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Eduardo M. da Cruz
Carol G. Vetterly
Editors

Critical Care of Children with Heart Disease

Basic Medical and Surgical
Concepts

 Springer

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To my wife Lina, my sons Rafael and Ricardo, and my grandson Daniel.
Ricardo Muñoz

To my wife Amy, and my children, Victor, Samuel and Oliver; for your love and support.

Victor O. Morell

To Tim, Jasmine, and Mom, for all of your patience...

Carol G. Vetterly

To Suzanne, Esteban and Tomas, as ever and forever...

Eduardo M. da Cruz

The Editors would also like to dedicate this book to all those caregivers who commit to care for children and young adults with critical congenital and acquired heart disease

We would like to express our sincere gratitude and appreciation for our illustrators, Steve Goldberg and Angelo Rutty, who created the exceptional surgical figures throughout the text. Their outstanding talents and contributions helped to make the book a valuable educational tool.

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Foreword

“Critical Care of Children with Heart Disease: Basic Medical and Surgical Concepts”

I am flattered to be invited to write a foreword for such a timely and comprehensive handbook of pediatric cardiac intensive care.

Having been intimately engaged in the management of congenital heart diseases for the greater part of the last 40 years, it has been rewarding to witness progress and interesting to reflect on what contributed to it. As in many endeavors, progress has been subtle and its underlying mechanisms have been multifactorial. There is little doubt that perioperative intensive care management has been a key component of this progress.

In many centers the overall mortality for pediatric cardiac surgery has fallen below the 2% mark. The morbidity, however, remains significant and the authors of this handbook must be congratulated for dedicating a large section to cardiac and extracardiac complications. Morbidity should become part of performance assessment.

It has been interesting to witness how postoperative morbidity has evolved. The postoperative capillary leak syndrome of the small infant in the 1970s has been replaced by the postoperative pulmonary hypertensive crises in the 1980s, to make room to the problems related to the imbalance between systemic and pulmonary blood flow in the Norwood patients.

The advent of the Norwood operation has been a cornerstone in the management of congenital heart defects. A successful Norwood implies accurate diagnosis, expert anesthesia and perfusion, impeccable surgery, deep understanding of the postoperative cardiopulmonary interactions, and taming of extracardiac problems, such as sepsis, gastrointestinal, and neurological impairments. The efforts deployed by many institutions to achieve excellence with the Norwood patients have uplifted their overall performance in the management of all congenital heart defects.

The impressive list of experts who have contributed to this book highlights the importance of multidisciplinary in the perioperative management of the sick cardiac patient.

Multidisciplinary is a two-edged sword. On the one hand, it provides knowledge, competence, commitment, and availability, which are key components of success. On the other hand, shared care can lead to conflicts and redundancy. It creates interfaces that require collaboration, hierarchy, and leadership. Too often those who are made responsible for problems arising within intensive care units do not have the authority to solve them. Several institutions over the past 30 years have faced difficulties in establishing the multidisciplinary structure of their cardiac intensive care units, which is most beneficial to their patients and most cost-effective to their institution. This is a delicate topic that often generates emotional if not legal argumentations. I am taking the liberty of alluding to this important issue even though it is not specifically addressed in this handbook.

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Foreword

Progress in medicine is compounded of two processes: small steps with intelligent “drift” toward best practice, and sea change with an occasional paradigm “shift.”

Ospina-Tascon, Buchele, and Vincent (*Critical Care Medicine* 2008; 36:1311–1322) were able to find in the literature only 72 large, randomized, controlled, intensive care trials with mortality endpoints. Of these, the trial intervention was a statistical success in ten. Often, progress in critical care takes place because reports that suggest but do not prove benefit, as well as lesser forms of evidence, become incorporated into clinical wisdom and medical practice by consensus. Ultimately, as norms drift, it may become impossible to test hypotheses by randomized, controlled trial because standard (control) treatment and trial intervention have become too alike. Outcome of new treatments must then be compared to historic controls because prospective trials are no longer possible.

In Pediatric Cardiology and Cardiac Surgery, the engine for change has seldom been the randomized controlled trial. Laboratory studies, case reports, small series, and staggering successes have fostered the “drift” and “shift” of cardiac care. Often, with little experimental foundation, one technique is modified or overthrown by another. New approaches are tried, and may become state-of-the-art virtually overnight.

The sea changes in pediatric cardiovascular surgery have been obvious. The first reported surgical ligation of a ductus arteriosus by Robert Gross, then 33 years old, was performed in 1938. Other pioneering “closed” procedures include the first excision of a coarctation of the aorta (Crafoord, 1944), the first subclavian to pulmonary artery shunt (Blalock and Taussig, 1944), and the first pulmonary artery band (Dammon-Muller, 1952). The surgical tradition is relatively receptive to steep “learning curves” in the adoption of new approaches. When cardiac bypass was introduced, between 1952 and 1954, 18 open heart operations were described in six separate reports, with an overall mortality of 94.5%. The bubble oxygenator was introduced in 1955. Then, in 1956, Lillehei, Cohen, Warden, and Varco reported the survival of a patient after total correction of tetralogy of Fallot. The sea changes have continued. More recent “paradigm shifts” include the introduction of deep hypothermic circulatory arrest, shelving of the Mustard and Senning procedures in favor of the arterial switch, Fontan’s approach to tricuspid atresia and the resulting sea change in the operative management of single ventricle defects, Norwood’s procedure for the hypoplastic left heart syndrome, and the introduction into postoperative care of extracorporeal membrane oxygenation and ventricular assist devices.

Some 50 years have elapsed since Lillehei’s report. Cardiac bypass has become a safe and well-established technique. Corrective open heart surgery is commonly

performed in small neonates. Most congenital cardiac defects can be either palliated or corrected, and many centers report overall mortality rates for congenital heart surgery at or below 2%. Much of this progress can be attributed to the more subtle process of “drift,” which has, by consensus, moved the age of corrective operation toward the first days of life, increased the specificity and accuracy of prenatal diagnosis, replaced routine cardiac catheterization with noninvasive diagnostic techniques like 2-D echocardiography and MR Angiography, and transformed many corrective procedures from surgical into transcatheter interventions.

In general, new discoveries and pioneering developments trigger sea changes. Intelligent adoption of a paradigm shift and cautious drift toward best practice occur by integration of the best evidence and by consensus building. That integration is the unwritten mission of a textbook such as this.

Consensus is a team activity and requires team work. The virtual exclusion of non-surgeons from postoperative care has ended. Interdisciplinary teams have been assembled to collaborate in this endeavor, improving outcome and accelerating the pace of progress. These teams include practitioners who first learn their craft as cardiologists, pediatric intensivists, pharmacists, and respiratory therapists, as well as cardiac surgeons who first learn their craft on adults (who are not just “big children”). It is the need for a literature to describe, explain, and teach critical care of the pediatric cardiac patient to trainees and collaborators of diverse backgrounds that has generated this textbook. In *Critical Care of Children with Heart Disease: Basic Medical and Surgical Concepts*, the authors embed the knowledge base of cardiology and congenital cardiac surgery into the context of intensive care, and advanced cardiac diagnostics and therapeutics. The product is not so much a cardiology text for intensive care physicians, as it is a text about the critical care of patients with pediatric heart disease.

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Foreword

The development of intensive care units can be traced, in part, to the challenge of ventilating dozens of patients with respiratory failure simultaneously during the polio epidemic in Copenhagen (1952–1953). The advantage of cohorting patients with “intensive care” needs became apparent and the value of an intensive care unit was established. During this initial experience dozens of patients were hand ventilated simultaneously via tracheostomy tubes (or subsequently with negative pressure ventilators) before there was adequate clinical appreciation of acid base balance. Numerous deaths were attributed to “a mysterious alkalosis.” By 1966, with the advent of positive pressure ventilators and the appreciation of arterial blood gas analysis, patient care was transformed into the field of critical care.

There is a striking parallel and temporal overlap to this discovery of mechanical ventilation and innovation in critical care: the development of cardiopulmonary bypass (1952–1953) and the need for cardiac intensive care. The early experience with cardiopulmonary bypass was predominantly in children. The poor results were discouraging for most; 17 of the first 18 patients died. But Walt Lillehei’s demonstration of the feasibility of repairing congenital heart disease using a parent as the functional source of pump and gas exchange in a cross circulation experiment propelled the field forward and motivated others to refine cardiopulmonary bypass techniques and successfully apply them to the repair of congenital heart disease.

By 1966 (when Rashkin introduced the balloon atrial septostomy in infants with transposition of the great arteries) cardiac intensive care units for children were emerging in Boston, Toronto, Minneapolis and elsewhere. In a 1966 landmark paper by Brown, Johnston and Conn in Toronto, the early results of mechanically ventilated patients in a postoperative care unit for children with congenital heart disease were reported. Although mortality exceeded 50% for those patients requiring 24 h of postoperative mechanical ventilation, there were many successes. Pediatric cardiac intensive care units were born. At first wedged between adult intensive care and adult cardiac surgical units, then mingling, merging with, evolving, and emerging from pediatric intensive care units, this subspecialty now exists in its own right with dozens of highly specialized units throughout the world. The subspecialists who populate the clinical leadership of these units, represent its multifaceted heritage: pediatric anesthesiologists, cardiologists, cardiac surgeons, and intensivists. It is further defined by specialized nursing dedicated exclusively to caring for critically ill children with heart disease. This book, *Critical Care of Children with Heart Disease: Basic Medical and Surgical Concepts*, is a wonderful testament to the collaborative expertise that must be brought to bear on this relatively new subspecialty. The textbook, like the discipline, is truly a multidisciplinary and multinational effort.

I have been honored to work with Dr. Muñoz in his early years, along with many of the other authors involved in this textbook. They, like many of those in this new field, chose to blend multiple conventional training programs and an unconventional number of additional years of training to help define the curriculum, qualifications and content of pediatric cardiac intensive care. It is my pleasure now to read and learn from those who represent the next and now current authorities in this field.

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Carol G. Vetterly has previously published under the name Carol G. Schmitt.

Preface

Pediatric cardiac intensive care patients pose special challenges to those practitioners caring for them.

The primary purpose of this textbook is to provide the health care practitioner with an overview of both the medical and surgical facets in caring for pediatric patients with congenital or acquired cardiac disease.

This book conceals a multitude of topics that may be encountered when caring for children in a cardiac intensive care setting. The first part of the text covers general aspects ranging from mechanical ventilation and cardiac anesthesia, sedation and pain management, to cardiopulmonary bypass, cardiac catheterization, echocardiography, in addition to describing the special monitoring required for pediatric cardiac patients. It also includes important recent developments in assessing and reporting risk factors.

The next sections address specific cardiac anomalies including acyanotic defects, right and left obstructive heart lesions, atrio-ventricular valve anomalies, vascular lesions, pulmonary hypertension, cardiomyopathies, pericardial diseases, and other complex heart defects. Specific chapters are dedicated to mechanical assistance, renal replacement therapy, transplant, arrhythmias, as well as the ethical and legal issues that involve the discontinuation of support of patients.

The last section reviews other challenging non-cardiac problems that caregivers in charge of pediatric cardiac patients have to face on a regular basis, including matters related to respiratory, gastrointestinal, nutrition, hematologic, renal and neurological systems, infectious disease, and skin protection.

A unique aspect of this text is the inclusion of drawings and descriptions of cardiac anomalies which serves as a valuable teaching and learning tool for cardiac intensivists, surgeons, fellows, residents, and nurses.

The editors sincerely acknowledge and express their gratefulness to the collaborating authors who were the successful artisans of this project.

It is our hope that practitioners will find this text useful in achieving the ultimate goal of providing the most superior quality of care to their pediatric cardiac intensive care patients.

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Part I

General Aspects

Chapter 1

Transition from the Fetal to the Neonatal Circulation

Daniel Sidi and Eduardo M. da Cruz

1.1 Introduction

To understand the rules and limitations of neonatal circulation in normal hearts and in those with congenital diseases, one must remember and understand the basic rules of heart physiology and apply them to the fetal and the neonatal circulations, with emphasis on the cardiovascular adaptation to the changes occurring at birth.

Birth is indeed a big challenge for the neonatal heart because of the dramatic changes in loading conditions occurring immediately or soon after birth when:

1. The placenta disappears, constraining the left ventricle (LV)
2. The pulmonary vascular bed opens, relieving the afterload on the right ventricle (RV) and increasing the preload on the LV
3. The atrial communication (patent foramen ovale) and arterial communication (ductus arteriosus) both close, inducing a complete change in the cardiovascular physiology with separated or “in series” systemic and pulmonary circulations

The first part of this chapter concentrates briefly on the study of the physiology of the normal heart and emphasizes the modern way to approach cardiac physiology through pressure/volume curves (cardiac loops). This approach allows the comprehension of heart properties (systolic and diastolic) along with their loading conditions.

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These figures will then be useful to look at the transition between the fetal circulation (with communications) and the neonatal circulation (in series).

This chapter also emphasizes some characteristics that have clinical and pharmacological relevance for fetal or neonatal interventions.

Finally, a brief illustration of the physiological approach to help understanding and treating some pathological examples will be given.

This chapter is influenced greatly by the work of Abraham M Rudolph in San Francisco CVRI, who with his team initiated and contributed greatly to the understanding of fetal circulation and its transition to neonatal circulation.

1.2 Part 1: Cardiac Physiology on a Pressure/Volume curve

Circulation is a combination of heart properties and loading conditions that are put together in order to achieve its main goal: adequate (optimal) perfusion, oxygenation extraction, and consumption by tissues.

This goal is achieved when aortic arterial pressure (AoP), cardiac output (CO), and appropriate flow distribution to the organs are adequate (according to their needs). It is a fine neurohormonal regulation, and not the heart, that decides on the needs and fulfills them through several cardiac and vascular interventions. The heart is just an executor.

The regulation in the heart is achieved through changes in its loading conditions (preload and afterload) and through a direct action on cardiac contraction

(heart rate and inotropic stimulation), in order to eject the necessary CO at the adequate AoP.

The vascular regulation is dedicated to the flow distribution and it acts through local changes in vascular resistances. These changes can occur locally in some organs with autoregulation systems (i.e., heart, brain, kidney) or through neurohormonal action on vascular tone (resistances), mainly by arteriolar vasoconstriction or dilatation. All this is achieved according to Poiseuilles' law, that states that there is a direct linear relationship between the mean pressure gradient (ΔP) amid the artery and the vein (or the tissue P for the heart), the flow (Q) within a given organ and the local vascular resistance (R):

$$\Delta P = Q \times R$$

It is crucial to realize that the heart acts as an executor and not as a commander. The control of the circulation mainly in the brain and the kidneys fixes the needs (AoP and CO) and the cardiac properties will then determine the filling pressures necessary to achieve the "work." The better the heart is, the less the filling pressure will be. This is the philosophy behind the Frank-Starling law that states that the heart acts like elastic, meaning it delivers more strength in systole (pressure and flow in the artery) if there are more fibers stretching during the diastole when the ventricles fill from the atria. The volume in the cavity is converted into diastolic pressure depending on the compliance of the ventricle. Therefore, any increase in venous return will result in an increase in cardiac output through improved cardiac contraction, but at the expense of a higher venous pressure. These ventricular filling pressures will be ensured by the venous and capillary pressures upstream to the heart (in the lungs for the left ventricle and in other organs for the right ventricle) and are "the price to pay" for the work to be done, as they may induce symptoms such as congestion, edema, or hydrops.

This Frank-Starling mechanism is present from the very beginning of fetal circulation. The analysis of the relation between pressure and volume in the ventricles is the objective representation of Starling law and allows the quantification of systolic (contractility) and diastolic (compliance) properties of the heart: The PV curve shown in Fig. 1.1 is for normal adult circulation; in Fig. 1.2 for the comparison of adult and neonatal circulation; in Fig. 1.3 for normal fetal circulation; in

Figs. 1.4 and 1.5 for abnormal fetal circulation; in Fig. 1.6 for the comparison between normal neonatal and fetal circulation and in Fig. 1.7 for one abnormal circulatory scenario.

Contractility is the property that allows the ventricle to develop pressure and then convert the hydrostatic pressure reserve (if the heart was not ejecting) into kinetic energy to eject the blood in the arterial tree. Contractility is well represented on a Pressure–Volume curve (Fig. 1.1) by the end systolic Pressure–Volume relationship (when the ventricle develops only pressure). This relation, named elastance, happens to be a straight line (Suga and Sagawa) and the tangent of this line is a very reliable indicator of contractility. The more shifted to the left (the ventricle can develop more pressure for the same volume, or it needs less volume for the same developed pressure) the better is the contractility. Note that in different figures the elastance is better for the left compared to the right ventricle, but the difference is small in the fetus and neonate and prominent in the adult subjects.

Compliance is the relationship between pressure and volume in diastole. It will determine the filling pressure in the ventricle, and also in the atria, veins and capillaries, as in diastole the atrio-ventricular valve is open and the pressure is the same from the subarterial ventricle to the capillaries (or the lungs for the left ventricle). The diastolic Pressure–Volume

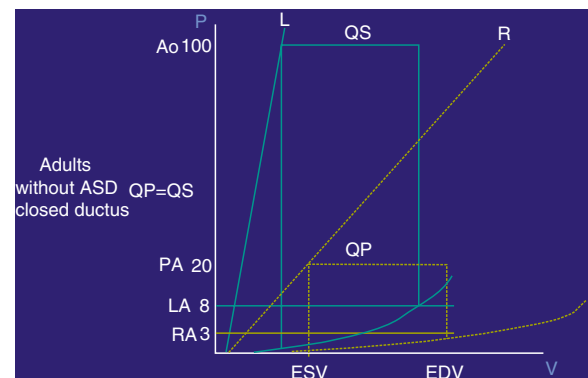


Fig. 1.1 Pressure–Volume curve in a normal adult. This figure shows a normal P/V curve. Note that the contractility (elastance) is much better for left ventricle (LV) than right ventricle (RV), but that the compliance is much better for RV than for LV. Also note that the circulation is in "series" with equal Qp and Qs. In the figure it is the ejection volume that is shown (QP or QS divided by heart rate). The RV pressure is lower than the LV pressure both in systole (because of the law PA vascular resistances) and diastole (because of the better compliance of the RV compared to the LV)

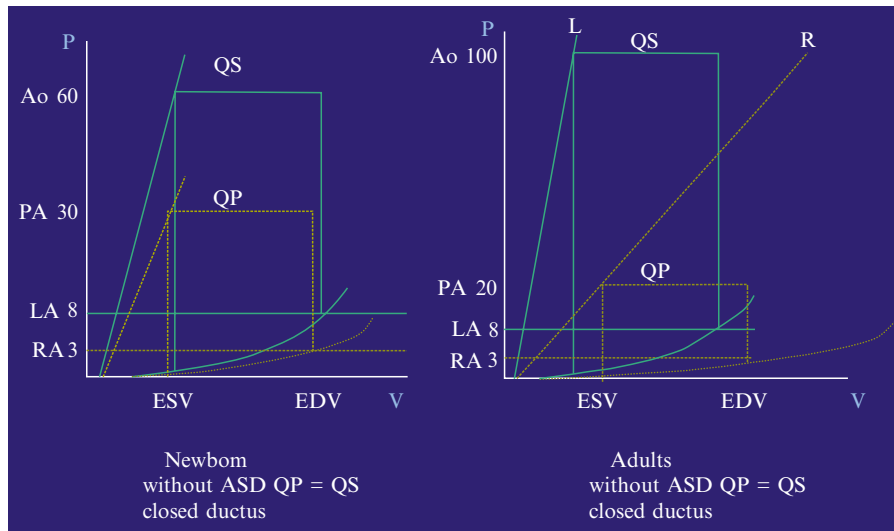


Fig. 1.2 Pressure–Volume curves in newborns as compared to adults: shows the main difference in neonatal and adult circulation. Note that there are only slight differences in ventricular contractility and compliance in the neonate (it changes quickly throughout the first few months of life) and that although the PA pressure has decreased immediately after birth, PA pressure is

higher in the neonate since PA vascular resistances are still relatively high (about 1/3 of systemic vascular resistance). The filling pressures are higher in the Left compared to the right ventricle (much more work) and compare with Fig. 1.7, where because of the presence of an ASD, the filling pressures are the same

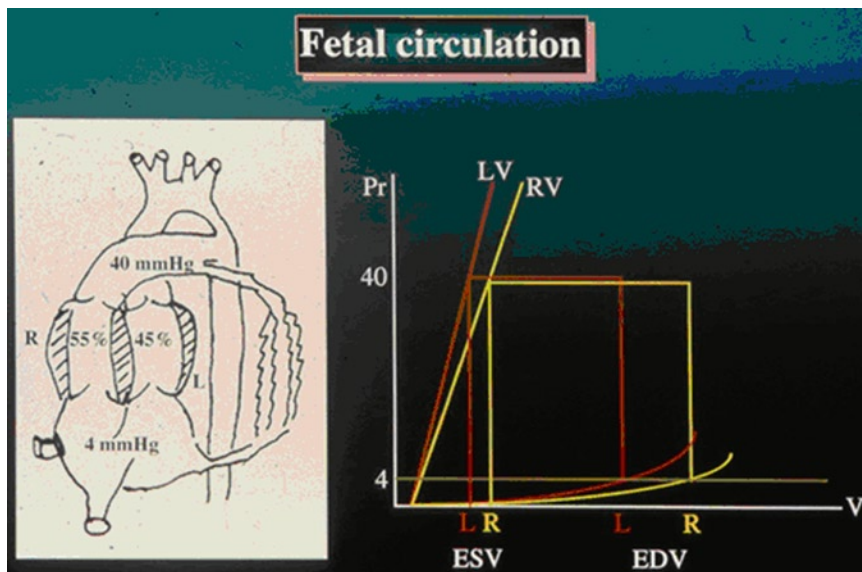


Fig. 1.3 Pressure–Volume curve in a fetus with same preload and afterload explaining the ventricular volumes: shows the anatomical reasons for the equalization in preload and afterload of both ventricles in the fetus. The LV has better contractility (less end systolic volume (ESV)) and worse compliance (less end diastolic volume

(EDV)) than the RV and the combination of both explains that the LV ejects a little less than the RV during the fetal life. After the carotida arteries there is limited blood with a physiological small thoracic Ao named isthmus (in contact with the ductus arteriosus (DA)) and where will eventually occur a coarctation of the aorta

curve is exponential, meaning that for low volume the pressure rises very slowly but for high volume the pressure rises quickly (stretching noncompliant myocardial fibers). *If the ventricle is very compliant the*

filling pressure will be low even with an enlarged ventricle with decreased contractility and there will be no congestion. *If the ventricle is noncompliant*, filling pressures may be quite high in a rather small ventricle

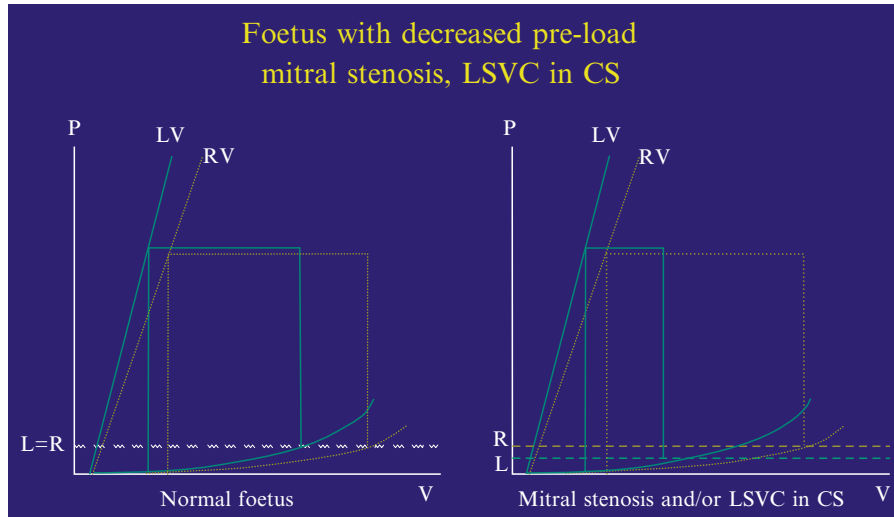


Fig. 1.4 Pressure–Volume curves in a fetus with decreased left ventricular preload: shows the consequences of a decrease filling of the LV on fetal circulation. The loss in preload pressure is

only a few mmHg but affects greatly the LV volume, instead of increasing the LA pressure (because the RV can eject into the Ao through the DA)

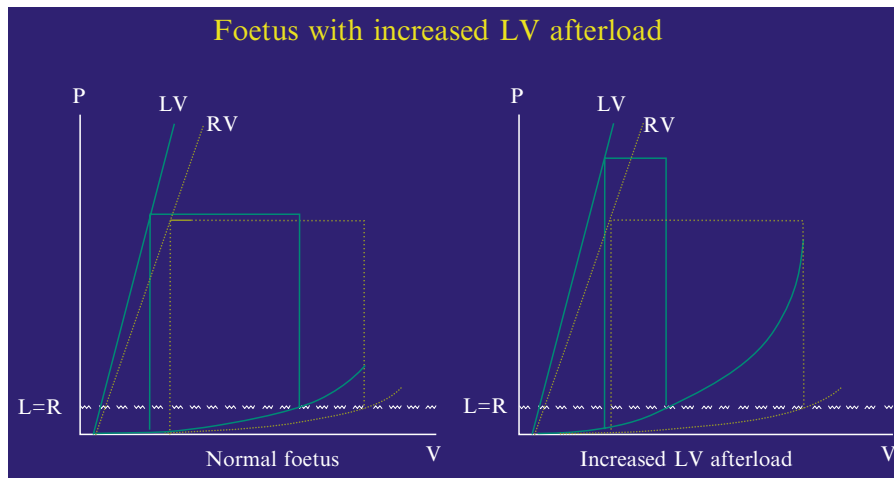


Fig. 1.5 Pressure–Volume curves in a fetus with increased left ventricular afterload: shows the consequences of an increase in LV afterload in the fetal circulation. The increased pressure in the LV due to Ao stenosis influence LV volume through

changes in compliance. It will affect even more the amount of blood flowing into the Ascending Aorta because of the increased ESV of the LV (unless the hypertrophy of the LV gives better contractility)

(good contractility) and congestion will be present. If the filling pressures are the same for both ventricles (large atrial septal defect like in fetal circulation), the respective right and left ventricular volumes will be a function of the respective compliances of both ventricles. Note that, the compliance is better for the right compared to the left ventricle at all ages but that this difference is mild in the fetus and neonate and significant in the adult.

1.2.1 Description of a Cardiac Loop (“Kitchen Recipe”)

Going from arteries to capillaries: start from end systolic relationship with an end systolic volume (ESV) that is the intersection of the contractility (elastance) line with the arterial pressure line (afterload). The ESV is the residual ventricular volume (or the volume required

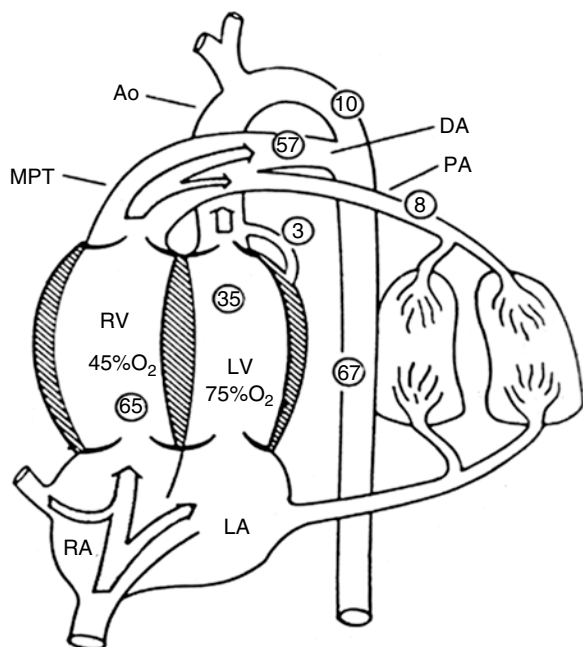


Fig. 1.6 Pressure–Volume curve changes at birth with the closure of the ductus arteriosus and the foramen ovale: shows the changes in circulation at birth when the neonatal heart is in series after closure of foramen ovale and DA. The loading conditions have changed dramatically for the two ventricles but that they are now ejecting the same volume. Note that birth is a big challenge for the LV that increases both pressure and volume whereas the RV is now working at low pressure with mild decrease in volume. This explains why the LV will hypertrophy and improve contractility while the RV wall will get thinner and improve compliance

in order to develop enough pressure to be able to eject blood into the arterial bed). Any added volume will be ejected and will constitute the ejected systolic volume (EV) that is the ratio of CO and the heart rate (HR). If ESV and EV are added, the end diastolic volume (EDV) is obtained, which represents the filling volume. The end diastolic pressure (EDP) is the intersection of this EDV and the compliance curve. This EDP (preload) is the filling pressure of the ventricle, responsible for the capillary pressure (or the pulmonary capillary pressures for the left ventricle and other tissue capillary pressures for the right ventricle).

In normal circumstances (heart in “series”), there is no communication between the right and the left heart, so that the ejected volume is the same but the pressures will be different, depending on vascular resistances, the systolic pressure and compliance of the diastolic pressure. It is a privilege for the cardiac function to allow

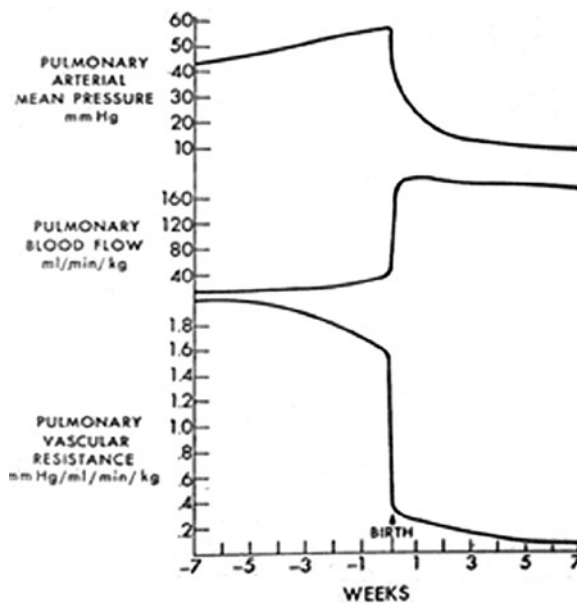


Fig. 1.7 Pressure–Volume curves at birth with a patent foramen ovale and abnormal left ventricular function: shows the difference of circulation in a neonate compared with a fetus in the case of an abnormal LV function in the presence of an atrial communication equalizing the atrial pressures at birth (forced foramen ovale or atrial septal defect). In the fetus, there was a compensation by the RV of the loss in volume of the LV (since the RV could eject in the Ao through the ductus arteriosus (even with retrograde flow in the Ao Isthmus to the brain). In the newborn, with a closed ductus, the LV has to accommodate on its own the systemic flow and if its function is impaired the LV (and LA) diastolic pressure will be increased (in order to dilate the LV according to Starling law). This increase in LA pressure will be transmitted to the right atrium through the ASD and the RV volume will increase a lot (according to the difference in compliance between the ventricles). This is why abnormal LV function decreases the size of the LV in the fetus and increases the size of the RV in the newborn with atrial shunting. The very dilated RV will eject a big amount of flow to the PA (coming back to the RV through the ASD). If the QP increases more than three times, the PA pressure will not decrease at birth. This is why when an ASD may be associated with PA hypertension; in most of the cases it is due to abnormal LV function (coarctation of the aorta, aortic or mitral abnormalities or even cardiomyopathy)

higher filling pressures in the left ventricle compared to the right ventricle, since pulmonary capillary pressures can rise to a higher level without edema than pressures in the vena cava and systemic capillaries. This privilege is not anymore present if there are wide communications between the ventricles and the atrial cavities.

In case of large communications, the pressure will equalize between the chamber at the level of the systemic circulation (usually LV and LA) and this

will impose the same pressure on the PA circulation (usually RV and RA). In these instances it is the pressure that is fixed and the flow that varies with shunts. These shunts are physiological in the fetus but not after birth. The PV curves allow to understand the direction and magnitude of the shunt in any cardiac malformation, by respecting the law that the systemic circulation is regulated (fixed by the demand) and the PA circulation acts passively according to the properties of the Heart and the loading conditions (Vascular resistances, regurgitation of valves or obstacle to the circulation).

1.3 Part 2: Cardiac Physiology in the Fetus and Newborn

In the fetus (Fig. 1.3), there are large communications between the atrium (so, the preload is the same for the right and the left ventricles) and the arteries (because of the large patent ductus arteriosus diverting the blood from the lung to the placenta) so that the afterload is roughly similar for both ventricles. In this condition, we can say that in the fetus the difference in EDV is related to the ventricular compliance and that the difference in ESV is function of the contractility of both ventricles. In normal fetuses, the right ventricle is slightly larger in systole and diastole compared to the left ventricle, indicating that the former is slightly more compliant and less contractile than the latter (Fig. 1.1). These characteristics have implications in the harmony of the future neonatal heart. Well balanced ventricles will be present if myocardial properties are roughly similar in the absence of valvular abnormalities. Conversely, ventricular hypoplasia will occur in case of even minor abnormalities in myocardial properties or loading conditions. Fig. 1.4 shows what happens if the preload of the LV is impaired by minor anomalies of the mitral valve or even by a persistent left superior vena cava decreasing by 2 mmHg the LV preload. The decreasing LV volume and increasing RV volume are evident in the graphic. Figure 1.5, shows what happens if the afterload of the LV is impaired by aortic stenosis with small changes in compliance of the LV affecting its size. The LV is still filled at the same Pressure as the RV because of the large Foramen Ovale with small LV and big RV. Infact, because of the communications up and down stream of the ventricles allowing a bypass

of the abnormal ventricle, the filling of this latest will be impaired and there will be a loss of its growth, without significant alteration of fetal oxygenation (assumed by the other ventricle), but with a decreased growth downstream of the sick ventricle (aortic hypoplasia and postnatal coarctation). This explains the flow theory on cardiac growth like in the case of the frequent association between coarctation of the aorta and aortic arch hypoplasia with mild congenital mitral valve stenosis, or even in the case of a persistent left superior vena cava dilating the coronary sinus (mild preload reduction) and/or of a bicuspid aortic valve (mild afterload increase). We can also explain by this flow theory the vicious circle of mitral valve stenosis inducing aortic hypoplasia, decreasing left ventricular filling through decreased compliance (showing the consequences of these abnormalities on the left ventricle and on the aortic growth as shown in Figs. 1.4 and 1.5).

We have to add another important feature concerning *fetal oxygenation* to this cardiac fetal physiology. The preferential flow from the umbilical vein to the left heart through the foramen ovale, (Fig. 1.8) gives a more oxygenated (O_2 saturation of 75% and Partial O_2 pressure (Pp) of 25 mmHg) blood flow to both the heart and the brain through coronary and carotid arteries from the ascending aorta, compared to the right heart that is filled with deoxygenated blood (O_2 saturation of 40% and Partial O_2 pressure (Pp) of 15 mmHg) which then flows across the pulmonary arteries (PAs) and back to the placenta through the ductus arteriosus (DA), the descending aorta and the umbilical arteries. Very low O_2 Pp in the fetal lung is partly responsible for the *intense vasoconstriction in the PAs* (Fig. 1.9). The other reason for the vasoconstriction is the fact that lungs are not ventilated and have compressed vessels. Both mechanical and gaseous abrupt changes at birth will open the pulmonary arterial vascular bed with a 15% decrease in their vascular resistances as shown by the birth simulation studies in the fetal and newborn lambs.

Another important physiological feature of fetal circulation concerns the reactivity of the DA and the reason why it stays open during fetal life and closes after birth. There are two major reasons for this; the first concerns the reactivity of the DA to O_2 Pp that is opposite to the PA reactivity. The DA dilates with low O_2 Pp and constricts with high O_2 Pp (above 60 mmHg). This explains why it is open in the fetus and closes after

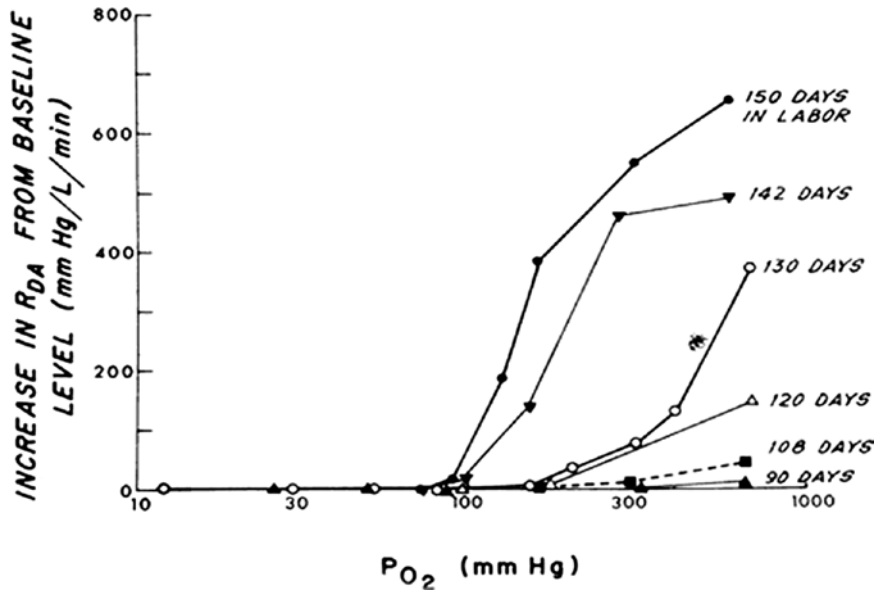


Fig. 1.8 Fetal circulation as seen by A. Rudolph: shows the difference in O₂ saturation in the right and left ventricles during fetal life due to the right-to-left predominant atrial shunt by

oxygenated blood coming from the umbilical vein. The lower PpO₂ in the PA of the fetus is one of the reasons for the very high PA vascular resistances during fetal life, as shown on Fig. 1.7

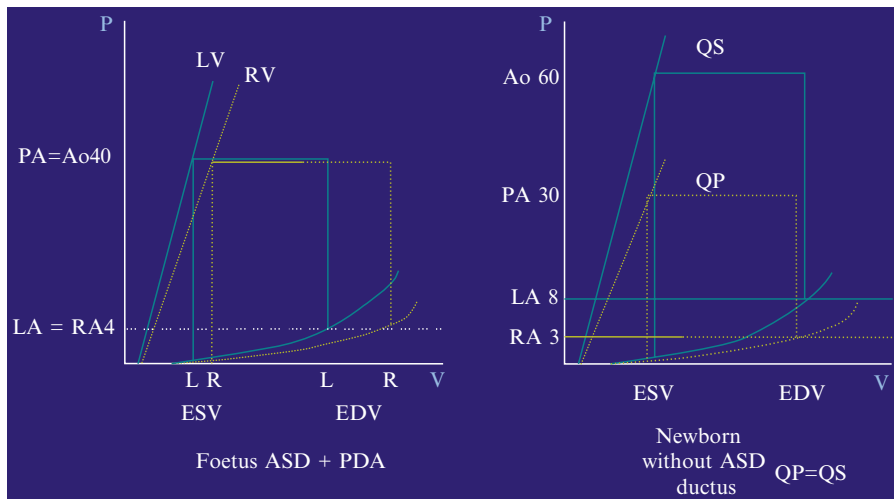


Fig. 1.9 Changes in pulmonary vascular resistances after birth: shows the changes in Pa vascular resistances at birth. The instantaneous dramatic decrease in PVR explaining the fall in Pa pressure after few minutes (there is no physiological PA hypertension in the neonate)

birth (Fig. 1.10). The second reason is due to the response of the DA to prostaglandin E₁ (PGE₁) levels which induces vasodilatation that persists regardless of the O₂Pp.

PGE₁ accumulates with high concentration in the fetus, because it is produced by the placenta and catabolized in the lungs, hence maintaining the DA

open; whereas at birth, PGE₁ concentration falls dramatically due to the removal of the placenta and to the fact that right CO goes entirely in the lungs, thus inducing ductal constriction. It is crucial in clinical practice to know that a perfusion of PGE₁ can maintain the DA open, even with high O₂Pp. It allows a left-to-right shunt ensuring pulmonary blood flow in case

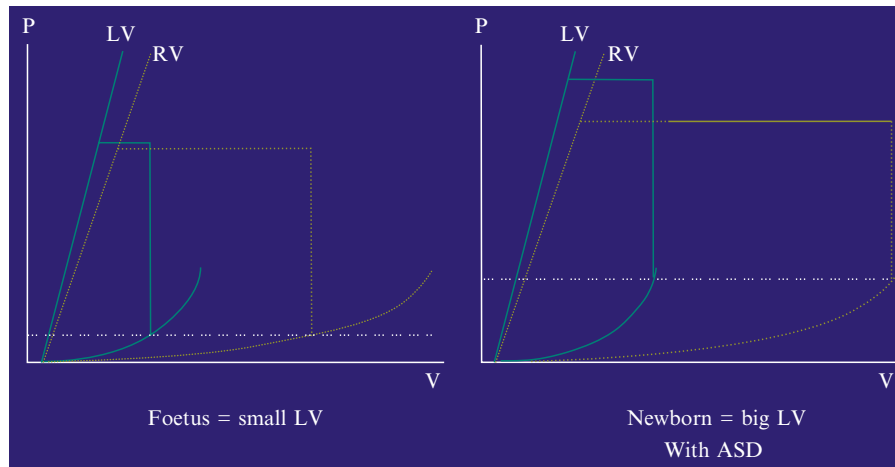


Fig. 1.10 Ductus arteriosus responses to ppO_2 : shows the reactivity of the DA to O_2 during fetal life. This reactivity increases

during the last trimester (explaining PDA in premature babies). Note that the DA constricts with PpO_2 above 50 mmHg

of right obstructive malformations (i.e., pulmonary atresia), and a right-to-left shunt warranting systemic blood flow in case of left obstructive lesions (i.e., aortic atresia or interrupted aortic arch).

In the neonate (Fig. 1.6), the loading conditions are very different for both ventricles, with an increase in the systemic vascular resistances (that augment by twofold when the placenta disappears) and with an enormous decrease in pulmonary vascular resistances (that fall by a factor of 15, secondary to the active vasodilatation related to ventilation, O_2 levels, and humoral changes in Prostaglandins, Thromboxane, and Leucotriene levels). In less than 1 h, the PVR are 1/3 of the SVR. In addition, with the closure of the foramen ovale and the DA, the heart can work with independent loading conditions. As shown in Fig. 1.6, preload and afterload become much higher for the left ventricle when compared to the right ventricle.

Figure 1.7 shows the difference in circulation in a neonate compared with a fetus with an abnormal LV function when the foramen ovale stays open (ASD) allowing atrial shunting. As per the explanation in Fig. 1.7, if the QP increases more than three times, the PA pressure will not decrease at birth. This is why when an ASD is associated with PA hypertension, in most cases it is due to abnormal LV function (coarctation, aortic or mitral abnormalities, or even cardiomyopathy).

For the cardiologist, birth is considered as a difficult challenge for the left ventricle, with a work

increase of more than 100% (60% increase in systolic pressure and 30% increase in CO), whereas it is a great relief for the right ventricle (100% decrease in pressure and 20% decrease in CO). This is the reason why the left ventricle has very limited inotropic reserves at birth and is so sensitive to any increase in afterload, while the right ventricle tolerates moderate pulmonary arterial hypertension very well. This is also the reason why the left ventricular mass and wall increases quickly improving its contractility, while the right ventricular wall mass significantly decreases with the increase in volume (the ventricle becomes thinner) with a dramatic improvement in right ventricular compliance.

1.3.1 Clinical Consequences of Fetal and Neonatal Cardiac and Circulatory Physiology

The left ventricle has limited reserves in neonates and left ventricular failure is frequent, particularly when facing afterload challenges (aortic coarctation or valvar stenosis). Myocardial ischemia may occur and myocardial VO_2 increases when the aortic pressure is not maintained. Mitral valve regurgitation from papillary muscle ischemia may occur and worsen the left ventricular function. The only way to improve neonatal left ventricular function is to reduce the afterload,

as long as the aortic and the coronary pressure are maintained within normal range. The other solution is to maintain an open DA and allow the right ventricle to participate in the systemic flow by a right-to-left shunt from the pulmonary arteries to the aorta.

1.3.2 *There is no Physiological Pulmonary Arterial Hypertension in a Newborn*

If pulmonary arterial hypertension is found, it is because either the DA is not closed leading to a mandatory left-to-right arterial shunt, or there are added problems:

1. The pulmonary vascular resistances did not fall normally (abnormal pulmonary arterial vascular bed or reactivity to lung disease).
2. There is a post capillary hypertension due to abnormal left ventricular function (Fig. 1.7) or to anomalous mitral or pulmonary veins.
3. Questions arise concerning the role of an atrial left-to-right shunt when the foramen ovale does not close or when there is an atrial septal defect. Normally, this shunt is trivial because, compliance at birth is not very different in the two ventricles (as a reminder, fetal right ventricular compliance is a little better than left ventricular compliance) so that the pulmonary flow does not significantly increase with the fall in pulmonary vascular resistances and therefore does not lead to pulmonary hypertension. If the neonate has pulmonary hypertension in the context of an atrial septal defect (and a closed DA), the left ventricle is dysfunctional and responsible for a substantial left-to-right atrial shunt (as opposed to a situation of high pulmonary capillary pressures).
4. Sometimes, neonatal pulmonary hypertension results from the association of increased flow and post capillary hypertension (when the foramen ovale is distended with a high velocity left-to-right shunt)

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Chapter 2

Triage and Transport of Infants and Children with Cardiac Disease

Bradley A. Kuch and Richard A. Orr

2.1 Principles and Practice

Advances in cardiology, intensive care, and surgical techniques have led to the survival of children with previously lethal congenital cardiac defects [1–3]. A large number of these children present to local community hospitals, nurseries, and emergency for their initial stabilization before being transferred to regional tertiary care centers for more invasive diagnostic, surgical, and/or critical care intervention. Because of this, pediatric transport systems have become a significant component of the pediatric cardiac care continuum.

The primary goal of any transport system is to provide a safe and timely transfer to a center specializing in the required care needed without an increase in morbidity or mortality. Accomplishing this goal requires a team capable of providing an extension of the pediatric cardiac critical care unit (i.e., skills and equipment) to the referring hospital [4].

A recent multicentered study demonstrated that nearly 10% of children requiring interfacility transport have a diagnosis of cardiac disease [5]. The main reason for transport in this group was cyanotic heart disease with others, including congestive heart failure (CHF), respiratory distress, and sepsis syndrome (Fig. 2.1) [5]. Initial stabilization and transport of these children is often complicated by an increased need for stabilizing interven-

tions [5], a lack of a confirmed diagnosis, and their underlying severity of illness. For these reasons, infants and children with congenital and/or acquired heart disease must be transported by a team with pediatric experience and more importantly, specialized training in the area of pediatric cardiac disease [6, 7].

2.2 Initial Call Triage

A successful transport always begins at the time of initial referral request, at which point the call is triaged by a command physician who collects pertinent patient information and gives recommendation for further stabilization efforts. In calls involving children with suspected or confirmed cardiac disease, either a cardiologist or cardiac intensive care unit (CICU) physician should be consulted. During the initial call a large amount of information must be collected, which can be accomplished with a brief report which should include the following:

- Past medical history
- Present condition
- Vital signs (ABC's = airway, breathing, circulation)
 - Airway patency
 - Respiratory rate
 - Heart rate
 - Blood pressure
 - Perfusion
- Neurologic assessment
 - Level of consciousness (LOC)
 - Glasgow coma scale (GCS)
 - Presence of seizure activity

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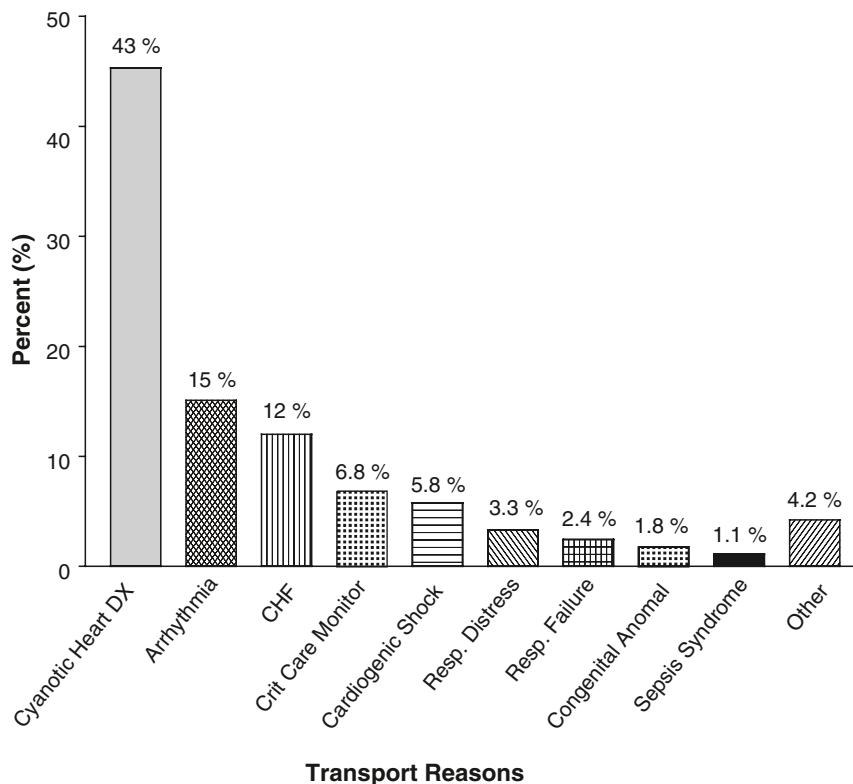


Fig. 2.1 Primary reasons of transport at the time of initial request for transfer data from an EMSC (1-H34-MC-00040-01) funded database of five regional pediatric specialty care teams.

DX disease; *CHF* congestive heart failure; *Crit Care Monitor* need for critical care monitoring; *Resp.* respiratory; *Congenital Anomal* multiple congenital abnormality

- Laboratory data
 - Blood glucose level
 - Complete blood count (CBC)
 - Electrolytes
 - Cultures (blood, urine, sputum)
- Radiological interpretations
- Interventions Administered

2.3 Physical Assessment

Airway: Assessment of the pediatric airway can be divided into two functional areas: *airway patency* and *airway protection*. Rapid assessment will lead the clinician to the next step in gaining control of the child's airway. It may be as simple as repositioning the child's head or as complex as endotracheal intubation.

Breathing: The initial assessment of breathing starts with a visual inspection of the child while entering the room, prior to interaction. Identifying the patient's position, respiratory rate and pattern, level of distress, and behavior will provide an immediate indication of the severity of the situation.

Circulation: Assessment of circulation and peripheral perfusion can be done simultaneously during the initial patient survey. Assessment should include heart rate, central versus peripheral pulses, capillary refill time, level of consciousness, and urine output. Early identification and resuscitation of children with poor perfusion is paramount in limiting the adverse outcomes associated with uncompensated shock and multi-organ dysfunction syndrome.

Sugar: A serum blood sugar level is easily obtained with a bedside glucometer and should be documented at the time of the initial transfer request and at the team's earliest convenience during transport. Evaluating blood glucose level is extremely important as it has been

reported that 18% of children requiring major intervention in the emergency department were found to be hypoglycemic (blood sugar <40 mg/dl) with an associated mortality rate of 55% [8].

2.4 Presentation and Stabilization

Stabilization is the shared responsibility of the referring facility, receiving institution, and transport team. Stabilization always begins at the time of the initial transport request and is focused around procurement of a patent airway, establishing effective respiration, ensuring adequate circulation, and identifying hypoglycemia or hypocalcemia.

For the purpose of this chapter, children with heart disease have been classified into four groups which are:

- a. Defects with increased pulmonary blood flow
- b. Defects with decreased pulmonary blood flow
- c. Special considerations
- d. Arrhythmias.

Each diagnosis will be discussed in terms of age of presentation and stabilization, following the ABC's algorithm.

2.4.1 Defects with Increased Pulmonary Blood flow [1–4]

Congenital cardiac defects with increased pulmonary blood flow frequently present with signs of pulmonary overcirculation. These children present with the symptom of CHF around 3 months of age. Younger infants (less than 8 weeks of age) with CHF should be evaluated for left heart outflow tract obstruction as the symptoms may proceed the closure of a patent ductus arteriosus (PDA) and onset of shock. Other causes of CHF include cardiomyopathy, infectious myocarditis, and tachyarrhythmias.

2.4.1.1 Clinical Presentation

As mentioned before, patient assessment must begin with the ABC's as recommended by the PALS and APLS curricula [6, 7]. Infants and children with lesions

resulting in CHF, present mainly with respiratory symptoms as a result of pulmonary edema or complicating infectious pneumonitis. A history from the parent(s) or care taker(s) will reveal a progressive increased work of breathing, poor feeding tolerance, and lack of weight gain. These children often appear Pale and thin but with normal length and head circumference.

A physical assessment reveals tachycardia, tachypnea with respiratory distress of varying degrees, and hepatomegaly. Auscultation of the lungs does not usually reveal rales, more commonly found are wheezes; however, some patients may present with clear breath sounds. These children rarely present with low cardiac output (CO) and shock, but more often are hypoxic and impending respiratory failure.

2.4.1.2 Chest Radiography

Chest radiograph will demonstrate cardiomegaly with or without increased pulmonary vascular markings [9]. The lungs may be either atelectatic or hyperinflated secondary to airway obstruction from bronchial wall edema.

2.4.1.3 Stabilizing Intervention

The initial management of these patients should focus around alleviating hypoxemia, lessening respiratory distress, and preventing the need for endotracheal intubation. Oxygen should be administered immediately to improve hypoxemia. Lowest concentrations, required to increase the arterial saturation level (SpO₂) to an acceptable level, should be used, as oxygen is a potent pulmonary vasodilator and may worsen the left-to-right shunt. Infants with an increased work of breathing but maintaining adequate gas exchange should be administered intravenous diuretics such as furosemide [10]. If supplemental oxygen and diuretic therapy does not alleviate the respiratory distress or if the condition of the child worsens, endotracheal intubation should be considered.

In situations with poor cardiac function, an inotropic agent with peripheral vasodilatory properties should be initiated. Epinephrine and dopamine are useful; however, phosphodiesterase III inhibitors such as amrinone or milrinone may also be used [11].

If an infant requires high levels of inotropic support, other diagnosis such as sepsis should be considered.

- *Atrial septal defects (ASD) and Ventricular septal defects (VSD)* may result in pure volume overload of the right heart and lungs. If an infant or child presents with CHF, oxygen, inotropes, and diuresis are indicated. Moderate fluid restriction, maintenance fluid rates of 60–80 cc/kg/h/day may be helpful in the absence of shock.
- PDA refractory to Indomethacin therapy requires transfer to pediatric tertiary care centers for surgical intervention. Oxygen should be used with caution in preterm infants with large PDA as it will further increase pulmonary overcirculation by decreasing PVR. If left untreated, the pulmonary overcirculation may result in pulmonary hypertension reversing the shunt thus resulting in hypoxia. A past medical history of a PDA may be associated with endocarditis in children.
- *Truncus Arteriosus (TA)* results in pulmonary overcirculation as the common “trunk” is exposed to systemic pressure causing a large left-to-right shunt. Severe hypoxia is rare. Older children who are post-TA repair may present with CHF secondary to truncal insufficiency or conduit stenosis.
- In *anomalous pulmonary venous return (APRV)* clinical presentation depends on the number, location, and presence of obstruction within the anomalous connection(s). In infants with a total anomalous venous return (TAPVR), cyanosis may present in the neonatal period due to the elevated PVR limiting pulmonary blood flow. As the PVR drops, pulmonary blood flow increases and the SpO₂ rises to the upper 80’s lower 90’s %. These infants usually present during first of age with right heart failure, unless there is an obstructed anatomic form, TAPVR, with venous obstruction usually presents in the first few days of life and requires urgent surgical intervention. Fluid overload must be avoided and initiation of prostaglandin E₁ (PGE₁) may not improve hypoxia in these infants as mixing occurs at the atrial and ventricular levels. However, PGE₁ should still be started as some infants may have restricted mixing at the atrial level requiring a PDA for systemic blood flow (see chapter Anomalous Pulmonary Venous Return, by Tsifansky M, Munoz R, Kazmerski T, Kreuter J, Morell V). This lesion is difficult to differentiate from primary pulmonary hypertension (PPHN) in the transport environment.

2.4.2 Left Heart Outflow Tract Obstruction

Obstruction to systemic output is the most common cause of cardiogenic shock in infants less than 1 month of age. These infants may present with symptoms of CHF prior to ductal closing. Once ductal patency is lost, the infant appears “septic” due to low CO and profound metabolic acidosis. For this reason, septic shock is the principal differential diagnosis and the infant should be treated for both conditions until further diagnostic elucidation. Infants with left heart outflow tract obstruction often become symptomatic over hours, however, they may present as late as 8 weeks of age.

2.4.2.1 Clinical Presentation

Physical examination reveals tachypnea with increasing respiratory distress or apnea, tachycardia, lethargy, irritability, hepatomegaly, and severe shock. Pulses may be weak or absent. Arterial blood gas analysis will reveal a severe metabolic acidosis (pH <7.20) with a low PaCO₂, and mild hypoxia with a PaO₂ between 50 and 70 torr. Hypoxemia is a result of pulmonary edema and/or right-to-left shunting across the PDA; however, the addition of oxygen may constrict the PDA limiting systemic blood flow and should be used with caution in these patients.

2.4.2.2 Chest Radiography

Chest radiograph will reveal cardiomegaly with pulmonary edema.

2.4.2.3 Stabilizing Intervention

The emergency stabilization of left heart obstruction focuses around re-establishing ductal patency and increasing systemic blood flow. PGE₁ infusions are critical for reopening the ductus arteriosus providing a pathway for this to occur. When systemic blood flow is improved, peripheral pulses will return, urine output will increase, and the metabolic acidosis will slowly clear. Severe acidosis will decrease myocardial function and should be buffered with sodium bicarbonate (NaHCO₃⁻). In cases where poor cardiac function is

present, intravenous inotropic support with dopamine and/or dobutamine should be initiated [11]. Amrinone or milrinone may be useful for increasing CO, peripheral vasodilatation, and lusitropic properties [11].

Endotracheal intubation is indicated in infants who have apnea, refractory shock, altered mental status (GCS <8 or 3 less than baseline), or in those who's respiratory status poses a risk of decompensation while en route. Advanced airway management should also be considered in infants receiving high dose PGE₁ infusions as clinically significant apnea may occur [12]. Ventilator management should be aimed at preventing pulmonary overcirculation by maintaining a pulmonary to systemic perfusion ($Q_p:Q_s$) ratio of 1:1. [9, 12]. Maintaining arterial oxygen saturations between 80% and 85%, and a PaO₂ in the 35–40 mmHg range is recommended [10].

- *Aortic stenosis* (AS) may present either during the immediate newborn period or childhood. Critical AS presents in the neonatal period when ductal patency is lost limiting systemic blood flow through a stenotic aortic valve. Blood pressure in all four extremities will be low as the obstruction is below the root of the subclavian arteries.

Undiagnosed AS in the older child presents with a history of fatigue, dyspnea on exertion, and less commonly syncope. These children rarely require interfacility transport. However, children in this age group may suffer from restenosis following repair leading to severe aortic insufficiency and ultimately left heart failure.

- *Coarctation of the aorta* (CoA) may present as late as 8 weeks of age and should be considered in any infant within this age group who has signs of cardiogenic shock. Assessment of pulses will reveal significant difference in the carotids and upper extremities compared to the femoral and lower limbs. Blood pressure measurements should be performed and recorded in all four extremities. The blood pressure will be greater above the obstruction (right arm) and lower below the obstruction (legs). In the setting of an aberrant right subclavian artery, the pressure gradient may not be present.
- *Hypoplastic left-sided heart syndrome* (HLHS) commonly presents within the first 7 days of life. Rapid deterioration occurs as the only source of systemic blood flow (PDA) closes resulting in profound cyanosis, hypotension, and metabolic acidosis. Endotracheal intubation and immediate initiation of PGE₁ are indicated. These infants often

require inotropes and multiple boluses of Na HCO₃⁻ for pH buffering. Maintaining $Q_p:Q_s$ ratio at 1:1 is essential for survival. Arterial blood gases should be in the ranges of pH 7.40, PaO₂ 35–40 mmHg, PaCO₂ 35–40 mmHg, HCO₃⁻ 24 mmol/L, and FiO₂ should be set to achieve a SpO₂ in the 70's [10]. Sedation and paralysis may be useful in controlling the aforementioned parameters. If SpO₂ rises and the metabolic acidosis worsens there is excessive pulmonary blood flow (Q_p) and if the SpO₂ drops there is too little pulmonary blood flow. Blood glucose and calcium level should be followed throughout transport.

2.4.3 Defect with Decreased Pulmonary Blood Flow

Cyanosis in the newborn presenting to a local community hospital without pediatric cardiology poses a significant diagnostic problem as the cause may be pulmonary, cardiac, or a combination of both. In a resource limited environment such as transport, distinctions must be made by obtaining an accurate familial and prenatal history, conducting a thorough physical exam, and utilizing specific lab data.

2.4.3.1 Clinical Presentation

Familial and prenatal history: Upon arrival, the transport team should quickly evaluate the family history for congenital heart defects, birth defects, syndromes, and early deaths [10]. A prenatal history should be reviewed for a maternal history of diabetes, or for any exposure to rubella, Coxsackie, or radiation. The onset of cyanosis and/or respiratory distress should also be noted as it may give important clues to whether the symptoms are related to the closure of the ductus arteriosus or the development of sepsis.

Physical Examination: The physical assessment should begin with the appearance and level of respiratory distress. Agitation, irritability, tachypnea, nasal flaring, grunting, and retractions suggest pulmonary pathology. Infants with cyanotic heart disease, usually have central cyanosis, appear comfortable with little to no increased work of breathing which is generally referred to as “quiet tachypnea.” Pre and post-ductal pulse oximetry is extremely useful in identifying the

presence of ductal shunting [13]. Evaluating the presence of differential cyanosis is also useful since blue upper extremities and pink lower extremities are highly suggestive of congenital heart disease.

2.4.3.2 Imaging and Laboratory Data

A chest X-ray with any of the following is suggestive of cyanotic heart disease: clear lung fields, cardiomegaly (cardiothoracic ratio >0.50), and decreased pulmonary vascular markings.

If any of the following are present, a *hyperoxia test* may be useful in identifying the etiology of the cyanosis. A right to left shunt is likely when the PaO_2 is <200 mmHg in 100% oxygen [10].

Immediate intervention is indicated in any cyanotic infant whose arterial blood gas reveals a $\text{pH} < 7.28$ or a $\text{PaCO}_2 > 50$ mmHg or a $\text{PaO}_2 < 50$ mmHg on a $\text{FiO}_2 \geq 0.5$ [10, 14].

2.4.3.3 Stabilizing Intervention

Prostaglandin E₁ should be initiated in any situation where there is a high suspicion of cyanotic heart disease. Some have recommended intubation prior to transport in all infants who require PGE₁ infusions to avoid clinically significant apnea and lessen the risk of severe hypoxia [10]. Further control in the respiratory status of the infant may be facilitated with the use of sedation and neuromuscular blockade.

- *Tetralogy of fallot* (TOF) in the newborn period may have little right-to-left shunting, occasionally referred to as “pink tetralogy.” A chest X-ray in this period may reveal a “boot shaped” heart. As the infant grows, the infundibular obstruction functionally becomes more significant, increasing right-to-left shunting resulting in hypoxia. Sudden onset of severe hypoxia or “tet spells” commonly occur between 2 and 4 months of age for reasons including fever, dehydration, anxiety, pain, and manipulation of an artificial airway, as for example suctioning. Tet spells are treated with supplement oxygen, administration of morphine sulfate and beta-blockers, administration of volume, initiation of vasoactive agents to increase the systemic vascular resistance, or simply placing the child in the knee-chest position [10]. Intubation may be indicated

which depends on the degree of cyanosis, acidosis, and the frequency of these hypercyanotic spells (see chapter Tetralogy of Fallot, by Chrysostomou C, Domnina Y, Kazmerski T, Morell V, Munoz R). Endocarditis should be considered in febrile children with a history of TOF.

- *Critical pulmonary stenosis* (PS) and *pulmonary atresia with intact ventricular septum* cause obstruction of forward flow across the pulmonary valve resulting in profound cyanosis. These infants require PGE₁ infusions to ensure adequate pulmonary blood flow, and in the presence of ventricular dysfunction may require inotropic support [11]. Older children with progressive PS rarely present with cyanosis; if present, its usual cause is an ASD with a right to left shunt [10].
- *Transposition of great arteries* (TGA) is the most common cyanotic heart defect [10]. It should be suspected in any infant with isolated, central, and progressive differential cyanosis: blue upper extremities and pink lower extremities. In the event there is little response from the administration of fluids, supplemental oxygen, then the initiation of PGE₁ is indicated; however, older infants may be unresponsive to the later and may require an urgent atrial septostomy to facilitate adequate mixing. Time to reach a pediatric tertiary center, where a emergent septostomy can be performed, is an important factor in the survival of these infants. Infants with an associated VSD may present in CHF. Inotropic support and diuresis are often indicated. Calcium should be monitored, keeping in mind the possibility of a DiGeorge syndrome.

2.4.4 Special Considerations

- *Cardiomyopathy* is a common etiology of pediatric heart failure. Dilated and hypertrophic cardiomyopathies are two types which pose a significant challenge to the transport team. Delineation of the two is based on clinical, hemodynamic, and structural features, of which there is some degree of overlap [14].

2.4.4.1 Clinical Presentation

Infants and children with either type present with symptoms of CHF. However, in more seriously ill children, it

presents as cardiovascular failure and shock. Children with poor cardiac function will appear anxious with tachycardia, tachypnea, possibly with grunting, prolonged capillary refill, and hypotension. Hypotension results from low cardiac output and in the most severe cases, fulminant pulmonary edema may be present. Stabilization is focused around decreasing myocardial workload on the failing heart while increasing its function.

2.4.4.2 Stabilizing Intervention

The level of cardiopulmonary compromise dictates the extent of stabilization. Noncritical patients may require only supplemental oxygen and diuretics to improve fluid homeostasis. In the most severe cases, airway control and work of breathing must be removed from the patient and controlled by the team. Removing the work associated with breathing will decrease the metabolic demands of both the respiratory muscles and heart, thus decreasing stress on the already failing cardiopulmonary system. In addition, a higher mean airway pressure will decrease intrapulmonary shunting created by the fluid filled alveolus. High levels of positive end-expiratory pressure (PEEP) should be used with caution as it may limit venous return to the heart. Following stabilization of the airway and breathing, continuous infusions of inotropic agents should be initiated. Sympathomimetic agents such as dopamine, dobutamine, and epinephrine have been advocated [15]. High doses of dopamine will amplify cardiac action but will also increase peripheral vasoconstriction, and may be proarrhythmogenic [15]. Amrinone or milrinone may also be useful in improving CO, promoting peripheral vasodilatation, and increasing systolic and possibly diastolic function [10]. Peripheral vasodilators such as nitroprusside and hydralazine may be useful in decreasing afterload [15]. In the presence of a metabolic acidosis, buffering with Na HCO_3^- is indicated, as severe acidosis further compromises myocardial function.

- *Dilated cardiomyopathy* (DCM) is the most common form of cardiomyopathy and a major reason for cardiac transplantation, with 31% of patients either succumbing to the disease or receiving transplantation within 1 year of diagnosis [16]. This type of cardiomyopathy is characterized by ventricular dilation and systolic dysfunction. A chest radiograph will show cardiomegaly often with pulmonary venous congestion [14].
- *Hypertrophic cardiomyopathy* is primarily a disease of the myocardium which is distinguished by left

ventricular hypertrophy without ventricular dilation [14]. Typically, a chest radiograph is normal [14, 17]. This type of cardiomyopathy is the leading cause of sudden death in children and adults.

2.4.5 Arrhythmias

The transport team's management of arrhythmias should be focused around those which may potentially, or at the time, be compromising hemodynamic stability. It is essential to assess and support the ABC's, since, often the underlying cause of the arrhythmia is related to compromise of the airway, breathing, circulation, or hypoglycemia (Table 2.1) [6, 7, 18].

Most transport monitors used today have the capacity to record and print rhythm strips which are potentially useful in diagnosing the exact arrhythmia which occurred. All strips should be saved in the presence of a suspected arrhythmia for a later evaluation by a pediatric cardiologist. A continuous ECG strip should also be obtained during any attempt at converting the arrhythmia by noninvasive methods such as vagal maneuvers or infusions of antiarrhythmics agents. Recording the onset and/or termination of an arrhythmia offers vital clues in identifying the most successful method of management.

2.4.5.1 Tachyarrhythmias

- *Supraventricular tachycardia* (SVT) most commonly occurs in infants under the age of 4 months and often presents as poor feeding, inconsolability, tachypnea, prolonged capillary refill time, and mottling [19]. It should be considered in any infant with a sudden onset narrow complex (≤ 0.08 s) tachycardia with a heart rate 220 or more or in any child with a heart rate 180 or more. SVT is associated with Ebstein's anomaly and with pre-excitation syndromes (i.e., Wolff-Parkinson-White syndrome).

Table 2.1 Treatable causes of arrhythmias: The four H's and four T's concept

Hypovolemia	Toxins
Hypoxia	Tamponade, cardiac
Hydrogen Ion (acidosis)	Tension pneumothorax
Hypo-/Hyper-kalemia	Thrombosis (coronary or pulmonary)
Hypoglycemia	Trauma (hypovolemia)
Hypothermia	

Adapted from references [6, 7, 19]

– Stabilizing Intervention

Treatment of SVT depends on the degree of hemodynamic instability. In stable infants and children ice may be applied on the face without occluding the airway [18]. In older children, carotid sinus massage or Valsalva maneuvers may be useful. If IV access is available, adenosine should be given rapidly via the two syringe technique. The technique is easily accomplished by using a stopcock or double lumen t-connector. One port is to push the adenosine and the second port used to flush with ≥ 5 mL of normal saline [18]. If the patient is unstable or IV access is unavailable, synchronized cardioversion at 0.5–1 J/kg should be administered [6, 7, 18]. If unsuccessful, a repeat shock can be delivered at 2 J/kg. Consider amiodarone or procainamide prior to the third shock [6, 7, 18].

- *Ventricular Tachycardia (VT)* is differentiated from SVT by a wide complex (≥ 0.08 s) and poor perfusion. Most children who present with VT have a history of congenital or acquired heart disease.

– Stabilizing Intervention

If the child is unstable and VT is suspected, immediate synchronized cardioversion should be performed at 0.5–1 J/kg when the airway and breathing is stabilized. A dose of adenosine may be useful in determining whether the rhythm is SVT with aberrant conduction, however, cardioversion should not be delayed [18]. If a second shock is required, it should be delivered at 2 J/kg [6, 7, 18]. If a second shock is unsuccessful or the VT recurs quickly, amiodarone or procainamide should be considered prior to a third shock. Close monitoring of the ECG and blood pressure should be performed during the administration of any antiarrhythmic agent. In the presence of VF with hemodynamic stability, an expert should be consulted, since all arrhythmia therapies have a significant potential for causing serious adverse effects [18]. In case of polymorphic VT, Torsades de Pointe ought to be considered and a dose of 25 mg/kg of magnesium sulfate should be promptly administered. In any of the above situations, electrolytic disturbances should be ruled out and aggressively rectified.

2.4.5.2 Bradycardic Arrhythmia

The most common cause of bradycardia in children is hypoxemia with or without hypoventilation. Other

etiologies include hypothermia, hypoglycemia, hypothyroidism, increased intracranial pressure, seizures, and vagal stimulation from the placement/adjustment of nasogastric tubes or endotracheal tubes. Children who have had cardiac transplantation have denervated hearts and often develop bradycardia.

Atrioventricular blocks (A/V blocks) are rarely symptomatic in children; however, will be discussed considering their varying etiologies. They include structural heart disease, infection, inflammatory, neurodegenerative disease, muscular dystrophies, infiltrative disorders, trauma, and drug intoxications.

- *First-degree AV block* is defined as a prolonged PR interval (PR >0.20 in any age group) [6, 7, 10, 18]. Neonatal PR interval is usually between 0.09 and 0.12. Rarely does this type of heart block present symptomatically, therefore, it is of little concern.
- *Second-degree mobitz type I or Wenckebach block* is defined as increasing prolongation of the PR interval eventually producing a nonconducted P wave. It is caused by the same etiologies stated above with the addition of Digoxin toxicity [20].
- *Mobitz type II second degree block and third degree heart block* indicate more serious cardiac pathologies and should be considered when the P waves are found to be “marching through” the ECG tracing with little to no association with the QRS complex. Both can present as a late postoperative complication when scarring begins to infiltrate the conduction system. Inflammatory disorders, such as myocarditis is another cause of these types of advanced heart blocks. Congenital complete heart block occurs in approximately 1 in 15,000–20,000 live births and should be considered in any infant who presents with complete heart block in the newborn period from a mother with history of connective tissue disease (commonly systemic lupus erythematosus) [10]. Acquired third degree block could also be identified in the context of complex cardiac defects (i.e., congenitally corrected transposition of the great vessels, heterotaxic anomalies) or long QT syndrome.

Stabilizing Intervention

The initial management of bradycardia and AV blocks is focused on the establishment of a patent airway, reversal of hypoxemia, and treatment of any underlying

metabolic derangement. The upper airway should rapidly be assessed for obstruction, easily identified by the presence of little or no airflow, upper airway stridor, or asynchronous chest and abdominal motion. Endotracheal intubation may be indicated. In severe symptomatic bradycardia, cardiopulmonary resuscitation must begin without delay. Intravenous administration of agents which modify the autonomic nervous system is indicated in case of persistent symptomatic bradycardia. These include atropine, which can be given as a single bolus (0.02 mg/kg) up to four doses, epinephrine (0.1–1 µg/kg/min), or isoproterenol (0.05–0.5 µg/kg/min [10]). Temporary transcutaneous pacing should be considered in any child with severe bradycardia unresponsive to pharmacological therapy [6, 7, 10, 18].

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Chapter 3

Airway Control, Mechanical Ventilation, and Respiratory Care

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3.1 Introduction

Mechanical ventilation is often required for infants and children with cardiovascular disorders. This chapter briefly reviews the physiology of lung inflation and deflation with tidal breathing, the principles involved with the practice of conventional ventilation, the design and functional characteristics of conventional ventilators, the theory and practice of respiratory care, and special forms of artificial respiration.

3.2 Physiology

The primary determinants of lung inflation are the pressure difference between the airway opening and the alveoli, the resistance of the conducting airways, and the compliance of the regional alveolar segments. *Time constant* is the product of compliance and resistance, and is defined as the time taken to cause a given change in lung volume with a constant distending pressure. One time constant is the time taken to cause a 63% change in volume, and three time constants is the time taken to cause a 95% change in volume [1]. Expiration is for the most part passive, because of the elastic recoil of the lung, which is attributable to alveolar surface tension and tissue elasticity. Since inspiratory and expiratory resistances are different, their time constants may be different. Increased airway resistance and decreased

chest and lung compliances would require a greater Ptp (trans-pulmonary pressure) to inflate the lung to the same lung volume. This imposes a greater work load on the respiratory muscles, and increases the oxygen cost of breathing (OCB). When the oxygen supply–demand balance to the respiratory muscles is perturbed, respiratory failure may ensue due to muscle fatigue.

Systemic arterial oxygenation depends upon the inspired oxygen concentration and tension, lung volume, cardiac output, ventilation–perfusion matching, and the magnitude of venous admixture or intrapulmonary shunting. A critical opening pressure is required to maintain both the patency of the terminal airways and alveolar volume. Alveolar collapse, which readily occurs below the critical opening pressure, leads to inadequate oxygenation due to increased intrapulmonary shunting resulting from ventilation–perfusion (V/Q) mismatch. Inadequate ventilation, reflected by an increase in arterial carbon dioxide (PaCO₂), results from a minute alveolar ventilation that is insufficient to meet the metabolic production of carbon dioxide.

3.2.1 Indications for Mechanical Ventilation

The primary indication for institution of assisted ventilation is respiratory failure. Apnea or respiratory arrest is an extreme form of respiratory failure and an absolute indication for mechanical ventilation.

Respiratory failure is generally defined as the presence of the following:

1. Inadequate oxygenation
2. Inadequate ventilation
3. Both

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Inadequate oxygenation, objectively, is defined as an arterial oxygen tension (PaO_2) less than 60 torr in room air, a $\text{PaO}_2/\text{FiO}_2$ ratio of <300 , and a calculated or measured intrapulmonary shunt fraction $>15\%$.

Inadequate ventilation is defined as an arterial carbon dioxide tension (PaCO_2) >50 torr in the absence of chronic hypercapnia. Impending respiratory failure characterized by rapidly rising PaCO_2 , progressive respiratory distress, PaCO_2 out of proportion to the respiratory effort, or fatigue of respiratory muscles is a relative indication for mechanical ventilation.

Intubation and institution of mechanical ventilation under these circumstances are likely to be more controlled than when full-blown respiratory failure develops. Therefore, in critically ill children, it is preferable to institute mechanical ventilation before respiratory failure develops.

Cardiovascular dysfunction can result in decreased respiratory reserve, can increase respiratory work, and may ultimately result in respiratory failure. Positive pressure ventilation decreases lactate production by respiratory muscles during circulatory shock, and withdrawal of ventilatory support results in a marked increase in cardiac work [2, 3]. Therefore, mechanical ventilation may not only decrease the work of breathing under these circumstances but also decrease the oxygen demand of the heart.

Acute neurologic disorders may require mechanical ventilation for the following reasons:

1. Decreased ventilatory drive and acute hypercapnia
2. Loss of airway protective reflexes
3. To deliberately hyperventilate in disorders associated with intracranial hypertension to produce hypocapnia and respiratory alkalosis
4. Decreased ventilatory effort.

3.2.2 Modes of Ventilation

A detailed review of the physical characteristics and functional design of ventilators is beyond the scope of this chapter, and the reader is referred to several excellent reviews on this subject [4–8]. When the termination of a breath is under the control of the mechanical ventilator, it is referred to as a *mandatory breath*. A mandatory breath may be initiated by the ventilator or it can be initiated by the patient. A mandatory breath is always

cycled by a preset time, pressure, or volume and is not under the control of the patient. Whether the mandatory breath is initiated by the ventilator or by the patient, the characteristics of the breath (changes in flow, pressure, and volume) and the inspiratory time of the breath are the same. *Assist-control* refers to a mode of ventilation when a patient receives a combination of ventilator-initiated and patient-initiated mandatory breaths. When the initiation and termination of a breath is under the control of the patient's breathing efforts, it is referred to as *spontaneous breaths*. A spontaneous breath with an inspiratory pressure that is greater than the expiratory pressure is referred to as a *supported* or an *assisted* mechanical breath for which the trigger can be either pressure or flow. When all minute ventilation is provided by the ventilator, it is referred to as *total ventilatory support*. When all breaths are mandatory breaths, it is referred to as continuous mandatory ventilation (CMV). Total ventilatory support is provided entirely by CMV. When spontaneous breathing is responsible for some of the minute ventilation and the rest by the ventilator, it is referred to as *partial ventilatory support*. Minute ventilation provided by ventilator-initiated mandatory breaths are referred to as controlled mechanical ventilation and those provided by assisted mechanical breaths (patient-initiated) they are referred to as assisted mechanical ventilation (AMV). When spontaneous breathing is responsible for the entire minute ventilation without any assistance from the ventilator, then it is referred to as complete spontaneous breathing. Partial ventilatory support can be provided by CMV, AMV, or a combination of both. The two most common forms of controlled mechanical ventilation are *pressure-regulated* and *volume-regulated ventilation*.

3.2.3 Volume-Regulated Mandatory Breaths

Volume-regulated ventilation can be delivered either by volume-cycled breath, where inspiration is terminated after a pre-set volume is delivered, and inspiratory time is allowed to vary, or by volume-regulated time-cycled breaths, where the cycling mechanism is pre-set time, and the tidal volume delivered is regulated by adjusting the inspiratory flow rate. In volume-regulated

ventilation, the tidal volume is delivered throughout inspiration. The peak inspiratory pressure (PIP) is variable and is dependent on the flow rate, the total resistance, and the total compliance of the ventilator circuit and the patient's lungs. Changes in resistance or compliance will be reflected by an increase in PIP, and the ventilator can be set to alarm at a pressure limit that is generally set 5–10 cm above the PIP.

Most modern ventilators deliver the pre-set tidal volumes quite reliably, but, the tidal volumes delivered to the patient on a breath-to-breath basis may not always be constant. The tidal volume delivered by the ventilator is distributed between the ventilator circuit, the airways, and the patient's lungs. The effective tidal volume (VT_{eff}) delivered to the patient can be approximated by the following formula: $VT_{eff} = VT_{del} - C_{vent}(PIP - PEEP)$, where VT_{del} is tidal volume delivered by the ventilator; and C_{vent} is the compliance of the ventilator circuit. VT_{del} is equal to the inspired tidal volume, when there is no leak in the total respiratory system. But, when there is a leak in the system, such as with the use of uncuffed endotracheal tubes, then VT_{del} is less than the inspired tidal volume. During exhalation, expiratory flow curves depend on the type of expiratory resistance or PEEP valve in the system.

3.2.4 Pressure-Regulated Mandatory Breaths

Pressure-regulated ventilation can be either pressure-cycled or pressure-limited and time-cycled ventilation. In pressure-cycled ventilators, inspiration is terminated when a pre-set pressure limit is reached. In this mode of ventilation, the inspiratory time may vary depending on the changes in resistance and compliance of the total respiratory system. This mode of ventilation is not widely used these days except for intermittent positive-pressure breathing treatments. Pressure-limited time-cycled ventilation is most commonly used in the neonate with respiratory distress syndrome and in children with ARDS. In this mode, inspiratory and expiratory times are constant, and the PIP reaches a preset limit quickly early in inspiration and is then maintained at that level during the rest of the inspiratory phase. Usually a high flow rate is used (4–10 L/kg/min). The tidal volume delivered depends on the compliance and resistance of the ventilator circuit and the

patient's lungs. Pressure-controlled ventilation results in higher mean airway pressure for the same amount of minute ventilation.

3.2.5 Intermittent mandatory ventilation

Intermittent mandatory ventilation (IMV) refers to a pattern of controlled ventilation where spontaneous breathing is permitted. Between mandatory machine breaths, the patient can breathe spontaneously and the required gas flow is delivered either through a continuous flow or a demand system [9]. The spontaneous breaths are not assisted by a ventilator breath. Therefore, the tidal volumes generated by the spontaneous breaths are dependent on the patient's effort alone and not on the ventilator support. When IMV is synchronized to the patient's inspiratory efforts, it is referred to as synchronized IMV (SIMV). Each time a synchronized breath is delivered, the machine recomputes the time required to deliver the next mandatory breath. In SIMV, the total number of mandatory breaths will only be equal to the preset frequency of mandatory breaths. SIMV breaths can be volume-regulated, or pressure-limited.

3.3 CPAP/PEEP

CPAP refers to the maintenance of positive airway pressure throughout the respiratory cycle with no positive pressure breaths being delivered to the patient. Positive end-expiratory pressure (PEEP) refers to the maintenance of positive airway pressure above atmospheric pressure at the airway opening at end expiration [10]. CPAP/PEEP can be applied by:

1. An underwater column
2. A water-weighted diaphragm
3. A venturi valve
4. A spring-loaded valve
5. A pressurized exhalation valve
6. A magnetic valve
7. A fixed or adjustable orifice

CPAP may be provided through the endotracheal tube, through specially designed nasal prongs or nasal cannula, or through a facemask.

3.3.1 Selection of Parameters for Mandatory Breaths

The first parameter is the VT_{eff} . A desirable VT_{eff} for most patients is 8–10 ml/kg. The end-inspiratory alveolar pressure should not exceed 40 cm of H_2O . During mechanical ventilation, end-inspiratory alveolar pressure can be estimated by measuring the end-inspiratory airway pressure using an end-inspiratory hold maneuver.

Ventilator rate is the next parameter to be selected and depends upon the age of the patient and the ventilatory requirements of the patient. The initial ventilator rate for a newborn infant usually ranges from 25 to 30/min; for a 1-year old, between 20 and 25/min; and for an adolescent, from 15 to 20/min.

The *inspiratory time* is selected to provide an inspiratory-to-expiratory time (I:E) ratio of at least 1:2 in most patients. Inspiratory time must be selected to allow sufficient time for all lung segments to be inflated.

Similarly, sufficient *expiratory time* must be provided for all lung segments to empty. If inspiration starts before the lung has completely emptied, this will result in air trapping and inadvertent PEEP.

PEEP is the next parameter to be selected. The level of PEEP will depend on the clinical circumstance. The goals of PEEP are listed below:

- 1) Increasing FRC above closing volume to prevent alveolar collapse
- 2) Maintaining stability of alveolar segments
- 3) Improvement in oxygenation
- 4) Reduction in work of breathing

The optimum PEEP is the level at which there is an acceptable balance between the desired goals and the undesired adverse effects.

Fraction of the inspired oxygen (F_iO_2) is the next parameter to be selected. F_iO_2 is adjusted to maintain an adequate PaO_2 . In certain cyanotic heart diseases, it may be desirable to use the lowest possible F_iO_2 to maintain an adequate balance between the pulmonary and systemic circulations.

3.3.2 Pressure-Support Ventilation

In pressure-support ventilation (PSV), the ventilator assists patient's own spontaneous effort with a mechanical breath with a pre-set pressure limit. The patient's

spontaneous breath creates a negative pressure (pressure-triggering) or a change in flow through the circuit (flow-triggering), which triggers the ventilator to deliver a breath. With initiation, the machine delivers high inspiratory flow to achieve a peak airway pressure level that is selected by the operator [11–13]. The pressure-limit stays constant as long as the patient's inspiratory effort is maintained with a variable gas flow rate from the ventilator [12, 13]. As inspiration continues, the inspiratory flow rate decreases. A threshold reduction in the flow rate is a signal for the termination of the inspiratory assist, with the opening of an expiratory valve, following which passive exhalation occurs [11–13]. PSV is entirely dependent on the patient's effort; if the patient becomes apneic, the ventilator will not provide any mechanical breath.

3.3.3 Dual Control Modes

Dual control modes are newer modes that allow the ventilator to control pressure or volume based on a feedback loop. They cannot control both at the same time, but rather one or the other. There are currently two techniques for performing dual control. In both these techniques of dual-control modes, there is an attempt made to assure a certain target tidal volume. These can be classified as dual-control within a breath or dual control breath-to-breath.

Two examples of dual control modes within a breath are volume-assured pressure support (VAPS) (Bird 8400ST and Tbird, Bird Corp., Palm Springs, CA) and pressure augmentation (PA) (Bear 1000, Bear Medical, Riverside, CA). Both these techniques can operate during mandatory breaths (pressure-limited time-cycled) or pressure-supported breaths.

Dual-control breath-to-breath mode with mandatory pressure-limited time-cycled breaths is referred to as pressure-regulated volume control (PRVC with Siemens 300), adaptive pressure ventilation (APV with Hamilton Galileo), autoflow (Evita 4), or variable pressure control (Venturi), depending on the manufacturer. In this form of pressure-limited, time-cycled ventilation, delivered tidal volume is used as a feedback control for continuously adjusting the pressure limit. All breaths in these modes are time- or patient-triggered, pressure-limited, and time-cycled. One difference between devices is that the Siemens 300 only allows PRVC in the CMV mode. The newer Servo_i ventilator and the

other ventilators allow dual control breath to breath using CMV or SIMV. In this mode, the ventilator attempts to target the “desired” tidal volume and makes adjustments to the PIP to achieve the goals.

Dual control breath to breath in the pressure support mode quite simply is closed loop pressure support ventilation, with tidal volume as the input variable. It is referred to as *volume support* (Siemens 300, Siemens Medical Systems, Inc., Danvers, MA) and *variable pressure support* (Venturi, Cardiopulmonary Corporation, New Haven, CT). All breaths are patient-triggered, pressure-limited, and flow-cycled. Volume support is selected with the mode selector switch, and the desired tidal volume is set. Similar to the PRVC mode described above, the pressure-support level is adjusted to maintain the set tidal volume with changes in compliance and resistance. In addition to the volume-support settings, a mandatory ventilator frequency must be set. This frequency is set based on the age of the patient.

3.4 Principles of Mechanical Ventilation

3.4.1 Alveolar Recruitment and Derecruitment

Alveolar recruitment with maintenance of lung volume by preventing derecruitment during mechanical ventilation is a goal during mechanical ventilation. The benefits of optimal lung recruitment and prevention of derecruitment are

1. A reduction in the intrapulmonary shunt fraction and venous admixture resulting in an improvement in arterial oxygenation
2. Improvement in lung compliance
3. Prevention of repeated alveolar collapse and reopening which may ameliorate or prevent ventilator-induced lung injury.

The primary determinants of alveolar recruitment and derecruitment are transpulmonary pressure and PEEP, respectively. Mean airway pressure has been shown to be an excellent marker of mean alveolar pressure [14]. Increasing mean airway pressure will improve oxygenation if there is alveolar recruitment. Recruitment of the lungs can be achieved by manual inflation to high airway pressures, increasing PEEP in a stepwise manner, application of a sign maneuver, using

pressure-limited time-cycled ventilation with a high PIP, or combining titrated levels of PEEP with increased inflation pressures. Ventilatory sighs are effective in recruiting alveoli in ARDS [15].

3.4.2 Heart Failure

The goals in respiratory management in congestive heart failure are relief of work of breathing and reversing alveolar collapse. This can be provided by a judicious combination of controlled ventilation, PEEP, and sedation. The greater the inotropic support a heart needs, the greater should be the respiratory support provided. In adults with congestive heart failure, positive pressure ventilation improves cardiac output by unloading the left ventricle [16, 17]. Cardiopulmonary interactions ought to be taken into account in specific scenarios (see chapter 4 on Heart-Lung Interactions in this book).

3.4.3 Postoperative Management after Repair of Congenital Heart Disease

Many infants and children require mechanical ventilation during the postoperative period. The duration of requirement of mechanical ventilation depends on several factors such as age of the patient, complexity of the cardiac lesion, complexity of the operative procedure, duration of bypass, duration of circulatory arrest, postoperative bleeding, and postoperative cardiopulmonary status. Prolonged intubation and mechanical ventilation are more likely in children under a year of age, with more complex heart lesions, prolonged bypass and prolonged circulatory arrest times, and postoperative respiratory failure and hemodynamic instability.

In the immediate postoperative period, patients should be on controlled mechanical ventilation until hemodynamic functions improve. Adequate PEEP should be applied to prevent and relieve atelectasis. The choice of ventilatory parameters depends on the goals for each individual patient. In patients with *pulmonary hypertension*, hyperventilation to provide respiratory alkalosis will decrease pulmonary vascular resistance and right ventricular afterload. In patients who

have undergone a *Fontan procedure*, early extubation is desirable, and if that is not possible, then spontaneous ventilation should be encouraged. Since these patients are totally dependent upon venous return for their cardiac output, airway pressures must be kept at a minimum. High intra-thoracic pressure may not only impede venous return, but also decrease pulmonary blood flow from increased pulmonary vascular resistance.

3.4.4 Diseases with Abdominal Distention

Positive intra-abdominal pressure tends to elevate the diaphragm, decrease Ptp in the lung bases, and decrease alveolar lung volumes in the lung bases. In order to maintain normal lung volumes a greater Ptp has to be generated. This increases the airway pressures during positive pressure ventilation, and increases work of breathing during spontaneous breathing. During positive pressure ventilation, a higher Ptp may cause hyperinflation of the apical regions while restoring normal volumes in the bases. Therapy should be directed primarily toward reducing the intra-abdominal pressure.

3.4.5 Altering Inspired Oxygen and Carbon Dioxide Concentration

A low alveolar oxygen tension increases pulmonary vascular resistance (hypoxic pulmonary vasoconstriction) [18]. With certain types of congenital heart diseases such as hypoplastic left heart syndrome, it is critical to control pulmonary blood flow and prevent pulmonary overflowing. One approach is to decrease the F_iO_2 to <0.21 by blending room air with nitrogen. The exact F_iO_2 delivered must be monitored to avoid administering excessively low inspired oxygen. The other approach especially in mechanically ventilated patients, both preoperatively and postoperatively, is to increase the inspired carbon dioxide concentration (F_iCO_2) [19], which increases pulmonary vascular resistance. The advantage of increased F_iCO_2 is the ability to ventilate without producing hypocarbia. The disadvantage is an increased spontaneous ventilatory

drive due to an increased $PaCO_2$. This increases the work of breathing and with marginal cardiac reserve may impose undue strain on the heart. Therefore, neuromuscular blockade and total ventilatory support may be necessary with increased F_iCO_2 to avoid an increased work load on the heart.

3.4.6 Inhaled Nitric Oxide

Inhaled nitric oxide produces selective pulmonary vasodilation. Indications for inhaled nitric oxide include diaphragmatic hernia, pulmonary hypertension after repair of congenital heart disease, primary pulmonary hypertension, and isolated right heart failure. In severely hypoxemic babies with pulmonary hypertension, inhaled NO rapidly increases arterial oxygen tension without causing systemic hypotension [20–23]. Nitric oxide binds to hemoglobin to produce methemoglobin. Therefore, methemoglobin levels should be monitored during administration of nitric oxide. In addition, nitric oxide combines with oxygen to form nitrogen dioxide. Nitrogen dioxide is known to cause lung injury. Therefore, the concentration of nitrogen dioxide should be monitored in the inspired gas to keep it below 1–2 ppm.

3.4.7 Negative Pressure Ventilation in Cardiovascular Disorders

Several studies have shown beneficial effects of *negative pressure ventilation*, specifically in certain children after cardiac surgery [24–28]. In patients with Fontan-type operations, negative pressure ventilation increased pulmonary blood flow and cardiac output and also decreased the pulmonary valvular incompetence in patients with restrictive right heart physiology after repair of Tetralogy of Fallot [25]. In children after repair of total cavopulmonary connection and Tetralogy of Fallot and after Fontan-type procedures, negative pressure ventilation provided using a Hayek external high-frequency oscillator improved cardiac output by 42–46% almost entirely by an increase in stroke volume with improvement in mixed venous oxygen saturation [26]. A similar finding was observed in children after transcatheter occlusion of an asymptomatic patent ductus

arteriosus and after open heart surgery [27]. Raine et al in 1992 reported that negative pressure ventilation is a viable alternative to positive pressure ventilation in patients with phrenic nerve palsy after pediatric cardiac surgery by reducing the need for diaphragmatic plication and facilitating weaning from positive pressure ventilation [28]. These studies show that negative pressure ventilation is a useful technique in selected patients after cardiac surgery where positive pressure ventilation is not desirable or results in unwanted hemodynamic effects.

3.4.8 High Frequency Ventilation

High frequency ventilation (HFV) refers to diverse modes of ventilation characterized in general by supraphysiologic ventilatory frequencies (>60 cycles/min) and low tidal volumes (less than or equal to physiologic dead space during conventional ventilation). Four distinct methods of HFV are recognized: high frequency positive pressure ventilation (HFPPV), high frequency jet ventilation (HFJV), high frequency oscillatory ventilation (HFOV), and high frequency chest wall oscillation (HFCWO). Only HFPPV, HFJV, and HFOV have been extensively used clinically. The principal theoretical advantage for the use of HFV lies in the ability to ventilate effectively at low airway pressures.

Recent studies have suggested a role for HFV in children after cardiac surgery and with ARDS [29–34]. HFJV has been shown to improve cardiac function after a Fontan procedure [29]. HFJV and HFOV have been shown to improve oxygenation and ventilation compared with conventional ventilation in children with respiratory failure [31–34]. There are many reported strategies while using HFV:

1. “High lung volume strategy,” which requires HFV to be provided at a mean airway pressure that is at least 3–5 cm higher than with conventional ventilation
2. Combined HFV and conventional ventilation (usually used with HFJV), where conventional tidal breaths are interposed during HFV usually at a rate of 5–8 breaths/min
3. Application of HFV at the same mean airway pressure as conventional ventilation. The high lung volume strategy seems to be the most promising one at least for HFOV.

3.5 Respiratory Care During Mechanical Ventilation

3.5.1 Pulmonary Hygiene

The goals of pulmonary hygiene are clearance of secretions for the prevention and relief of atelectasis. The most effective method of clearing secretions is a combination of changing body position and vigorous coughing by the patient [35]. When the patient is unable to cough effectively, it is common practice to resort to chest physiotherapy and active suctioning of the trachea. Chest physiotherapy refers to a variety of respiratory maneuvers performed to aid in the clearance of airway secretions and promoting lung expansion. These are

1. Postural drainage
2. Chest percussion and chest vibration
3. Deep breathing exercises

The efficacy of chest physiotherapy in intubated patients is unclear. For details on the specific types of secretion clearance techniques, the reader is referred to several other reviews [36, 37].

3.5.2 Weaning from Mechanical Ventilation

Weaning is defined as liberation from mechanical ventilation while allowing spontaneous breathing to assume the responsibility for effective gas exchange. It can be considered a success when a patient can maintain effective gas exchange with complete spontaneous breathing. It can be considered a failure when spontaneous efforts are incapable of sustaining effective gas exchange without mechanical ventilator support. Extubation is defined as the removal of an endotracheal tube. The timing of extubation should coincide with an assessment that the patient is capable of maintaining effective gas exchange without any mechanical ventilator support. It is important to avoid both premature extubation and unnecessary prolongation of mechanical ventilation. Weaning should start

1. When the underlying disease process is improving
2. When gas exchange is adequate

3. When no conditions exist that impose an undue burden on the respiratory muscles, such as cardiac insufficiency, severe hyperinflation, severe malnutrition, and multiple organ system failure
4. When the patient is capable of sustaining spontaneous ventilation as ventilator support is decreased without expending an excessive amount of energy

Patients cannot be arbitrarily forced to wean. The pathophysiologic determinants of weaning outcome include the following:

1. Adequacy of pulmonary gas exchange
2. Respiratory drive
3. Respiratory muscle performance and capacity
4. Respiratory muscle load
5. Amount of deadspace ventilation
6. Work of breathing and ventilatory requirements

3.5.3 Weaning Problems

Trial failure is defined as a failure to sustain effective gas exchange and breathing during a trial of spontaneous breathing while still intubated [38]. *Extubation failure* is defined as the requirement for re-intubation within 48 h after extubation. Some patients take longer than others to wean. Factors that prolong the weaning process are

1. Slow resolution of the underlying disease process
2. Ventilatory pump failure
3. Psychological factors

In many instances, weaning is delayed due to the slow resolution of the underlying disease process. Phrenic nerve injury usually results as a complication of birth trauma or operative procedures involving the heart and other thoracic structures [39–42]. This may result in either paresis or paralysis of one or both hemi-diaphragms.

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Chapter 4

Heart–Lung Interactions

Shekhar T. Venkataraman

4.1 Introduction

One of the key functions of the respiratory and circulatory systems is to transfer oxygen from the atmosphere to the tissues, and carbon dioxide from the tissues to the atmosphere. To accomplish this, the two systems need to act in concert and consequently interact with each other in many different ways. Broadly, these interactions can be classified into *neural*, *humoral*, *functional*, and *mechanical*.

The central nervous system exerts control over both the respiratory and circulatory systems through afferent feedback and efferent effectors. Neural interactions refer to the changes in one system that is mediated by these neural connections when the other system is perturbed. For example, hypoxemia stimulates peripheral chemoreceptors that trigger a ventilatory response of hyperventilation and hyperpnea [1]. Similarly, lung inflation can induce reflex changes in heart rate. These are examples of neural heart–lung interactions.

Many humoral substances are released, processed, filtered, or metabolized by the lungs. These include cytokines, prostaglandins, and vasoregulatory peptides [2]. Cardiovascular function may be affected by many of these substances. These are referred to as humoral heart–lung interactions.

When the heart fails, breathing and gas exchange can be compromised. Heart failure may result in pulmonary edema, which increases the work of breathing

and increases intrapulmonary shunting resulting in hypoxemia. Similarly, chronic lung disease may increase pulmonary vascular resistance (PVR) and cause pulmonary hypertension, which may result in right ventricular failure. These are referred to as functional heart–lung interactions.

Mechanical heart–lung interactions refer to those interactions that are due to lung inflation and deflation. This chapter deals exclusively with the mechanical heart–lung interactions.

4.2 Primary Determinants of Hemodynamic Effects of Ventilation

Both spontaneous and positive pressure ventilation (PPV) increase lung volume during inspiration. During spontaneous breathing, intrathoracic pressure (ITP) is negative, whereas during positive pressure breathing, it is positive. Both lung inflation and ITP can independently affect the function of the heart. Heart–lung interactions can, therefore, be grouped into interactions involving changes in lung volume or ITP. Since lung volume changes are similar, the interactions can be grouped into three phenomena:

1. Inspiratory increase in lung volume
2. Decrease in ITP with spontaneous inspiration (SV)
3. An increase in ITP with PPV

Heart–lung interactions can also be understood by the effect of lung inflation and changes in ITP on the factors that affect global cardiac performance, i.e., heart rate, preload, contractility, and afterload.

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4.3 Changes in Heart Rate

Heart rate may be affected by lung inflation and changes in ITP by many mechanisms. Lung inflation at normal tidal volumes increases heart rate by inhibiting the vagus nerve [3]. Heart rate may also be affected by changes in cardiac output induced by heart–lung interactions as discussed subsequently.

4.3.1 Right Ventricular Preload

Right ventricular (RV) preload is determined by systemic venous return. Venous return is determined by the gradient between mean systemic pressure (Pms) and the right atrial (RA) pressure [4]. Mean systemic pressure, which is the upstream pressure for venous return, is determined by blood volume, vascular tone, and blood flow distribution within the vascular reservoirs. RA pressure (Pra) is directly affected by changes in ITP. Venous return is maximized at a Pra that is just below atmospheric pressure. SV decreases Pra and increases the gradient to venous return and results in an increased right ventricular preload. On the other hand, PPV increases Pra and decreases the gradient to venous return and therefore, decreases right ventricular preload. Under normal conditions, SV results in an increase in RV preload and an increase in cardiac output. Venous return becomes maximal due to flow-limitation with more negative pressure swings such as that may occur during severe airflow obstruction with status asthmaticus. Under normal conditions, PPV results in a decrease in RV preload and therefore a decrease in cardiac output. The decrease in RV preload due to PPV can be mitigated by fluid administration, which increases the circulating blood volume and the mean systemic pressure. Ventilation can also alter venous return by affecting Pms. During inspiration, diaphragmatic descent can increase intrabdominal pressure, which increases Pms. Recent studies by Fessler et al. [5] showed that PEEP applied during mechanical ventilation decreased venous return by compression of the intrathoracic inferior vena cava by the hyperinflated lung.

4.3.2 Right Ventricular Afterload

PVR is lowest at functional residual capacity (FRC). A change in lung volume on either side of FRC increases

total PVR. The increase in PVR below FRC is primarily due to two mechanisms:

1. Alveolar hypoxia and hypoxic pulmonary vasoconstriction
2. Kinking of vessels with atelectasis

The increase in PVR above FRC is primarily due to alveolar vessel compression. The lung blood vessels can be partitioned into alveolar and extra-alveolar vessels based on their behavior during lung inflation [6]. Alveolar vessels are compressed while extra-alveolar vessels dilate during lung inflation. The increase in PVR with PPV can be explained by the West's zones of the lung [7]. The blood flow through a lung segment is determined by the pressures in the pulmonary artery (Ppa), alveolus (Palv), and pulmonary vein (Ppv). Under Zone 3 conditions, the pulmonary blood flow (PBF) is determined by the difference between Ppa and Ppv, and not affected by Palv. Under Zone 2 conditions, the PBF is determined by the difference between Ppa and Palv, and is not affected by Ppv. PBF is then directly proportional to the Palv. Under Zone 1 conditions, there is, theoretically, no flow possible through the alveolus. In neonatal animals, studies have shown that mechanical ventilation with PEEP increases PVR and the increase in PVR is directly proportional to the increase in mean airway pressure or level of PEEP applied [8, 9]. In neonatal animals, the increase in PVR with PEEP has two components: one due to compression of alveolar vessels, and the other due to active vasoconstriction. This PEEP-induced pulmonary vasoconstriction is Ca^{2+} -channel dependent and is dose dependent with PEEP. PEEP-induced pulmonary vasoconstriction may have clinical implications for those children with a very reactive pulmonary vasculature [9].

4.3.3 Left Ventricular Preload

Left ventricular (LV) preload is affected by many mechanisms. Changes in RV preload will directly affect LV preload. During spontaneous inspiration, RV preload increases followed by a few beats later with an increase in LV preload. Instantaneous effects are, on the other hand, mediated through ventricular interdependence. For example, when RV end-diastolic volume increases, LV end-diastolic volume and compliance decrease, leading to reduced LV filling. This is thought to be the mechanism for pulsus paradoxus. An increase in PVR

may increase RV volume causing the interventricular septum to shift into the LV. This will also decrease LV compliance and filling. When the lung is inflated, it can cause deformation and compression of the cardiac fossa [10].

4.3.4 Left Ventricular Afterload

Left ventricular afterload can be defined as the maximal systolic wall tension. It can be calculated as the transmural pressure of the ventricle during systole, which is the intracavitary pressure minus the pericardial pressure. When ITP increases, pericardial pressure increases as well. With SV, transmural pressure increases and with PPV, transmural pressure decreases. Since transmural pressure is reflective of ventricular afterload, PPV decreases LV afterload and spontaneous breathing increases LV afterload. The practical application of this concept is given below.

4.4 Practical Applications of Heart–Lung Interactions

4.4.1 Functional Heart–Lung Interactions

Normally, oxygen cost of breathing under resting conditions is about 5% of the total oxygen consumption [11]. When the oxygen demand of the respiratory muscles outstrips the cardiovascular system's ability to supply it, respiratory pump failure ensues [12].

4.4.2 Use of Respiratory Variation in Hemodynamics to Predict Preload Responsiveness

During spontaneous breathing, the pleural pressure decreases. If the right atrial pressure drops in response to a spontaneous inspiration, it indicates that the venous return curve is intersecting the ascending part of the cardiac function curve. If the heart is on the ascending part of the cardiac function curve, it should respond to an increased preload with an increased output. If, on the other hand, the venous return curve intersects the

plateau of the cardiac function curve, then spontaneous inspiration does not result in a decrease in right atrial pressure and such a heart will not be preload responsive. This has been demonstrated to be true in patients [13].

Variations in systolic arterial pressure can also be used to determine preload responsiveness. In a preload responsive heart, there is an increase in systolic blood pressure followed by a fall in blood pressure during the inspiratory phase of mechanical ventilation. The normal difference between the peak increase and peak decrease is about 5–10 mmHg. In adults, the magnitude of this systolic pressure variation predicts responsiveness to increased preload [14–16]. Thus, if the pulse pressure variation was greater than 15%, then cardiac output always increased, and if it was less than 15%, then cardiac output did not increase in response to fluid loading [17]. On the other hand, in a preload independent heart, such as with congestive heart failure, positive pressure inspiration will result in an increase in systolic blood pressure during inspiration due to a decrease in left ventricular afterload with no decrease below the baseline.

4.4.3 Effects of Initiating Mechanical Ventilation in Patients with Heart Failure

Mechanical ventilation may improve cardiovascular performance in patients with heart failure by many mechanisms. By reducing the work of breathing, the demand on the heart is reduced. PEEP applied during PPV decreases alveolar edema formation and improved gas exchange. PEEP also helps recruit atelectatic lungs, thereby improving lung mechanics. Moreover, PPV decreases LV afterload and improves LV emptying [18]. PPV decreases lactic acid production by respiratory muscles during circulatory shock, and withdrawal of ventilatory support results in a marked increase in cardiac work [19, 20]

4.4.4 Mechanical Ventilation and Postoperative Issues after Glenn or Fontan Procedures and Surgery for Univentricular Hearts

A simple Fontan procedure for tricuspid atresia where the PBF is passive, any increase in ITP will not only

decrease venous return but also increase PVR. Therefore, PPV may be detrimental to cardiac output in these patients. Early extubation and spontaneous breathing are to be encouraged. Some patients may develop atelectasis and may need lung inflation or a distending pressure to maintain adequate lung volumes. Negative pressure ventilation offers an attractive alternative to these patients. In patients with Fontan-type operations, PBF and cardiac output increase with spontaneous inspiration, and PPV decreases antegrade PBF [21–23]. These studies show that negative pressure ventilation is a useful technique in selected patients after cardiac surgery, whereas PPV is not desirable, or it results in unwanted hemodynamic effects.

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Chapter 5

Cardiac Catheterization

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5.1 Introduction

Invasive pediatric cardiology developed as a subspecialty over the past four decades after first pediatric angiogram was performed by Agustin Castellanos in 1937 [1]. With the introduction of the balloon septostomy by William Rashkind to alleviate cyanosis in transposition of the great arteries [2], the field of interventional pediatric cardiology was initiated and subsequently expanded explosively. It plays a role in almost every heart defect. Although urtrre conia the use of diagnostic cardiac catheterization has decreased with the advances in noninvasive imaging, it continues to be a significant tool in the management of many complex congenital heart defects. This chapter summarizes basic aspects of diagnostic cardiac catheterization including hemodynamic evaluation, angiography and indications, review the role of cardiac catheterization in the critically ill, and the role therapeutic cardiac catheterization plays in pediatric cardiology. Possible reasons for admission to the intensive care unit (ICU) after cardiac catheterization the discussed in each section.

Nowadays, transcatheter intervention has replaced surgery for many simple defects. In complex heart disease the role of catheter interventions is hand in hand with surgery, increasing treatment strategies and allowing an improved outcome.

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5.2 Diagnostic Cardiac Catheterization

5.2.1 Indications

Although, the use of preoperative diagnostic cardiac catheterization has decreased and continues to decrease significantly for most lesions with the advances of non-invasive testing, there are specific conditions for which it is thought to be necessary:

1. Pulmonary atresia with intact ventricular septum, to rule out coronary anomalies which would preclude a biventricular repair.
2. Tetralogy of Fallot with pulmonary atresia, multiple aortopulmonary collaterals, and other conditions when collaterals are suspected or when central pulmonary arteries are very small or cannot be identified.
3. Single ventricle variants, prior to Stages II and III palliation.
4. Primary or secondary pulmonary artery hypertension, particularly outside of infancy.
5. Pulmonary vein anomalies with or without stenosis (if anatomy cannot be well identified by noninvasive methods).
6. Coronary artery anomalies (although, noninvasive technologies continue to advance in resolution, for most children, angiography continues to be the gold standard to diagnose coronary artery abnormalities).
7. Postoperative evaluation: To evaluate postoperative conditions, diagnostic cardiac catheterization continues to be used routinely, often as a first step prior to transcatheter interventions (see below). Examples include evaluation of homograft or

conduit stenosis, residual shunts, palliated single ventricle patients, or evaluation of most postoperative lesions unexplained fully by noninvasive testing.

8. Pre transplant evaluation.
9. Prior to transcatheter intervention: Diagnostic cardiac catheterization is performed in all patients with indication for transcatheter intervention, to determine the need for intervention, which is performed during the same procedure. Immediately after intervention, repeat diagnostic cardiac catheterization is performed to assess the results of the intervention.
10. Other: Diagnostic cardiac catheterization may also be necessary in patients with common conditions and unusual clinical presentation, and whenever symptoms cannot be explained fully by noninvasive testing.

It is likely that over time the use of diagnostic cardiac catheterizations will continue to evolve, with a significant decrease in its use for common lesions and increased demand of studies on patients with complex postoperative conditions, of which in the past survivors would have not existed. Nowadays, simple diagnostic cardiac catheterizations are indeed a rarity. Almost 50% of planned diagnostic cardiac catheterizations in patients with single ventricle physiology result in interventions. These include, for example, coil occlusion of venous or arterial collaterals, balloon dilation and/or stent placement for venous or arterial stenoses, or device closure of baffle leaks or fenestration.

5.2.2 Access

Most common sites of vascular access are the femoral artery and vein at any age, and the umbilical vessels in the newborn [3]. Other access sites (subclavian, jugular, hepatic) may be necessary when standard sites are not available, or in patients with complex anatomy (i.e., post bidirectional Glenn), or when certain interventions are planned (i.e., transhepatic access in a patient with occluded femoral vessels and need for transeptal puncture or internal jugular access for transcatheter closure of an apical ventricular septal defect). The preferred and most commonly used technique for access is the percutaneous Seldinger technique, [3] which has become highly successful in children, making surgical cut-downs almost historical.

The smallest French size of catheter and/or sheath which would allow adequate hemodynamic and angiographic evaluation should be chosen.

Heparin is administered intravenously (100 Units/kg) at the start of the procedure and ACTs are monitored to be kept above 200 s [4].

5.2.2.1 Hemodynamic Evaluation

Pressure and saturations: Accurate pressure measurements are essential for hemodynamic diagnosis. Two simultaneous transducers are used, and should be accurately calibrated. Normal tracings have been published widely (Table 5.1) [5, 6]. The most common sequence of measurements include:

- Superior vena cava (SVC) saturation; occasionally pressure is recorded as well (patients with surgical caval anastomoses, transvenous pacing wires, or history of indwelling lines, in whom a pull back from superior vena cava to right atrium should be recorded)
- Right atrium (RA) (pressure and saturation)
- Right ventricle (RV) (pressure and saturation)
- Pulmonary arteries (PA) (pressure and saturation) and bilateral wedge pressures simultaneous with systemic ventricular end-diastolic pressure
- Measurement of oxygen consumption (this can be selectively measured or assumed according to tables normalized by heart rate and age)
- Second set of saturations in pulmonary artery, aorta, and superior vena cava, which should be consistent

Table 5.1 Hemodynamic values considered normal in children #

Site of pressure measurement	Average normal	Range
Right atrial mean	3 mmHg	0–8 mmHg
Right ventricular	24/4 mmHg	15–35 mmHg
Pulmonary artery (mean)	21/9 (12) mmHg	11–26/2–14 (8–19)
Pulmonary capillary wedge or left atrial mean	8 mmHg	2–12 mmHg
Left ventricular	96/8 ^a	60–130/–12 ^a
Systemic arterial	110/65 ^a	Largely variable with age

^aPressure variable with age normal values for systemic blood pressure

[#]Values derived from combination of published normal hemodynamic data

with the initial values obtained, assuming an unchanged condition

- Pull-back tracings from pulmonary artery to right atrium and systemic ventricle to descending aorta

The sequence of measurements may vary according to the underlying diagnosis. In all patients with cyanosis, pulmonary venous saturation should be measured whenever possible. Pulmonary venous wedge pressures are measured to determine PA pressures in patients with difficult access to the pulmonary arteries. An abnormal value above 20 mmHg should be confirmed with direct pulmonary artery pressure measurement. Gradients across lesions can be determined with two catheters (one positioned proximal and one distal to the stenosis) (Fig. 5.1) or via pull-back recordings.

Cardiac output and shunts: Based on the Fick's principle, by measuring oxygen consumption (VO_2) and oxygen content in systemic arterial, systemic venous, pulmonary arterial, and pulmonary venous blood, it is possible to determine the cardiac output (CO) or Q_s , the pulmonary blood flow or Q_p , and calculate shunts. The cardiac index is estimated by relating the CO to the body surface area [6]. The saturation of

the superior vena cava is considered the best representative of the mixed venous saturation [6, 7].

$$CO \text{ or } Q_s(l / \text{min}) = \frac{VO_2(\text{mlO}_2 / \text{min})}{\text{Systemic artery O}_2 \text{ content-mixed venous O}_2 \text{ content}(\text{mlO}_2 / \text{liter blood})}$$

$$\text{O}_2 \text{ content}(\text{mlO}_2 / \text{l}) = \text{saturation} \times \text{Hb g / dl} \times 1.36 \text{ ml O}_2 / \text{g Hb} \times 10 + \text{pO}_2 \times 0.03 \text{ ml O}_2 / \text{liter blood}$$

In patients receiving inhaled O_2 and an arterial pO_2 over 100, dissolved O_2 should be accounted for. This is particularly important for the determination of lability of pulmonary vascular resistance to selective pulmonary vasodilators in patients with pulmonary hypertension and shunts.

$$Q_p(l / \text{min}) = \frac{VO_2(\text{mlO}_2 / \text{min})}{\text{Pulmonary vein O}_2 \text{ content-pulmonary artery O}_2 \text{ content}(\text{mlO}_2 / \text{liter blood})}$$

Q_p/Q_s can be determined to estimate clinical significance of left to right shunt, and is more useful than shunt calculations per se. The effective pulmonary blood



Fig. 5.1 Pressure tracings are demonstrated from the left ventricle (arrow) and the ascending aorta simultaneously. There is a peak gradient of 44 mmHg, indicating moderate aortic stenosis

flow (Qe) is the amount of deoxygenated blood which gets oxygenated.

$$Q_e(l/min) = \frac{VO_2(mlO_2/min)}{\text{Pulmonary vein } O_2 \text{ content} - \text{systemic vein } O_2 \text{ content}(mlO_2/liter \text{ blood})}$$

The absolute left to right shunt is the difference between the Qp and the Qe. Similarly, the absolute right-to-left shunt is the difference between the Qs and the Qe.

In patients with no source of right-to-left or left-to-right shunting, cardiac output can be accurately determined by thermodilution [7]. This is particularly useful in patients with left-sided obstructive lesions (i.e., congenital aortic stenosis) or cardiomyopathies. Thermodilution would be inaccurate in patients with pulmonary regurgitation (i.e., postoperative Tetralogy of Fallot), severe peripheral pulmonary artery stenosis or tricuspid regurgitation, and cannot be used in the presence of any intracardiac shunting. A normal CI is 3–3.5 l/min/m².

Resistances: Vascular resistances are determined by dividing the pressure difference through the circulation being considered by the flow (l/min) across it, and are expressed in mmHg per l/min (Wood units or hybrid resistance units), or converted into metric resistance units (dyne sec cm⁻⁵) or absolute resistance units, by multiplying by 80. These units are more commonly used in adults, and not in children, for whom resistances are expressed by body surface area, giving a resistance index. A normal pulmonary vascular resistance is less than two Indexed Units (mmHg l/min/m²) [6].

$$PVR = \frac{\text{Mean pulmonary artery pressure} - \text{Mean left atrial pressure or pulmonary vein pressure}}{Q_p \text{ indexed}}$$

$$SVR = \frac{\text{Mean arterial blood pressure} - \text{Mean right atrial pressure}}{Q_s \text{ indexed (or CI)}}$$

Calculations should be performed in room air or baseline. Different specific conditions may need to be studied according to the patient's diagnosis, such as drug testing (i.e., response of pulmonary vascular resistance to nitric oxide), or transcatheter balloon testing (i.e., test occlusion of atrial septal defect in a patient with mitral stenosis or small left sided structures, or test occlusion of a source of right-to-left shunt through an atrial septal defect or Fontan fenestration). To accurately estimate the pulmonary vascular resistance in patients with branch pulmonary artery stenoses, it is

necessary to determine the distribution of pulmonary blood flow to each lung by lung scintigraphy or MRI. Since the resistances are in parallel, the total resistance can then be calculated using the formula:

$$\frac{1}{\text{Total resistance}} = \frac{1}{\text{Right lung resistance}} + \frac{1}{\text{Left lung resistance}}$$

This would be important to take into consideration when evaluating hemodynamics in a patient with single branch pulmonary artery proximal stenosis. The pressure may be elevated in the contralateral lung, but the overall resistance may be normal if calculated accurately.

Valve areas: Valve areas in pediatrics are calculated similarly as in adults, using the Gorlin and Gorlin formulae. A valve area is directly proportional to the flow across the valve and inversely related to the square root of the mean pressure drop across it [6].

$$\text{Aortic or pulmonary valve area} = \frac{\text{Systolic flow}(ml/s)}{(44.5) \times \left(\text{square root of mean systolic gradient} \right)}$$

$$\text{Systolic flow}(ml/s) = \frac{(C.O.) \times (R \text{ to } R \text{ interval})}{(60) \times (\text{systolic ejection time})}$$

$$\text{Mitral or tricuspid valve area} = \frac{\text{Diastolic flow}(ml/s)}{(31.5) \times \left(\text{square root of mean diastolic gradient} \right)}$$

$$\text{Diastolic flow}(ml/s) = \frac{(C.O.) \times (R \text{ to } R \text{ interval})}{(60) \times (\text{diastolic ejection time})}$$

The mean gradient can be accurately obtained by planimetry. Otherwise, it can be approximated from the average of the gradients measured from vertical lines placed 1 mm apart throughout the area in between the pressure tracings (either ventricular and arterial, or auricular and ventricular).

5.2.3 "Test" Conditions

The hemodynamic response to specific conditions can be tested in the Catheterization Laboratory to plan

further surgical or catheter intervention. Examples of these include:

1. Balloon test occlusion of an atrial septal defect or a fenestration prior to the closure in patients with right-to-left shunting and abnormal right heart structures
2. Test occlusion of a Blalock-Taussig shunt before coil embolization
3. Test occlusion of a patent ductus arteriosus to determine the presence of aortic coarctation or ductal-dependant hypoplastic arch
4. Drug studies (testing of response of the pulmonary vascular bed to selective vasodilators in pulmonary hypertension; or the effect of intravenous verapamil in patients with hypertrophic cardiomyopathy)
5. Rhythm modification (i.e., patients with Fontan circulation and junctional rhythm can be tested in the catheterization laboratory with atrial pacing to determine the hemodynamic benefit of pacemaker implantation; some with cardiomyopathy can be studied to test effects of biventricular pacing or different pacing modalities). Hemodynamics and calculations are determined before and after 10 min in the new condition.

5.2.3.1 Angiographic Evaluation

Angiography is most commonly performed using angiographic catheters (i.e., Pigtail or Berman) connected to a power injector [8]. For small structures, selective injection can be performed by hand using any end-hole catheter. Occasionally, balloon occlusion angiography is preferred, where the injection occurs proximal (Berman catheter) or distal (wedge end-hole catheter) to the balloon. Biplane angiography is preferred in congenital heart disease, and particularly, necessary in infants and in patients of any age when interventional procedures are being considered. Common angiographic views for diagnosis of congenital heart defects are [8]:

- Straight AP 0°/Lateral 90°: (a) Right ventriculogram in normally related to great arteries, transposition, double outlet right ventricle, pulmonary atresia intact ventricular septum and postoperative tetralogy of Fallot, and most single ventricle ventriculograms. (b) Venous pathways, systemic and pulmonary arteries, pulmonary veins.

- Cranial frontal (+20°–30°) and straight lateral: Particularly used to visualize the right ventricular outflow tract and main pulmonary artery with bifurcation in tetralogy of Fallot or in patients with pulmonary stenosis.
- Caudal frontal, extreme (–30° to 45°): (a) A “laid back” @ aortogram technique, particularly useful in transposition of the great arteries to visualize coronary artery anomalies (Fig. 5.2) [9] or after Norwood to visualize distal arch. (b) Branch pulmonary artery stenosis, to visualize bifurcation.
- Long axial oblique (70° left anterior oblique and 20°–30° cranial on the lateral camera): particularly useful for left ventriculogram to visualize ventricular septal defects and left ventricular outflow tract (Fig. 5.3).
- Hepatoclavicular view (40° right anterior oblique in the AP camera; 40° left anterior oblique and 40° cranial on the lateral camera): useful for left ventriculogram to visualize inlet ventricular septum and septal defect in tricuspid atresia and endocardial cushion defects.

Modified views can be adapted in specific conditions, such as complex branch pulmonary artery stenosis, or postoperative arch obstruction.

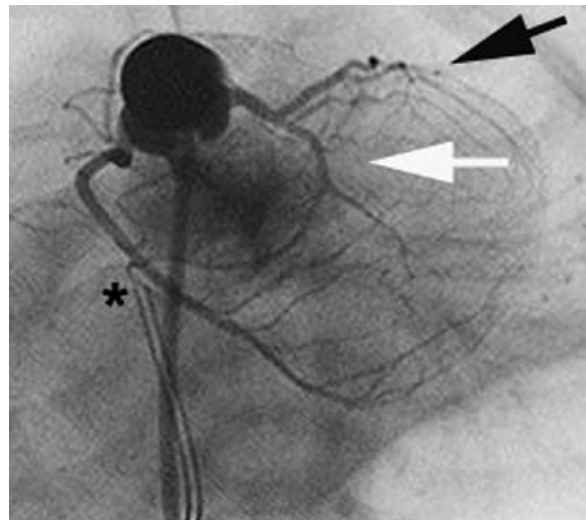


Fig. 5.2 Laid-back aortogram in a patient with {S, D, D} transposition of the great arteries and normal coronary artery anatomy for d-transposition. Note the right coronary artery (*) comes off the rightward facing sinus of Valsalva. The left coronary artery comes of the leftward and anterior sinus, giving off the circumflex (*white arrow*) and the left anterior descending coronary artery (*black arrow*)

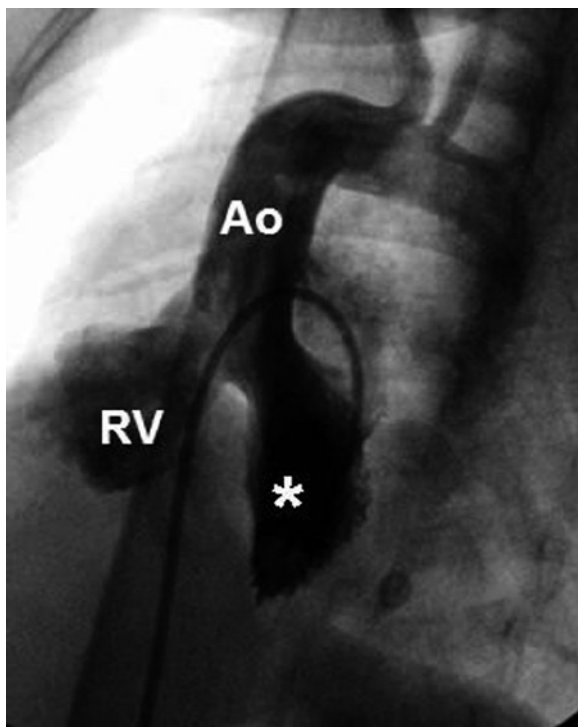


Fig. 5.3 Transvenous left ventriculogram performed in long axial oblique projection demonstrates a large cono-ventricular septal defect (often called perimembranous). *: left ventricle; Ao: Ascending aorta; RV: right ventricle

5.2.4 Complications

Even though diagnostic cardiac catheterizations are performed in patients of increasing risk, and in spite of a substantial increase in the number and complexity of interventional procedures, the incidence of complications has consistently decreased over the years. Currently, mortality from a cardiac catheterization is exceedingly rare, in the order of 0.1%, and almost exclusively occurring in infants or high risk patients undergoing interventional procedures [10]. The reported incidence of all adverse events is approximately 8%, including the complications related to interventions. Within this group, the incidence of major complications (e.g., death, cardiac arrest, cardiac perforation, complete heart block, ventricular tachycardia or fibrillation, decreased pulse requiring surgery, or cardiac tamponade) is 1–2%. Common minor complications include fever in the 12 h following the procedure and hematoma at the vascular access site.

Complications of cardiac catheterization and transcatheter intervention may be a reason to admission to the ICU.

Some of the complications are specifically related to the intervention performed. For instance, the presence of segmental high perfusion pulmonary edema following pulmonary artery angioplasty procedures, or an arterial pulse loss associated with retrograde aortic balloon valvotomy. These problems will be discussed in more detail in the specific sections to follow.

5.3 Interventional Cardiac Catheterization

Table 5.2 provides a summary of transcatheter interventions in congenital heart disease.

Interventions can be classified according to the purpose to treat:

- 1) Valvular obstruction
- 2) Vascular stenosis
- 3) Creation or enlargement of defects
- 4) Closure of defects
- 5) Other

5.3.1 Valvular Obstruction

5.3.1.1 Pulmonary Valve Stenosis/Atresia

Intervention for pulmonary valve stenosis is indicated if a peak to peak gradient is above 40 mmHg as measured by cardiac catheterization. Balloon dilation has become the standard first line therapy, with very high success rate [11, 12]. However, patients with so-called dysplastic pulmonary valves as seen in Noonan syndrome, with markedly thick leaflets and often associated stenosis at the sinotubular junction (supravalvar), have traditionally had lower success. Nowadays, the use of high pressure balloon valvotomy for these resistant valves can achieve success in most patients, so that surgical intervention is limited only to very few. Patients are recovered overnight and discharged the following morning. Rarely severe dynamic subpulmonary stenosis can develop post dilation. In some cases, this can be severe, specially in the absence of a right-to-left shunt at atrial level, can lead to a low output state (“suicidal right ventricle”), requiring admission to the ICU and intravenous beta-blockers.

Table 5.2 Summary of transcatheter interventions

Therapeutic goal	Intervention	Indicated in patients with:
Create or enlarge an ASD	Balloon atrial Septostomy	TGA/IVS w/ restrictive ASD (electively or with severe cyanosis) TGA/VSD or DORV with poor mixing and severe cyanosis Tricuspid atresia or PA/IVS w/ restrictive ASD (rarely)
	Blade or balloon atrial septoplasty	HLHS w/ restrictive or absent ASD Other complex CHD with left atrioventricular valve stenosis or atresia and restrictive or absent ASD
Balloon Valvuloplasty	Pulmonary balloon valvotomy	Critical PS (newborn) Moderate to severe PS Severe PS in TOF with hypoplastic pulmonary arteries and high surgical risks Other complex CHD with severe PS, hypoplastic pulmonary arteries and high surgical risks
Angioplasty and/or Stent implantation	Aortic balloon valvotomy	Critical AS (newborn) Moderate to severe AS
	Pulmonary artery	Branch pulmonary artery stenosis (isolated or in association with other CHD) Hypoplastic pulmonary arteries (isolated or in association with other CHD)
	Coarctation	Native coarctation of the aorta Postoperative recurrent coarctation
	Systemic vein	SVC syndrome and SVC obstruction (postoperatively, secondary to indwelling lines or cannulation sites)
	Pulmonary vein	Severe pulmonary vein stenosis (only indicated as a bridge to heart–lung transplantation to relieve symptomatology)
	PDA	Ductal dependent lesions, or other with decreased pulmonary blood flow
Closure	Device or Coil	Patent ductus arteriosus Atrial septal defect Ventricular septal defect Aortopulmonary collaterals (patients with dual source of pulmonary blood flow: central pulmonary artery and collateral) Arteriovenous malformation (i.e., pulmonary) Pulmonary sequestration (i.e., in Scimitar Syndrome)
Miscellaneous	Balloon dilation/stenting local thrombolysis	PDA stenting (patients with ductal dependent lesions awaiting transplantation; HLHS as part of hybrid approach) Blalock-Taussig shunt reopening APC dilation/stenting or reopening post failed unifocalization
	Endomyocardial Biopsy	Myocarditis and cardiomyopathies
	Foreign body retrieval	Retained intracardiac lines (i.e., post cardiac surgery)

ASD atrial septal defect; *AS* aortic stenosis; *APC* aortopulmonary collateral; *CHD* congenital heart disease; *DORV* double outlet right ventricle; *HLHS* hypoplastic left heart syndrome; *IVS* intact ventricular septum; *PDA* patent ductus arteriosus; *PS* pulmonary stenosis; *TGA* transposition of the great arteries; *TOF* tetralogy of Fallot; *VSD* ventricular septal defect

In the newborn and infant with an open atrial communication, variable degree of right-to-left shunting at atrial level causing cyanosis is common.

Though balloon dilation may result in valvar regurgitation, given that the pulmonary artery pressure is normally quite low, the physiologic consequences of the insufficiency are rarely significant. Thus, the main long term issues are observation for the rare case of restenosis and the continued need for endocarditis precautions.

A special group of patients are the newborns with critical pulmonary valve stenosis, and ductal dependent circulation. It is common to see the associated

variable degrees of right ventricular hypoplasia, although overtime the right ventricle is almost always adequate to allow a biventricular circulation [13, 14]. However, it may take several weeks or months for the right-to-left shunting at the patent foramen ovale to be eliminated or significantly reduced. Typically, prostaglandins are discontinued immediately following balloon dilation, although, most patients require on-going prostaglandins for a few more days or weeks, especially if the severity of the right ventricular hypoplasia is marked. Patent ductus arteriosus (PDA) stenting or surgical intervention (placement of

a Blalock-Taussig shunt +/- a right ventricular outflow tract patch) may be necessary for those patients who cannot wean off prostaglandins after 14 days of dilation.

Radiofrequency-assisted valve perforation followed by balloon valvotomy [15] can be performed in patients with membranous pulmonary atresia (Fig. 5.4). Although successful perforation has been reported in up to 75–90% of selected patients, the procedure is definitive for only 35%, as they commonly require additional intervention either transcatheter or surgical.

Patients with pulmonary valve atresia may have right ventricular dependent coronary circulation which would contraindicate right ventricular decompression. Typically, patients with this condition have small right ventricles and small tricuspid valve annulus. For these patients, cardiac catheterization is typically purely diagnostic.

5.3.1.2 Aortic Valve Stenosis

Balloon valvotomy is considered as the procedure of choice for management of severe or critical aortic valve stenosis in most centers. In the newborn, severe aortic stenosis can present as critical, ductal-dependant lesion [16, 17]. Transcatheter balloon dilation can be performed antegrade (femoral vein or umbilical vein to left ventricle and aorta across foramen ovale), or retrograde (umbilical artery or femoral artery). For premature babies, the carotid artery approach via surgical carotid cut down is a good alternative to avoid femoral arterial damage. Other approaches for access have also been reported (axillary, subscapular, transventricular). Currently, the procedure can be performed using low profile balloons advanced via femoral approach through a 3F sheath in the newborn, with which the incidence of iliofemoral artery thrombosis in the retrograde approach has significantly lowered. A gradient of over 50 mmHg is considered the cut-off for intervention, although smaller gradients may not correlate with severity in patients with severe LV dysfunction, or cardiomyopathy.

Some degree of aortic insufficiency is commonly present after the procedure, although more than moderate regurgitation is rare. Attempts to completely alleviate obstruction by using large balloons result in an unacceptable amount of regurgitation [18]. Thus, after successful balloon dilation, it is common for patients to have residual obstruction in the mild to moderate range and/or insufficiency. In most cases, the

residual physiologic abnormality is mild with average residual gradients of 22–35 mmHg. Moderate or severe aortic insufficiency occurs in about 10% of patients, and this incidence tends to increase during follow-up [16, 17]. When subsequent intervention is needed it may be due to recurrent obstruction, insufficiency, or both. In the first case, repeat valve dilation is an option. When aortic insufficiency becomes severe, surgery is required.

5.3.1.3 Mitral Stenosis

Isolated congenital mitral valve stenosis is very rare, occurring more commonly in association with other left sided obstructive lesions in patients with Shone's syndrome or other complex congenital heart disease. Congenital mitral valve stenosis has proven to be somewhat an intractable condition, except in those patients with isolated supravulvar mitral ring, in whom surgical resection is the procedure of choice [19]. Infants with severe congenital mitral stenosis have been reported to have a poor outcome regardless of treatment modality. Given the palliative nature of any intervention, newborns who present with this condition are typically managed as patients with hypoplastic left heart syndrome (Norwood Stage I procedure, followed by subsequent surgeries for a single ventricle palliation). The therapeutic options for symptomatic infants and children outside the newborn period presenting with severe mitral stenosis and pulmonary hypertension are few. In the presence of a supravulvar mitral ring, surgical resection should be performed. Depending on the underlying anatomy mitral balloon valvotomy has been reported to immediately reduce the gradient in the majority, although, sustained symptomatic improvement is only seen in less than half of the patients. Given the lack of better options, mitral valve balloon valvotomy can be considered as a palliative procedure to delay the need for mitral valve replacement in these patients.

5.3.2 Vascular Stenosis

5.3.2.1 Pulmonary Artery Stenosis

Peripheral pulmonary artery stenosis can be congenital or acquired post cardiac surgery, and constitutes 2–3%

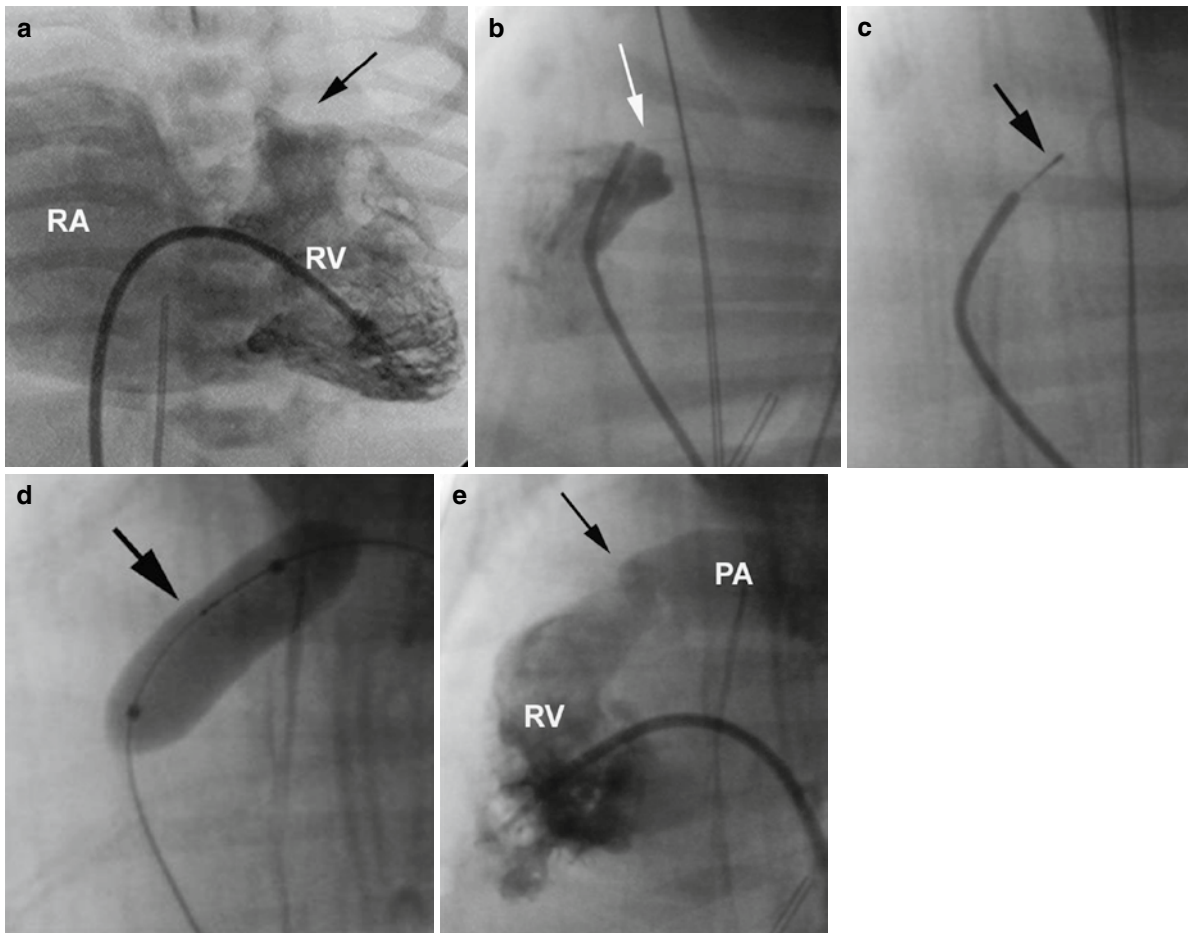


Fig. 5.4 (a) The right ventricular demonstrates membranous pulmonary valve atresia (arrow), with severe tricuspid valve regurgitation, with contrast filling the right atrium (RA). The right ventricle (RV) is well developed. (b) In the lateral projection the right ventriculogram demonstrates membranous atresia (arrow). A right coronary catheter is used to position its tip under the atretic valve, in preparation for

radiofrequency perforation. (c) The radiofrequency wire has been advanced across the atretic valve. (d) After a wire is advanced across coaxial catheter, a balloon is inflated across the valve. (e) A right ventriculogram post radiofrequency perforation and balloon valvotomy demonstrates a widely open pulmonary valve (arrow). RV: right ventricle; PA: pulmonary artery

of congenital heart disease. Congenital pulmonary artery stenosis occurs in isolation or association with other congenital heart defects (most commonly, Tetralogy of Fallot +/- pulmonary atresia). As a primary lesion, it may be idiopathic or occur in presence of syndromes, such as congenital rubella, Williams syndrome, and Alagille syndrome. Results of surgery for such branch pulmonary artery stenoses have been quite unsatisfactory, commonly leading to more severe stenoses than preoperatively. In addition, surgery cannot treat peripheral stenosis. Therefore, balloon angioplasty remains the first line and only therapy for many of these patients [20–22].

Indications for balloon dilation include elevated right-to-left ventricular pressure ratio of over 50%, right ventricular failure, angiographic narrowing, contralateral pulmonary arterial hypertension, and abnormal perfusion by lung scintigraphy. Although there are no contraindications to this procedure by age or size, newborns with severe branch pulmonary artery stenosis would undergo balloon angioplasty only if symptomatic and associated with systemic or higher right ventricular pressure, or ventricular dysfunction. Either discrete stenoses or long diffuse hypoplastic pulmonary arteries can be successfully dilated to variable degree [22]. Reported results indicate a rate of

success of 50–75%, [22] the latter with the use of high pressure balloons. Most recently, the introduction of the cutting balloon and novel balloon technology (over 25 ATM of burst pressure) has increased the success rate of balloon pulmonary angioplasty to the order of over 92% [22–24]. The cutting balloon has microsurgical blades longitudinally and creates a predictable intimal tear. Stent implantation allows a further significant improvement in success (over 90%); [25, 26] (Fig. 5.5) however, not all lesions are stentable, and there are limitations in the available technology, as the cutting balloon is manufactured only up to 8 mm in diameter. Most stents implanted in children can be redilated at a later time to adult size diameters [27].

Stents in infants offer some theoretical disadvantages: need for a larger introducer (more difficult vascular access), and for subsequent dilations to keep up with somatic growth. Still, some lesions that do not respond to dilation alone or to previous surgery can be successfully managed with stent implantation, regardless of the age.

Balloon dilation of peripheral pulmonary artery stenosis carries a procedural related mortality of 0–3% [28], related to vessel rupture (tears) or cardiac arrest in high risk patients – those with suprasystemic right ventricular pressure and poor right ventricular function. Immediate transcatheter management of significant pulmonary artery trauma using coil closure of unconfined tears or implantation of covered stents can be lifesaving, [27] and likely will almost eliminate mortality in the future. In addition, high risk patients with suprasystemic right

ventricular pressures and dysfunction may benefit from creation of an atrial level communication prior to balloon dilation to allow a pop-off. The incidence of morbidity related to the procedure is in the order of 10%, including nonfatal pulmonary artery tears, segmental pulmonary edema, distal vessel aneurysm formation, and deep vein thrombosis [28, 29]. Patients with hyperperfusion pulmonary edema may need to remain mechanically ventilated for 24 h in the ICU on PEEP and be managed with diuretics for a few days.

5.3.2.2 Aortic Coarctation

Balloon dilation of native coarctation of the aorta [30–32] remains a controversial subject in pediatric cardiology. Generally, indications for intervention in infants and children, whether surgical or transcatheter, include the presence of anatomic coarctation associated with a systolic pressure gradient between upper and lower extremities of over 20 mmHg, or a systolic blood pressure greater than 95% for age, or the presence of left ventricular dysfunction. In the newborn, surgery is indicated only in symptomatic patients, with congestive heart failure, failure to thrive, or upper extremity hypertension associated with left ventricular dysfunction, given that during the first month of life there is a higher postoperative restenosis rate. Surgery is considered as the management approach of choice for neonates and young infants with severe

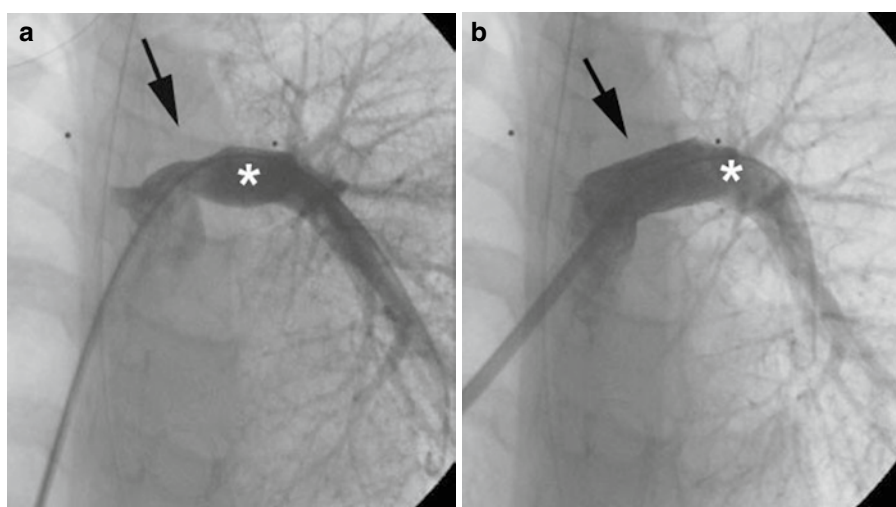


Fig. 5.5 (a) The left pulmonary angiogram demonstrates proximal left pulmonary artery stenosis (arrow). (b) Following stent implantation there is significant improvement in vessel diameter without any residual stenosis (arrow). *: Left pulmonary artery

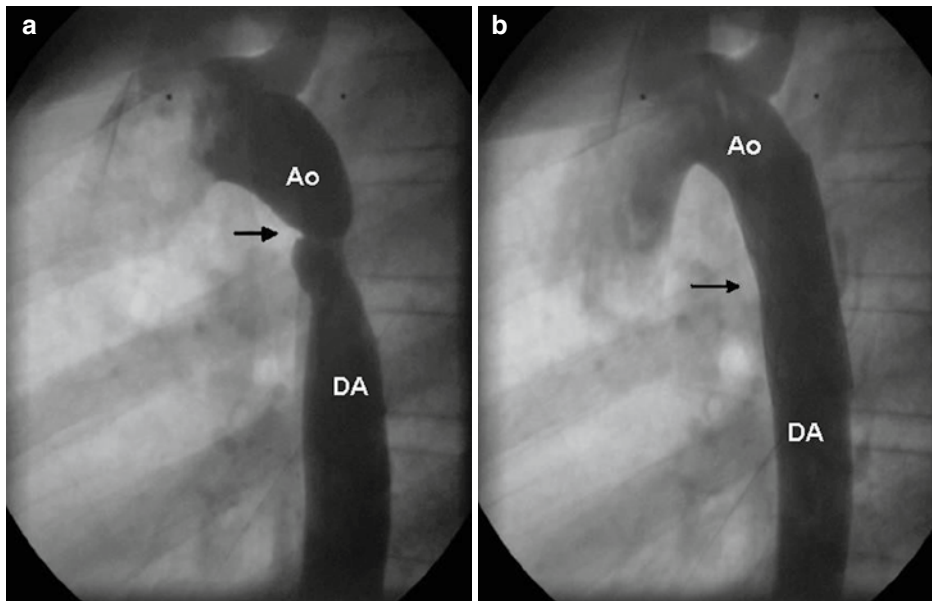


Fig. 5.6 (a) Aortogram demonstrates coarctation of the aorta with a narrow and tortuous course (arrow). (b) Following stent implantation there is no residual coarctation (arrow). Ao: Aorta; DA: Descending aorta

coarctation, given the unacceptably high incidence of restenosis following balloon angioplasty (at least 50%). However, there are specific clinical conditions where balloon dilation of the native coarctation in infants can be considered: patients with high surgical risks (i.e., severe left ventricular dysfunction and unstable hemodynamic condition, severe pulmonary hypertension, or other pulmonary diseases that would significantly increase the risk of thoracotomy, recent intracranial hemorrhage, or other major systemic conditions), or if coarctation is identified at the time of cardiac catheterization for balloon valvotomy of congenital aortic valve stenosis.

Recurrence of stenosis post balloon dilation, decreases as the age of the patient increases, reaching about 10% for children over 2 years of age. The procedure is generally safe, with a mortality of less than 1% and aneurysm formation rates of variable incidence reaching up to 14% in some reports. Recent long term data supports balloon dilation of native coarctation as an acceptable therapeutic option for discrete coarctation of aorta in patients older than 1 year of age with discrete stenosis. However, the long term significance of an aortic aneurysm in the adult is unknown.

In patients who are diagnosed during late childhood, adolescence, or in adulthood, stenting of the coarctation

at catheterization is widely gaining acceptance as a first line treatment [33] (Fig. 5.6), particularly in the absence of any significant collaterals, given that the surgical repair is at risk of spinal cord ischemia. Long term results of coarctation stenting are still scarce. The lack of approved covered stents for generalized in the United States make the risk of vessel dissection particularly worrisome. Stents result in effective relief of the obstruction in between 92 and 100% of cases. At follow-up, recurrent coarctation can be managed with repeat balloon dilation and/or re-stenting.

For infants with postoperative recurrent or residual coarctation balloon angioplasty is considered as the procedure of choice, regardless of the type of previous surgical repair [34, 35] (Fig. 5.7). Mortality is 0.7%, with a low incidence of aneurysm formation (less than 2%). Success occurs in over 90% with a restenosis rate of less than 20%, and can be managed with repeat balloon dilation.

5.3.2.3 Systemic or Pulmonary Vein Stenosis

Symptomatic systemic venous obstruction can occur in infants and children following cardiac surgery or after placement of chronic indwelling lines.

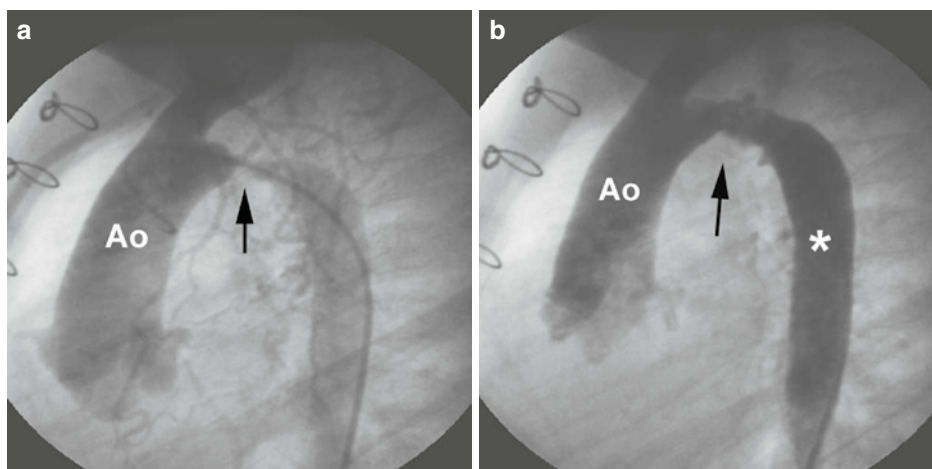


Fig. 5.7 (a) The aortogram demonstrates severe coarctation of the aorta (arrow) after surgical arch repair. (b) Following balloon angioplasty there is significant improvement in vessel diameter. Ao: Ascending aorta; *: Descending aorta

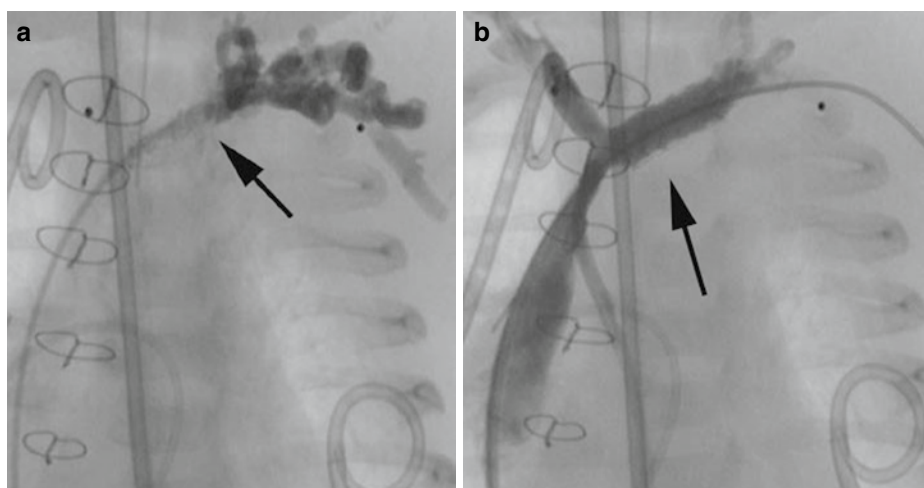


Fig. 5.8 (a) Venogram performed in the left subclavian vein demonstrates near extensive occlusive thrombus in the innominate vein (arrow). (b) After use of Angiojet, balloon dilation and stenting, patency has been re-established (arrow)

Indications for intervention include symptoms of systemic venous hypertension, SVC syndrome, and chronic effusions. Balloon dilation of venous stenoses has been performed since the mid 1980s. The immediate success rate is over 90% for balloon dilation alone, but the restenosis rate is over 50%, for what primary stent implantation is preferred (Fig. 5.8) [25].

Recanalization of completely thrombosed systemic veins can be performed using the angiojet technique (transcatheter mechanical thrombolysis) or using

catheter or RF perforation, followed by balloon dilation/stenting (Fig. 5.9).

Pulmonary vein stenosis is generally an intractable disease, occurring either congenital or postoperatively. Balloon dilation and stent implantation [36] can only serve as a short term palliation for symptomatic patients as a bridge to heart–lung transplantation. The use of drug eluting stents, or the cutting balloon may provide alternative options of more durability, although the experience with these techniques is only anecdotal.

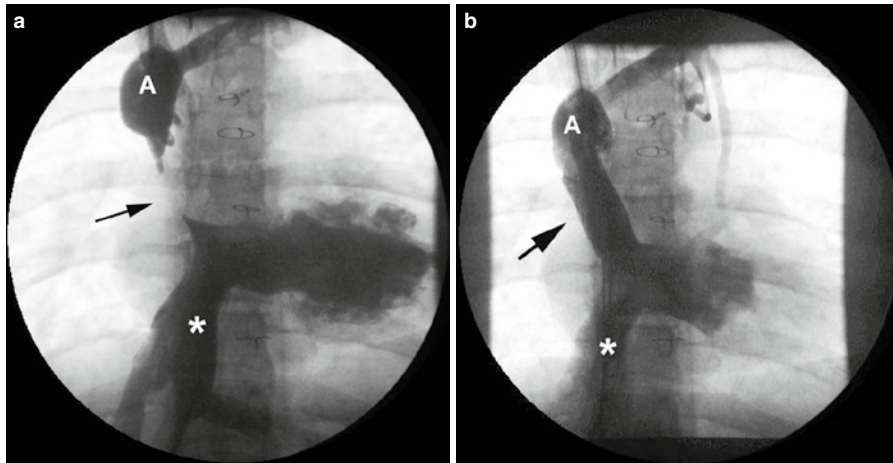


Fig. 5.9 (a) The angiogram demonstrates complete occlusion (arrow) of the superior limb of the Mustard baffle in a patient with transposition of the great arteries. (b) Following transcatheter recanalization and stenting patency is reestablished (arrow). (a): superior vena cava; * Inferior vena cava baffle

5.3.3 Creation or Enlargement of Defects

5.3.3.1 Balloon Atrial Septostomy (BAS)

Following its initial introduction by Rashkind and Miller in 1966 [2], BAS has become an essential intervention in the management of most patients with transposition of the great arteries and other forms of congenital heart disease with transposition-like physiology (i.e., double outlet right ventricle). At most centers, BAS is performed routinely on patients with d-transposition of the great arteries and intact ventricular septum, often in the ICU under echocardiographic guidance. In patients with left-sided obstructive lesions, thick atrial septum, small left atrium, and restrictive atrial septal defect, BAS is rarely successful [37]. For these patients, other techniques of atrial septal defects (ASD) creation and septoplasty are preferred (see below). The success rate of balloon atrial septostomy in newborns is over 98%, with a procedural mortality of less than 1%, and an incidence of major complications reported in the order of 0–3% [54].

5.3.3.2 Atrial Septoplasty/Blade Septostomy

Blade septostomy [38] is almost not used nowadays, having been replaced by the use of a combination of Brockenbrough transeptal puncture [37], followed by

serial balloon dilations using angioplasty balloons, including the use of the cutting balloon, and occasionally stent implantation.

5.3.4 Closure of Defects

5.3.4.1 Atrial Septal Defects (ASD)

Now, most ASD secundums are closed via transcatheter devices. Some are still not candidates for device implantation, given the lack of good rims of tissue around the defect to anchor the device. ASDs of the sinus venosus or ASD primums cannot be closed with devices. Although devices are available to close very large holes (up to 40 mm in diameter) the larger devices will fit only in the heart of a large adult. Currently, there are two devices approved for use in the USA for closure of ASD: the amplatzer septal occluder [39, 40] (which accounts for the vast majority of implants); and the Helex [41] occluder. The CardioSEAL device was in the past used for this purpose while under investigation, and is now approved for closure of ventricular septal defects. A newer generation of this device is under investigation for closure of the PFO. The procedure is performed under transesophageal or intracardiac echocardiographic guidance. Patients receive low-dose aspirin for 6 months and adhere to bacterial endocarditis prophylaxis precautions for 12 months.

Several studies have documented efficacy of device closure comparing the method to surgery: in general, they show no or little difference in efficacy rates between the two strategies (complete closure rates of 95–98%), [39, 40] with longer hospital stay and higher rate of complications after surgical closure. The actual numbers reported for complications as well as length of stay, vary substantially, but severe complications are very rare. The main difference in complication rate between surgical closure and device closure can be attributed to post-procedure pericardial effusion, which is relatively common after surgery and rare after device closure. The timing and underlying cause for effusions differ for both methods. While post operative effusions are thought to relate to postpericardiotomy syndrome, post device effusions are typically thought to be related to erosion or perforation of the atrial wall caused by the device or the catheters used during the procedure. These have been reported to occur early or late, even several years after device implantation, and are thought to be in the order of 1:1000–5000.

5.3.4.2 Ventricular Septal Defects

Most ventricular septal defects (VSD) cannot be closed with devices, due to their significant size in relatively small hearts as well as the proximity to intracardiac valves. An option to overcome the limitations of

the technique in an infant is a hybrid or combined surgical–catheter approach [42]. In this method, the heart is exposed via a thoracotomy and the device delivery catheter advanced through the free wall of the right ventricle and across the VSD, under echocardiographic guidance. This technique has the advantage of avoiding cardiopulmonary bypass and eliminating the risk of vascular damage in small children.

The Cardioseal device was the only one approved by FDA for closure of muscular VSDs in the USA. This device requires a large introducer sheath for delivery (10–11F), and cannot be retrieved once opened up. The Amplatzer muscular VSD occluder [43] has recently received FDA approval. This device has been used widely and offers attractive properties and high success rate for closure of muscular ventricular septal defects. The amplatzer membranous VSD occluder designed for perimembranous VSDs is also under investigation. The incidence of complete heart block even late after implantation is concerning.

5.3.4.3 Patent Ductus Arteriosus (PDA)

Small and moderate PDAs are typically closed in the catheterization laboratory with either embolization coils [44] or devices (Amplatzer duct occluder) [44] (Fig. 5.10), while large symptomatic PDAs in the newborn are treated surgically. Transcatheter closure

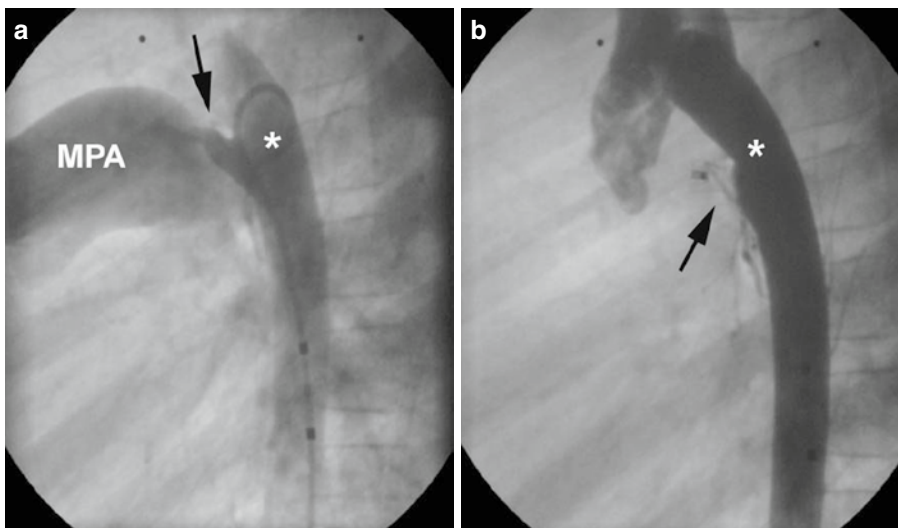


Fig. 5.10 (a) The aortogram demonstrates a moderate size patent ductus arteriosus (arrow). (b) Following implantation of an Amplatzer PDA occluder there is no residual PDA flow (arrow). *: Descending aorta; MPA: Main pulmonary artery

of PDA has been extensively studied. A European registry series reported an overall efficacy of 95% in over 1,200 procedures performed between 1994 and 2001 [44]. In this series, successful occlusion was less likely in larger PDAs. Since that report, the closure device described above (Amplatzer PDA Occluder) has been approved in the USA, achieving high closure rate of close to 100% [45]. Thus, nowadays, the use of coils for small PDAs and devices for moderate and large ones, allows a high efficacy of greater than 97% with a very low complication rate.

5.3.4.4 Other

Closure of Collaterals

Lesions amenable to closure by embolization therapy include systemic venous anomalies [46] (i.e., left superior vena cava to left atrium) or collaterals (abnormal vessels which are seen in patients with single ventricle palliation), aortopulmonary collaterals, pulmonary sequestration, or congenital arteriovenous malformations [47, 48]. Coil embolization of collaterals is one of the most common procedures in children with congenital heart disease, particularly in patients with functional single ventricle. It is safe and highly successful, with over 95% complete closure rate. The use of platinum coils rather than that of stainless steel allows for future cardiac MRI imaging. In tetralogy of Fallot variants and diminutive or absent central pulmonary arteries, coil embolization is indicated for those collaterals to lung segments with dual sources of pulmonary blood flow.

Transcatheter Thrombolysis

Reopening of thrombosed vessels or surgical anastomoses [49] can be performed nowadays with good results, although, the experience in pediatrics is relatively limited. Often thrombolysis is associated to balloon angioplasty and stenting to achieve success.

Other interventions include retrieval of foreign bodies, preservation of ductal patency using stents, coil embolization of coronary artery fistula and some novel catheter interventions, such as prenatal interventions (for opening of stenotic valves, or restrictive atrial septum) and transcatheter pulmonary valve implantation.

These novel procedures are likely to become common procedures during the next decade.

Preservation of Ductal Patency

Stenting of the patent duct can be performed instead of surgical Blalock–Taussig shunt in some newborns. The procedure can be performed using self expanding stents or balloon expandable stents [50]. Conditions for which this can be considered include:

- Hypoplastic left heart syndrome: Stenting of the PDA in patients awaiting heart transplantation, or as part of the interventions performed with the hybrid management approach for hypoplastic left heart syndrome [51, 52].
- Pulmonary atresia and intact ventricular septum, following transcatheter perforation and valvotomy, in patients who cannot wean from PGE₁.
- Some complex single ventricle with diminished pulmonary blood.

There are limiting factors to the consideration of PDA stenting in a newborn. The ideal approach is transvenous, via the femoral vein, into the pulmonary artery and down the PDA. This way, it is likely that a 5F or 6F could be used without much risk for vessel damage and allowing the use of a self expanding stent if desired. If on the other hand, the stent has to be performed transarterially, depending on the size of the newborn, the intervention may not be feasible without significant risk of vessel damage. The only stent which could be used for transarterial implantation would be a coronary stent, for what the PDA would have to be relatively small to begin with. Given the risk of vessel tear, if the PDA stent cannot be implanted transvenously, the risks/benefits ratio of transarterial stenting versus surgical shunting should be considered.

Prenatal Catheter Interventions

The pioneering work by the interventional group at Children's Hospital of Boston introduced a new management option for fetuses with congenital aortic stenosis. Fetal echocardiography has demonstrated the natural history of fetal aortic stenosis [53]. Fetuses who present in mid gestation with dilated and/or dysfunctional left ventricles and retrograde aortic flow

are highly likely to develop hypoplastic left heart syndrome during fetal development. Fetal aortic balloon dilation is offered for these fetuses with the aim to alter the natural history and prevent left ventricular growth arrest and hypoplastic left heart syndrome (HLHS). The procedure is done percutaneously and transabdominal, providing both mother and fetus anesthesia, requiring 50% of the time laparotomy. The approach is via ultrasound guidance and needle puncture. The valve is dilated with a coronary balloon premounted on a coronary wire. The results demonstrate that 20% of fetuses only become candidates for biventricular circulation. It is not certain whether there is any benefit for the remaining fetuses, especially if some increase in antegrade aortic flow might be associated with improved brain development. The intermediate and long term results are still unknown.

5.4 Specific Problems

5.4.1 Cardiac Catheterization in a Patient on Extracorporeal Membrane Oxygenation (ECMO)

ECMO has been used increasingly for the management of the cardiac pediatric patients, often initiated semielectively postoperatively [54, 55]. Cardiac catheterization is performed commonly in these patients to determine the underlying cause of the cardiovascular collapse, or the failure to wean from the ECMO circuit. When a residual anatomic problem exists, interventional cardiac catheterization is often indicated and can be lifesaving. Indeed, it has been reported that over 80% of such studies end up requiring transcatheter intervention procedures, specially if ECMO was initiated immediately postoperatively.

From a technical stand point, hemodynamic assessment has to be interpreted according to the flow condition of the time. Partial or total clamping of the ECMO cannulas is necessary to evaluate hemodynamics. If decreasing ECMO flows is not an option, hemodynamic assessment is impossible to perform. Still, angiographic assessment can be most helpful in diagnosing these patients. Angiography has to be performed with transient clamping of the ECMO canulas, as otherwise, visualization of the anatomy will be poor as the contrast will get diluted with the ECMO flow.

In some patients with decreased systemic ventricular function and no interatrial communication, the left atrial pressure may reach severely elevated levels, which induces pulmonary venous hypertension, and elevation in pulmonary artery pressures/pulmonary edema and potential lung damage. This could become a vicious circle that would prevent the patient to ever wean from ECMO. Left atrial decompression has to be performed emergently in this setting, and is done with transeptal puncture and balloon dilation. Rarely, stenting of the atrial septal communication may be required [56].

Transport of the patient on ECMO to the cardiac catheterization laboratory is a team effort. Multiple experienced individuals are involved, including ECMO technicians, ICU nurses, anesthesiology team, cardiologist, and intensivist. Despite the severity of the condition of the patient's, cardiac catheterization and transcatheter interventions are performed with a relatively low incidence of complications (3–7%).

5.4.2 Specific Post Cardiac Catheterization Complications

Some specific complications post cardiac catheterization can lead to admission to the cardiac ICU. Among these are:

5.4.2.1 Arterial Pulse Loss

Following arterial puncture, lower extremity pulses are checked every 15 min for 1 h, every 30 min for 2 h, and every hour for the initial 6 h. Pulse loss can be transient associated with arterial vasospasm. In those cases, the distal pulses return to normal within half an hour post line removal. The risk of pulse loss is related to the size of the sheath and the size of the vessel. The use of intravenous heparinization during the procedure lowers the chance of arterial loss. The treatment of pulse loss following cardiac catheterization [57, 58] includes heparinization for the first 12–24 h (drip starts at 20 Units/kg/h plus heparin bolus depending on the ending ACT measured in the Catheterization Laboratory and the time evolved since then). If no response by 24 h (or sooner if extremity is cold), it is recommended to start thrombolytic therapy, with tPA infusion. The patient should be monitored in the ICU. A bolus of 0.1 mg/kg is initiated followed by 0.5 mg/

kg/hour drip for 2 h, then off. Heparinization is continued for 6 h at 12–17 Units/kg/hour. If the pulse has not returned, the bolus and drip of TPA are repeated, followed by heparin infusion for another 6 h. The success rate with this protocol is quite high (95%).

5.4.2.2 Post Angioplasty Hyperperfusion Pulmonary Edema

This occurs when a severely stenotic pulmonary artery (with very low distal pressure) is successfully dilated and the distal mean pressure increases to over 25 mmHg due to a significant increase in flow. It can affect just one segment of the lung, may involve a lobe, or the whole unilateral lung [29]. Pulmonary edema of the site takes place, often affecting oxygenation and requiring positive pressure ventilation for 24–48 h. Sometimes significant bloody fluid can be suctioned. Use of diuretics is needed. The edema typically resolves within 1–2 days. Short term use of diuretics is prescribed, and patients usually extubate within that time period, being able to discharge home at 2–4 days after the procedure.

5.4.2.3 Hemorrhage/Vessel Trauma

Vessel trauma associated to transcatheter intervention can be life threatening. Angiographic evaluation following each angioplasty is essential, as early identification of problem would allow specific therapy. Tears can be confined [28] (extravasation of contrast is retained within the perivascular tissue), or nonconfined. Nonconfined tears need to be treated emergently in the catheterization laboratory with coil occlusion of the site of bleeding or use of covered stents.

5.4.2.4 Arrhythmias

Complete heart block associated to cardiac catheterization can occur specially in patients with tetralogy of Fallot S/P repair with a bifacular block when the catheter is positioned retrograde into the left ventricle for angiography. Other predisposing conditions include patients with {S, L, L} segmental combination, or patients with d-TGA during specific catheter manipulation (catheter crossing the right ventricular outflow tract into the ascending transvenously for angiography). Typically,

it is transient and can be treated successfully in the Cath Lab with removal of the catheter, atropine, and if needed a temporary transvenous pacemaker.

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Chapter 6

Echocardiography

Cécile Tissot, Adel K. Younoszai, and Christina Phelps

6.1 Introduction

Echocardiography in its current form, several generations removed from its origin in the 1950s [1], has become an invaluable tool in a modern cardiac intensive care unit environment. Coupled with a clinical examination and monitoring techniques, echocardiography can provide real-time rapid and reliable diagnostic answers that are invaluable to patient care. This noninvasive test can be used to reliably evaluate cardiac anatomy of both normal hearts and those with congenital heart disease and has replaced cardiac angiography for the preoperative diagnosis of the majority of congenital heart lesions [2–4]. In congenital or acquired cardiac disease, echocardiography may be further used to estimate intracardiac pressures and gradients across stenotic valves and vessels, determine the directionality of blood flow and pressure gradient across a defect, and examine the coronary arteries. Within the realm of critical care, echocardiography is useful to quantitative cardiac systolic and diastolic function, detect the presence of vegetations from endocarditis, and examine the cardiac structure for the presence of pericardial fluid and chamber thrombi. As with all tools, however, a thorough understanding of its uses and limitations are necessary before relying upon the information it provides.

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6.2 Principles of Echocardiography

Echocardiography uses ultrasound technology to image the heart and associated vascular structures. Ultrasound is defined as sound frequencies above the audible range of 20,000 cycles per second. The primary components of an ultrasound machine include a transducer and a central processor. The transducer converts electrical to mechanical (sound) energy and vice versa. Electrical energy is applied to piezoelectric crystals within the transducer resulting in the generation of mechanical energy in the form of a series of sinusoidal cycles of alternating compression and rarefaction. The energy produced travels as a directable beam which may be aimed at the heart. The sound beam travels in a straight line until it encounters a boundary between structures with different acoustical impedance, such as between blood and tissue. At such surfaces, a portion of the energy is reflected back to the same crystals within the transducer, and the remaining attenuated signal is transmitted distally. Within the ultrasound, machine is circuitry capable of measuring the transit time for the beam to travel from the transducer to a given structure and back again then calculate the distance traveled. A cardiac image is constructed from the reflected energy, or so called ultrasound echoes.

Differing properties of tissues affect the portion of acoustic energy transmitted versus reflected. For example, air reflects the majority of the signal it receives and, therefore, prevents images from being obtained through windows where it is present. Anything hindering or augmenting the reflection of this acoustic signal, such as air, bone, dressings, an open chest, or lines, tubes, or other foreign bodies, will diminish the overall quality of the examination. Therefore, in the intensive care unit, an ultrasound study may be limited by difficulty in finding a good acoustic window to allow for accurate analysis [5].

6.3 The Anatomical Echocardiographic Examination

In order to obtain the best imaging windows, whenever possible, patients are placed in a left lateral decubitus position during a transthoracic echocardiogram. During two-dimensional (2D) echocardiography, all planes are described in reference to the heart and not the heart's position within the body. For a complete

pediatric study, standard views (see Fig. 6.1–6.5) are obtained from the high left chest just lateral to the sternum (parasternal window), the left lateral chest just inferior and lateral to the nipple (apical window), sub-xyphoid area (subcostal window), and the suprasternal notch (suprasternal window). In patients with more complex anatomy, additional windows, such as the high right parasternal border, may be used to obtain additional information.

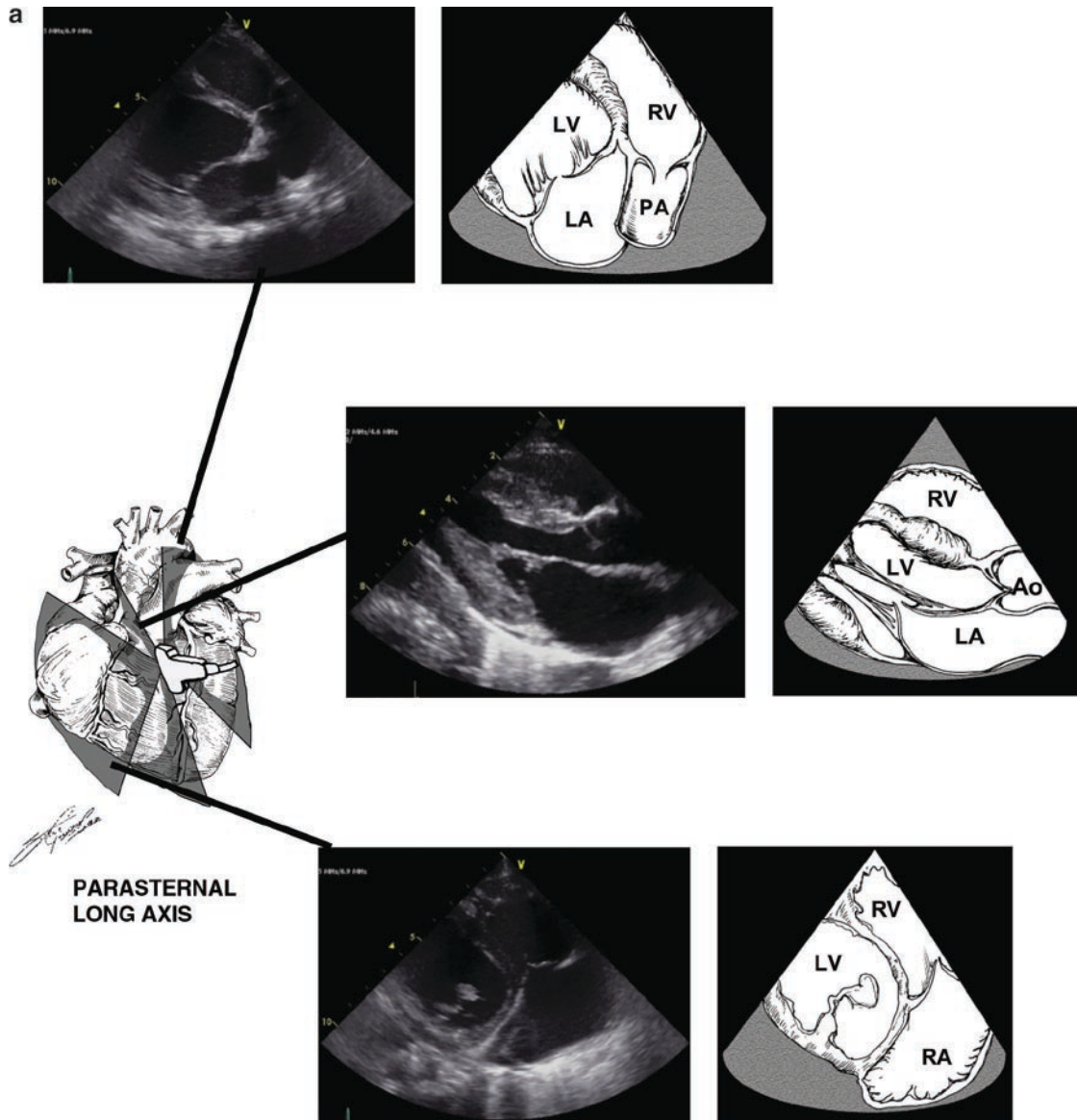


Fig. 6.1 Standard echocardiographic image planes from the high left chest just lateral to the sternum (parasternal window (a) and (b)), the left lateral chest just inferior to the nipple (apical window (c)), sub-xyphoid area (subcostal window (d)), and the suprasternal

notch (suprasternal window (e) and (f)). *RA* right atrium; *RV* right ventricle; *LA* left atrium; *LV* left ventricle; *Ao* aortic valve; *CS* coronary sinus; *RVOT* right ventricular outflow tract; *SVC* superior vena cava (drawing from Steven P. Goldberg, MD)

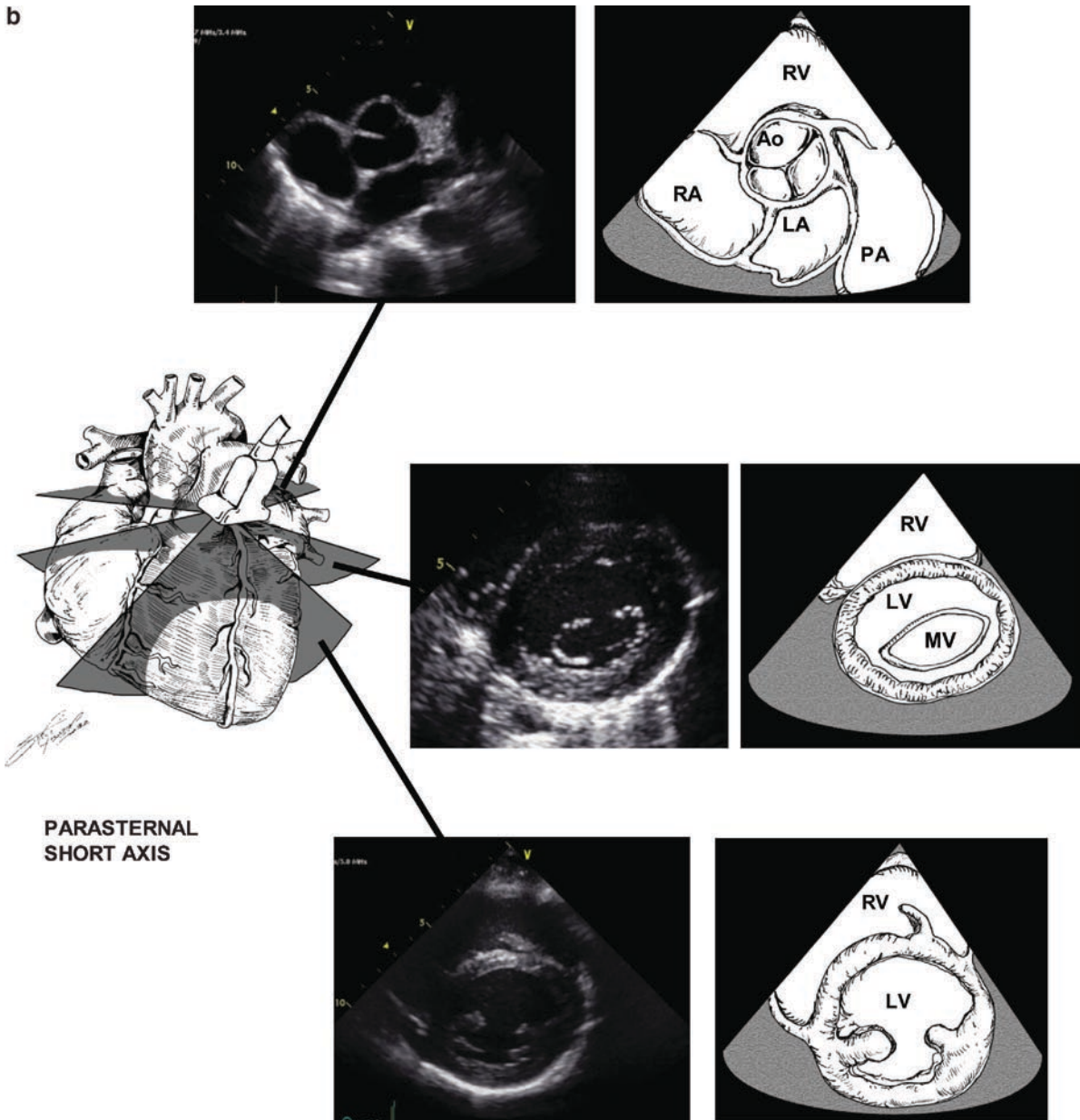


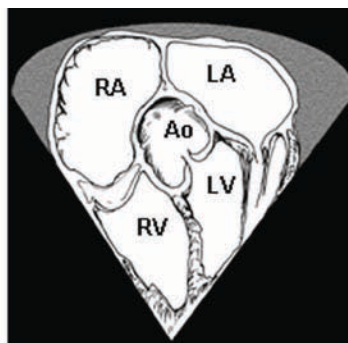
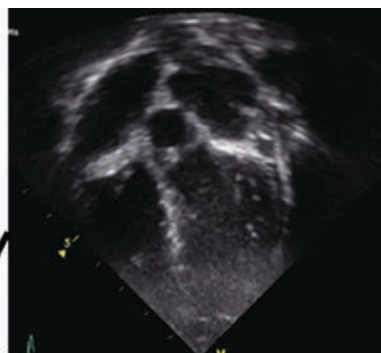
Fig. 6.1 (continued)

6.3.1 Parasternal Window

In the anatomically normal heart, the parasternal window allows visualization of the heart aligned along its long axis and short axis. In the long axis (Fig. 6.1a), the left ventricular inflow and outflow tracts can be seen well. As a result, comments can be made from this view regarding the aorta, including its annulus, the

sinuses of Valsalva, and the proximal portion of the ascending aorta, as well as its relationship to the mitral valve. Additionally, the ballet-slipper appearance of the left ventricle is featured as the inferoposterior wall and interventricular septum are visualized. The anterior and posterior leaflets of the mitral valve can be visualized. By angulating the transducer and performing a sweep, the right ventricle is brought into focus

c



APICAL VIEWS

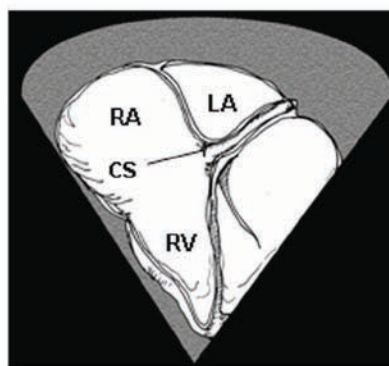
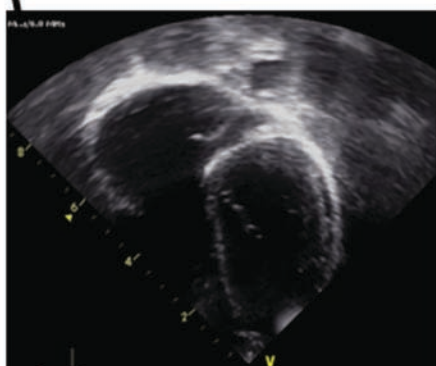
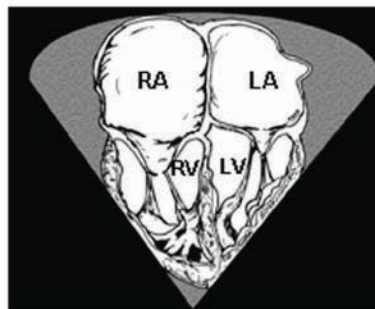
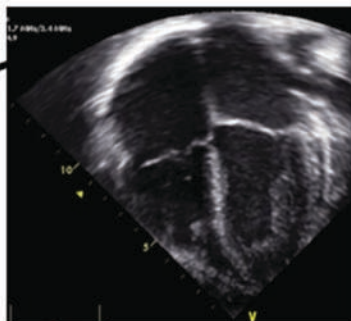


Fig. 6.1 (continued)

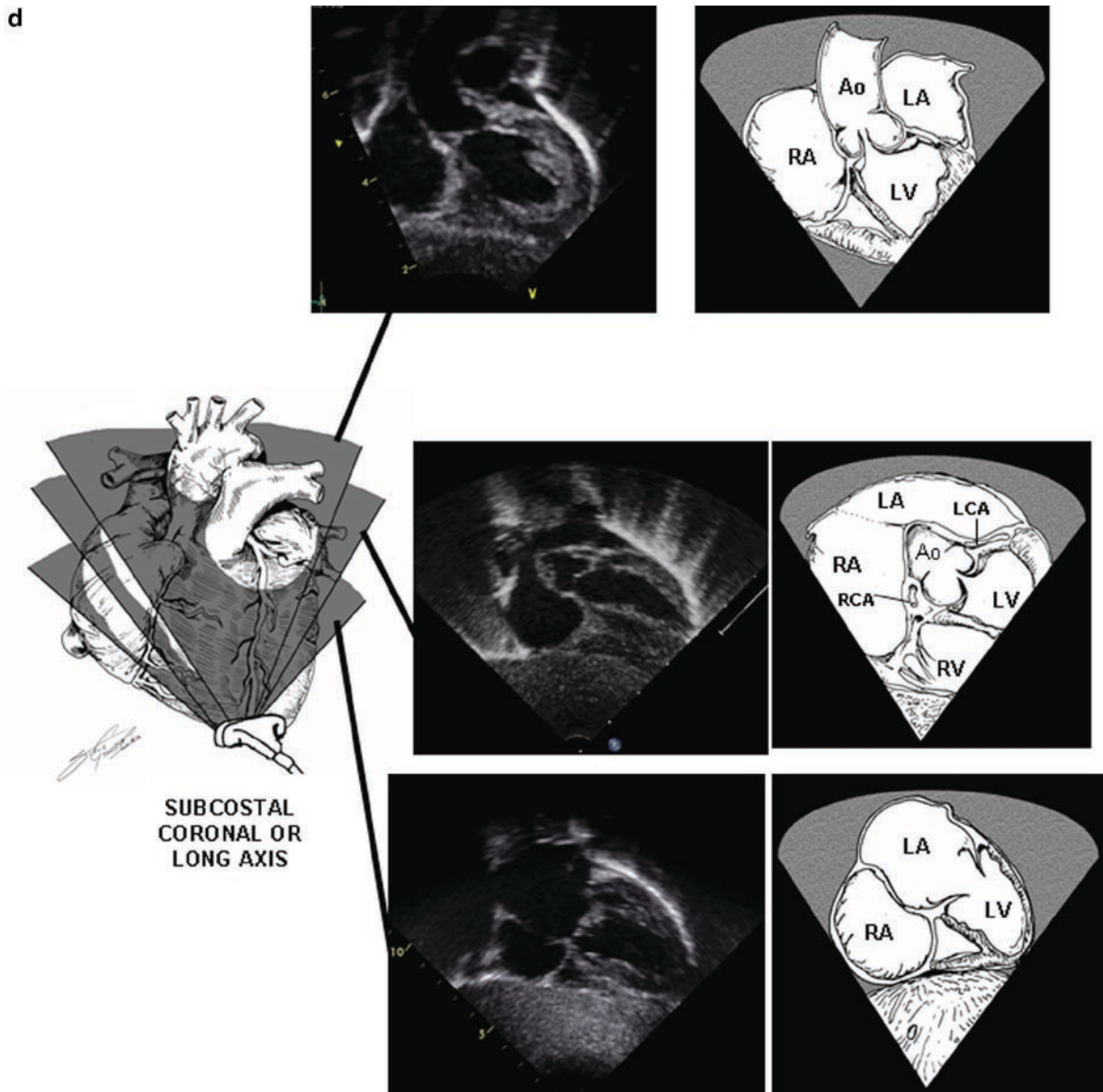


Fig. 6.1 (continued)

and an examination of both its inflow including the right atrium and tricuspid valve and its outflow tract, including the pulmonary valve can be performed.

The transducer may be rotated 90° providing a series of short-axis views (Fig. 6.1b) that assist in the evaluation of the chambers of the heart, the semilunar and atrioventricular valves, and the coronary arteries. Sweeping from the apex of the heart toward the base will allow a close cross-sectional examination of the

ventricular chambers. The normal left ventricle has circular geometry with symmetric contraction, whether it is visualized at the level of the mitral valve, papillary muscles, or apex. In contrast, the normal right ventricle appears as a more trabeculated crescent-shaped structure when visualized at or below the level of the mitral valve. Sweeping farther toward the base of the heart, the mitral valve's papillary muscles and the valve itself are viewed. Progressing to the base of the normal heart,

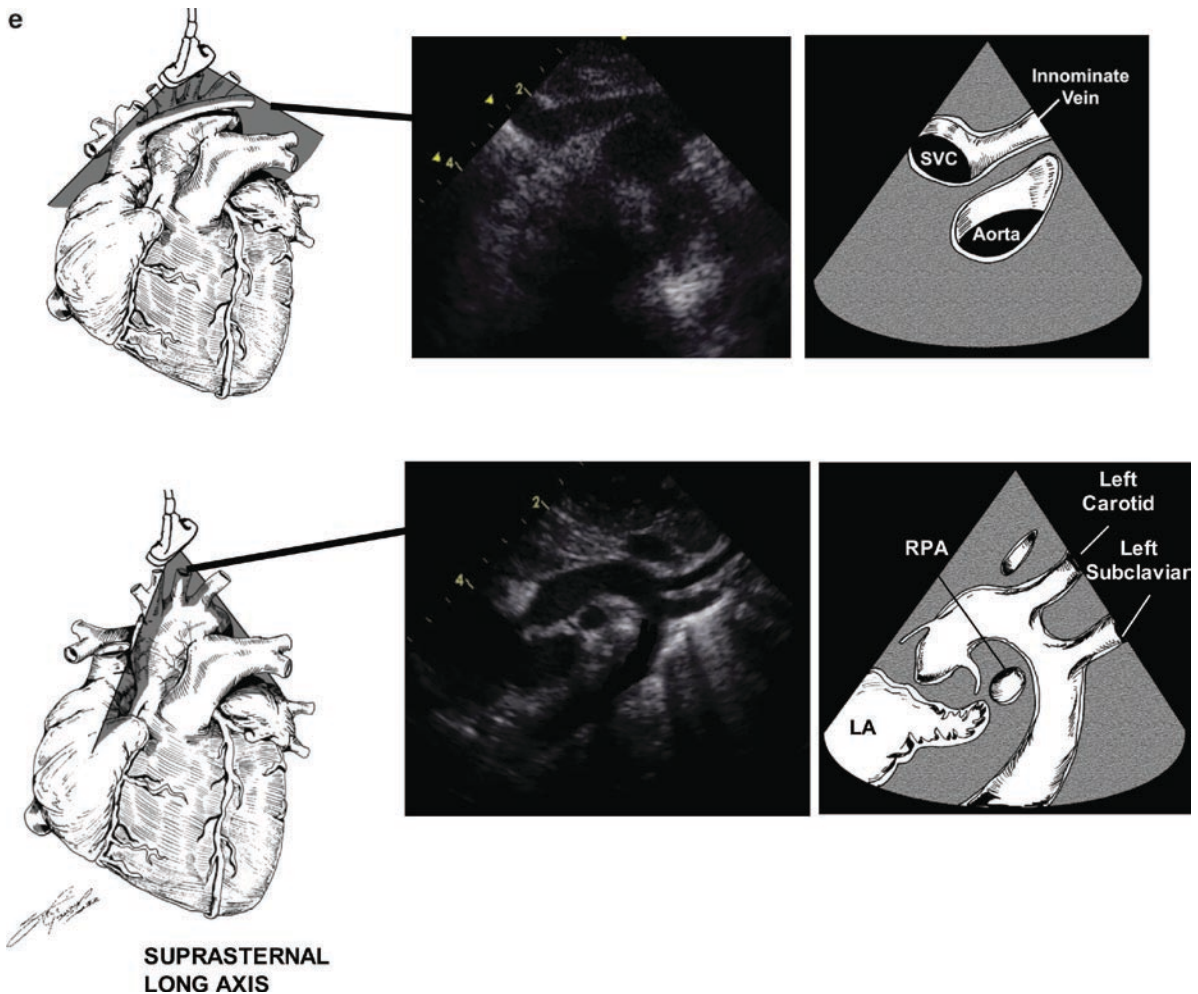


Fig. 6.1 (continued)

the tri-leaflet aortic valve takes the center stage with the right ventricular outflow tract and pulmonary wrapping in an inverted “U” anteriorly and leftward. Additionally a portion of the atrial septum and the tricuspid valve may be profiled. Finally, continuing the sweep allows for the examination of the atrial appendages, ascending aorta in cross-section and branch pulmonary arteries.

6.3.2 Apical Window

For those not trained in echocardiography, the images obtained with the transducer in the apical position (Fig. 6.1c) are perhaps the most intuitive as it allows for visualization of all four chambers and valves in the heart

with a simple left-to-right orientation. Imaging is begun in the four-chamber view, in which the anatomic right and left ventricles may be identified. Sweeps of the transducer from this position identify the posterior coronary sinus and may indicate abnormalities such as a left superior vena cava or unroofed coronary sinus. Proceeding more anteriorly to a five-chambered view, the atrial and ventricular septa may be visualized looking for defects and the left ventricular outflow tract and ascending aorta may be examined. The four chamber view allows for the examination of the anterior and posterior mitral valve leaflets and pulmonary veins as they enter the left atrium. By rotating the transducer to 90° from the four-chamber view, a two-chamber view of the left ventricle and left atrium can be obtained to evaluate the anterior and posterior left ventricular wall function.

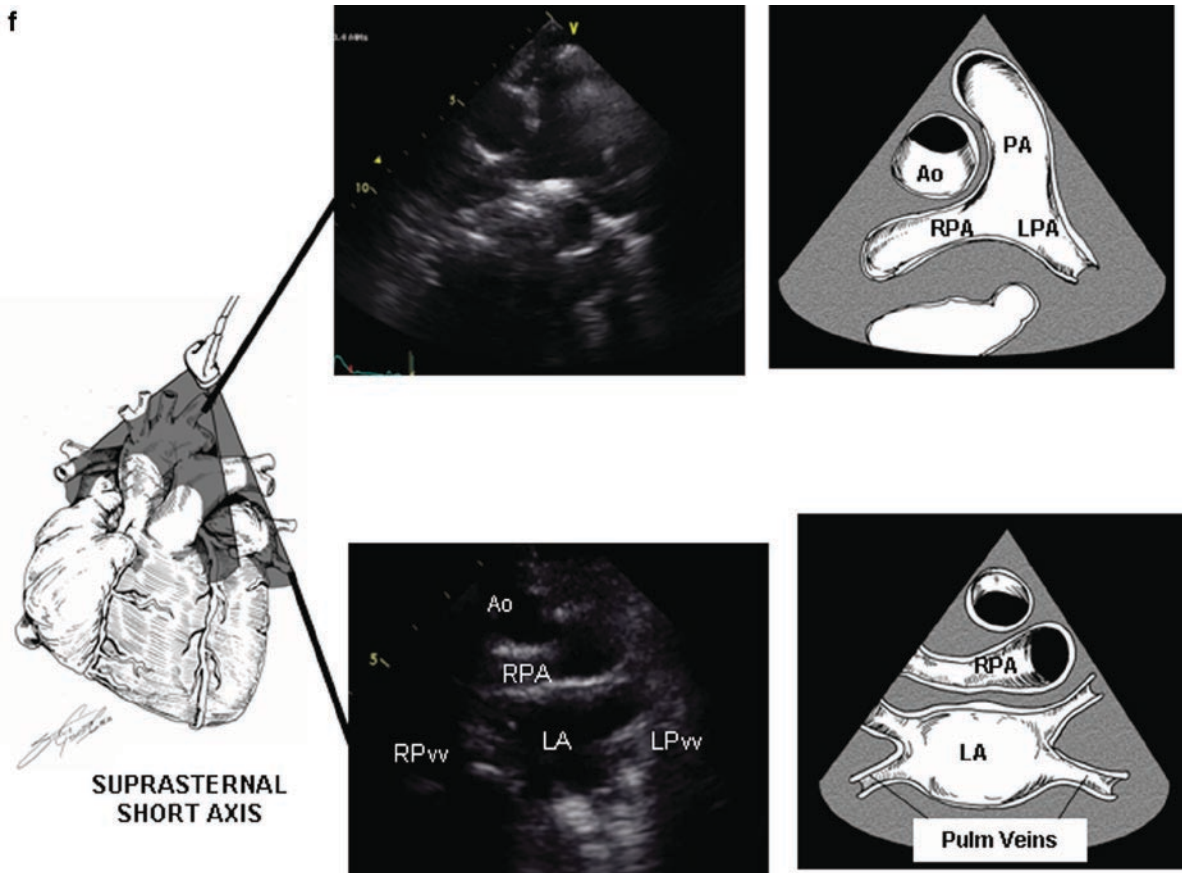


Fig. 6.1 (continued)

6.3.3 Subcostal Window

For pediatric patients with complex cardiac anatomy, the subcostal position (Fig. 6.1d and Fig. 6.1e) provides the most detailed information and is often the best starting place. In order to obtain images in this position, patients are placed supine with the transducer in the subxiphoid position. In larger cooperative patients beyond the infancy period, image quality may be improved by having the patient participate in the examination with held inspiration that allows the heart to move downward toward the transducer. Initial views in this position should determine visceral situs as well as the relationship of the inferior vena cava and aorta. Subsequent views and sweeps will provide detailed analysis of the atrial septum as well as the images related to the ventricular septum, the atrioventricular valves, atrial and ventricular chambers, and drainage

of systemic veins. With the rotation of the transducer both ventricular outflow tracts may be visualized. Additionally in some patients the branch pulmonary arteries and the entire aorta may be examined from this position.

6.3.4 Suprasternal Window

The views are obtained in this position by placing the transducer in the suprasternal notch (Fig. 6.1.f and Fig. 6.1.g) with the neck extended. The suprasternal long- and short-axis views provide detailed information regarding arch sidedness, anomalies in the ascending and descending aorta and head and neck vessels, the size and branching of the pulmonary arteries, as well as anomalies of systemic and pulmonary venous systems.

6.4 M-Mode Imaging

One of the earliest applications of ultrasound technology that remains an important tool in the evaluation of cardiac function, dimension, and timing, the M-mode echo provides an “ice-pick” view of the heart. An M-mode echo is obtained with the ultrasonic transducer placed along the left sternal border and directed toward the part of the heart to be examined. A single line of interrogation is repeatedly produced and the resultant image is displayed with time along the x-axis and distance from the transducer along the y-axis (see Fig. 6.2). M-mode obtains an estimate of ventricular function by measuring the short axis shortening fraction and wall thickness.

6.5 Doppler Evaluation

Frequently in an intensive care setting the clinician is concerned with new or residual flow disturbances from shunt lesions, an abnormal cardiac valve, or narrowing of a blood vessel. While 2D echocardiography determines anatomical relationships, additional information

regarding movement of the blood or myocardium is provided by looking for Doppler shifts in the reflected ultrasound waves. The Doppler principle, first described by Johann Christian Doppler, states that for a stationary object, the frequency of ultrasound reflected is identical to the transmitted frequency. Inherently the heart and the blood it pumps do not fit this basic definition. Therefore, when performing a cardiac ultrasound, the moving objects alter the frequency of the reflected signal (the Doppler shift) according to the direction and velocity with which they are moving in relation to the fixed transducer [6].

Additional insights to intracardiac and vascular hemodynamics may be obtained when velocity data is collected. Doppler data are typically displayed as velocity rather than the actual frequency shift. The velocities can then be translated into pressure data using the modified Bernoulli equation: $P_1 - P_2 = 4[(V_2)^2 - (V_1)^2]$. If one assumes that the level of obstruction and therefore the velocity of V_1 is negligible compared with the obstruction at V_2 the formula becomes even simpler: $DP = 4(V_{max})^2$. Although the modified Bernoulli equation can only be applied in appropriate situations, it does help predict the pressure drop across an abnormal valve or septal defect to give a general estimate of

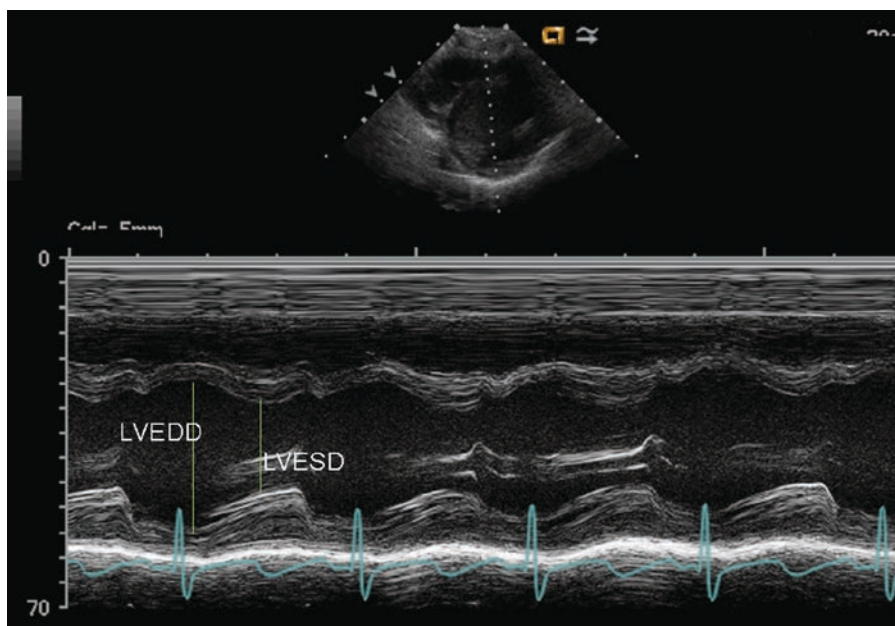


Fig. 6.2 M-mode echocardiography obtained in the parasternal short axis through the right and left ventricular chambers at the level of the papillary muscles. *LVEDD* left ventricular end-diastolic dimension; *LVESD* left ventricular end-systolic dimension

the severity of the lesion which can prove to be valuable information to help manage patients in the intensive care setting.

Of note, during Doppler imaging it is clinically important to recognize the angle of interrogation of blood flow and its impact on the accuracy of our velocity measures. It is important when performing Doppler studies that the line of beam interrogation should be directly in the line of flow, resulting in as little distortion of data as possible. The more off-angle the approach is, the increasingly more severe the underestimation of the true velocity will be. For practical purposes, an angle of interrogation less than 20° is essential to ensure clinically accurate information.

Two commonly used techniques are pulsed and continuous wave Doppler. Pulse wave Doppler allows determination of direction and velocity at a precise point within the imaged cardiac field. However, it is limited in its maximum detectable velocity by the Nyquist limit making it unusable for quantification of high-velocity flow (e.g., as seen with severe obstruction). In contrast, continuous wave Doppler interrogates all points along a given beam. Continuous wave Doppler imaging is not constrained by velocity limits and can hence record velocities exceeding those of pulsed Doppler imaging. The drawback is that while the line of interrogation is identifiable, knowledge of anatomy must already be obtained to identify the precise location of the maximum velocity. Clinically these two techniques are commonly used sequentially to identify the area of interest and then to obtain the maximum velocity.

6.5.1 Color Flow Doppler

Color flow Doppler is powerful technique for obtaining additional hemodynamic and anatomic data for patients undergoing echocardiography in the intensive care unit. Color flow Doppler allows velocity information to be overlaid on a 2D anatomic image therefore providing data regarding intracardiac and extracardiac shunts, valvar insufficiency or stenosis, and vessel obstruction. By convention, shades of red are used in identifying blood flowing toward the transducer and blue to indicate blood flowing away from the transducer. Therefore, color flow Doppler defines the presence and direction of shunts and is used to grade the severity of valvar insufficiency.

6.6 Current Clinical Applications

Clinical applications of echocardiography within the intensive care unit may be divided into the following major areas:

1. The diagnosis and post-intervention evaluation of anatomic lesions.
2. Evaluation of cardiac function.
3. Diagnosis of intracardiac masses and extracardiac effusions.
4. Guidance of intervention within the intensive care unit

6.7 Anatomic Lesions Pre and Post Intervention

Advances in technology have enabled most congenital heart defects to be diagnosed by echocardiography avoiding the risks, time, and cost of invasive cardiac catheterization [2–4]. In addition, for infants and pediatric patients admitted to an intensive care unit due to being succumbed to shock, echocardiography may be useful for differentiating anatomic causes of shock from functional causes. Patients with obstruction to outflow on the left side of the heart who go undiagnosed at birth frequently present with signs of diminished cardiac output (CO) or frank shock. These lesions including aortic valve stenosis, coarctation of the aorta, and variations of hypoplastic left heart syndrome may be identified and defined by echocardiogram alone.

Following surgical or catheter-based intervention patients convalesce in the intensive care unit. Most patients undergo a postprocedural echo before getting discharged home to document adequacy of the repair and lack of significant complications. In postoperative patients this assessment may prove more complicated as access to the patient and the correct windows may be severely compromised by dressings, intracardiac lines, and chest tubes. Occasionally postoperative patients in the intensive care unit may be found to have unexpected residual lesions (see Fig. 6.3). For example, following repair of septal defects, echocardiography may be useful to screen for the presence of residual shunts which may be less well tolerated secondary to myocardial changes following cardiopulmonary

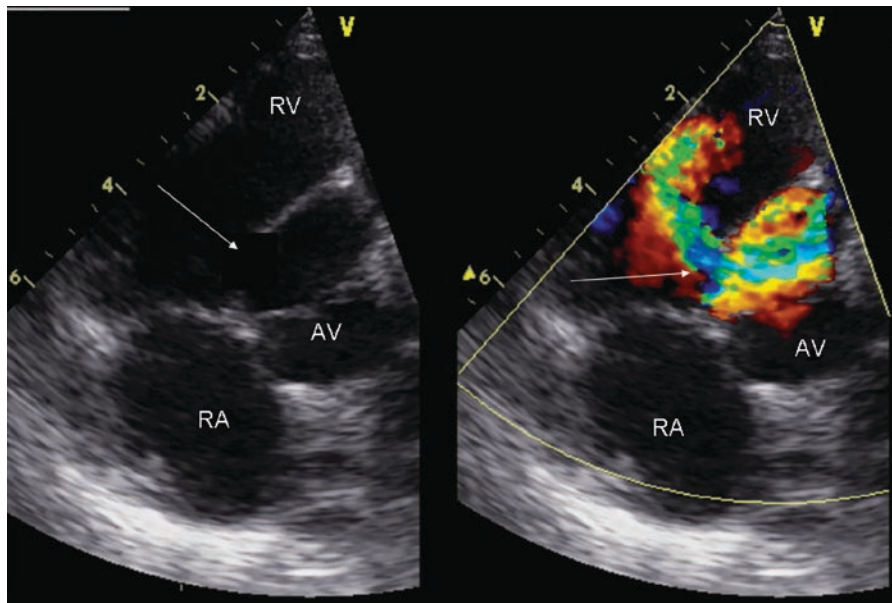


Fig. 6.3 Parasternal short axis image in a patient with pulmonary atresia/VSD who acutely decompensated. White arrows demonstrate the large residual VSD than resulted when a patch dehiscid. *RA* right atrium; *RV* right ventricle; *AV* aortic valve

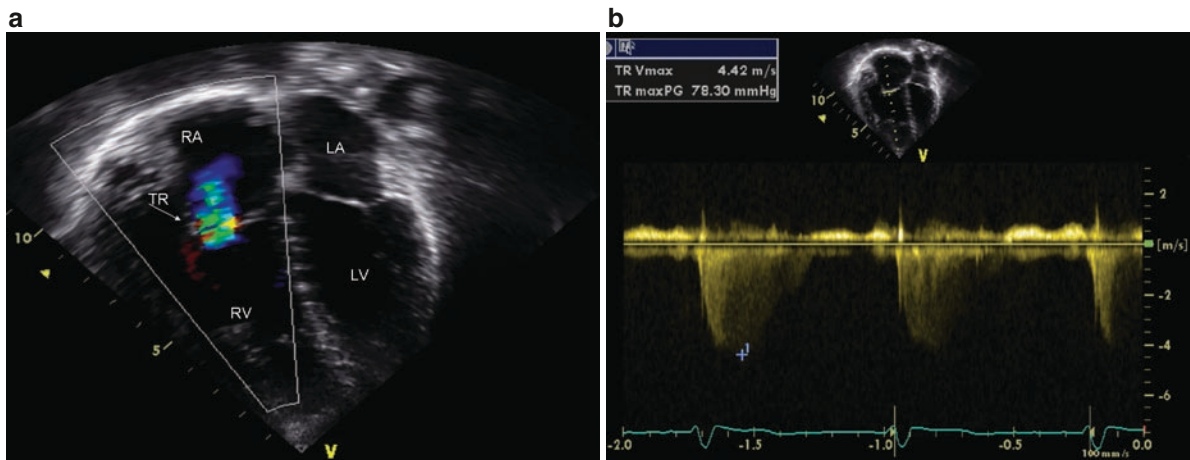


Fig. 6.4 (a) and (b): Four chambered view demonstrating color Doppler of tricuspid regurgitation and the corresponding spectral Doppler pattern. The velocity obtained by spectral Doppler may be utilized to estimate pulmonary artery pressures in the absence of downstream obstruction.

A complete envelope by pulse wave or continuous wave Doppler provides the velocity of the regurgitant jet which may be translated into pressure data using the equation: $\Delta P = 4(V_{\max})^2$. *RA* right atrium; *RV* right ventricle; *LA* left atrium; *LV* left ventricle

bypass [7]. Often, the presence of a residual lesion is known in the operating room through transesophageal echocardiography or direct discussion with the surgeon. An important role of echocardiography is to distinguish those lesions with hemodynamic consequences

from those whose presence has no impact on post-operative care. Transthoracic echocardiography may be used to diagnose and assess the hemodynamic sequelae of shunt lesions, residual stenosis, and function. More complicated is the assessment of coronary flow, right

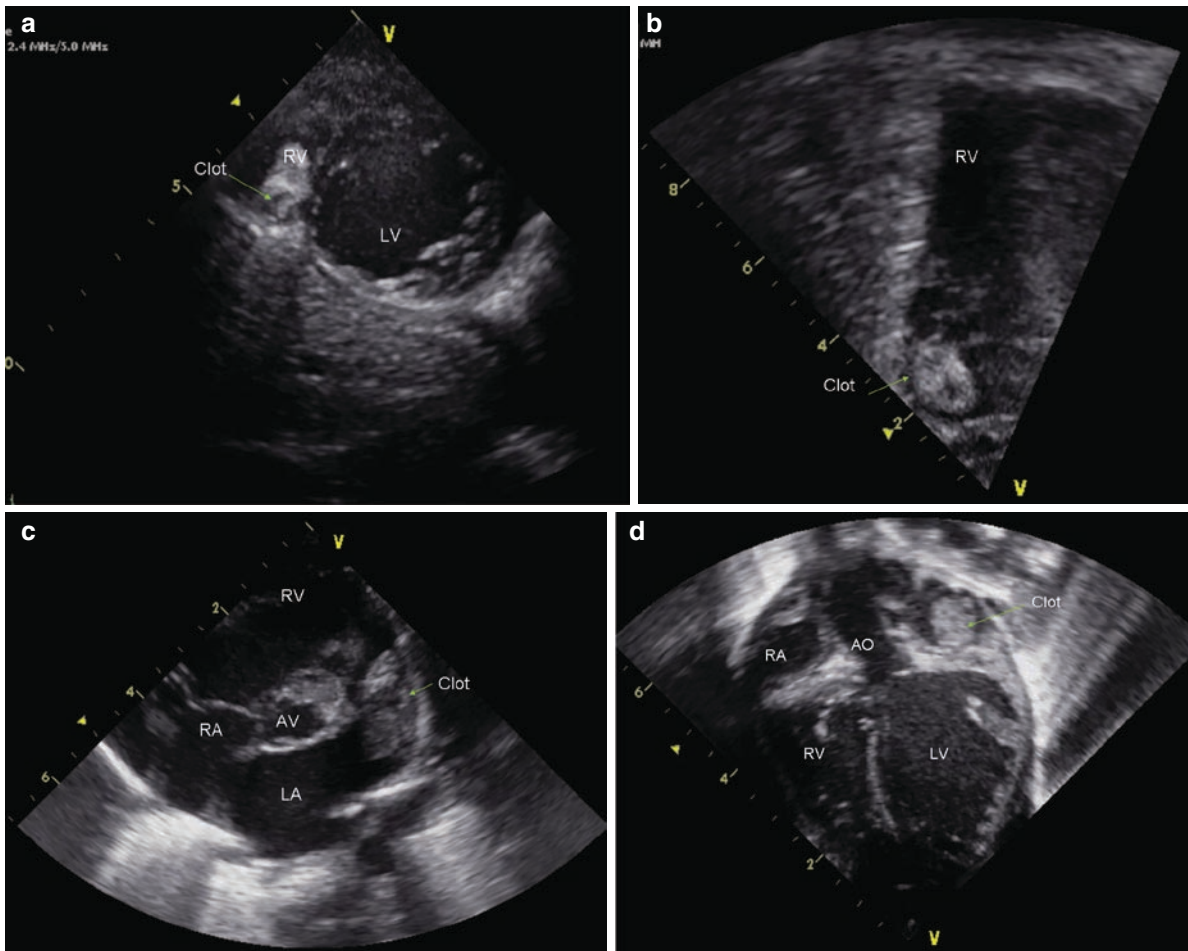


Fig. 6.5 Demonstrate a thrombus in the right ventricle seen in parasternal short axis (a) and modified four-chamber (b) views. *RV* right ventricle; *LV* left ventricle. (c) and (d): Demonstrate a

thrombus in the left atrial appendage in both parasternal short axis and a modified four chamber views. *RA* right atrium; *RV* right ventricle; *AV* aortic valve; *AO* ascending aorta; *LV* left ventricle

ventricular dynamics, and distal obstruction following intervention. In patients who are experiencing arrhythmias postoperatively, special attention should be paid to the flow within the coronary arteries to ensure that it has not been compromised or that a line or mass in the heart is not causing ectopy.

Unanticipated pulmonary arterial hypertension may slow the progress of a patient in the intensive care unit. In the absence of a Swan Ganz catheter or a direct pulmonary arterial monitoring, echocardiography may be used to estimate the pulmonary artery pressures. There are several methods that may be used to deter-

mine the pulmonary artery pressures. In a patient with tricuspid regurgitation, the velocity of the jet estimates the difference in pressure in the right atrium and the right ventricle (see Fig. 6.4). If there is no stenosis of the pulmonary arteries, pulmonary valve, or right ventricular outflow tract, the difference in pressure between the right atrium and right ventricle plus the right atrial pressure (CVP) provides an estimate of the pulmonary arterial pressures. In the absence of tricuspid valve insufficiency, interventricular septal geometry may be used to help quantify the degree of pulmonary hypertension.

6.8 Analysis of Ventricular Function

One of the most frequent uses of echocardiography in the ICU is related to the evaluation of ventricular performance. Improvements in technology allow assessment of both systolic and diastolic function with increasing accuracy.

6.8.1 Systolic Function

Accurate and timely assessment of systolic function should be an integral part of the medical management of the hemodynamically unstable critically ill patient. Global assessment of LV contractility includes the determination of ejection fraction (EF), circumferential fiber shortening, and cardiac output (CO). There are several methods that may be used to garner this information. Each has its limitations and assumptions which are paramount to understand prior to clinically applying the information gathered. For assessment of left ventricular function, perhaps the simplest quantitative approach is to use M-mode echocardiography (see Fig. 6.3) in either the parasternal short axis at the level of the papillary muscles or in the parasternal long axis at the tips of the mitral valve leaflets to measure the left ventricular end-diastolic dimension (LVEDD) and left ventricular end-systolic dimension (LVESD) for the determination of the fractional shortening (FS) percentage.

Fractional shortening is derived by the following:

$$FS(\%) = \frac{LVEDD - LVESD}{LVEDD} \times 100$$

Normal values for fractional shortening in children and infants vary slightly with age, falling typically between 28 and 44% [8–10].

Fractional shortening, therefore, provides a method of assessing circumferential change but has several obvious drawbacks. This method assumes that the ventricle being examined has a circular shape in the axis in which it is examined. As a result, changes in diameter may be mathematically related to circumferential fiber-shortening providing an estimate of ventricular function. Therefore anything that alters the circular shape of the left ventricle (anatomic abnormalities intrinsic to congenital heart disease, pre and afterload changes, or

ventricular–ventricular interactions) may affect the assessment of fractional shortening by altering the movement of the septum and causing an under or over estimation of the either end-systolic or diastolic dimension.

A second method of assessing ventricular function is via ejection fraction. Ejection fraction is a volumetric appraisal of ventricular fiber shortening. Echocardiographically the most common method of calculating ejection fraction is the biplane estimation of volumes from the apical four- and two-chamber views. One of the more commonly used mathematical algorithms is the Simpson method in which the left ventricle is traced manually at the end diastole and end systole along the endocardium. Using the method of disks the left ventricle is divided into a series of parallel planes and the resultant disks are individually summed to create each volume [11, 12]. Ejection fraction is calculated using the following equation:

$$EF(\%) = \frac{\text{End diastolic volume} - \text{End systolic volume}}{\text{End diastolic volume}} \times 100$$

Unfortunately, the determination of an accurate ejection fraction is also subject to ventricular shape with the left ventricle assumed to be its normal prolate elliptical shape. Variations from this shape, which occur frequently in pediatrics, significantly alter the relationship between fiber shortening and volume dependence upon when this equation is applied. In addition, patients in the intensive care environment frequently have suboptimal imaging windows making the endocardium difficult to distinguish and trace.

Not infrequently in active pediatric intensive care units, a patient's heart and/or lung function must be supported for a period of time. Two such modalities of support are extracorporeal membranous oxygenation and ventricular assist devices. Often the pediatric echocardiographer is asked to assist in the management of these patients by providing insight into the recoverability of cardiac function. This request can be one of the more challenging uses of echo in an intensive care setting. As discussed above, many of the techniques commonly used to determine ventricular systolic function and CO are dependent on the loading conditions of the heart as well as contractility. As a result, both of these support systems which unload the heart in an effort to allow recovery time severely limit echo's utility as a prognostic indicator. Several newer methods of determining myocardial function including Tissue Doppler Imaging (TDI), strain and strain rate,

color m-mode, calcium gating, and three-dimensional (3D) echocardiography are entering the realm of echo in the intensive care unit. These newer modalities may prove to be more efficacious than current standard echocardiography is at present.

6.8.2 Diastolic Function

Accurate assessment of diastolic function by echocardiography is an evolving field that has made great strides in the past few years. Diastolic heart failure and its impact on postoperative management also deserve consideration. Spectral Doppler evaluation is a relatively easy and useful method for evaluating diastolic function noninvasively at the bedside. A prominent pulmonary vein atrial reversal wave (a wave) is a marker of diastolic dysfunction. This finding represents marked flow reversal into the pulmonary veins during atrial systole in response to a noncompliant ventricular chamber. The mitral inflow Doppler pattern can also be a useful marker for diastolic dysfunction. Mitral inflow is composed of 2 waves – an E wave representing early passive ventricular filling (preload dependent) and the A wave representing active filling as a result of atrial systole. The E:A ratio, velocity of E wave deceleration and duration of the A wave can be altered in patients with diastolic dysfunction.

Tissue Doppler imaging (TDI) is a newer technique for assessing diastolic ventricular function. TDI allows recording of the low Doppler velocities generated by the ventricular wall motion and directly measures myocardial velocities. In spectral TDI, pulsed Doppler is placed along the myocardial wall (mitral, septal, or tricuspid annulus) recording the peak myocardial velocities. Three waveforms are obtained: a peak systolic wave (Sa), an early diastolic wave (Ea), and an end-diastolic wave (Aa) produced by atrial contraction [13]. The tissue Doppler systolic mitral annular velocity has been shown to correlate with global LV myocardial function [14]. TDI has also been used to estimate diastolic function, and is relatively independent of preload condition [15, 16]. The pulsed Doppler peak early mitral inflow velocity (E) divided by the TD early diastolic mitral annular velocity (Ea) results in a ratio that correlates with the pulmonary capillary wedge pressure [17]. The E/Ea ratio is also useful in estimating mean LV filling pressure [18]. At this time, TDI represents

one of the most accurate techniques to assess diastolic function and is therefore of particular interest in the critical care population in whom abrupt changes in preload and afterload are common, making Doppler evaluation of diastolic function less reliable.

6.9 Detection of Intracardiac Masses and Extracardiac Effusions

An abnormal area of dense reflectance that is well localized within an echo may represent a mass, thrombus, or calcification. In the postoperative or critical care patient with multiple lines in place, especially in the setting of low flow, care must be taken to evaluate these areas for thrombus formation. Echo is the imaging modality of choice for elucidating and evaluating cardiac mass lesions [19]. Differentiating an area of concern from artifact, can be challenging. Areas that move appropriately throughout the cardiac cycle and the presence of an abnormality in more than a single view, suggest a mass rather than an artifact (see Figs. 6.5a–d). These findings must in turn be distinguished from such anatomical variations as a prominent Eustacian valve or Chiari network.

Major factors that predispose a patient to the development of intracardiac thrombi are the presence of intracardiac lines, diminished CO, and localized stasis in addition to changes within the clotting cascade from sepsis, bypass, intrinsic clotting disorders, or heparin use. Echocardiographic evaluation of patients within the intensive care setting must include an awareness of the increased incidence of thrombus formation and a careful evaluation of areas predisposed to become a nidus for thrombus.

Following cardiac surgery it is not uncommon for patients to develop small collections of fluid in the pericardial space (see Fig. 6.6). Typically, this is of little concern to the clinician; however, in a postoperative patient experiencing tachycardia and/or hypotension, the necessity of recognizing the potential for and screening for cardiac tamponade becomes paramount. In young infants and children, it is frequently difficult to rely on physical exam findings of increased jugular venous pressure or the late finding of pulsus paradoxus. In this instance, a directed and easily performed 2D and Doppler echocardiography can confirm the presence of an effusion and provide accurate assessment of its hemodynamic significance.

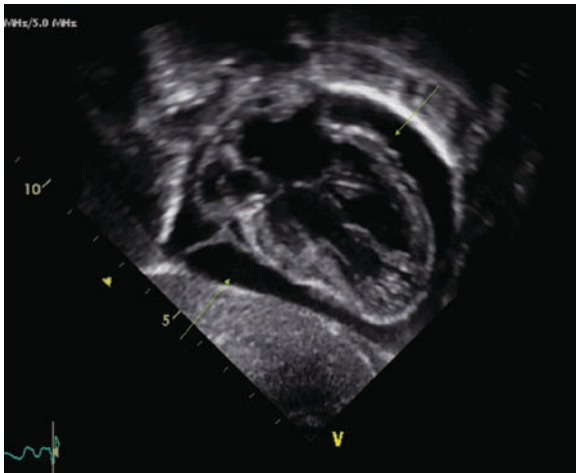


Fig. 6.6 Subcostal image demonstrating a large circumferential pericardial effusion (green arrows)

The size and extension of a pericardial effusion may be diagnosed from parasternal, apical, or subcostal windows. The apical view is the easiest for obtaining information regarding the effusions hemodynamic significance. From the apical four chamber view both the mitral and tricuspid valve flow patterns are evaluated with the respiratory monitoring in place. Examining the changes in inflow hemodynamics with respiration allows for the evaluation of tamponade physiology. Greater than 25% variability in maximal e wave velocity of the mitral valve with inspiration or 50% of the e wave velocity of the tricuspid valve (see Figs. 6.7a, b) is indicative of significant hemodynamic compromise resulting from the effusion [20]. Additionally, collapse (differentiated from contraction) of the free wall of the right and left atrium (see Figs. 6.8a, b) when the pericardial pressure exceeds the atrial pressure may be seen from this view in a patient with a significant effusion [21–26].

6.10 Echocardiography Guided Procedures

6.10.1 Pericardiocentesis

Performing “blind” percutaneous pericardiocentesis as a treatment for significant pericardial effusion dates back to the early eighteenth century and it is historically fraught with complications [27]. Improved techniques in the 1970s with the advent of 2D echo allowed more

accurate localization of the fluid and the development of echo-guided pericardiocentesis [28]. Echo-guided pericardiocentesis (see Fig. 6.9) has been found to be a safe and effective procedure with insertion of a catheter for drainage used to reduce the rate of recurrence found to complicate simple needle drainage and is considered the primary and often the definitive therapy for patients with clinically significant effusions [29, 30].

6.10.2 Balloon Atrial Septostomy (BAS)

Part of any echocardiographic assessment of a patient with congenital heart disease should include evaluation of the atrial septum. Cardiac lesions such as transposition of the great arteries, hypoplastic left heart syndrome, and tricuspid atresia require an adequate atrial communication. In the setting of a restrictive atrial septal communication or intact septum, a BAS is required to improve mixing and CO. In the past, the procedure, originally described by William Rashkind was performed in the cardiac catheterization laboratory under fluoroscopic guidance [31, 32]. However, during the last decade BAS has been routinely performed at the bedside in the intensive care unit under echocardiographic guidance (see Figs. 6.10a–d). Most commonly either a subcostal view that includes a focused look at the atrial septum, pulmonary vein, and mitral valve or an apical four-chamber view is used. For the echocardiographer, the primary role is to provide continued visualization of the catheters and communicate well with the interventionalist. Advantages of this technique are multifactorial; echocardiography is superior to fluoroscopy during BAS due to a lack of radiation, the ability to perform the procedure at bedside rather than transporting to a catheterization laboratory, and direct, continuous visualization of the atrial septum, pulmonary veins, and mitral valve. The disadvantages of this technique include the potential for interference with maneuverability for both echocardiographer and catheter operator around a small neonate and therefore the risk of contamination of the sterile field. Additionally there is the possibility of poor acoustic windows in an ill neonate who may be mechanically ventilated. However, with proper planning and communication, the limitations of transthoracic echocardiographic guidance of BAS may be minimized [33–36].

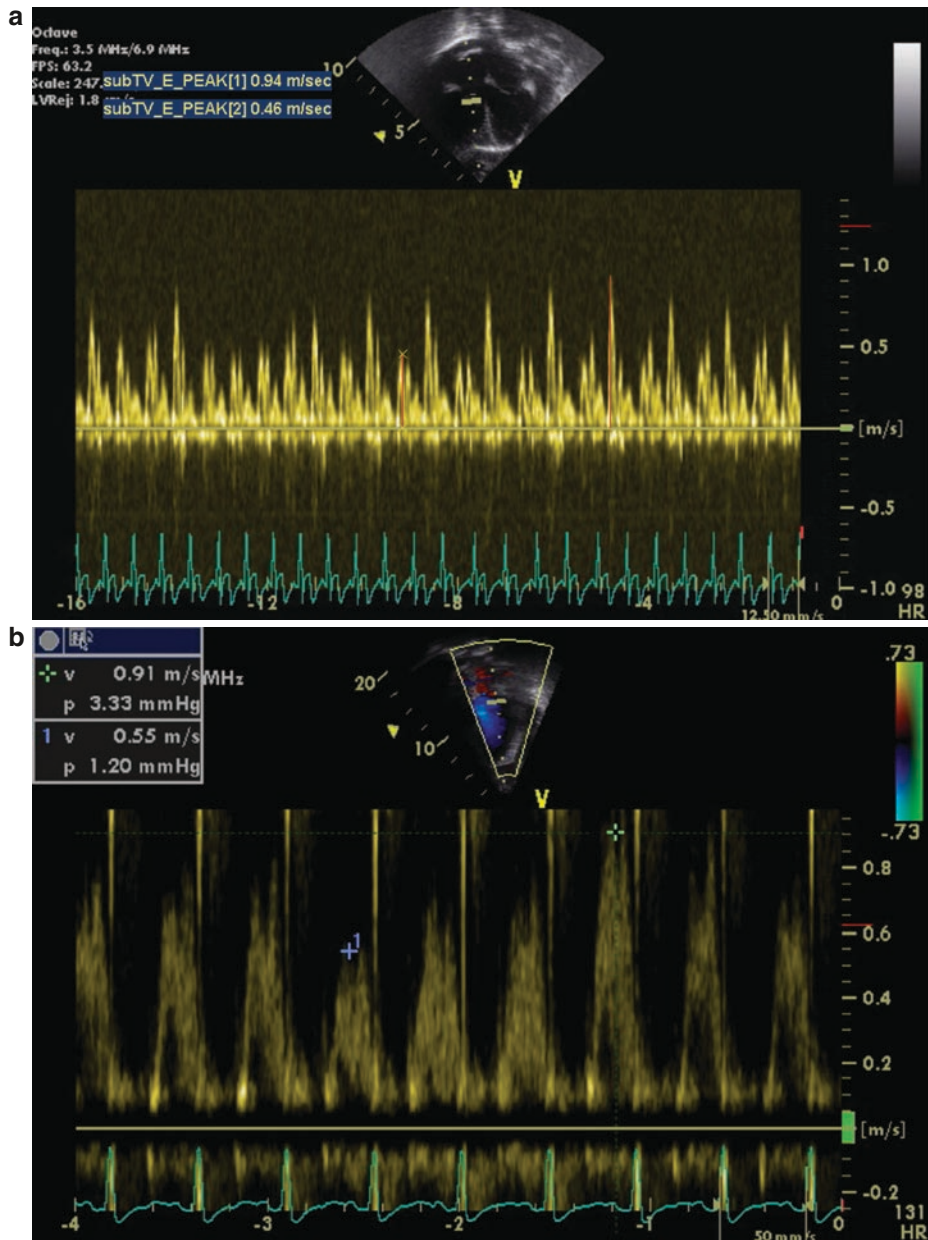


Fig. 6.7 (a) and (b): Respiratory changes in the mitral and tricuspid valve e wave Doppler patterns consistent with tamponade physiology. The tricuspid valve inflow demonstrates more than

50% variability between inspiration and expiration (a). During mitral valve inflow Doppler, the peak E wave velocity alters more than 30% between inspiration and expiration (b)

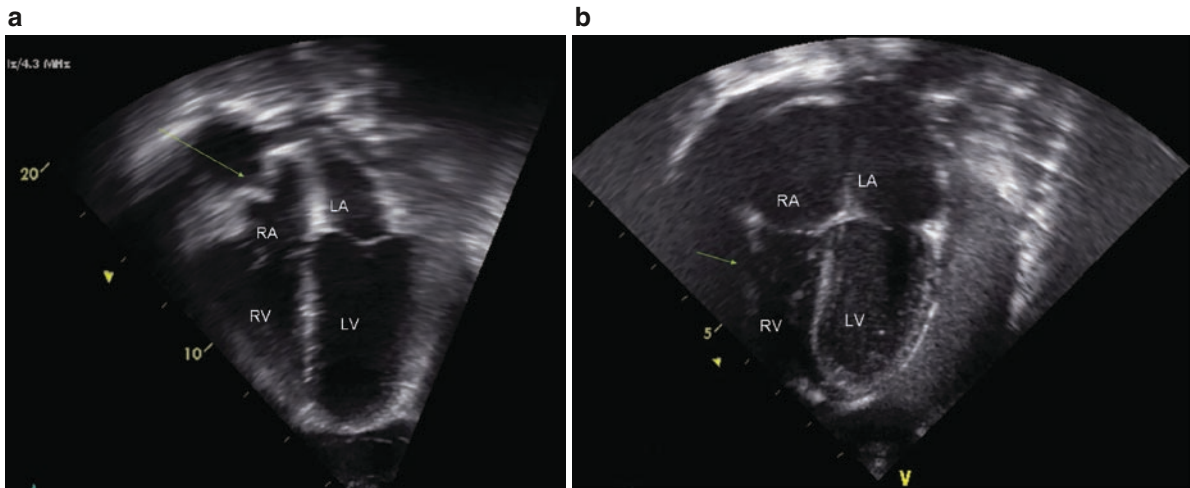


Fig. 6.8 (a) and (b): Four chambered views demonstrating right atrial and right ventricular collapse (green arrows) as a finding of tamponade physiology. RA right atrium; RV right ventricle; LA left atrium; LV left ventricle

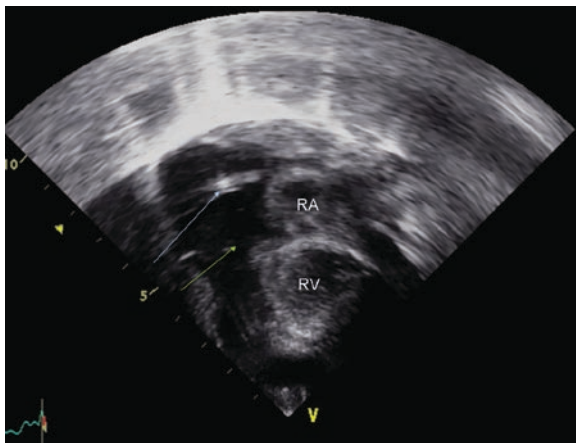


Fig. 6.9 Echoguided pericardiocentesis. Green arrow is in the pericardial space demonstrating the large fluid collection. Blue arrow is pointing to the needle that has been advanced into the pericardial space to drain the fluid collection. The large effusion allows the echocardiographer to direct the individual performing the pericardiocentesis away from areas that could lead to complications such as perforation of the myocardium

6.11 Future Directions

There are several areas of advanced imaging that are becoming more commonplace in the practice of pediatric echocardiography. Primary assessment of cardiac mechanics by evaluating myocardial motion, strain,

and strain rate has been validated in healthy children and provides additional information regarding myocardial performance.

Three-dimensional real-time echocardiography has a growing role in evaluating anatomic defects, valves, and right and left ventricular function independently of geometric assumptions that constrained the previous methods.

6.11.1 Myocardial Mechanics

In the past several years, myocardial strain and strain rate have emerged as promising quantitative measures of myocardial function and contractility. Strain (ϵ) is a dimensionless parameter defined as the deformation (L) of an object relative to its original length (L_0), and is expressed as a percentage. Strain rate (SR) is defined as the local rate of deformation or strain (ϵ) per unit of time, and is expressed in 1/s. Strain and strain rate measurements can be obtained from data acquired by Doppler Tissue Imaging or 2D tissue tracking. Strain and strain rate should be of great help in the future in the evaluation of ventricular function, since conventional M-mode and 2D echocardiography have limitations due to complex morphology of the right ventricle and altered left ventricle morphology that occurs in

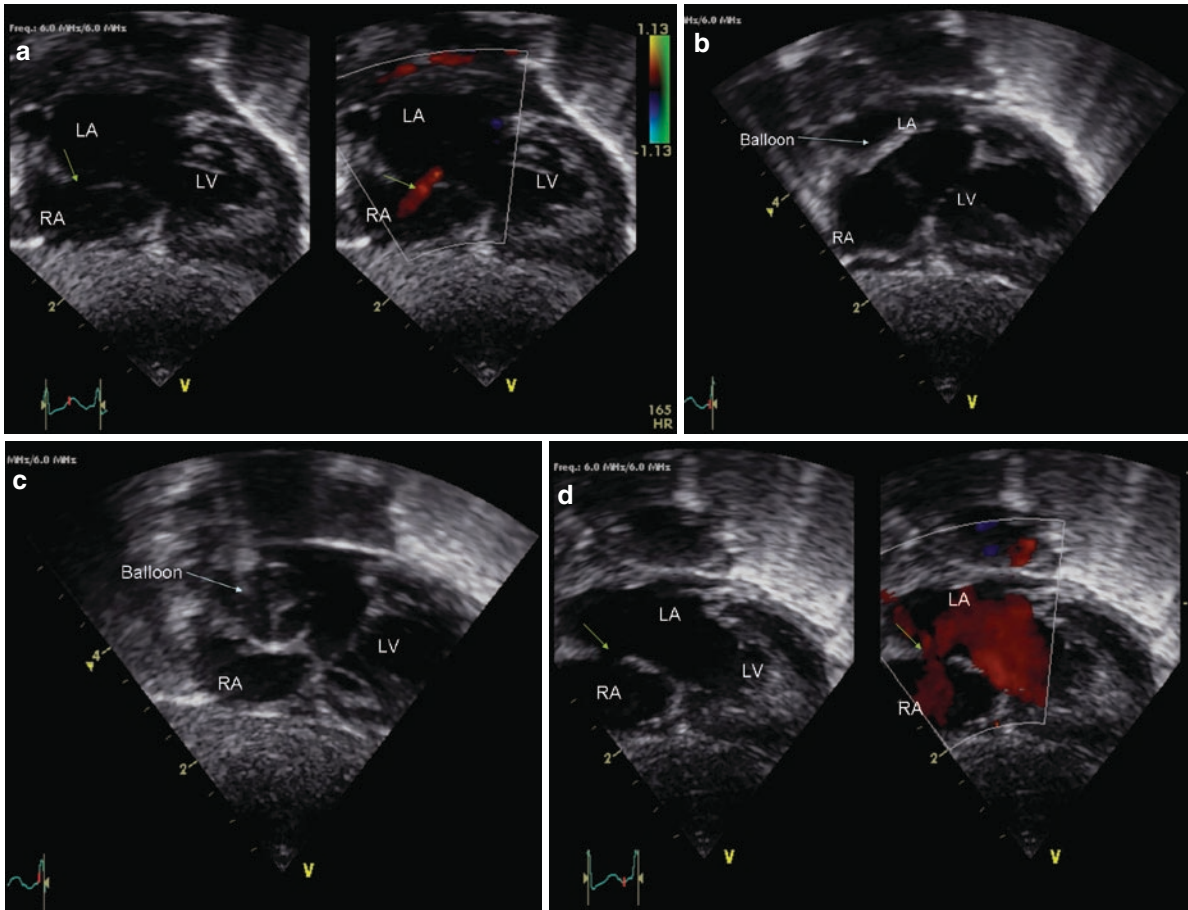


Fig. 6.10 Subcostal images demonstrating echo-guided balloon atrial septostomy (BAS). (a): shows the initial small atrial communication in both 2 dimensional (2D) and color Doppler imaging. (b): reveals the deflated balloon that has been advanced across the atrial communication. It is important during this portion of the procedure for the echocardiographer to ensure that the balloon has not been advanced across the left

atrioventricular valve. (c): demonstrates the inflated balloon within the left atrium. It is important to note the balloon's position away from the mitral valve and pulmonary veins. (d): demonstrates the atrial communication following septostomy using both 2D and color Doppler imaging. RA right atrium; RV right ventricle; LA left atrium; LV left ventricle; Green arrows atrial communication

complex congenital heart defects [37]. Left and right ventricular values of strain and strain rate are available for healthy children [38].

6.11.2 3D Echocardiography

Off-line 3D reconstruction consists of acquisition of sequential 2D slices which are converted to a rectangular coordinate system for 3D reconstruction and provides

accurate anatomic information suitable for quantitative analysis [39–42].

Left ventricular volume, mass, and function can be accurately assessed using RT3D independently of geometric assumption, and ejection fraction can be calculated. The wideangle mode is often used to acquire the entire LV volume, from which further analysis allows determination of global and regional wall motion. Wall motion is evaluated from base to apex with multiple slices from different orientations. The advantage of 3D over 2D is the ability to manipulate the plane to

align the true long axis and minor axis of the LV, thus avoiding foreshortening and oblique image planes. LV volume assessment by RT3D is rapid, accurate, reproducible and superior to conventional 2D methods [43] and is comparable to MRI, which represents the gold standard [44–48]. Three dimensional reconstruction of the tricuspid valve has been shown to be helpful for anatomical assessment of Ebstein's malformation [49, 50] or after atrioventricular septal defect repair [51]. 3D echocardiography is a useful adjunct to standard 2D imaging and should be increasingly used in the future.

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Chapter 7

Cardiac Anesthesia

Edmund H. Jooste

7.1 NPO Guidelines

Prolonged preoperative fasting times in children may lead to dehydration, hypovolemia and hypoglycemia. This is especially true in the cyanotic child and children with single ventricles as they may have increased hematocrits and are dependent on an adequate preload to maintain their cardiac output. Current guidelines suggest allowing clear up to 2 h preoperatively; breast milk, up to 4 h preoperatively; infant formula, up to 6 h preoperatively and any solids will require an 8-h fasting period [1, 2].

7.2 Premedication

Children with congenital heart disease (CHD) and their parents are frequently apprehensive about surgery and anesthesia. Because these children have undergone frequent procedures, they benefit greatly from the use of appropriate premedication that provides amnesia and reduces anxiety, excitement and oxygen requirements. Premedication is generally administered to cardiac surgical patients older than 8 months of age. The most commonly used medication is midazolam. Midazolam can be administered by the oral, nasal/buccal, rectal and intravenous routes.

The oral formulation of midazolam is a syrup. The recommended oral dose is 0.25–0.75 mg/kg with a maximum dose of 20 mg. It is administered 20–30 min prior to the procedure. For children with intravenous

catheters in place, intravenous midazolam is effective just before going to the operating room. The intravenous preparation of midazolam can also be administered through the buccal or rectal routes. Nasal midazolam, 0.2–0.3 mg/kg with a maximum dose of 5 mg, is also effective. The peak effect is at 10–15 min, but nasal midazolam can cause burning on administration. Rectal midazolam has been used, and a dose of 1 mg/kg was shown to be optimal. For the older patient who might prefer tablets, PO lorazepam (1–2 mg) or diazepam (5–10 mg) 20–30 min prior to the scheduled start time are appropriate alternatives [3].

7.3 Midazolam [4, 5]

Mechanism of action: Midazolam binds to stereospecific benzodiazepine receptors in the CNS where it enhances the inhibitory tone of GABA receptors resulting in sedation and amnesia.

Pharmacokinetics: Midazolam is metabolized in the liver mostly by CYP3A4 of the P450 enzyme system. Following a single intravenous bolus, midazolam rapidly redistributes, and its peak CNS effect occurs within 2–5 min. Following an oral dose, midazolam's peak clinical effect occurs at 15–20 min. The half-life of midazolam is approximately 1–4 h.

7.3.1 Pharmacodynamics

Central Nervous System: In the CNS, midazolam causes sedation and amnesia but has no analgesic effect. Midazolam has anticonvulsant properties and also can act as an antispasmodic for muscle spasms.

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Cardiovascular System: Midazolam causes mild vasodilation and reduced cardiac output. The heart rate may decrease or remain unchanged.

Respiratory System: Respiratory depression is frequently associated with midazolam and is poorly correlated to dose and not reversed by naloxone.

Dosing: [6]

Adverse effects: Additive respiratory and cardiovascular depression occur when midazolam is administered with an opioid. Midazolam administration in the first trimester of pregnancy is associated with birth defects (cleft *palate*).

Reversal: Flumazenil is a competitive antagonist to all benzodiazepines. Dosed in increments of 0.01mg/kg (maximum 0.2mg/dose) every minute up to a total of 1 mg. Repeated dosing may be necessary as it has a short duration of action [7].

7.4 General Anesthesia

The type of anesthesia induction depends on the patient's age, underlying cardiac reserve, presence of an intravenous catheter, potential of a difficult airway and the preference of the child. In stable patients without an intravenous catheter, inhalational inductions are commonly preferred. In patients with an intravenous catheter already in place or in patients with little cardiac reserve, intravenous inductions are preferred. If the cardiac function is adequate, propofol is generally administered. If the cardiac function is decreased, etomidate, ketamine or an opioid are used to induce anesthesia [8].

7.4.1 Intravenous

7.4.1.1 Propofol

Propofol or 2,6-diisopropylphenol, is prepared as a 1% or 2% isotonic oil-in-water emulsion and contains egg lecithin, glycerol, soybean oil and EDTA [5, 9].

Mechanism of action: The exact mechanism of propofol's action is unclear, but it is thought to enhance inhibitory GABA synapses.

Pharmacokinetics: Propofol is metabolized in the liver. Propofol produces unconsciousness within 30–45 s following intravenous injection, and its duration of action after a single bolus is 3–10 min. This short duration of action is attributed to the redistribution of propofol.

Pharmacodynamics

Central Nervous System: At high doses, propofol produces general anesthesia while at lower doses propofol can be used for procedural sedation. Propofol has both anticonvulsant and proconvulsant properties. Propofol has some anti-emetic properties and no analgesic effects.

Cardiovascular System: Propofol causes a dose-dependant decrease in blood pressure and cardiac output.

Respiratory System: Propofol is a potent respiratory depressant, and blunts the response to hypercarbia and exhibits a dose-dependent decrease in both respiratory rate and tidal volume.

Dosing:

Induction: Child (2.5–3.5 mg/kg), adult (2–2.5mg/kg) IV

Maintenance: Child (125–300 µg/kg/min), adult (150–200 µg/kg/min) IV

Sedation: Child (25–75 µg/kg/min)

Doses should be reduced in hemodynamically unstable patients and always titrated to effect.

Adverse effects: Pain is extremely common during IV propofol injection. The pain can be attenuated by using large veins or the prior administration of lidocaine or an opioid. Propofol is solubilized in an emulsion that supports bacterial growth, and therefore, propofol should be administered to patients within 6 h of having been opened. Propofol should be avoided in patients who have an allergy to egg whites because the preparation contains egg lecithin. A "propofol infusion syndrome" has been described in patients who have received high-dose and/or a prolonged infusion. Symptoms of propofol infusion syndrome include severe, sporadic metabolic acidosis and/or lactic acidosis. The acidosis may be associated with tachycardia, myocardial dysfunction, and/or rhabdomyolysis. Propofol should be used cautiously in patients with disorders of lipid metabolism.

7.4.1.2 Etomidate

Etomidate is a carboxylated imidazole structure. Etomidate is a commonly used agent for the induction of anesthesia in hemodynamically unstable patients [5, 9].

Mechanism of action: Like propofol, etomidate enhances inhibitory GABA synapses.

Pharmacokinetics: Etomidate is metabolized in the liver and produces unconsciousness within 30–60 s. Following intravenous administration, etomidate's duration of action following a single bolus is 3–10 min and this short duration of action is attributed to redistribution of the drug.

Pharmacodynamics

Central Nervous System: With induction doses, etomidate produces unconsciousness and has no analgesic properties.

Cardiovascular System: Etomidate produces minimal changes in heart rate, blood pressure and cardiac output.

Respiratory System: Etomidate produces a dose-dependent decrease in respiratory rate and tidal volume but to less of a degree as compared to propofol.

Dosing: IV induction dose for adults and children is 0.2–0.6 mg/kg IV.

Adverse effects: Pain on IV injection occurs almost as frequently as with propofol. Myoclonus can occur. Nausea and vomiting occurs more frequently than when using other induction agents. Etomidate inhibits 11- β -hydroxylase, an enzyme important in adrenal steroid production. Even a single induction dose can block the normal stress-induced increase in adrenal cortisol production for 4–8 h. Etomidate is no longer used as a continuous infusion for sedation in the ICU because of an increased mortality, possibly because patients may not be able to respond to stress. However no clinical problem has been identified with a single dose for induction of anesthesia.

7.4.1.3 Ketamine

The ketamine molecule is similar structurally to phencyclidine. Ketamine is often used for induction of anesthesia in hemodynamically unstable patients.

Ketamine is also administered intramuscularly in combative patients or patients who have poor IV access [5, 9].

Mechanism of action: Ketamine is an *N*-methyl-D-aspartate (NMDA) receptor antagonist that acts in the cortex and limbic systems.

Pharmacokinetics: Ketamine is metabolized in the liver. With IV induction, it produces unconsciousness with IV induction in 30–60 s and lasts 10–15 min. Intramuscular administration produces unconsciousness in 5–10 min and lasts 12–25 min.

Pharmacodynamics

Central Nervous System: Ketamine induces a dissociative state and provides both amnesia and analgesia. Ketamine also increases cerebral blood flow, cerebral metabolic rate and ICP.

Cardiovascular System: Ketamine releases endogenous catecholamines (epinephrine, norepinephrine) which maintain blood pressure and heart rate. Ketamine has direct myocardial depressant effects and should be used cautiously in patients with hypovolemia or patients who have maximal sympathetic stimulation.

Respiratory System: Ketamine mildly decreases respiratory rate and tidal volume. Ketamine is an excellent bronchodilator and maintains laryngeal reflexes longer than with other induction agents.

Dosing:

Induction: 1–2 mg/kg IV; 5–10 mg/kg IM

Sedation: 0.2 mg/kg IV titrated to effect.

Adverse effects: Emergence reactions, confusion, or irrational behavior may occur up to 24 h following ketamine administration. These reactions may be reduced by pretreatment with a benzodiazepine (midazolam). Children seem less affected by these hallucinations but it should be avoided in patients with psychiatric disorders.

Patients should also be given an antisialagogue (e.g., glycopyrrolate) because ketamine markedly increases oral secretions.

Myoclonic movements of the limbs and eye movements (e.g., nystagmus) are common following ketamine administration.

Ketamine raises both intracranial and intraocular pressure and should be avoided in patients with head trauma and in patients having ophthalmologic procedures.

7.4.2 Inhalational Agents

General principles: Dosages of inhalational anesthetics are expressed as minimal alveolar concentration (MAC). MAC is the concentration of a volatile anesthetic when used as the sole anesthetic, expressed as a percentage, which inhibits movement in response to a skin incision in 50% of patients. The blood-gas partition coefficient defines how easily the inhalational agent is absorbed into the blood. The more soluble the vapor is in the blood, the higher the number. This blood-gas partition coefficient is inversely related to the rate of induction, i.e., an inhalational agent with a low blood-gas coefficient partition (insoluble agent), e.g., sevoflurane (0.69), has a faster speed of induction compared to the more soluble agent, isoflurane, which has a blood gas coefficient of 1 [4, 8, 9].

7.4.2.1 Nitrous Oxide

Nitrous oxide is a clear and odorless gas used as an adjunct to inhalation and intravenous anesthetics (MAC=104; blood-gas=0.47) [5, 9].

Mechanism of action: Nitrous oxide is a general CNS depressant that may act similarly to inhalational general anesthetics, i.e., stabilizing axonal membranes to partially inhibit action potentials leading to sedation.

Pharmacokinetics: The uptake and elimination of nitrous oxide is extremely rapid (2–5 min). Nitrous oxide is eliminated by exhalation and undergoes no metabolism.

Pharmacodynamics

Central Nervous System: Because of its high MAC (104%), nitrous oxide it is not used as a sole anesthetic. Rather, nitrous oxide is used in combination with other agents. Nitrous oxide activates opioid receptors and provides analgesia. At concentrations greater than 60%, nitrous oxide provides amnesia.

Cardiovascular System: Central sympathetic stimulating action of nitrous oxide supports blood pressure, systemic vascular resistance, and cardiac output. Nitrous oxide may increase pulmonary vascular resistance.

Respiratory System: Mild respiratory depressant, but it does not depress carbon dioxide drive to stimulate breathing.

Dosing: Nitrous oxide is added to anesthetic gas mixture to create a concentration of 50–70%.

Adverse effects: Diffusion hypoxia occurs at the discontinuation of nitrous oxide because nitrous oxide diffuses so rapidly out of the blood and back into the lung. This rapid diffusion into the alveolus can dilute the oxygen content in the lung. Because nitrous oxide is 31 times more soluble in the blood than nitrogen, it diffuses into closed spaces quicker than nitrogen can diffuse out, thus leading to the expansion of the space, e.g., pneumothorax. A theoretical concern regarding nitrous oxide is that methionine synthase, a vitamin B12 dependent enzyme, is inactivated following prolonged administration of nitrous oxide, and the subsequent interference with DNA synthesis prevents production of both leukocytes and red blood cells by bone marrow. Therefore, it should be used with caution in pregnant patients and patients with Vitamin B12 deficiency.

7.4.3 Volatile Agents

Volatile agents are liquids that are vaporized to produce anesthesia. The most frequently used potent inhaled agents include sevoflurane, desflurane and isoflurane. [5, 9]

Mechanism of action: Volatile anesthetic agents, CNS depressants. The exact mechanism of action of the volatile anesthetic agents is unclear. They are thought to stabilize axonal membranes and partially inhibit action potentials, thus lead to sedation.

Pharmacokinetics: The speed of an inhalational anesthetic induction is determined by the rate of rise of the alveolar anesthetic concentration and the second gas effect. The quicker the rate of rise of the alveolar concentration, the faster the anesthetic induction. Numerous factors influence the alveolar rate of rise:

(1) The lower the blood-gas partition coefficient, the lower is the vapor's solubility, and therefore, the quicker the increase in alveolar concentration and the faster the induction. (2) The higher the inspired concentration and (3) the greater the alveolar ventilation, the quicker the increase in alveolar concentration and the faster the induction [4].

Conversely, an increase in the cardiac output results in an increase in uptake of the vapor into the blood and

a corresponding decrease in the alveolar concentration resulting in a slower induction. The second gas effect also affects the rate of anesthetic induction. The second gas effect occurs when two inhalational anesthetics are administered at the same time, and one of them, e.g., nitrous oxide, gets absorbed quicker than the other vapor ("second gas"). This leads to a proportionate increase in the alveolar concentration of this second gas and a faster induction. Anesthetic effects are terminated when the anesthetic gases are discontinued. The main route of elimination of anesthetic agents is via exhalation. Some metabolism of the anesthetic agents in the liver does occur but is believed to be clinically insignificant.

7.4.3.1 Pharmacodynamics

Central Nervous System: All of the inhalational anesthetic agents produce a dose-dependent unconsciousness and amnesia. They all decrease both EEG and somato-sensory evoked potentials. Inhalational anesthetic agents increase cerebral blood flow and intracranial pressure but decreases cerebral metabolic rate.

Cardiovascular System: Inhalational anesthetic agents cause a dose-dependant cardiac depression. The agents all sensitize the myocardium to the arrhythmogenic effects of catecholamines, but to varying degrees.

Respiratory System: Inhalational anesthetic agents cause dose-dependant respiratory depression. At sufficient concentrations, inhalational agents are all potent bronchodilators.

Dosing: If used as an anesthetic induction agent, it is dosed initially at 3–4 times its MAC value, but during maintenance of anesthesia, it is dosed between

0.5–2 times its MAC value depending on the use of other anesthetic adjuncts and the degree of surgical stimulation.

Adverse Effects: Sevoflurane may have a potential for renal toxicity if used at low flows for an extended period of time.

Desflurane needs a special vaporizer because of its vapor pressure. Desflurane is very irritating to airways and can not be used for inhalational induction.

Isoflurane has the potential to induce a coronary steal phenomenon. Isoflurane is a potent coronary artery vasodilator and may cause coronary blood flow to be redistributed to non-diseased, normally responsive coronary arteries.

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Chapter 8

A Pharmacokinetic and Pharmacodynamic Review

Carol G. Vetterly and Denise L. Howrie

Important pharmacodynamic and pharmacokinetic differences in drug handling are observed in newborns, infants, and children when compared to adult patients. Therefore, knowledge of pharmacokinetic and pharmacodynamic principles in the pediatric population may better assure safe and effective medication prescribing.

8.1 Definitions

Pharmacodynamics is the study of the biochemical and physiological action or effects of drugs on living organisms. Pharmacokinetics is the study of the processes by which drugs move through the body, generally, referring to processes of absorption, distribution, metabolism, and excretion.

8.2 Absorption

Drugs that are administered extravascularly undergo absorption. The bioavailability of a drug is defined as the fraction of a given drug dose that is available in the systemic circulation to exert a pharmacologic effect. The extent or efficiency of systemic drug absorption is dependent upon characteristics including hydrophobic or hydrophilic properties, molecular weight, and drug ionization at biologic pH. Drug penetration through biologic membranes, most often occurs through passive diffusion dependent upon drug concentrations. The absorption of a drug is also dependent upon

the dosage form selected and the pharmaceutical characteristics of the formulation.

Orally-administered medications require drug absorption in the gastrointestinal tract, determined by variables including surface area of the gastrointestinal tract, rates of stomach emptying and intestinal transit, pH of the stomach and small intestines, as well as blood flow to the absorption site [1]. There are important considerations regarding the use of oral medication and drug absorption in pediatric patients. For example, gastric pH in newborns is high, around 6–8 at birth, decreasing to a pH of 1–3 within 24 h of birth [2], and reaching adult values by 3–7 years of age. This is an important consideration when administering acid labile medications via the oral route. For example, higher serum concentrations of penicillin may be achieved in early infancy [1] while weak acids, such as phenobarbital or phenytoin, may require higher daily doses to achieve comparable serum concentrations due to pH values.

Medications may also be absorbed through the respiratory tract via the inhalation route. Water soluble particles will be absorbed to a greater extent from the lung alveoli. Small particles (<1 μm) can penetrate into the tracheobronchial area. During respiratory administration of drugs, it should be noted that inadvertent swallowing of drug into the gastrointestinal tract may significantly contribute to systemic bioavailability.

The skin is also a route of drug absorption. The stratum corneum is the most important layer in the regulation of medication penetration. Cutaneous absorption of medications may be increased in children due to a greater relative body surface area to body mass ratio compared to adults [1, 3]. The topical route in infants and children has potential for a greater risk of systemic absorption as a result of a greater skin-surface-to-body-weight-ratio, a decreased subcutaneous fat layer, as well as a thinner stratum corneum and epidermis [1, 2].

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In pediatric patients, and specifically newborns, efficiency of intramuscular drug absorption may be decreased and unpredictable due to decreased muscle mass and tone, reduced muscle blood flow and decreased muscle activity.

8.3 Distribution

Drug distribution is extensively altered in children when compared to drug handling in adults. Drugs are distributed throughout the body through tissues and fluids under the control of variables including body composition (body water, fat, bone, muscle etc.), extent of plasma protein binding, and organ blood flow [4]. Total body water varies depending on the age of a pediatric patient. Total body water ratio, when compared to body mass progressively, decreases with age: pre-term newborns 85%, term newborns 75%, infants approximately 78%, a one year old approximately 75%, adults 60% [2, 3]. Variation in total body water content effects distribution of hydrophilic medications, so that higher loading doses and maintenance doses (when compared by body weight) may be required. For example, aminoglycoside daily dose requirements are increased: 7.5 mg/kg/day in infants and young children as compared to adult doses of 3–5 mg/kg/day to achieve similar therapeutic serum concentrations.

A hypothetical drug “volume of distribution” (Vd) may be calculated, reflecting the extent of distribution into body fluids and tissues, and relates the amount of drug in the body to the measured plasma concentration. An apparent Vd may be calculated as:

$$Vd \text{ (L/Kg)} = \text{dose (mg/kg)} / \text{plasma concentration (mg/L)}$$

The larger the volume of distribution, the larger the medication dose needed to achieve a target drug concentration. For example, if the Vd of a particular drug is 1 L/kg, and the therapeutic serum concentration is 20 mg/L, then the necessary loading dose of the medication would be 20 mg/kg. Phenytoin and phenobarbital loading doses in status epilepticus are examples of clinical applications of this pharmacokinetic principle.

Plasma protein binding is another important determinant of drug distribution, as many important drugs in pediatrics demonstrate high extent of binding to albumin and alpha-1-acid-glycoproteins. Lower serum

albumin concentrations and decreased affinity of acidic drugs at albumin binding sites, most evident in newborns and young infants, result in higher free concentrations for drugs such as phenytoin, valproate, and salicylates with risks of enhanced toxicity and/or enhanced clearance, and subtherapeutic effects. Drug displacement interactions may also be more evident in infancy where highly albumin-bound drugs such as ceftriaxone or sulfonamides, for example, may displace bilirubin and other physiologic substances from albumin-binding sites resulting in toxicity.

Plasma concentration of alpha-1-acid-glycoprotein, a carrier of basic drugs, is decreased in newborns, reaching approximately 50% of adult values during infancy and slowly increasing during the first year [3]. Effects of age-based changes may be important for agents such as lidocaine. Disease states can also affect changes in alpha-1-acid glycoprotein, with elevations as an acute phase reaction caused by inflammation (e.g., myocardial infarction in adults). This could result in lower free concentrations of drugs, including quinine, lidocaine, and propranolol, necessitating careful laboratory and clinical monitoring.

8.4 Metabolism

Drug metabolism is the process by which a substance is biochemically transformed through chemical reactions in the body. Primary route of drug metabolism is via the liver, but metabolism also may occur to lesser extents in the kidney, gastrointestinal tract, lung, blood, and kidney. Drugs may demonstrate “first pass effects” in which metabolism of an orally administered medication occurs in the intestinal lumen and liver before reaching systemic circulation. Medications which demonstrate high first pass effects include beta-blockers such as propranolol, opioids such as hydromorphone, isoproterenol, and nitroglycerin. It is important to note that when a drug has a high first pass effect, the oral dose of the medication is considerably greater than the intravenous route, and dosing conversions from parenteral to oral routes or vice versa may result in errors.

Hepatic drug metabolism may occur through a variety of processes. Phase I reactions including oxidation (CYP450), reduction, and hydroxylation [3] allow formation of more polar, water soluble molecules

that can be more easily eliminated by the body. Rates of metabolism through Phase I pathways generally are approximately 50% of activity at birth and mature over time [3]. Phase II reactions, including conjugation, glucuronidation, sulfation, and acetylation, vary in activity from 20 to 70% at birth and mature with age [5].

The cytochrome P450 enzyme system is responsible for oxidative metabolism. Four major isoenzyme pathways are responsible for metabolism of approximately 95% of all drugs: CYP3A4, CYP2D6, CYP2C9, CYP1A2. Knowledge of drug metabolism via these enzyme pathways is useful because significant drug–drug interaction may be anticipated.

The CYP3A4 enzyme pathway is responsible for metabolism of the greatest number of medications. Drugs may act as substrates for this enzymes family; drugs may also act as inhibitors or inducers of this family. Examples of medications that are substrates include prednisone, dexamethasone, cyclosporine, tacrolimus, benzodiazepines, calcium channel blockers, “statins,” and lidocaine [6]. Medications that are inhibitors of this enzyme pathway such as amiodarone, erythromycin, azole anti-fungals such as fluconazole and voriconazole, and diltiazem may produce significant drug–drug interactions through reduced drug metabolism of competing substrates. Medications that are enzyme “inducers” such as carbamazepine, phenytoin, rifampin, and phenobarbital would decrease substrate drug concentrations and, therefore, therapeutic responses. There are large differences reported in CYP3A4 activity with a four to thirteen fold variations in clearance rates [7].

CYP2D6 isoenzyme family encompasses approximately 25% of medications. Substrates of this pathway include tricyclic antidepressants, opioids, mexilitine, flecainide, haloperidol, and beta blockers. Dextromethorphan is the standard marker for efficiency of drug metabolism through this pathway. Examples of CYP2D6 inhibitors include amiodarone, haloperidol, and quinidine; inducers include phenytoin, phenobarbital, carbamazepine, and rifampin.

CYP2C9 enzyme substrates include: omeprazole, phenytoin, S-warfarin, diazepam, and propranolol. Inhibitors include amiodarone, fluconazole, omeprazole, and topiramate. Inducers include phenytoin, phenobarbital, carbamazepine, and rifampin.

The CYP1A2 isoenzyme family is responsible for approximately 5% of medications such as theophylline, R-warfarin, and caffeine. Inhibitors include:

erythromycin, clarithromycin, fluconazole, and ciprofloxacin. Example of inducer include: phenytoin, carbamazepine, phenobarbital, and rifampin.

8.5 Excretion

Excretion of drugs and metabolites occurs primarily through the urine and feces, although other routes include saliva, sweat, respiratory tract, tears, semen, and breast milk. Renal excretion of drug proceeds via glomerular filtration, tubular secretion, and tubular reabsorption. There is age-specific maturation of renal processes of elimination that affects rates of drug elimination. For example, glomerular filtration function is reduced in premature infants and newborns, with progressive maturation by 8–12 months of age. Therefore, drugs such as vancomycin and gentamicin require extended dosing intervals in neonates due to immature renal function.

8.6 Describing Drug Pharmacokinetics Through Pharmacokinetic Models

Pharmacokinetic parameters expressed in mathematical terms may be used to generate visual descriptions of drug movement. The most simplistic model of drug movement is referred to as a single compartment model in which the body is a single compartment, there is no absorption phase and the drug rapidly equilibrates through all tissues (Fig. 8.1). In this model, it is assumed that a drug follows first order elimination when the amount of drug eliminated from the body in a specified amount of time is dependent upon the rate of elimination and the concentration of drug at that time. An increase in drug dosage results in increased serum concentrations and the amount of drug eliminated over that period (Fig. 8.2). For example, the amount of drug eliminated from the body may change, but the fraction of the drug removed over a period of time remains constant [8]. Aminoglycosides, cephalosporins, and vancomycin follow first order elimination.

Pharmacokinetic models may reveal pattern of elimination best described as zero order elimination, also referred to as non-linear or Michaelis–Menten kinetics. Zero order pharmacokinetics describes drug

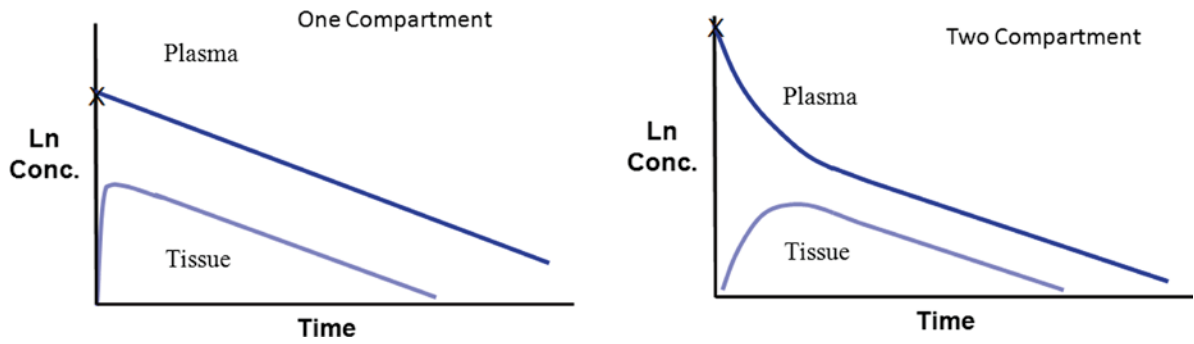


Fig. 8.1 Log of concentration vs. time for one and two compartment models

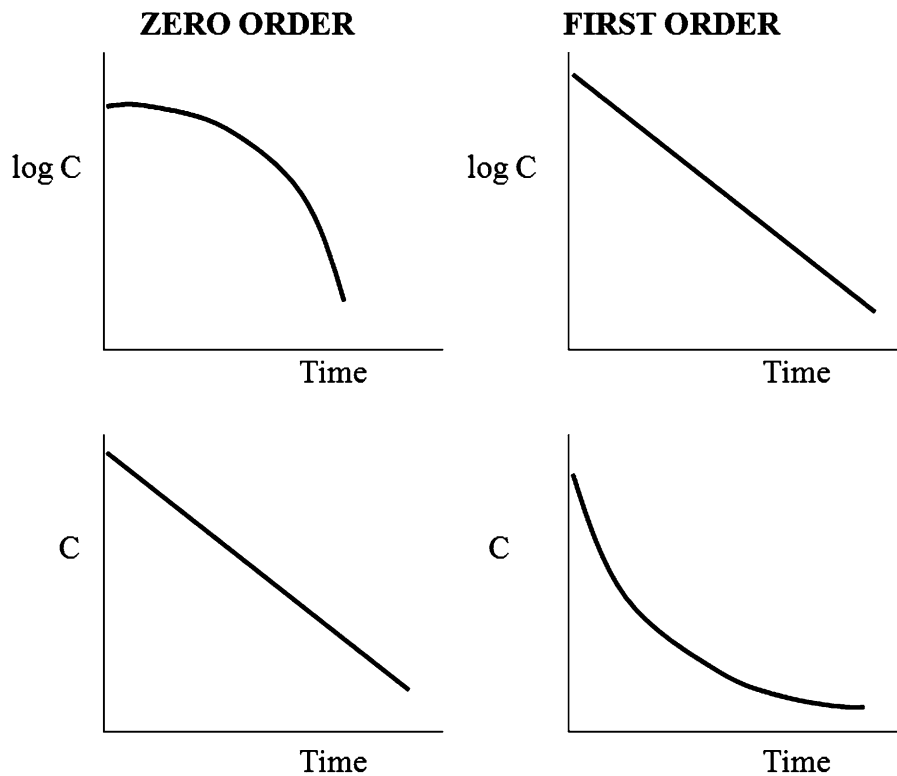


Fig. 8.2 Log of concentration vs. time for first and zero order pharmacokinetic models

elimination as a saturable process at the serum concentrations commonly achieved in patients. In zero order elimination profiles, the amount of drug eliminated does not change with the amount (concentration) of drug in the body at a given time; however, the fraction of drug that is removed changes [8] (Fig. 8.2). Aspirin, phenytoin, and ethanol are example of medications that exhibit zero order kinetics within recommended dosage regimens. The impact of this pharmacokinetic

profile can be understood in its application to practice for phenytoin. A given patient may require a dosage increase to achieve a targeted therapeutic plasma concentration. With zero order elimination, phenytoin dose increases by 15% and will result in a disproportionate increase in serum concentration, as much as two to three -fold, resulting in serious toxicity. In this setting a fixed amount of drug is eliminated per hour regardless of serum concentration.

8.7 Drug Half-life

Another important pharmacokinetic concept is half-life, defined as the time for drug concentration to decrease by one-half of its initial value. Clinical application of this value lies in the ability to predict timing of steady-state drug concentrations when the rate of drug administration equals the rate of drug elimination. For example, as serum steady concentrations are achieved at approximately 4–5 half-lives, dosage adjustments are best made at that time [8].

In conclusion, understanding pharmacokinetic and pharmacodynamic principles for specific drugs and age-related differences in the pediatric population may aid in therapeutic decision-making. Anticipation of patient-specific variable, such as hepatic and renal function and drugs affecting the CYP450 enzyme system, enhances appropriate drug selection, dosage, and therapeutics.

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Chapter 9

Sedation and Analgesia

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The major goals for postoperative sedation and analgesia in infants, undergoing cardiothoracic surgery are to alleviate pain and to aid the transition of patients from the intensive care unit to home. The type of agents used for pediatric sedation varies with the medical needs of the patients. For postoperative pediatric patients, children need to be comfortable and nonagitated. Ideal sedative analgesic agents should have a rapid onset and offset of action, and be nontoxic, noncumulative, nonaddictive, and have minimal interactive effects with other drugs. In addition, ideal sedatives should provide the patient with cardiorespiratory stability and be cost effective. Historically, intravenous midazolam, lorazepam, and opioids were the mainstay sedative agents used in pediatrics. However, respiratory depression, tolerance, and withdrawal syndromes frequently complicate their use. More recently, the use of alpha-2 agonists, the administration of intravenous opioids, and the intraoperative placement of neuroaxial opioids have been used for postoperative sedation and analgesia.

9.1 Alpha-2 Adrenergic Agents

The use of alpha-2 adrenergic agonists has emerged as adjunct for pediatric anesthesia and sedation. Specifically *dexmedetomidine*, either as a sole agent or in conjunction with opioids and benzodiazepines, has evolved as a sedative agent for children [1–4].

Alpha-2 adrenergic receptors are composed of G proteins. These consist of 3 isoreceptors (alpha-2a, alpha-2b, and alpha-2c), which bind both agonists and

antagonists with similar affinity. The receptors are present in both the central and peripheral nervous system at autonomic ganglia and at pre and postsynaptic sites. Activation of central nervous system leads to sympathetic inhibition, while binding of alpha-2 agonists in the spinal cord results in analgesia. Central nervous stimulation and sympathetic stimulation in the locus ceruleus in the brainstem affect sedation and anxiolysis [5].

The titrateable alpha-2 agonist for sedation is dexmedetomidine. Dexmedetomidine is a member of the imidazolines subclass. It exhibits a high affinity to the alpha-2 receptor compared to the alpha-1 receptor. At present, dexmedetomidine is FDA approved for use in adult patients in the intensive care unit, when its use is limited to a short-term sedation of less than 24 h. However, a number of off-label uses involving the use of dexmedetomidine in children have been reported.

9.1.1 Pharmacokinetics

Dexmedetomidine is 94% protein-bound and undergoes hepatic elimination. In healthy adult volunteers, the pharmacokinetic profile of dexmedetomidine includes a rapid distribution phase $T_{1/2}$ of 6 min, a terminal elimination half-life of 2 h, and a steady state V_D of 118L. In adult patients with hepatic failure, there is an increased V_d , increased elimination half-life, and a decreased clearance [6]. Pediatric PK studies are limited. In a study of 36 children aged 2–12 years from Canada and South Africa, where patients received a 10-min infusion of one of three different doses of dexmedetomidine, Petroz, and others noted no dose-dependent changes in the kinetics and that the kinetic parameters in children were similar to that in adults [7].

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9.1.2 Pharmacodynamics

Central Nervous System: The sedative effects of dexmedetomidine are similar to the properties of natural sleep. Dexmedetomidine appears to have little effect on ICP. However, it does lower mean arterial pressure, and consequently, it reduces the cerebral perfusion pressure [8, 9] Dexmedetomidine has cerebral vasoconstricting properties and will decrease cerebral blood flow. Dexmedetomidine also lowers intraocular pressure [10].

Dexmedetomidine has been reported to have both pro and anticonvulsant properties. Dexmedetomidine lowers the shivering threshold and has been reported to be effective in treating postoperative shivering [11].

Cardiovascular System: There is generally a biphasic response to intravenous administered dexmedetomidine. The initial increase in blood pressure and decrease in heart rate results from stimulation of peripheral postsynaptic alpha-2b adrenergic receptors which results in vasoconstriction. The second phase of decrease in blood pressure and heart rate results from the central presynaptic alpha 2a adrenergic receptors stimulated by sympatholysis. Cardiac output decreases, bradycardia and sinus arrest have been reported. Myocardial oxygen consumption may decrease. The effect of dexmedetomidine on pulmonary vascular resistance is unknown [12]. Dexmedetomidine has also been reported for its anti-arrhythmic effect in the context of junctional ectopic tachycardia.

Respiratory System: Dexmedetomidine increases resting PaCO₂ and decreases minute ventilation both at rest and in response to a CO₂ challenge. However, these changes are modest compared to other sedative modalities [13, 14].

9.1.3 Dosing

The recommended dose varies depending on the need of the patient. Hemodynamic instability (increase blood pressure, decreased heart rate) is associated with rapid bolus dose administration and large doses. For sedation purposes, an intravenous bolus dose is generally followed by a continuous intravenous infusion. Initial bolus doses range from 0.3–1 µg/kg administered over 10 min. The continuous infusion is then started at 0.5–1 µg/kg/h.

The *side effects* of dexmedetomidine include over sedation, cardiovascular instability (hypertension followed by hypotension, bradycardia, sinus arrest), and an analgesic and anesthetic sparing effect. In the concentrations administered clinically, dexmedetomidine does not appear to decrease adrenocortical function.

9.2 Opioids

Fentanyl, remifentanyl, and morphine are the most commonly used opioids during general anesthesia and are continued in the postoperative period for sedation. Their predominant effect is analgesia, and they also produce sedation but do not provide any amnesia. They are seldomly used as a sole agent except when used in high doses during certain cardiac procedures or with critically ill patients. When used in the ICU it is better to administer continuous infusions to provide a constant serum concentration rather than on a PRN basis [15–18].

9.2.1 Mechanism of Action

Opioids bind to stereospecific opioid receptors in the central nervous system and peripheral tissues resulting in decreased neurotransmissions through various mechanisms, and ultimately analgesia. The Mu-1 receptor produces analgesia whereas the Mu-2 receptor has some analgesic effect but is responsible for hypoventilation, bradycardia, constipation, urinary retention, and physical dependence. Kappa receptor activation has mild analgesic properties; opioid agonists–antagonists often act at these receptors but can also result in dysphoria, which gives it a low abuse potential. Delta receptor activation is thought to modulate the activity of the Mu receptors, and therefore, its activation has similar effects as Mu receptor activation.

9.2.2 Pharmacokinetics

After IV administration, the onset of action is within minutes, the greater the lipid solubility the quicker the onset. The main elimination is by the liver with the inactive metabolites being excreted by the kidneys.

Remifentanyl is unique in that it is broken down by ester hydrolysis in the blood and skeletal muscles.

9.2.3 Pharmacodynamics

For each specific opioid, the pharmacodynamic effect depends on which receptor is bound, the binding affinity and whether the receptor is activated.

Central Nervous System: Opioids exert a potent analgesic effect, sedation, and sometimes euphoria. When given in large doses they will produce loss of consciousness and amnesia (but not reliably).

Cardiovascular System: Minimal changes in cardiac contractility, mild bradycardia, and mild decrease in SVR is due to decreased sympathetic reflexes (exception: morphine's histamine release may lead to large decrease in SVR).

Respiratory System: Opioids may induce a dose-dependant respiratory depression resulting in apnea, decreased response to PaCO₂ and hypoxia, as well as decreased cough reflex.

9.2.4 Dosing

Opioids can be administered via different routes, including transdermally, intranasally, orally, intramuscularly, intravenously, or into the central neuraxial compartment and can be dosed by either bolus or continuous infusion. Increased dosing may be needed in patients already taking long-term opioids.

9.2.5 Adverse Effects

Hypoventilation: Mediated via respiratory centers in the brainstem

Muscle rigidity: This centrally mediated muscle contraction may occur after large bolus dosing, affects mainly abdomen and chest wall, and can lead to inability to ventilate. Muscle rigidity can be treated by the administration of neuromuscular relaxants or opioid antagonist.

Nausea and vomiting: Caused by direct stimulation of the chemoreceptor trigger zone and by decreased

motility on the intestinal tract. May also cause biliary colic secondary to sphincter of Oddi contraction.

Urinary retention: Secondary to the contraction of the vesical sphincter.

Physical dependence: Tolerance and physical dependence can develop with repetitive opioid usage.

Constipation: A major problem with the chronic use of all opioids. Also one of the few side effects that a person does not develop tolerance to, and therefore, all patient receiving long-term opioids should be on a bowel regime.

9.2.6 Reversal

Naloxone is a pure competitive opioid antagonist. It is used to reverse unwanted side effects of opioids like respiratory depression and sedation; however, it will also reverse the analgesic effects and should be used with great caution in postoperative patients and patients on long-term treatment. It is dosed in 1–10 µg/kg boluses (adult dose 0.4–2 mg per dose) until the desired effect is achieved. Its peak effect is within 1–2 min, and lasts for approximately 30 min, so it should be administered as a continuous infusion if one is concerned about the return of the unwanted side effects. Side effects include hypertension, tachycardia, pulmonary edema, and even cardiac arrest.

9.2.7 Morphine

Morphine is the opioid to which all other opioids are compared. Its onset is reasonably rapid (15–30 min) after IV and IM administration and lasts up to 4 h. This slower onset is due to its relatively poor lipid solubility which slows down its penetration into the CNS and gives it a smaller volume of distribution. Its elimination half life is 115 min. It is metabolized in the liver by conjugation to glucuronic acid to form morphine 3-glucuronide and morphine-6-glucuronide which is an active metabolite. This by-product may accumulate in patients with renal disease leading to a prolonged morphine effect and potential respiratory depression.

Dosing: IV bolus for acute pain (0.03–0.1 mg/kg IV q20min); continuous infusion (0.04–0.06 mg/kg/h).

Side effects: Hypotension and histamine release (prevented by minimizing size and speed of bolus dose and keeping the patient supine), nausea, and vomiting.

9.2.8 Fentanyl

Fentanyl is an extremely potent synthetic opioid, roughly 100 times as strong as morphine. Its rapid onset and shorter duration of action is due to its high lipid solubility, however, when dosed as an infusion or in high doses it saturates inactive sites and becomes a long acting opioid-like morphine. Its elimination half life of 180–220 min is actually slightly longer than that of morphine, primarily due to its large volume of distribution. It is metabolized in the liver and its breakdown products can accumulate in renal failure which may result in poor pain control and delirium.

Dosing: IV for acute pain (1–2 µg/kg IV q10min); surgical anesthesia (50–150 µg/kg IV); continuous infusion (1–5 µg/kg/h).

Transmucosal: (fentanyl lollipop) 200–1600 µg / unit. Sometimes used as a premedication to decrease anxiety but associated with high incidence of post-operative nausea and vomiting.

Transdermal: (25–100 µg/h patch q72 h) does provide excellent stable fentanyl serum concentrations and is mostly used in the treatment of chronic pain syndromes.

Side effects: Potent respiratory depression, bradycardia, and muscle rigidity

9.2.9 Remifentanyl

Remifentanyl is a potent synthetic opioid structurally similar to fentanyl, but unique in that it has ester linkages that allow for rapid hydrolysis to inactive metabolites by blood and tissue nonspecific esterases. This makes it the only true ultra-short acting opioid with no accumulation and an elimination half life of 10–20 min, no matter how long the infusion time or how large the dose used. Its rapid onset of action is due to its high lipid solubility, like fentanyl.

Dosing: IV for acute pain (1 µg/kg IV q5 min), Continuous infusion (0.1–1 µg/kg/min).

Side effects: Potent respiratory depression, bradycardia, and hypotension (may enhance the cardiac depressant effects and muscle rigidity of other medications).

9.3 Neuroaxial Drugs

The third technique for sedation and analgesia in postoperative pediatric cardiac patients involves the use of neuroaxial drugs. In 1971, Bromage first demonstrated that the stress response associated with major abdominal and thoracic surgery could be attenuated with neuraxial blockade [19]. Neuraxial anesthesia with opioids and/or local anesthetics appears to be more effective in inhibiting the stress response to surgical intervention than intravenous opioids [20]. As efforts to fast track pediatric cardiac surgical patients increases, goals of early extubation in the operating room and earlier discharge from the intensive care unit preclude the use of large doses of systemic opioids [21–28]. Thus, alternative treatment strategies that control post-operative pain without the detrimental side effect of respiratory depression are now being used.

Neuraxial analgesia involves the use of intrathecal or epidural opioids with or without the concomitant use of local anesthetic agents. The use of neuraxial analgesia in combination with general anesthesia in children having cardiac surgery has been reported to attenuate the stress response of surgery as well as to facilitate early tracheal extubation [26–29].

The stress response is a collection of physiologic responses to surgical stimulation that include alterations in circulatory, metabolic, immunologic, and hematologic systems that can affect patient morbidity and mortality. These physiological alterations include tachycardia, vasoconstriction, catabolism, impaired immune response, and platelet activation [30, 31]. In addition, the stress response also elevates plasma concentrations of epinephrine, norepinephrine, cortisol, glucagon, β-endorphin, glucose, and lactic acid [32]. The stress response also effects thyroid function and results in a decrease in triiodothyronine (T3) [33]. Intravenous anesthetics, do not completely attenuate the stress response of surgery and CPB. Gruber et al. noted that dosing strategies using fentanyl with or without midazolam failed to blunt the hormonal and metabolic stress response in infants having cardiac surgery [34]. However, in infants, epidural analgesia with local anesthetic agents can attenuate the stress response of surgery more effectively than intravenous fentanyl [35]. In fetal lambs, total spinal anesthesia has been shown to completely block the stress response to surgical manipulation and cardiopulmonary bypass (CPBP) [36].

Other reported benefits of neuraxial analgesia in patients undergoing cardiac surgery include improved pulmonary mechanics, faster return of gastrointestinal function, enhanced cardiovascular stability, and enhanced postoperative pain relief. In addition, the benefits of earlier tracheal extubation may reduce the costs and complications associated with postoperative mechanical ventilation [21]. However, for each patient, the benefits of neuraxial analgesics must be weighed against the potential adverse effects of hypotension, postoperative respiratory depression, and epidural hematoma formation.

9.3.1 Adverse Effects of Neuraxial Analgesia

The most serious complications associated with neuraxial analgesia are respiratory depression, hypotension, and epidural hematoma formation.

Respiratory depression following epidural opioid administration is a function of drug dose and the hydrophobic/hydrophilic nature of the opioid. Hydrophobic drugs (Morphine) are more likely to cause a delayed onset of respiratory depression as a result of its greater rostral spread. Respiratory depression is unlikely with epidural morphine doses less than 0.05 mg/kg [37–40] and intrathecal doses of 0.02–0.03 mg/kg [41–43].

Systemic arterial hypotension is an undesirable side effect of both intrathecal and epidural local anesthetic administration. In adults, local anesthetic blockade of the cardiac sympathetic fibers improves coronary blood flow, alleviates angina, and improves ventricular function. However, blockade of the upper thoracic dermatomes can also produce hypotension and a decrease in coronary artery perfusion [44–49]. In infants and young children, local anesthetic blockade of T3–T5 does not result in any appreciable heart rate or blood pressure change [50]. This lack of hemodynamic effect may be related to the immaturity of the sympathetic nervous system or to a decreased sympathetic innervation of the lower extremities.

The most serious complication of neuroaxial anesthetic administration is neurological compromise from spinal cord compression, secondary to an epidural hematoma. This risk is believed to be increased in cardiac surgical patients undergoing cardiopulmonary bypass, because of the patient's need to be heparinized

for the surgical procedure, although this has not been demonstrated. The formation of epidural hematoma following spinal or epidural puncture is a rare but a potentially catastrophic complication. In an analysis of 20 adult studies involving over 850,00 epidural and 650,000 spinal anesthetics, only three case reports of epidural hematoma were documented [51, 52]. Chaney reported no cases of epidural hematoma in 4,000 adult patients undergoing vascular surgery who were administered with either epidural or spinal anesthesia prior to their being heparinized [53].

Data regarding neuraxial hematoma in children is sparse [54]. In one large study of 961 pediatric patients undergoing cardiac or thoracic surgery, in which epidural anesthesia was administered through either a caudal, lumbar, or thoracic site, blood was observed in the needle or catheter in 7.9% of patients, but no neurologic deficits were noted in any patient.

9.3.2 Techniques

Neuraxial analgesics can be administered either in the epidural or intrathecal space and the drugs can be administered either as a bolus or as a continuous infusion. Epidural techniques using a continuous infusion require a catheter to be placed in the epidural space. These catheters allow for additional dosing of local anesthetic agents and/or opioids. Because of the risk of bleeding in a heparinized patient, catheters and continuous infusions are less frequently used.

The drugs commonly used for neuraxial anesthesia include local anesthetic agents, opioids, and alpha-2 agonists. Local anesthetic agents effectively block nerve conduction and have a quick onset of action. Opioids are administered in the neuroaxial space to provide long acting analgesia. The opioids are divided into two groups: hydrophilic (morphine) and hydrophobic (fentanyl, hydromorphone). In general, the hydrophilic class of drugs tends to last longer, have a delayed onset of action, spread rostrally, and are associated with a greater likelihood of respiratory depression and sedation. Although lipophilic drugs like fentanyl do not cause respiratory depression, their analgesic effect is short lived and may not offer any more benefit than opioids administered intravenously. Alpha-2 agonists (clonidine) are frequently administered in the neuroaxial space along with the opioid and local anesthetic

combination, because alpha-2 agonists can potentiate the analgesic effects of neuraxially administered local anesthetic and opioid. In doses frequently used, clonidine (1–2 µg/kg), can also cause sedation.

The epidural technique, most commonly used in small children undergoing cardiac surgery, is the single bolus injection in the caudal space. Local anesthetic agents coupled with morphine are frequently used because of poor lipid solubility of morphine and its propensity to spread rostrally to the thoracic dermatomes [55, 56]. The caudal dose of morphine used is 0.05–0.10 mg/kg and is administered after the induction of general anesthesia. When epidural opioids are administered, co-administration of intravenous opioids can potentiate the delayed respiratory depression associated with neuroaxial opioids. Consequently, if intravenous opioids are used, they must be administered in a much lower dose and the patient must be carefully monitored.

If a continuous epidural infusion is desired, the recommended morphine dose is an initial bolus dose (0.04 mg/kg) followed by a continuous infusion (0.0075 mg/kg/h). If in the postoperative period the patient appears overly somnolent, the infusion is incrementally decreased. The continuous infusion can be continued for 48–72 h.

Another neuraxial analgesic technique used in pediatric cardiac surgery involves the *intrathecal*

administration of drugs. Intrathecal drugs require lower doses and produce a more profound analgesia and nerve block compared with epidural blocks. In general, the technique involves a local anesthetic tetracaine mixed with the opioid administered as a single bolus injection. The dose of tetracaine is adjusted for age, in accordance to the estimated volume of cerebrospinal fluid.

9.3.3 Side Effects of Neuraxial Opioids

Neuraxial opioids have some potential side effects associated with their use. These include nausea and vomiting, pruritus, urinary retention, somnolence, and respiratory depression. Nausea, vomiting, and pruritus are relatively uncommon in infants and are primarily seen in children over the age of 3 years. These side effects are more commonly seen with morphine than with hydromorphone or fentanyl [57]. Respiratory depression is also more frequently seen in association with morphine as compared to hydromorphone [44, 48] Urinary retention occurs most commonly during the first 24 h. However, the majority of patients have urinary catheters already in place. Treatment strategies for side effects related to neuraxial opioids are given in Table 9.1.

Table 9.1 Treatment strategies for side effects related to neuraxial opioids

Side effect	Treatment	Comments
Nausea/Vomiting	<i>Metoclopramide 0.1–0.2 mg/kg IV Q6h PRN</i>	Extrapyramidal reactions uncommon but occur
	Maximum dose 10 mg	
	<i>Diphenhydramine 0.5–1 mg/kg IV Q6h PRN</i>	Very sedating avoid if somnolent
	Maximum dose: 50 mg	
	<i>Ondansetron 0.1–0.2 mg/kg IV Q6h PRN</i>	May substitute other 5-HT ₃ antagonist
Pruritus	Maximum dose: 4 mg	
	<i>Nalbuphine 0.1 mg/kg IV Q6h PRN</i>	
	<i>Naloxone 0.001–0.005 mg/kg/h infusion</i>	Excessive doses may compromise analgesia
	<i>Propofol 0.5–10 mg/kg/h infusion</i>	
	<i>Diphenhydramine 0.5–1 mg/kg IV Q6h PRN</i>	Very sedating, avoid if somnolent
Somnolence	Maximum dose: 50 mg	
	<i>Nalbuphine 0.1 mg/kg IV Q6h PRN</i>	
	<i>Naloxone 0.001–0.005 mg/kg/h infusion</i>	Excessive doses may compromise analgesia
Respiratory Depression	Decrease epidural opioids infusion	Consider low dose naloxone infusion (above)
	Severe: Administer 100% O ₂	Initiate mechanical ventilation if needed
	<i>Naloxone 0.001–0.010 mg/kg IV</i>	Stop epidural infusion Mild/Moderate: Increase O ₂ as needed
Urinary retention	<i>Naloxone 0.001–0.005 mg/kg/hr infusion</i>	Reduce epidural opioids infusion
	Replace urinary catheter PRN	

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Chapter 10

Monitoring of the Cardiac Patient

Evelyn Lechner

In the cardiac patient, especially during the first postoperative night, rapid hemodynamic changes may occur. The use of invasive continuous monitoring devices helps to detect complications early. Everyone working bedside has to keep in mind that repeated careful clinical observation by the experienced nurse and medical doctor is fundamental in all bedside monitoring. If monitoring devices show ambiguous results, a careful clinical examination usually resolves the problem. The best “monitor” is the intelligent, experienced, and committed caregiver.

10.1 Basic Monitoring

Sophisticated modern bedside patient monitors are designed to match the pace and unique needs of adult, pediatric, and neonatal cardiac intensive care. They are usually easy to use, operate on a networked platform, and can be individually configured to suit specific requirements.

10.1.1 Electrocardiography (ECG)

Three lead cardiographic monitoring, ideally equipped with a 24 h real time memory function is mandatory. It allows the early detection of arrhythmias as well as brady- and tachy-cardias. Recording of a 12 lead surface ECG is performed in any suspected pathology.

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Temporary epicardial atrial pacing wires are most often seen in postoperative open-heart surgery patients and can be used for diagnostic purposes. These wires provide a method of detecting atrial electrical activity in an uncertain rhythm when the p-wave is unclear or obscured on a traditional surface ECG. A unipolar or bipolar atrial ECG can be obtained by either using the five-lead port of the ECG bedside monitor or a 12-lead ECG machine. Atrial ECGs are used to determine the relationship between atrial and ventricular activity by exaggerating the P-wave relative to the QRS-complex. Using an atrial ECG has been shown to be more accurate in diagnosing atrial dysarrhythmias as opposed to using the standard ECG recording [1] (Figs. 10.1 and 10.2).

10.1.2 Pulse Oximetry

Pulse oximetry is a simple noninvasive method of monitoring the percentage of hemoglobin (Hb), which is saturated with oxygen using a probe attached to the patient’s finger or ear lobe. A source of light originates from the probe at two wavelengths (650 nm and 805 nm). The light is partly absorbed by hemoglobin, by amounts, which differ depending on whether it is saturated or desaturated with oxygen. The oximeter is dependant on a pulsatile flow and produces a graph of the quality of flow. The unit displays the percentage of Hb saturated with oxygen. Pulse oximetry detects hypoxia before the patient becomes clinically cyanosed.

Major limitations in the use of pulse oximetry are:

- At saturations below 80% pulse oximeters have a high potential for errors. Thirty percent of values were found to be in error by more than 5% [2].

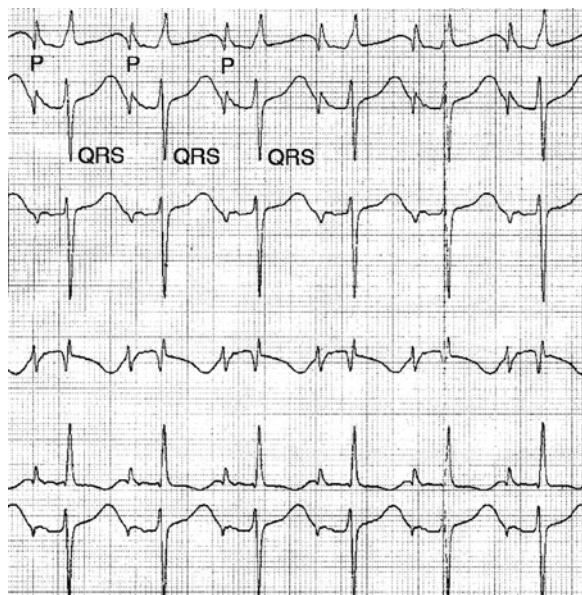


Fig. 10.1 Atrial electrocardiography (ECG) showing normal sinus rhythm. Each p-wave (P) follows a QRS-complex (QRS)

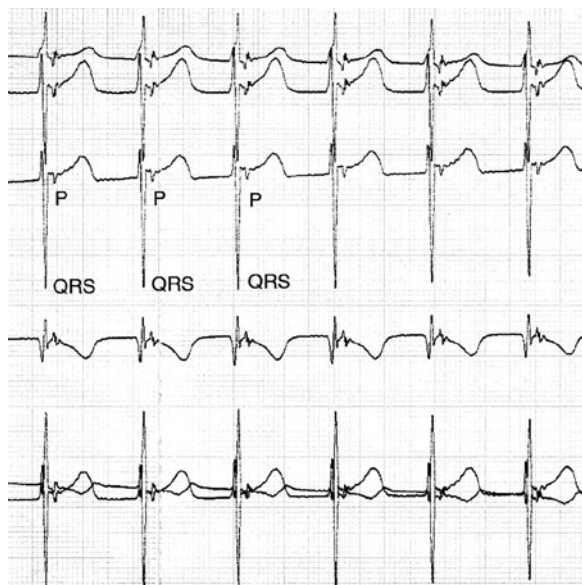


Fig. 10.2 Atrial ECG showing junctional ectopic tachycardia, where the p-wave (P) follows the QRS-complex (QRS) indicating retrograde stimulation of the atria

For children with congenital heart disease it is common to have saturations between 70 and 88%, therefore, the value of the pulse oximeter is always to be compared with blood gas analyzes of PaO_2 and should be regarded more as a useful indicator of trends.

- At saturations above 90–95%, the oxygen dissociation curve flattens out so that large changes in PaO_2

causes small changes in pulse oximetric saturation. Hyperoxia is not detectable with pulse oximetry. This fact is important in the avoidance of hyperoxia in the premature infant.

10.1.3 Transcutaneous Oxygenation (PaO_2) and Carbon Dioxide (PaCO_2) Monitoring

Transcutaneous monitoring of PaO_2 and PaCO_2 are widely used in neonatal and pediatric intensive care. A sensor is fixed to the skin over the anterior chest or the abdomen on an occlusive contact medium and held in place by an adhesive ring. Reported correlations for PaO_2 monitoring are 0.90–0.95 and for PaCO_2 monitoring 0.90–0.93 [3]. As transcutaneous derived gas tensions result from complex interactions between hemodynamic, respiratory, and local factors, which can hardly be defined in hemodynamically instable patients; these methods are of inferior value in the care for the early postoperative cardiac patients. However, in patients with prolonged ventilation the use of PaCO_2 monitoring to control mechanical ventilation is useful and reduces the need of blood gas analyzes. As in pulse oximetry, the value of the transcutaneous PaCO_2 monitoring is always to be compared with blood gas analyzes of PaCO_2 and should be regarded as a useful indicator of trends.

10.1.4 Endtidal CO_2 (ETCO_2) Monitoring

In patients with normal pulmonary function and matching of ventilation–perfusion, ETCO_2 monitoring provides an accurate estimation of arterial CO_2 . Capnometers use infrared spectroscopy in the exhaled gas to analyze the CO_2 content. In pediatric intensive care, mainstream monitors are commonly used because they can be incorporated at the proximal end of an endotracheal tube. Correlation of arterial PaCO_2 and ETCO_2 reveals important informations in the postoperative cardiac patient. An increase in the ETCO_2 may occur with increase in cardiac output, injection of bicarbonate solution, and hypoventilation. A decrease in the ETCO_2 indicates hyperventilation, decrease in cardiac output, mismatching of ventilation–perfusion, or obstruction of the endotracheal tube.

10.1.5 Blood Pressure Monitoring

10.1.5.1 Noninvasive Blood Pressure Monitoring

Oscillometry is the most commonly used means of indirect blood pressure measurement in automated devices. It is based on the principle that pulsatile blood flow through an artery creates oscillations of the arterial wall. Oscillometric devices like Dinamap® (acronym for Device for Indirect Non Invasive Mean Arterial Pressure) utilize a blood pressure cuff to sense these oscillations that appear as tiny pulsations in cuff pressure. By measuring and analyzing at various cuff pressures, the amplitude and frequency of these pulsations. Oscillometric devices can noninvasively determine blood pressure and pulse rate. Accuracy of Dinamap® blood pressures has been validated in children, and it correlates well with direct intravascular radial artery pressures [4]. Accuracy of this technique is related to the correct size of the cuff. If the cuff is too narrow the pressure recorded will be erroneously high and if too wide may be too low. The width of the inflatable bladder should be 40% of the midcircumference of the limb and the length should be twice the width.

Noninvasive blood pressure monitoring is inadequate in patients with low cardiac output, hypotension, arrhythmias with beat-to-beat changes in blood pressure, vasoconstriction, and significant edema. Due to these limitations in patients after cardiopulmonary bypass, intravascular arterial blood pressure measurement is mandatory.

10.1.5.2 Invasive Blood Pressure Monitoring

Intra-arterial access is used to provide continuous monitoring of systemic arterial blood pressure and offers the opportunity for intermittent arterial blood gas analysis. Commonly, the radial, femoral, dorsalis pedis, and posterior tibial arteries are used. Less often, the brachial and in neonates the umbilical artery can be used. Usually, percutaneous entry is possible but occasionally a cut-down may be required to get vascular access. Local insertion site complications, such as hematoma, hemorrhage, thrombosis, and infection can occur. Although the complication rates are low [5], the potential for devastating injury exists and deserves the greatest respect whenever placement of an arterial catheter is considered.

To avoid infection a closed continuous flush system with a disposable transducer monitoring system is used; all components should be kept sterile and the number of manipulations and entries into the pressure monitoring system should be minimized.

Invasive arterial blood pressure measurement reveals systolic, diastolic, and mean pressure values, and the shape of the pressure curve provides important additional informations (Fig. 10.3). The expected age-dependent arterial pressures are shown in Table 10.1.

10.1.6 Central Venous Access

Central venous lines offer the opportunity to measure central venous pressure, deliver potent drugs or high osmolarity nutritional solutions, and monitor venous oxygen saturation. The cardiac anatomy and physiology affects the information derived from pressure transduction and blood sampling and dictates the decision, where the line is placed. In the patient with single ventricle physiology who has undergone Glenn operation, a line inserted via the upper limb or neck veins measures pulmonary artery pressure. As thrombosis or occlusion of the caval vein restricts pulmonary blood flow in these patients so venous lines should be placed elsewhere. With the catheters inserted from below, an accurate assessment of central venous pressure is only possible, if the tip of the catheter reaches the inferior caval-atrial junction.

Commonly the internal or external jugular, subclavian, or femoral veins are used. In patients with complete arterial or ventricular mixing, care must be taken with line flushing or bolus since, administration of drugs infusion of air or clot has the potential to result in systemic embolism. The most common complications caused by central venous lines are thrombosis and infection. To avoid catheter related bloodstream infections, central venous catheters should be removed after a maximum of 7–10 days [6]. When signs of infection are observed catheter removal should be considered independent of the duration of placement.

10.1.7 Left Atrial Pressure Monitoring

An intraoperatively surgically-placed intracardiac line for continuous measurement of the left atrial pressure is

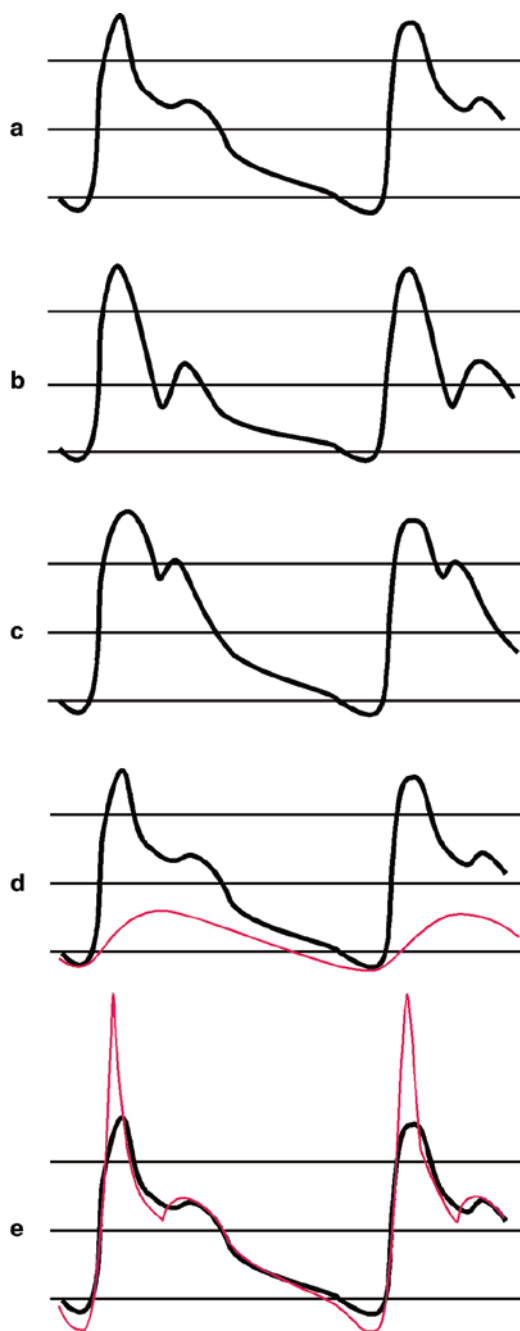


Fig. 10.3 Typical arterial wave forms: (a), normal arterial wave form, (b) low endsystolic pressure, (c) high endsystolic pressure, (d) flattened (red line) curve due to air in the system, thrombotic formations on the catheter or arterial spasm, (e) normal curve (black line) and systolic overshoot (red line), which leads to over-estimation of arterial blood pressure

helpful, especially during the early postoperative period in hemodynamically instable patients, and in elucidating atrial dysrhythmias and assessing atrioventricular

Table 10.1 Age dependent normal values of mean systemic arterial blood pressure

Age	Mean arterial pressure (mmHg)
Neonate	35–45
Infant	40–45
Small child	45–55
School age	50–65
Adolescents	60–75

synchrony during pacing. Intracardiac lines should be removed, as soon as the condition of the patient improves.

10.1.8 Pulmonary Artery Pressure Monitoring

Pulmonary artery pressure monitoring is possible via an intraoperatively placed intracardiac line or using a bedside inserted pulmonary artery Swan–Ganz catheter. Modern pulmonary artery catheters allow direct, simultaneous measurement of right atrial, right ventricular, pulmonary arterial, and pulmonary capillary wedge pressure, which reflects left atrial pressure. If the catheter is equipped with a thermistor, cardiac output can be estimated by thermodilution technique. Pulmonary artery catheter insertion may be indicated in patients with myocarditis, cardiomyopathy, pulmonary hypertension, or respiratory distress syndrome (RDS) complicating congenital heart disease. Percutaneous insertion of such catheters is best from the left subclavian or right internal jugular veins, but can also be performed from the femoral vein. The most common complications of pulmonary artery catheterization are ventricular tachycardia, pulmonary artery rupture, infection, endocarditis, venous thrombosis, and pulmonary infarction.

10.1.9 Cardiac Output Monitoring

Adequate tissue oxygen delivery (DO_2) has to be ensured in any intensive care patient. The components of DO_2 include cardiac output, blood hemoglobin concentration, and the degree of oxygen saturation of the hemoglobin molecule.

$DO_2 = \text{cardiac output} \times 1.34 \times \text{haemoglobin concentration} \times \text{oxygen saturation}$

Cardiac output measurements never should be interpreted or treated isolated, but used in conjunction with qualitative indicators of adequacy of flow (like blood lactate, mixed venous saturation, urine output, capillary refill).

10.1.9.1 Invasive Methods for Cardiac Output Monitoring

Dilution Techniques

Invasive cardiac output determination is usually done by an indicator technique, where the principle is that blood flow can be calculated after central venous injection of an indicator by measuring the change in indicator concentration over time at a point downstream of the injection site. Dye (e.g., Evans blue, brilliant red, indocyanine green) or cold saline may be used as indicator. Pulmonary artery thermodilution is the most common clinically used method. Automated systems reveal accurate and reliable measurements in adults [7], but have to be evaluated in children.

In transpulmonary thermodilution techniques the thermistor is percutaneously placed in a large artery (femoral or brachial artery). This technique is validated in children [8,9], and systems are commercially available for patients as small as 3 kg.

All dilution techniques are of limited value in the cardiac patient, because they are not accurate in the presence of intracardiac shunts or significant valvular regurgitation.

Fick's Principle

Fick's principle states that the rate of diffusion is proportional to the difference in concentration. Similarly, the volume of oxygen consumed per unit time is proportional to the difference in oxygen content between arterial and venous blood. The degree of proportionality depends on the volume of blood pumped per unit time, or cardiac output. Therefore, cardiac output can be calculated from the equation:

Cardiac Output = Systemic oxygen consumption / (systemic arterial O₂ saturation - systemic venous O₂ saturation)

This technique is limited by the difficulty of measuring oxygen consumption in the intubated and ventilated patient.

The advantage of the Fick's principle is that it can be used when an intracardiac shunt is present.

Indirect assessment of cardiac output can be accomplished by following mixed venous saturation, using a fiberoptic catheter for continuous measurement of venous oxygen saturation placed either in the pulmonary artery or right atrium. In the presence of intracardiac shunts, the saturation in the superior caval vein can be monitored to estimate cardiac output.

10.1.9.2 NonInvasive Cardiac Output Monitoring

Transesophageal Doppler Methods

This technique is minimally invasive and uses the Doppler principle and pulse contour analyzing for the estimation of blood flow in the descending aorta via an esophageal probe. Pediatric Doppler probes, which allow the use of this technique in patients of at least 3 kg of bodyweight, and a pediatric nomogram allows derivation of stroke volume and cardiac output [10,11].

Bioimpedance

In this technique voltage sensing and current transmitting electrodes are placed on the chest, which may be regarded as a conductor whose impedance is altered by changes in blood volume and velocity with each heartbeat. In the postoperative cardiac patient this technique is limited, because it is less accurate in the presence of skin edema.

10.1.10 Near Infrared Spectroscopy (NIRS)

Probes placed on the skin of the forehead provide a continuous, noninvasive method to measure regional changes in cerebral tissue oxygenation. The regional cerebral oxygenation has been shown to correlate with SvO₂ in children with cyanotic and noncyanotic heart defects during cardiac catheterization [12], cardiac surgery [13] and in the postoperative cardiac patient [14], as well as in critically ill neonates without congenital heart defect [15]. This technique is increasingly

used in postoperative cardiac intensive care, where in special conditions it is extremely helpful like in estimating cerebral blood flow in patients after bidirectional Glenn–Shunt or in patients with extracorporeal life support.

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Chapter 11

The Effects of Cardiopulmonary Bypass Following Pediatric Cardiac Surgery

Ana Maria Manrique, Kent Kelly, and Steve E. Litchenstein

The recent advances in pediatric cardiac surgery have focused on early primary repair and shown a marked improvement in outcome. Currently, the average mortality is 3.5% in children older than 1 year of age undergoing open-heart surgery and between 10 and 40% for repair undertaken in the neonatal period.

Intra-operative advances include a better understanding of the inflammatory process caused by cardiopulmonary bypass (CPBP) and its management. Astonishing changes have arisen since Gibbon's first CPBP in 1953. However, postoperative problems induced by CPBP, which include vital organ damage, and neurologic dysfunction are a current challenge in the management of pediatric patients undergoing cardiac surgery.

The deleterious effects of CPBP are related to the activation of cellular and humoral inflammatory pathways in response to the exposure of the circulating blood volume to the cardiopulmonary bypass circuit.

11.1 Physiologic Differences and Inflammatory Response to CPBP in the Pediatric Population

The cellular activation and the release of cytokines produced by CPBP have a great impact on physiologic function.

Some of the most relevant physiological differences between pediatric patients and adults explain the significant changes required for the management of CPBP in children.

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Some of the most important differences include the following:

1. Larger priming volume of the CPBP circuit relative to the blood volume of the small child
2. Immaturity of the liver
3. Immaturity of the hemostatic and immunological systems
4. Increased renal vascular resistance and decrease in renal perfusion and glomerular filtration rate
5. High pulmonary vascular resistance in newborns.

The transition in cardiopulmonary circulation toward the mature state during the first 6 months after birth and its development is not complete until the second to third year of life. During this critical period, any alteration in the pulmonary artery pressure and flow may produce permanent anatomic changes in the pulmonary peripheral vasculature. Furthermore, the pulmonary vasculature in newborns is even more sensitive to other metabolic alterations such as hypoxemia, hypercarbia, acidosis, and hypothermia [1].

11.2 Inflammatory Response to CPBP

CPBP induces a complex systemic inflammatory response (SIRS), which involves the activation of multiple, interdependent cellular pathways.

Polymorphonuclear cell activation releases proinflammatory cytokines such as interleukins (IL-1, IL-6), tumor necrosis factor (TNF- α), adhesion molecules, and chemokines (IL-8, monocyte chemoattractant protein). This produces endothelial cell injury, adhesion molecule up-regulation, and the initiation of the coagulation cascade.

The activated leukocytes have three phases:

1. *Rolling*: The leukocytes form temporary bonds with the endothelium; this is mediated by a selectin
2. *Adhesion*: Stronger bonds are formed through the interaction between leukocytes, integrins (CD11, CD18), and intercellular adhesion molecules (ICAM-1, ICAM-2)
3. *Migration*: The leukocytes migrate into surrounding tissues assisted by interleukin-8 and platelet-endothelial cell adhesion molecule-1.

The complement system plays a central role in the systemic inflammatory response. Over 20 proteins and protein fragments make up the complement system. The end result of its activation is a massive cascade and amplification of the cellular response and activation of the cell-killing membrane attack complex. The complement system has two pathways: classic and alternative (Fig. 11.1).

The *classic pathway* is initiated through the interaction of protein C1 with foreign cell regions of antibodies bound to the target antigens. The *alternative pathway* is an antibody-independent pathway that is activated by numerous triggers such as foreign surfaces, damaged tissue, shear forces, tissue plasminogen activator (tPA), and hypoxia-induced, oxygen-derived free radicals. These triggers amplify the continuous low-level basal activation of C3. The complement system is activated by components of other inflammatory pathways such as kallikrein, plasmin, thrombin, and factor XII [2, 3].

All of these pathways ultimately converge to form C3 convertase, an enzyme that cleaves C3 to its activated form C3a and C3b. C3b subsequently cleaves C5 to generate C5a, a potent anaphylatoxin, and C5b, which binds C6, C7, C8, and C9 to form C5b-9, the membrane attack complex.

The membrane attack complex creates a trans-membrane channel that allows the influx of ions and

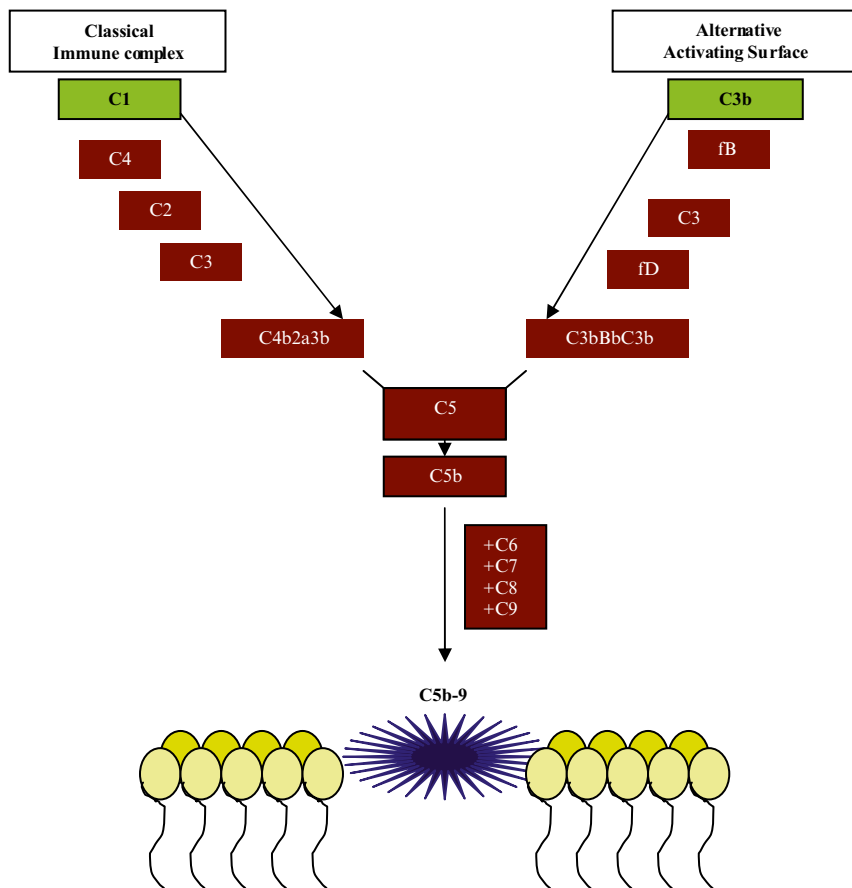


Fig. 11.1 Complement system activation

water into the cell, which disables the maintenance of osmotic and chemical equilibrium and ultimately leads to cell lysis and death.

In addition, the membrane attack complex induces the up-regulation of leukocyte adhesion molecules and the secretion of interleukin and chemokines.

The activation of the complement produces contraction of the smooth muscle and the endothelium, increase in vascular permeability, activation of neutrophils, production of oxygen-derived free radicals, and release of histotoxic products.

The CPBP also generates the activation of the coagulation system and the production of thrombin, which activates platelets and endothelium-inducing chemotaxis of the monocytes and neutrophils. The fibrinogen produced contributes to the inflammatory response by up-regulating the production of cytokines and chemokines [4, 5].

It has been reported that levels of proinflammatory cytokines (TNF- α , IL-1, IL-6, IL-8) are correlated with the duration of CPBP, myocardial ischemia, and the development of multi-organ failure. The systemic response from the ischemic/reperfusion injury during CPBP results in pulmonary dysfunction, excessive total body fluid, and low cardiac output [6].

The inflammatory response during CPBP is worse in pediatric patients than in adults. The causes of this amplified response are related to:

1. Hemodilution
2. Longer surgical time
3. Changes in temperature
4. Deep hypothermic circulatory arrest
5. Lower perfusion rates
6. Higher shear stress of blood cell components
7. Higher metabolic requirements
8. Variable response to anticoagulation due to immaturity of the system

11.3 Coagulation System

Bleeding and alterations in the coagulation system are some of the most common causes of morbidity and mortality after pediatric cardiac surgery.

Clotting and fibrinolysis are balanced in an auto-regulated coagulation that maintains its integrity by the interaction between its components.

Infants and children have an imbalanced system with most of the components differing in plasma concentrations compared with adults. Coagulation factors II, VII, IX, X, XI, XII, pre-kallikrein, high-molecular-weight kininogen (HMWK), antithrombin, Protein C and S, and heparin cofactor II approach 50% of the adult levels secondary to hepatic immaturity and more rapid clearance. Factors VIII, XIII, V, fibrinogen, and von Willebrand factor are close to adult levels. Inhibitors of coagulation, such as C1 esterase, exceed adult normal values. Furthermore, underlying congenital disorders are associated with additional alterations in the coagulation system.

CPBP causes a severe imbalance between the prothrombotic and fibrinolytic systems. This effect is produced by several factors:

Hemodilution can decrease coagulation factors over 50%.

Hypothermia decreases activity of Antithrombin III. Furthermore, low temperature is associated with loss of platelet adhesion receptors.

Direct damage to the endothelial surface stimulates the contact activation system (factor XII and XI, pre-kallikrein, and HMWK).

Generated kallikrein and HMWK will produce bradykinin and plasminogen activating the fibrinolytic system.

Activation of factor XII will initiate the coagulation pathway.

Those effects will result in the down-regulation of anticoagulant components and the up-regulation of procoagulant components.

The activation of the coagulation and kallikrein systems will result in microvascular thrombosis, ischemic–reperfusion injury, and the elaboration of inflammatory mediators. The formation of diffuse microemboli will result in a microcirculatory “no-reflow” phenomenon that increases ischemia–reperfusion injury [7].

In children, postoperative bleeding is mainly associated with platelet dysfunction after CPBP.

11.4 Pulmonary System

Pulmonary complications after CPBP in pediatric cardiac surgery are associated with:

1. Chest wall is highly compliant, resulting in a relatively low transpulmonary pressures and an increased tendency for collapse of the small peripheral airways.
2. Inflammatory response of the pulmonary epithelium in association with CPBP
3. Previous changes in the mechanical properties of the lung associated with congenital heart disease
4. Decrease in compliance after CPBP

Clinical consequences of these effects are

5. Atelectasis/microatelectasis: decrease or interruption of the pulmonary circulation (after aortic clamping), results in a decrease in lung volume and an increase in viscous resistance and elastance of the parenchyma, therefore a loss in the stability of the alveolar geometry.
6. Decrease in functional residual capacity (FRC):
7. Hydrostatic pulmonary edema
8. Inflammation of the alveolar epithelium
9. Hypoxemia and alteration of the gas exchange: Lung ischemia induces an inflammatory response by the release of tumor necrosis factor α and IL-8 from endothelial cells. After lung postischemic reperfusion, pulmonary neutrophil activation and release of myeloperoxidase cause direct injury to lung ultrastructure [8].

Maintaining ventilation and pulmonary artery perfusion during CPBP have shown some benefits in limiting pulmonary platelet and neutrophil sequestration; however, maintaining ventilation during CPBP may affect the degree of lung ischemia by altering the balance of collateral blood flow to the lungs, and bronchial mucosal blood flow [9].

11.4.1 Myocardial Ischemia/Reperfusion and Surgical protection

The Pediatric Myocardium: The myocardial structure changes after delivery, with a progressive increase in the number of muscular fibers and an evolving organization of the myocytes.

1. In the newborn only 30% of the myocardial mass comprises contractile tissue compared with 60% in the mature myocardium.

2. Pediatric myocardium has fewer mitochondria and less oxidative capacity.
3. Autonomic innervation is incomplete after birth, with less sympathetic innervation and decreased catecholamine reserves
4. The immature myocardium is more sensitive to extracellular calcium levels than mature myocardium
5. In mature hearts most of the calcium required for myocardial contraction is provided by the sarcoplasmic reticulum. However, in the immature heart the T-tubular system and the sarcoplasmic reticulum are underdeveloped with reduced capacity for calcium.
6. The activity of the sarcoplasmic ATPase responsible for calcium reuptake into the sarcoplasmic reticulum is also reduced. Thus, the ability of immature myocardium to release calcium after the stimulation of the sarcoplasmic receptors is decreased.
7. Immature heart has lower intracellular calcium concentration with a greater dependence on extracellular calcium levels
8. Immature myocardium depends on glucose oxidation as energy provider (in adults, fatty acids are the most important source of energy)
9. Acidosis and production of free radicals during ischemia are increased due to its decreased capacity for antioxidant enzymatic activity.
10. The immature myocardium has a decreased ventricular compliance and is more vulnerable to stretch injury.
11. Both ventricles are arranged in series; the right ventricle (RV) function may significantly affect the left ventricular (LV) function through ventricular interdependence. RV end-diastolic volume increases owing to increased RV loading; it can only occur at the expense of the space devoted to the left ventricle, this reduced LV end-diastolic volume is accompanied by decreases in LV diastolic compliance.
12. Cardiac output in pediatric patients is more dependent on heart rate and sinus rhythm.
13. Increase on afterload will produce significant hemodynamic impairment.
14. Despite the greater tolerance of the immature myocardium to ischemia, the ultimate myocardial performance will depend on the degree of ventricular distension [10].

Cardioplegia: A solution composed of crystalloid and/or blood, nutrients, and electrolytes that permit an

elective temporary cessation of cardiac activity. It is used during cardiac surgery to protect the heart from ischemic injury and postoperative heart failure. The solution is administered in an initial dose of 20 ml/kg through the aortic root after aortic cross clamping followed every 20–30 mins by a dose of 10 ml/kg. In some circumstances (i.e., severe aortic regurgitation), it may be administered retrogradely through the coronary sinus.

Cardioplegia composition varies widely and currently there are more than 150 types. The most common solution used contains a high concentration of potassium, which produces a depolarization arrest. The other essential components of the cardioplegia include buffering agents, free radical scavengers, and energy substrate supplementation [11].

Metabolic myocardial stress occurs during ischemic arrest with cardioplegia and is associated with inadequate suppression of metabolism. The first structural change after cardioplegia is an increase in permeability of the capillaries resulting in edema. This occurs early on and can be documented immediately after aortic clamping. The lesions involve both endothelium and the myocytes. More severe irreversible changes in the myocardium are the consequence of ischemia with an imbalance of sodium ions and changes in the levels of calcium ions. There is not a definitive clinical trial indicative of the most effective cardioplegia solution or technique.

Most of the studies that compare crystalloid and blood cardioplegia have been unable to demonstrate differences in clinical outcomes between them. However, the use of blood cardioplegia has been associated with a lower reduction in myocardial adenosine triphosphate (energy substrates), lower plasma troponin I, and lower lactate plasma levels, all those indicating a lower grade of ischemic injury. Furthermore, decreased incidence of early postoperative LV dysfunction and mitral regurgitation are associated with the use of blood cardioplegia. Hypothermia or cold cardioplegia provides additional protection to the myocardium [12].

11.5 Neurologic system

Neurologic dysfunction remains the most significant complication associated with CPBP. One third of

patients with congenital heart disease have neurologic abnormalities including:

1. Cerebral dysgenesis
2. Alteration in cerebral blood flow
3. Alteration in neuronal repair (genetic polymorphisms of apolipoprotein E)
4. White matter injury
5. Cerebral atrophy changes

Neonates have a particular vulnerability to hypoxia, chemical, and inflammatory injury. The incidence of periventricular leukomalacia in this group after surgery has been reported as high as 54%.

The mechanisms of central nervous system (CNS) injury in infants undergoing cardiac surgery include:

1. Hypoxia (ischemic/reperfusion injury)
2. Emboli
3. Inflammatory microvasculopathy
4. Activation of oxygen-derived free radicals

Oxygen-derived free radicals cause cellular apoptosis, they are produced at multiple sites within the CNS, including leukocytes, endothelium, mitochondria, and local inflammatory cells. After periods of ischemia and reperfusion, some areas remain without perfusion; the so-called “no-reflow” phenomenon. There are two main components of the “no-reflow”: “physiologic” related to sustained vasoconstriction after injury and “mechanical” caused by obstructed capillary beds.

Younger patients with complex surgery and prolonged deep hypothermic circulatory arrest (DHCA) or those with circulatory support prior to surgery have an increased risk for postoperative neurologic injury.

Early neurologic complications include stroke, cerebral bleeding, and seizures. Long-term outcomes focus on neurodevelopmental activity such as abnormal school performance, learning disabilities, and behavioral issues.

11.5.1 Neurologic Protection and Selective Perfusion

Neuronal injury is produced by the release of accumulated metabolic products during reperfusion and to the leukocyte activation process. Factors associated with neurologic outcome include:

1. Type of perfusion strategy
2. Temperature
3. pH management
4. Hematocrit management
5. Glucose management
6. Oxygenation strategy
7. Pharmacological protection
8. Systemic Inflammatory response
9. Presence of aorto-pulmonary collaterals

11.5.1.1 Perfusion Strategy

Several strategies have been developed to achieve neurologic protection: In 2001, Pigula et al. [13] reported on the application of selective cerebral perfusion whereby surgical correction of complex aortic arch pathology was accomplished without prolonged periods of DHCA. Both cerebral hemispheres were perfused by way of the right innominate artery using low flow techniques. Since then, several modifications have been made according to the surgical group's preferences. In general, those techniques include:

1. Intermittent perfusion
2. Regional, continuous low-flow and selective cerebral CPBP
3. Low-flow CPBP
4. Deep hypothermic circulatory arrest

Intermittent Perfusion (IP)

This technique is achieved with the use of full pump flow for 2 min every 20 mins during DHCA. The required rate is 80 ml/kg/min. Intermittent systemic recirculation during DHCA prevented cerebral anaerobic metabolism. Experimental studies demonstrated that IP reduces astroglial changes and no-reflow phenomenon when compared to DHCA.

Regional, Continuous Low-Flow and Selective Cerebral CPBP

Selective cerebral perfusion has evoked renewed interest in recent years, and has become the primary brain protection method in many centers. Regional low-flow perfusion (RLFP) can be used to limit or exclude the use of circulatory arrest. Direct cannulation of the

innominate artery and selective clamping of the proximal innominate, left carotid, and left subclavian arteries, achieves continuous regional brain perfusion. Flow rates vary between 20 and 30 ml/kg/min. Continuous low-flow and SCP are associated with the preservation of cerebral energy stores, improved cerebral perfusion, histologic outcome, and neurologic function when it is compared with prolonged DHCA (60–120 min). However, it cannot be reliable in 40 min DHCA. SCP extends the period during which surgical procedures on the arch can be safely performed. The incidence of neurologic impairment ranges from 2 to 30% independently of the neurologic protection strategy used [14].

Several studies have demonstrated that low-flow bypass is superior for high-energy phosphate preservation, cerebral oxygen metabolism, CBF, cerebral vascular resistance, and lower brain lactate levels. The minimum safe level of low flow has not been established. In a prospective, randomized study from Boston, children with transposition of the great arteries underwent repair using low-flow CPBP at 50 ml/kg/min. However, the neurologic outcome is directly associated with the temperature and perfusion pressure used during the low flow. The same study from Boston indicated that a minimum cerebral perfusion pressure of 13 mmHg was necessary to maintain flow during hypothermic bypass. Finally, the Boston group found in this study that children who had DHCA had lower motor function scores and had more speech abnormalities than those who had low-flow bypass [15].

11.5.1.2 Hypothermia and Deep Hypothermic Circulatory Arrest (DHCA)

Hypothermia produces:

1. Decrease in cerebral metabolism and energy consumption (cerebral metabolic rate decreases 5–7% for each degree Celsius decrease in body temperature).
2. Reduce the extension of degenerative processes including the excitotoxic cascade, microglial activation, oxidative stress, and inflammation.
3. Suppress specific pathways of the apoptosis, such as cytochrome C release, caspase activation, and DNA fragmentation.

These properties of hypothermia help in the process of organ protection. However, excessively low temperatures in the myocardium may cause a sudden release of

intracellular calcium increasing the resting myocardial tone interfering with the recovery function during the rewarming.

In children, hypothermia during cardiac surgery is usually performed with moderate temperature (28–32°C).

DHCA was introduced 30 years ago. It involves the complete cessation of the CPBP flow when the temperature is close to 15–18°C. It is a useful tool to perform complex congenital cardiac repair during a longer period with a clean surgical field.

The metabolic requirements decrease with hypothermia, therefore the flow rate is decreased. The decrease in the flow rate permits a better exposure of the structures in the surgical field.

The cooling should occur slowly with a difference between arterial and venous temperature of no more than 4–6°C. During the rewarming phase, the temperature gradient between the venous and the arterial blood should be not more than 10°C. Time on DHCA is also an important factor; prolonged exposure (>40 min) is directly correlated with neurologic impairment. Currently, hypothermia is a subject of study in terms of neurologic protection and long-term outcomes.

The Boston Circulatory Arrest Trial prospectively observed the neurological outcome of 171 neonates with D-transposition of the great arteries that were randomized either to DHCA or to low-flow CPBP for the arterial switch operation. In the immediate postoperative period, the incidence of seizure activity was higher in the DHCA group. One year after surgery, children of the DHCA group had a higher risk of delayed motor development compared with the low-flow CPBP group, and the risk of neurologic abnormalities increased with the duration of circulatory arrest. In the same study investigators found nonlinear relationship between the duration of DHCA and neurodevelopmental outcomes; however, there was no significant decline in the neurologic outcomes in children subjected to a period of DHCA lasting less than 41 min. After 8 years of surgery there were no differences in neurologic development between the groups [16].

11.5.1.3 pH Management During CPBP (pH stat–Alpha stat)

The optimal pH management strategy for cardiovascular procedures use cardiopulmonary bypass, and hypothermia is unknown.

The two main strategies used are *alpha-stat* and *pH-stat*.

Changes of the Acid–Base Status with Temperature

During cooling, the CO₂ increases in solubility and produces a decrease in the paCO₂ resulting in a metabolic alkalosis (with a high pH).

Body temperature of poikilotherms or cold-blooded animals directly varies with the ambient temperature. They permit an increase in their blood pH when they are at a lower temperature, which approximates alpha-stat management. Conversely, deep hibernators or warm-blooded animals do not drop temperature more than a few degrees during the winter season. In spite of its low body temperature, the hibernating animal retains a remarkably rigid control of its internal environment; its pH remains at 7.40. It requires an increased total body CO₂ content to maintain neutrality. This is achieved with a relative acidification of the intracellular fluids produced by the adoption of a modified breathing pattern that is typified by periods of apnea lasting up to 2 h that are interspersed with 3–30 min intervals of rapid ventilation. This approach is pH-stat management.

For pH management during CPBP, these two strategies have been adopted. When the *alpha stat* strategy is used, the pH is allowed to freely arise without performing any correction to the ABG. With *pH-stat* strategy, the ABG's are mathematically corrected for the actual temperature and carbon dioxide is added to reach a normal pH (7.40).

pH-stat strategy: causes cerebral vasodilatation above metabolic demands (loss of autoregulation) and a more homogenous cooling. Defenders of the pH-stat management argue:

1. Improvement in oxygen delivery by counteracting the leftward shift in the oxyhemoglobin dissociation curve associated with alkalosis.
2. Increased cerebral blood flow.
3. Suppression of cerebral metabolic rate.
4. pH-stat is particularly beneficial in cyanotic neonates and infants because it shifts more CPBP flow away from the aortopulmonary collateral circulation and toward the cerebral circulation, both improving cerebral cooling and oxygen supply.

During cooling the addition of CO₂ could potentially improve the distribution of the cold perfusate to deep brain structures.

However, while pH-stat facilitates earlier peri-operative return of electroencephalographic activity, developmental and neurological outcomes revealed no significant differences attributable to pH management strategy. Other disadvantages include that low intracellular pH results in impaired intracellular enzymatic function.

Alpha-stat requires that neutrality is maintained only at 37°C, and permits the hypothermic alkaline drift. Thus, additional CO₂ is not needed and cerebral autoregulation is maintained.

Defenders of the *alpha-stat* argue:

1. Preserves cellular transmembrane pH gradients, intracellular electrochemical neutrality, protein functioning, and enzyme activity are more normal when the pH is allowed to drift alkaline in parallel with the temperature. This concept is based on the notion that the pK of the histidine imidazole group changes with temperature in a manner nearly identical to physiologic blood buffers. Therefore, the ionization state of this group stays the same, irrespective of temperature. Ionization state is a determinant of intracellular protein function.
2. Relatively alkaline pH is beneficial before the ischemic insult of circulatory arrest. Despite considerable laboratory and animal research into these mechanisms, substantial controversy remains.

Some studies have shown significantly higher cerebral oxygenation when a pH-stat strategy is used at the end of cooling and during early rewarming. However, the higher cerebral blood flows associated with pH-stat also have the potential to carry more particulate emboli. In addition, the relative acid load induced by pH-stat had a negative effect in the enzymatic function after cerebral rewarming.

Results from several studies favor the pH-stat strategy during neonatal cardiopulmonary bypass. Data also suggest that pH-stat management results in better outcomes with shorter ventilation times and intensive care unit stays after pediatric cardiac surgery. In 2000, the group from Duke proposed the use of a combined strategy with pH management during cooling, followed by an *alpha-stat* strategy before the initiation of cardiac arrest. Currently, the use of moderate hypothermia may reduce the importance in the management on these strategies [17–19].

11.5.1.4 Hematocrit and Hemodilution

Hemodilution during CPBP was introduced in the 1950s to decrease homologous blood use and to improve microcirculatory flow. During moderate hemodilution, total body oxygen delivery is maintained because of reduced blood viscosity and vascular resistance, resulting in an increased tissue blood flow.

The adequate hematocrit level during pediatric cardiac surgery is not clearly defined. Physiologically important changes in cerebral oxygen supply might occur at hematocrit levels of 12% at 18°C, 15% at 28°C, and 18% at 38°C under CPBP conditions [20].

Higher levels of creatine kinase-BB (CK-BB), a marker of brain injury, are seen in children with low hemoglobin levels during the first hours after DHCA [14]. In addition, children with low hematocrit had worse peri-operative outcomes with decreased cardiac index and higher serum lactate levels. Evidence of better neurologic protection has been demonstrated with a hematocrit level of 30%. In the author's experience, hematocrit level during CBP are maintained not lower than 23%.

11.5.1.5 Aorto-Pulmonary Collaterals

Aorto-pulmonary collaterals decrease the rate of cerebral cooling, blood flow, and increase cerebral metabolic derangement after DHCA. Their presence has been associated with high incidence of choreoathetosis.

11.5.1.6 Oxygenation Strategy

At low temperatures, the quantity of dissolved oxygen is increased. Hyperoxia may be beneficial because the brain uses mainly dissolved oxygen during profound hypothermic cardiopulmonary bypass.

11.5.1.7 Glucose Management

Causes of hyperglycemia during heart surgery:

1. Glucose-containing fluids
2. Stress response
3. Changes in insulin secretion and resistance

The correct glucose level during cardiac surgery is not known.

During cerebral ischemia, hyperglycemia may increase the release of excitatory neurotransmitters. By contrast, in the adult population, hyperglycemia is not associated with neurologic impairment; instead, hypoglycemia is deleterious and should be avoided [21].

Experimental pharmacological neuroprotection has not been proven as beneficial but in clinical practice some of the medications used have included thiopental, steroids, and aprotinin.

11.6 Circuit

11.6.1 Cannulation and CPBP Initiation

11.6.1.1 Venous Cannulation

When a bicaval cannulation is necessary, the cannulation is performed using right-angle cannulae into the superior vena cava and the inferior vena cava. These cannulae decrease the risk of flow obstruction. Special considerations are required with the presence of a left superior vena cava or interrupted inferior vena cava. Venous cannulation is also achieved with a single cannula inserted into the right atrium. This type of cannulation is preferred if the atrium does not need to be opened or when DHCA will be used.

11.6.1.2 Arterial Cannulation

This is performed with a single cannula into the aortic root (some cases require a different position according to the surgery). The size of the arterial cannula should be wide enough to provide adequate flow without causing obstruction or trauma to the aorta. As with venous cannulation, adequate position of the cannula is crucial.

When the arterial and the venous cannulae are in adequate position, they are connected to the circuit. The venous blood is drained by gravity into the venous reservoir and then using either a roller or centrifugal pump, pumped through the oxygenator (which has an integrated heat exchanger) back into the systemic circulation through the arterial cannula. (Fig. 11.2)

The development of new reservoirs and oxygenators has reduced the priming volume used in pediatric extracorporeal circuits. This significant hemodilution

produces a deep effect over all systems including impairment in hemostasis. This effect also requires the use of blood products increasing the risk of infection, allergic reactions or immunologic responses. Additionally, there can be endothelial damage related to non-laminar flow generated during the CPBP.

In the past several years, CPBP has been vastly improved in terms of using superior circuit components [22].

11.7 Components of CPBP

11.7.1 Pumps

Currently, there are two types of pumps available for pediatric cardiac surgery: *Roller* and *centrifugal*.

Roller pumps are preferred to control low-flow when needed. Moreover, their compatible circuit requires the lowest prime volume. Each revolution propels the blood forward in the tubing (Fig. 11.3). Roller pumps are able to deliver <0.5 L/min.

Centrifugal pumps entrain the blood into the pump by a high-speed rotor, spinning impeller blades, or rotating cones. Those pumps were less used in the past due to their inability to provide low flow rates. The flow generated depends on afterload. They are less traumatic to the blood cells.

11.7.2 Tubing

There are two types of clinically relevant heparin-coated circuits:

1. Heparin-releasing surfaces
2. Heparin-immobilizing surfaces

The first subgroup, heparin is bound so that it may be slowly released into the circulation directly from the surface. The second subgroup includes those surfaces with heparin covalently immobilized on the polymer surface.

A third new group of biocompatible surfaces uses properties of modified protein adsorption, which secondarily influence biocompatibility. It is believed that the addition of alternating hydrophilic and hydrophobic

Fig. 11.2 Schematic diagram of cardiopulmonary bypass circuit

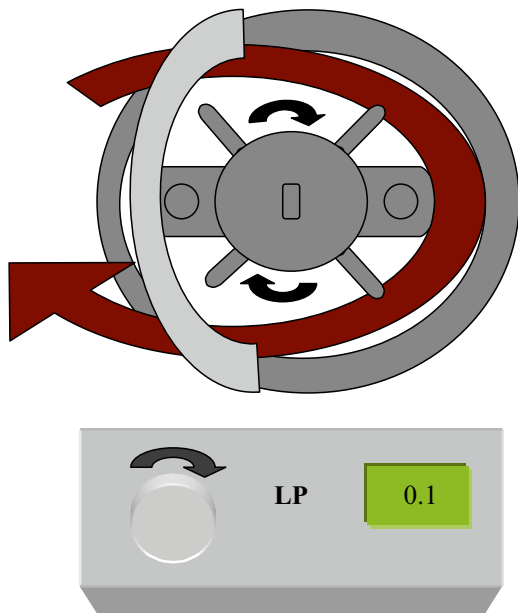
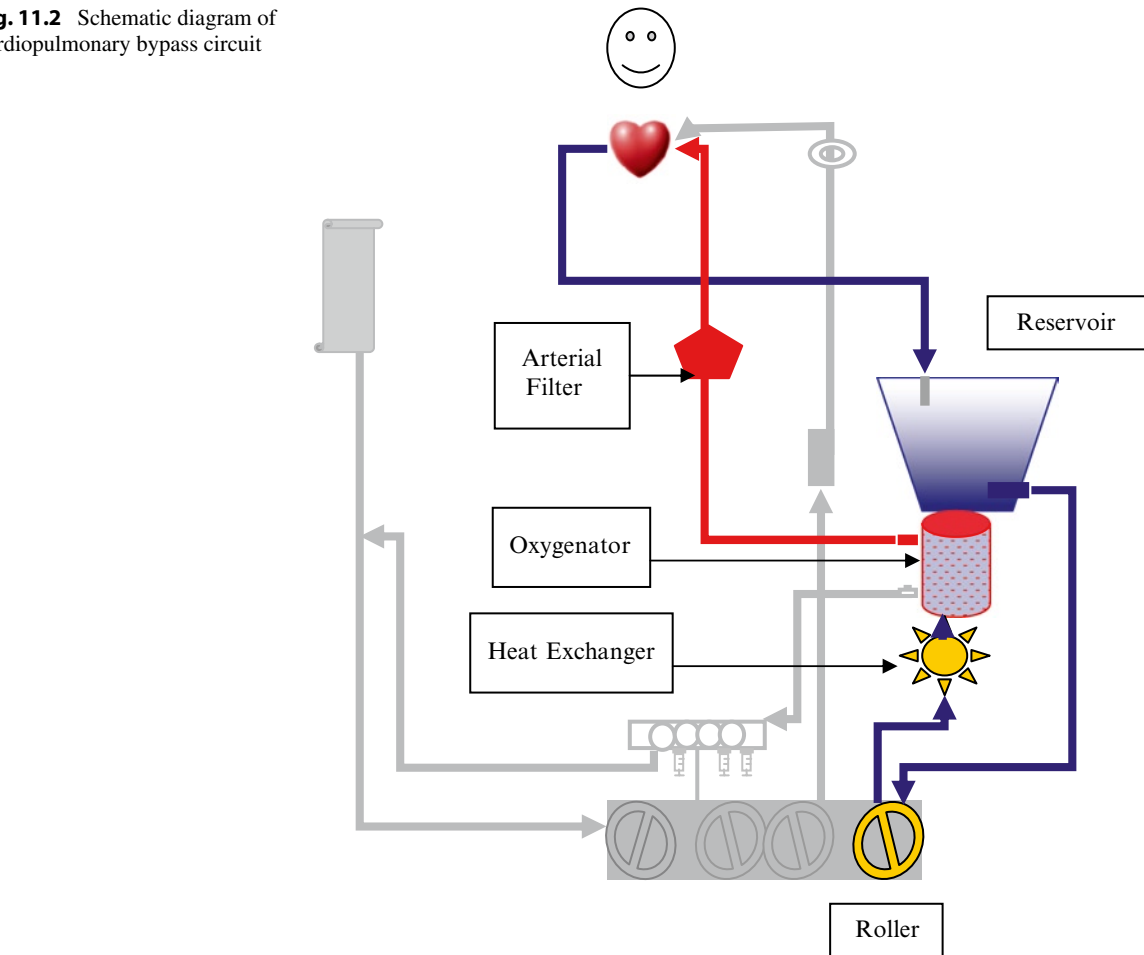


Fig. 11.3 Roller pump

regions modify fibrinogen adsorption, thus changing its ability to interact with circulating platelets. Some studies of the use of these circuits are associated with a drop in tissue plasminogen activator release and preservation of platelet numbers with less platelet activation.

11.7.3 Oxygenators

Oxygenators are able to perform gas exchange, and are the place where volatile anesthetics can be delivered. New oxygenators are being developed for use in pediatric cardiac surgery that require less priming volume. The smallest oxygenator available is 0.3 m² in surface area developed to provide less than 0.8 lpm of flow. Historically, rotating disks and bubbles were used during the first CPBP and were associated with massive air embolism. Currently, the oxygenators that are used are membrane oxygenators, there are two types:

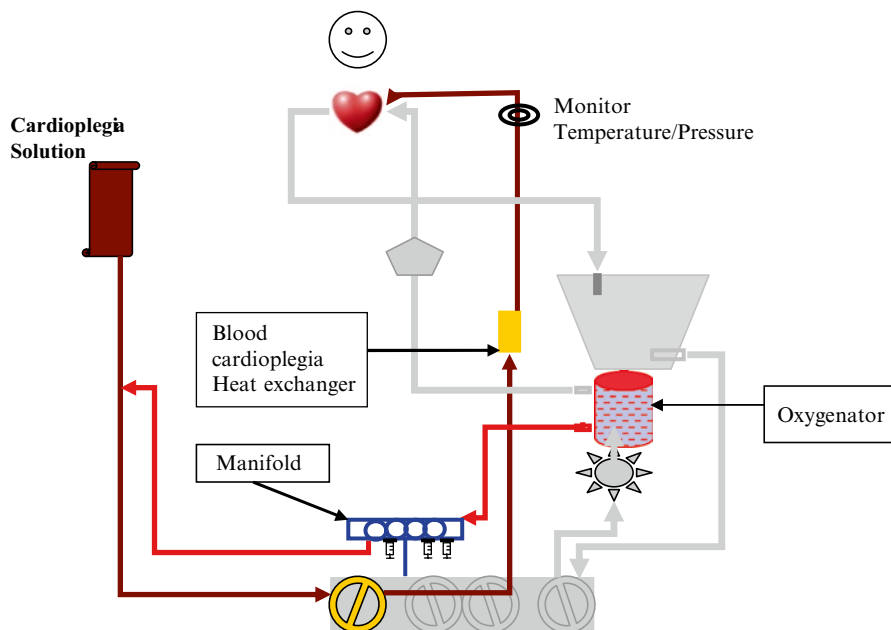


Fig. 11.4 Cardioplegia delivery system

“True membrane” and micro-porous membrane. Hollow fiber oxygenators are a type of membrane oxygenator made up of polypropylene fibers, which are porous. The new oxygenators are smaller and allow high flow rates with higher gas transfer rates. Hollow fiber oxygenators cannot be used for a prolonged period because of the leak of proteins and serum through the small pores. These proteins can occlude the membrane and decrease its efficiency.

The *heat exchanger* is integrated into the oxygenator and allows cooling and rewarming of the blood.

11.7.4 Venous Reservoir

The venous reservoir is the component of the CPBP where blood is collected from the venous line at the initiation of the CPBP. Transfusion products, crystalloids solutions, and blood obtained from suction systems (which aspirate blood and air from the field and the heart chambers) drain into the reservoir as well.

11.7.5 Cardioplegia Delivery System

This system is connected to an independent roller pump to drive blood from the cardioplegia solution

into the aortic root. The system also has an independent heat exchanger, and the pressure and temperature are also independently monitored. Blood from the oxygenator is mixed with the crystalloid cardioplegia solution before transfer to the aortic root (Fig. 11.4).

11.7.5.1 Venting of the Left Heart

The left ventricle normally receives venous blood flow from the bronchial and Tebesian veins during CPBP, this flow is collected in the right superior pulmonary vein. Bronchial blood flow is increased in cyanotic patients and abnormal blood flow to the left ventricle is present in patients with left superior venous cava, PDA or aortic regurgitation. Adequate drainage of the left ventricle prevents distension, decreases wall tension, improves subendocardial perfusion, and also improves surgical exposure. The decreased wall tension and improved subendocardial perfusion are essential to the pediatric population where the compliance of the small chambers is decreased.

11.7.5.2 Filters and Bubble traps

Micropore filters trap the air decreasing the risk for embolization. They are located at various sites through

the system. Leukocyte-depleting filters prevent the activated leukocytes from reaching the systemic circulation although their clinical benefit has not been proven.

Residual blood from the CPBP after finish support can be processed by the cell saver and is usable during the first 4 h after surgery, it is an usual practice from our surgical group.

Small improvements in early postoperative lung function and attenuation of the reperfusion injury at a cellular level in patients receiving systemic leukodepletion was reported. However, it is not reflected on hospital stay or survival.

11.7.5.3 Circuit Miniaturization

Current advances in the design of the CPBP circuit help to reduce the use of peri-operative blood products. Recent studies in neonates have shown clinical benefit with its use, which includes reduction of the postoperative edema, improvement of the systolic blood pressure, and reduced mechanical ventilation time.

The prime volume used is 115 ml in patients with less than 6 kg of weight [23].

11.7.6 Hemoconcentrators and Ultrafiltration

Hemofiltration and ultrafiltration are techniques used to remove water (with inflammatory molecules) from the circulatory blood flow. This effect is achieved through the filtration of water across a semi-permeable membrane as the result of a hydrostatic pressure gradient. The blood flows through a hemoconcentrator (which is composed by a bundle of hollow fibers) creating a positive pressure that drives water across the membrane through an ultrafiltration reservoir system (Figs. 11.5 and 11.6).

There are three approaches to ultrafiltration in pediatric cardiac surgery:

1. Conventional ultrafiltration (CUF) (performed during the CPBP)
2. Modified ultrafiltration (MUF) (after termination of the CPBP)

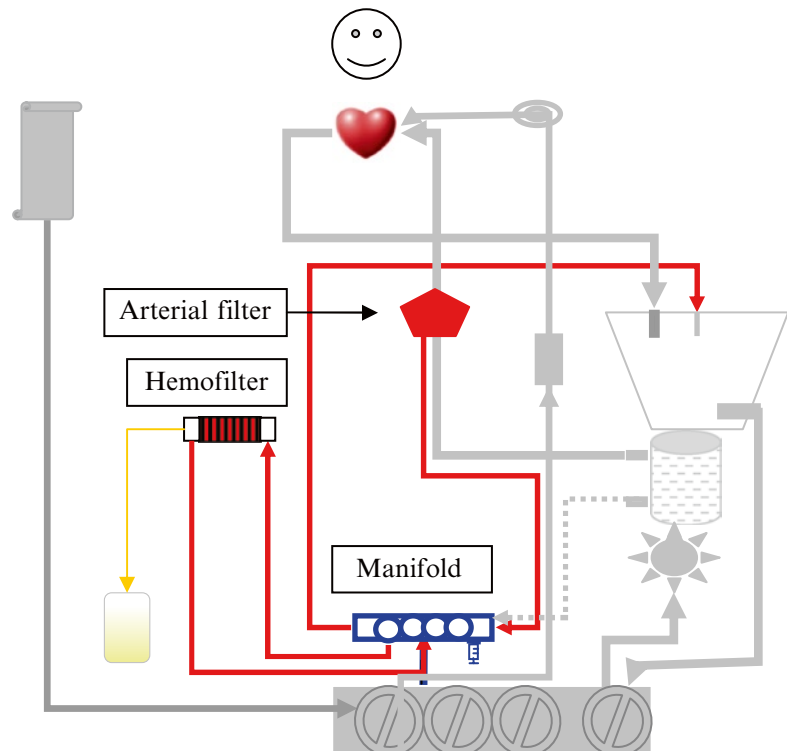
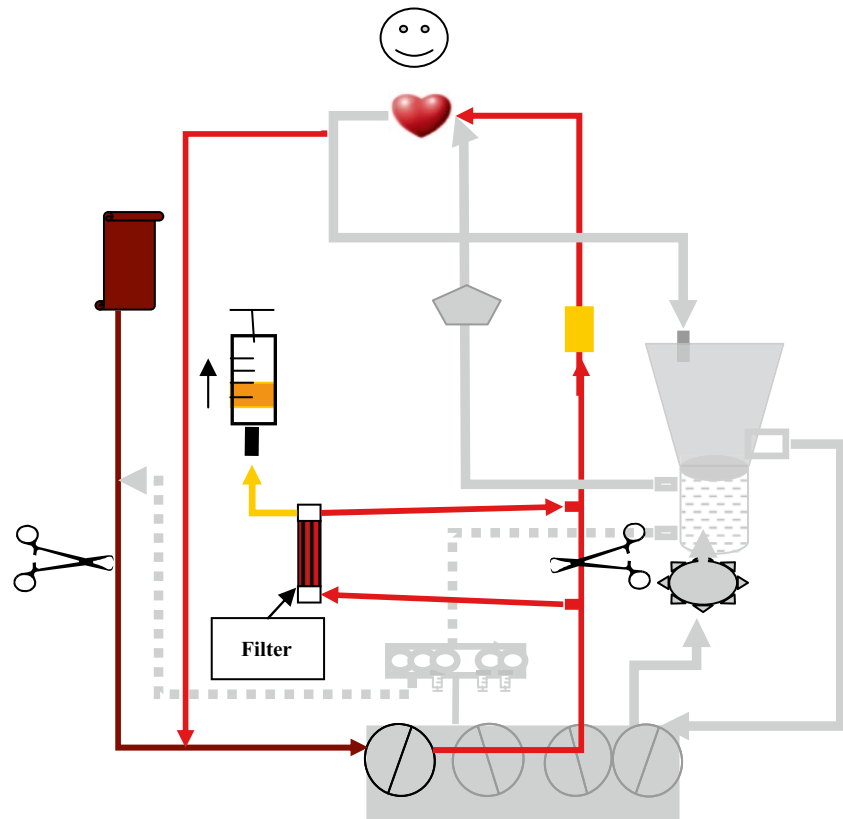


Fig. 11.5 Continuous hemofiltration system

Fig. 11.6 Modified ultrafiltration system



3. Ultrafiltration of the prime (PUF) (before the onset of the CPBP, it is performed occasionally when the CPBP circuit is primed with blood products).

In 1991, Naik et al. reported the use of MUF [24]. It is initiated after separation from CPBP; the blood from the aortic cannula is pumped through the hemofilter and then warmed by a heat exchanger and returned through the cardioplegia circuit to the patient's venous cannula(s) [25]. There is not a global consensus about the amount to be removed, but in general, the fluid is removed depending on arterial pressure, CVP, and left atrium pressure. This technique is generally used for patient less than 10 kg of weight [26].

The major advantage of ultrafiltration is to remove excess fluid from patients, which leads to an increase in the hematocrit level and coagulation factors. MUF decreases the level of low-molecular weight inflammatory mediators and other deleterious substances.

Several clinical trials have demonstrated the clinical benefits of CUF and MUF after pediatric cardiac surgery, however, controversy remains regarding the optimal ultrafiltration strategy [27].

MUF and CUF reduce blood loss, blood transfusion, and mechanical ventilation time.

Other demonstrated effects of the use of MUF include:

1. Improvement in the postoperative hemodynamics
2. Improvement in the alveolar–arterial oxygen difference.
3. Decrease pulmonary vascular resistance.
4. Decrease the incidence of pleural effusions (after superior cavopulmonary connection and Fontan procedure)
5. Decrease myocardial edema.
6. Improvement in the left ventricular function.

There is lack of consensus in the type of MUF (arterio-venous, venovenous), duration of ultrafiltration during CPBP, volume of ultrafiltrate, and the type of hemofilter to be used, leading to difficulty in the interpretation of the published studies and the definition of the best method of filtration [28].

Hemofiltration carries the potential for human and equipment error and increases plasma heparin

concentration. The removal of blood from the systemic circulation may result in hemodynamic instability or impaired aortopulmonary shunt flow. High flow rates through the ultrafilter decrease cerebral blood flow velocities and cerebral mixed venous oxygen saturation [29].

11.8 Conduct and Medications Used During CPBP

11.8.1 Priming the Pump

There is no universally agreed protocol for prime solution preparation; most centers have developed their own preferred regimen.

Priming of the circuit is performed with crystalloid solutions (Plasmalyte A) or blood products (packed red blood cells, plasma, or whole blood). In children, to avoid excessive hemodilution, homologous blood (packed red blood cells) is used, minimizing the amount of colloid and crystalloid transfused. Among natural colloids used in this group of patients, fresh frozen plasma is favored [30].

Stored homologous blood has a deranged electrolyte and acid–base status. Priming the pump with blood results in a high concentration of potassium, especially if irradiated blood is used. However, children with impaired T-cell immunity do require irradiated blood. The citrate in citrate–phosphate–dextrose (CPD) (which is added to stored blood as an anticoagulant), binds to the serum Ca^{2+} producing hypocalcemia. Due to the anaerobic metabolism of the red blood cells, the lactate and pyruvate levels are increased, making stored blood more acidotic [31].

The assessment to determine the type of fluid used for priming (Crystalloid vs. blood products) depends on desired hematocrit. Despite recent advances in technology, the majority of neonates and infants still require peri-operative transfusion of homologous blood components.

Historically, whole blood (WB) was preferred due to the benefit of use a single donor. WB also provides all blood components at the same time. Using packed red blood cells (PRBC) instead of WB has been shown to reduce mechanical ventilation time and intensive care stay [32, 33].

Hemodilution decreases blood viscosity and increases velocity of the blood flow through the capillary network. This decreases platelet activation and allows adequate flow.

Prime volume depends on the size of the circuit and size of the patient varying from 115 to 1500 ml in an adult circuit.

Oncotic pressure is maintained with the addition of albumin.

Steroids are used to decrease the inflammatory response.

Mannitol is added to decrease platelet binding to the circuit surface and is used to increase diuresis.

Magnesium, calcium, sodium bicarbonate are also added to the prime solution to maintain the electrolyte and acid–base equilibrium [34].

The addition of other medication is dependent on the surgical group's preferences. Other medications include antifibrinolytics such as aprotinin, tranexamic acid (TXA), or epsilon aminocaproic acid (EACA). TXA and EACA are lysine analogs that reversibly bind to the lysine-binding site on plasminogen, thus inhibiting the conversion of plasminogen to plasmin. Aprotinin is a polypeptide extracted from bovine lung that inhibits a number of plasma serine proteases, including kallikrein, trypsin, plasmin, and elastase. Aprotinin has the potential to preserve platelet function and decrease the systemic inflammatory response. Previous studies have found them to be effective in reducing blood loss and the need for transfusion. Data from some trials suggest an advantage of aprotinin over the lysine analogs TXA and EACA in terms of decreasing inflammatory response. However, aprotinin has been discontinued from the market in the USA, due to several randomized trials demonstrating the association between its use and the increased risk for stroke, thrombosis, myocardial infarction and death in adults. In pediatric patients, aprotinin has shown to have a wide benefit in decreased postoperative bleeding, but its use in this population remains uncertain [35].

11.8.2 Pharmacokinetics and Pharmacodynamics of Medications During CPBP

Changes in pharmacokinetics result from hemodilution, hypothermia, altered organ perfusion, acid–base status, and drug sequestration in the lungs and circuit.

1. *Hemodilution* of circulating carrier proteins produces an alteration of the free fraction of the medications and decreases their ability to bind to their target tissue. Most of the medications suffer a transient decrease, usually no more than 5 min. The free drug concentration increases as protein concentrations fall.
2. Change in perfusion pressure to the target organs produces an increase in the elimination of half-time due to a decrease in glomerular filtration rate. In addition, peripheral vasoconstriction produces a decrease in the drug absorption and consequently in the tissue distribution. There is also a decrease in the metabolic rate of the enzymatic reactions.
3. The reperfusion of the ischemic tissues releases sequestered medications increasing plasma concentrations of those during the rewarming period.
4. Heparin releases free fatty acids, which can displace drugs from protein-binding sites and increases free drug concentration for enhancing its pharmacologic effect.

The pharmacokinetics of infants and children vary greatly from adults. Neonates, infants and children have different volumes of distribution, rates of metabolism, and immaturity of metabolic systems.

Fentanyl, midazolam, propofol, isoflurane, nitroglycerine and vancomycin are some medications sequestered by the membrane of the oxygenator affecting the drug concentration [36, 37].

Effects of ultrafiltration and hemofiltration on drug concentration in children are not completely clear. A recent study demonstrating a net effect of MUF in increasing plasma concentrations of Milrinone by approximately 35% in neonates after HLHS stage I repair with the effect persisting for 12 h after surgery. Highly variable aprotinin concentrations have been found in children when the administered dose is given according to the adult data [38, 39].

11.8.3 Pump Flow

The blood flow depends on physiologic parameters of perfusion (venous mixed saturation, lactate, and perfusion pressure). The amount of flow will determine the cardiac index. Normal cardiac index is maintained between 1.5 to 3 L/m², when temperature drops, metabolic demands decreases, and the cardiac index is lowered.

Currently, research in pulsatile perfusion demonstrated significant increases in vital organ blood flow and microcirculation. Furthermore, the use of pulsatile perfusion reduces systemic inflammatory response, decreasing inotropic support, intubation time, and hospital stay [40].

11.8.4 Anticoagulation

Adequate anticoagulation is essential to minimize the thrombin generation that occurs as response of the contact of the blood with the extracorporeal circuit. Thrombin formation is age-dependent. Children experience reduced thrombosis during CPBP. Inadequate anticoagulation may cause both thrombosis and severe bleeding. However, the optimal dose of heparin in infants and children undergoing CPBP is not defined.

Children have low antithrombin III (ATIII) levels, which reduces the efficacy of heparin to neutralize thrombin generation during CPBP. However, increased heparin levels have been associated with a decrease in the platelet function. In addition, the decreased level of fibrinogen in children overestimates the real anticoagulation level [41].

Monitoring of anticoagulation is performed with the measure of the activated clotting time (ACT). Hattersley introduced this method in 1966. Whole blood from the CPBP is introduced into a tube or cuvette containing celite or kaolin as activators. A plastic stirring plunger is lifted up every 2 s until blood thickens sufficiently and the plunger is slowed.

Current devices use in its majority Kaolin as substrate. Aprotinin, hypothermia, hemodilution, thrombocytopenia, and protamine prolong ACT.

Interpretation of the ACT is not adequate in neonates due to the lack of linear relation between ACT level and heparin level. Monitoring of heparin levels may provide a more accurate guide for the administration of heparin during neonatal CPBP [42].

Thromboelastography (TEG) is an indicator of coagulability state. This tool is useful in examining the rapid phase of the clot formation indicating the platelet function and interaction of the coagulation factors.

Doses of alternative anticoagulants such as the direct thrombin inhibitors (argatroban and lepirudin) are not completely established in pediatrics, but may be useful in specific scenarios like a documented heparin-induced thrombocytopenia [43].

11.8.5 Monitoring

New monitoring devices permit real-time measurements of venous mixed saturation, Hemoglobin, K^+ and blood arterial gases. Tympanic, nasopharyngeal, or esophageal temperature is monitored to give an approximation of the cerebral temperature and the lower side of the body is monitored using a rectal or bladder thermometer.

Several monitors have been studied as tools for neurologic assessment:

1. Bispectral index monitoring (BIS) detects cerebral hypoperfusion and cerebral air embolism.
2. Near infrared monitoring (NIRS) detects cerebral ischemia.
3. Transcranial Doppler (TCD) ultrasound is a sensitive, real-time monitor of cerebral blood flow velocity (CBFV) and emboli during CHD surgery.

The NIRS displays a numeric value, the regional cerebral saturation index (rSO_{2i}), which is the ratio of oxyhemoglobin to total hemoglobin in the light path. The rSO_{2i} is reported as a percentage on a scale from 15 to 95%. In the brain, the major source of tissue oxygen content is the saturation of blood in the micro-circulation. Thus, rSO_{2i} reflects brain tissue oxygen content, which is influenced by cerebral oxygen delivery, oxygen consumption, and arterial/venous blood volume ratio [44, 45].

11.9 Strategies to Decrease Inflammatory Response and New Perspectives

11.9.1 Corticosteroids

Systemic inflammatory response and multi-system organ failure are most prominent between 8 and 24 h after CPBP. Their use is associated with the prevention of organ injury by minimizing lysosomal enzyme release and inhibition complement-induced neutrophil aggregation. However, the clinical evidence does not support the use of prophylactic steroids in pediatric patients to reduce postoperative complications [46, 47].

Methylprednisolone (30 mg/kg) can attenuate the increase in the proinflammatory mediators interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor- α (TNF- α), and plasma endotoxin. The mechanism of corticosteroids remains unclear. Dexamethasone administration before cardiopulmonary bypass in children resulted in a significant decrease in cardiac troponin I levels at 24 h postoperatively [48, 49].

A recent meta-analysis of randomized controlled trials from the Cochrane Heart Group demonstrated weak evidence in favor of prophylactic corticosteroid administration for reducing intensive care unit stay, peak core temperature, and duration of ventilation in pediatric cardiac surgery. The available studies differ in the type of steroid, the dose, and method of administration, the timing of the administration (pre, intra, and postoperative), and the clinical and laboratory parameters used to measure the therapeutic response [50].

The development of more biocompatible circuits decreases the platelet and fibrinogen adhesion. Minimization of the air–blood interface, air–blood contact, particularly in the venous reservoir, is another potential source of CPBP improvement. A study demonstrated that the use of a closed (collapsible) venous reservoir significantly decreased hemolysis during early stages of the CPBP. Its use was also associated with a decrease in the generation of complement C3a, fibrin degradation products, and elastase [51, 52].

Reduction of the use of blood products and the size of the CPBP circuit is possible by the use of modern oxygenators, decrease in the length, and diameter of tubing sets, and optimal positioning of arterial pump with vacuum-assisted venous drainage. The new strategy involves the use of a CPBP circuit composed of a biomaterial with enhanced biocompatibility. This biomaterial simulates the antithrombotic behavior of natural membranes such as the phospholipids (phosphorocholine) of the external erythrocyte membrane [53, 54].

Although most studies have demonstrated the effective blockade of complement activation by complement inhibitors, the results from studies that evaluated clinical outcomes have, unfortunately, been disappointing.

Several anti-inflammatory strategies have been implemented to reduce this response, including leukocyte removal from the circulation using specialized filters [55, 56].

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Chapter 12

Nursing Care of the Pediatric Cardiac Patient

Erin L. Colvin, Dana Shiderly, Tamara Maihle, and Dana Casciato

12.1 Introduction

Thorough assessment and support of cardiopulmonary function are essential in caring for every patient in the pediatric cardiac intensive care unit (CICU). The patient population in the CICU ranges from the preoperative patient awaiting cardiac surgery, the child with congestive heart failure, cardiomyopathy, or arrhythmias to the postoperative patient who has undergone palliation or corrective surgery for congenital heart disease. Nurses working in this environment must have exceptional assessment skills, clinical expertise, and a sound judgment to respond to constantly changing and potentially emergent situations. In addition, with the practice of holistic family-centered care, nurses must extend compassion and empathy to each child as well as to their parents, and extended family throughout their experience in the CICU. This chapter outlines basic cardiac assessment essential for the critical care nurse and defines clinical skills needed to care for the pediatric medical and surgical cardiac patient. The developmental needs of children in the CICU will be discussed within the context of a family-centered environment of care.

12.2 Cardiac Assessment

A thorough cardiac assessment is essential for the effective management of patients with congenital and acquired heart disease. For a bedside nurse,

exceptional assessment skills are vital. Continued assessment and reassessment of the patient must occur frequently. Knowledge of the patient's anatomy, disease process, and surgical intervention are all important to the management of the patient. Table 12.1 explains normal and abnormal finding in a head to toe cardiac assessment [1].

12.3 Hemodynamic Monitoring

Invasive hemodynamic monitoring of infants and children in the CICU is performed routinely. Invasive hemodynamic monitoring can provide valuable information in the care of a critically ill infant or child. It is imperative to use numeric hemodynamic data along with clinical assessment skills to make sound clinical decisions.

12.3.1 Central Venous Pressure Monitoring

Central venous lines serve many purposes in the management of cardiac patients. These lines can be placed directly into the right atrium, internal jugular, or subclavian vein. The ideal position of a central venous line is the proximal superior vena cava. When positioned in the proximal superior vena cava, the line directly measures the central venous pressure (CVP) and the right atrial (RA) pressure. Hemodynamic monitoring of CVP reflects intravascular volume status and right ventricular function. Normal CVP in infants is 0–4 mmHg and in children 2–6 mmHg. A high CVP may be caused by poor right ventricular

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Table 12.1 Cardiac assessment

System	Components of assessment	Abnormalities
General Survey	Overall general state	Cyanosis, pallor, mottling
	Color	Irritability, anxiety
	Affect	Lethargy, obtundation,
	Level of consciousness	Facial grimace, asymmetry
Vital Signs	Facial expression	
	Temperature	Hypothermia, hyperthermia
	Heart rate	Tachycardia, bradycardia, irregularity
	Respiratory rate	Tachypnea, apnea
	Non-invasive blood pressure	Hypotensive or hypertensive for age, wide pulse pressure
Skin	Arterial blood pressure	Hypotensive or hypertensive for age, wide pulse pressure, pulsus paradoxus
	Central venous pressure	High, low, cannon "A" waves
	Temperature	Cool
	Color	Pallor, mottled, cyanotic, jaundice
	Moisture	Diaphoretic
Cardiovascular	Turgor	Tenting
	Integrity	Rashes, lesions, scars, bruising
	Heart rate	Tachycardia, bradycardia, irregular
	Heart sounds	Distant, muffled, murmur, rub, clicks, gallop
	Rhythm	Arrhythmia
	Pulses	Weak, absent, bounding
	Capillary refill	Prolonged or flash
Respiratory	Lactate	
	Mixed venous Co-oximetry	
	Rate	Tachypnea, apnea
	Rhythm	Periodic, Kussmaul, Cheyne-Stokes, shallow
	Work of breathing	Retractions, head bobbing, use of accessory muscles, nasal flaring, grunting
	Arterial blood gases	Acidosis, alkalosis, hypoxemia, hypercarbia
Fluids, electrolytes	Breath sounds	Stridor, wheezing, grunting, obstruction, rales, rhonchi
	Chest rise	Asymmetry, shallow
	Sodium	
	Potassium	
	Chloride	
	Magnesium	
	Calcium	
	Bun	
	Creatinine	
	Fluid balance	
	Urine output	Less than 1 ml/kg/h
	Drain output	Greater than 5 ml/kg/h
Urological	Level of consciousness	Altered, confusion, irritability, somnolence, disoriented, unresponsive
	Pupil size and reaction	Asymmetry, nonreactive, dilated, nystagmus
	Fontanel	Bulging, sunken, tense
	Strength and movement of the extremities	Asymmetry, weakness, seizure activity, paralysis
GI/Nutrition	Sensation	Tingling, blunting, numbness, paraesthesia
	Glascow Coma Scale	
	Liver/Spleen Palpation	
	Abdominal girth	
	Abdominal inspection	
	Bowel sounds	
	Daily weights	
Caloric intake		

(continued)

Table 12.1 (continued)

System	Components of assessment	Abnormalities
Pain	Location Characteristics/ Frequency Onset/Duration Intensity/Severity Precipitating Factors Use of appropriate scale	Uncontrolled pain

function, hypervolemia, tricuspid stenosis or insufficiency, or with positive pressure ventilation. Low CVP measurements may indicate hypovolemia [2].

12.3.2 Arterial Blood Pressure Monitoring

Arterial lines are placed to continuously monitor blood pressure and blood sampling. Common sites for arterial lines include radial, ulnar, femoral, axillary, umbilical, and dorsalis pedis arteries. Assessment of the extremity distally from the site of origin of the arterial catheter is important to prevent neurovascular complications [3].

12.3.3 Pulmonary Artery Pressure Monitoring

Pulmonary artery (PA) catheters are useful tool in the diagnosis and treatment of infants and children with cardiopulmonary failure and pulmonary hypertension. PA catheters measure the direct pulmonary artery pressure. Laboratory studies, such as mixed venous oxygen saturations, may be obtained from these lines [2, 4]. These lines may be placed through a major blood vessel into the pulmonary artery or placed directly into the pulmonary artery at the time of cardiac surgery.

12.3.4 Left Atrial Pressure Monitoring

A catheter is placed into the left atrium following surgical repair/palliation to allow for direct monitoring of the left ventricular function. Infusions or lab draws should be avoided due to the risk of emboli. Left atrial lines are common in patients with transposition of the great arteries and Shone's complex [2].

12.4 Preoperative Assessment and Diagnosis

In children with known cardiac conditions who are scheduled to undergo surgery electively, preparation of the child and family begins prior to admission to the hospital. Each patient and family is scheduled for a preoperative assessment that takes place one to two weeks prior to the anticipated surgery in the cardiothoracic surgery outpatient setting. During this visit, a complete history and physical assessment is performed. Knowledge of baseline health, developmental, social, and family information obtained about the child is essential in providing holistic family-centered care to the child preoperatively, intraoperatively, and postoperatively. Any significant findings or concerns that arise during this evaluation can then be communicated to appropriate members of the health care team which include anesthesia, operating room, perfusion, cardiac intensive care unit, or social work staff [5].

The preoperative visit is also a time when the child and family will discuss the existing cardiac condition and the planned surgical intervention. Careful assessment of the child's developmental level, as well as the most efficient method of relaying information to the family, is of paramount importance. The use of pictures, models, videos, or websites to explain the anatomy and the surgical procedure often helps the family to comprehend the proposed surgical plan. Hands-on exploration of samples of materials, implants, and devices used during surgery are also helpful in reducing anxiety and eliminating fear of the unknown for children as well as parents [6].

A tour of the CICU is offered as part of the preoperative evaluation. This tour, often conducted by the cardiac social worker, provides an additional opportunity for families to address concerns regarding financial stressors, lodging, and absence from employment and school. Families are encouraged to speak with

nurses in the CICU so that questions that are prompted by viewing the unit can be answered. Education regarding the child's heart defect or disease, proposed surgical procedure, the predicted hospital course, and familiarization with the hospital environment and staff serves to optimize the ability to cope effectively during a time of stress and anxiety [7].

12.5 Nurse's Role in Postoperative Care

12.5.1 Preparation of the Cardiac Intensive Care Unit

The bed space is prepared while the child is in the operating room. The actual bed is stocked with all the equipment needed to transport the patient from the Operating Room (OR) to the CICU. This equipment includes primed and labeled transducers, transducer holder, manual resuscitation bag, appropriate sized masks, full oxygen tank, transport monitor, and bed linens as appropriate. The bed is taken to the OR so that the patient can be transported from the OR suite to the CICU in the bed in which they will recover.

The bedside in the CICU is also set up while the child is in the OR. Table 12.2 lists the equipment that is needed at each bedside to accept a postoperative patient.

The RN who is going to receive the patient from the OR will receive a phoned report from the OR nurse.

Table 12.2 Equipment needed at the post-operative bed space

1. Ensure that monitor is in mode that reflects patient group-Adult/Pediatric/Neonatal
2. Bedside monitors should have appropriate limits set for patient
3. Obtain appropriate cables/modules for the patient
4. Extra infusion pumps
5. Resuscitation bag and mask appropriate for the patient
6. Appropriate sized airway kit with intubation equipment
7. Mechanical ventilator should be prepared with appropriate settings
8. Emergency medication sheet prepared according to weight
9. Suction set up for anticipated number of chest tubes
10. Blood tubes and laboratory requisitions for postoperative bloodwork
11. Typical postoperative medications including albumin, potassium, calcium, and additional IV fluids.
12. Temporary pacemaker with extra battery

This will give the RN 45 min to 1 h to finalize the bedside in preparation of the child's arrival. When the child is admitted, it is important to designate one person to receive report from the anesthesiologist and surgeon. Appendix provided is an example of a checklist that is helpful to ensure all information is conveyed to the CICU team.

12.6 Developmental Needs and Family-Centered Care

12.6.1 Developmental Needs

Hospitalization is known to cause high levels of stress and anxiety for children and their families. For children facing hospitalization, the event can be confusing and frightening. The child, removed from his safe home environment, finds himself exposed to new sights, sounds, and people. Procedures, exams, and routine tests are perceived as potentially harmful or painful. The child's developmental level plays an important role in determining how the stress of illness and hospitalization is handled. In addition to the recognition of the child's psychosocial and cognitive development, acknowledgment of the family's previous experience with illness and hospitalization, their cultural beliefs, and ongoing family stressors will enable the health care team to provide exceptional levels of care and support [8].

Family-centered care is based on the recognition that family is constant in a child's life. Family is the primary source of support for the child during hospitalization. That support must be upheld by the health care team throughout the child's stay in the CICU. Nurses are responsible for fostering healthy parent-child relationships over the entire developmental continuum from infancy through adulthood. Family-centered care assures the health and well-being of children and their families through a respectful partnership between families and professional caregivers. Consideration is given to the strengths, cultural values, beliefs, and expertise that each individual brings to this partnership. Family-centered care has been shown to improve outcomes and anxiety, decrease recovery time, and increase patient, family, and staff satisfaction [9].

As an integral part of this partnership with families, the CICU nurse must be acutely aware of the events and

situations which families perceive as anxiety-provoking. One of these events is the time that a diagnosis of cardiac disease is determined and communicated to families. This event can elicit feelings of sadness, anger, confusion, guilt, and fearfulness. An understanding of the spectrum of coping mechanisms employed by parents in dealing with a diagnosis of heart disease is essential in providing family-centered care. These coping mechanisms range from denial, overprotection, extreme diligence, and monitoring of the child's condition to more severe responses that can include depression and anxiety disorders [10].

The anticipation of surgery is another very stressful time for families. Knowledge is generally empowering to families as they prepare for a major intervention like cardiac surgery or cardiac catheterization. Keeping in mind the family's capacity for receiving and processing information, nurses can effectively explain the child's anatomy and planned surgery while drawing on their prior experience and utilizing teaching tools such as pictures, videos, and models.

Once viewed as a time of exclusiveness from family involvement, daily patient rounds has recently emerged as a forum for families as well as the health care team to exchange concerns and ideas while providing an opportunity for education and mutual development of the child's plan of care. The concept of family input in patient rounds has historically been met with skepticism, but reports from teaching hospitals that invite families to be involved have been overwhelmingly positive [11]. CICU nurses can be instrumental in this process by encouraging families to be involved and assisting them in preparation for rounds each day. Throughout the day, the CICU nurse is available as a resource to the family to answer questions that pertain to the established plan of care.

Undoubtedly, the most challenging time for children, families, and caregivers is when poor outcomes are encountered. The relationship between the CICU nurse and the family implies the unique responsibility to assess and provide for the needs of the family during this critical situation. Communication must remain open, and all available resources must be used to support families in crisis. The astute CICU nurse will anticipate each family's individual needs for the

support of extended family, pastoral care, social work, or hospice.

Providing family-centered care in the CICU is both challenging and rewarding. CICU nurses must be adept at maintaining the focus of the entire health care team on the child within the protective context of the family.

12.7 Appendix

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Chapter 13

Cardiac Database and Risk Factor Assessment. Outcomes Analysis for Congenital Cardiac Disease

Jeffrey P. Jacobs

13.1 Introduction

Over the past two decades, tremendous progress had been made in the field of congenital heart disease outcomes analysis [1–85]. Efforts are ongoing to continue to improve the techniques and technologies available to evaluate the outcomes of treatments for congenital heart disease. The rationale for this goal is multifactorial. The techniques and technologies of outcomes analysis for congenital heart disease can function as tools to support a variety of purposes:

- a. Patient care for the one million new patients born worldwide each year with congenital heart disease (130,013,274 births per year estimated for 2005 with 8 children per 1,000 births with congenital heart disease=1,040,106 new patients each year with congenital heart disease)
- b. Research
- c. Teaching
- d. Practice management
- e. Resource allocation
- f. Outcomes analysis designed to lead to quality improvement

In order to perform meaningful multi-institutional outcomes analysis designed to improve the quality of care in congenital heart surgery, one must use a database that incorporates the following six essential elements:

1. Use of a common language and nomenclature [5–40, 45–53, 56, 57, 60, 61, 66–72, 75–77, 80–84]
2. Use of an established uniform core dataset for collection of information [2, 4–6, 38–40, 42, 43, 45, 46, 49–52, 54–57, 59–61, 66, 67, 70, 75–77, 81–85]
3. Incorporation of a mechanism of evaluating case complexity [1, 3, 41, 43, 44, 51, 52, 54–58, 60–63, 65, 67, 69, 74, 75, 78, 79, 81, 85]
4. Availability of a mechanism to assure and verify the completeness and accuracy of the data collected [56, 57, 60, 61, 64–67, 69, 70, 75, 81]
5. Collaboration between medical and surgical subspecialties [75, 81]
6. Standardization of protocols for lifelong follow-up [73, 81]

13.2 Nomenclature

During the 1990 decade, both The Society of Thoracic Surgeons (STS) and The European Association for Cardio–Thoracic Surgery (EACTS) created congenital heart surgery outcomes databases. [6] Beginning in 1998, these two organizations collaborated to create the International Congenital Heart Surgery Nomenclature and Database Project [5–37]. By 2000, a common congenital heart surgery nomenclature, along with a common core minimal dataset, were adopted by The EACTS and The STS and published in the *Annals of Thoracic Surgery* [5]. In 2000, The International Nomenclature Committee for Pediatric and Congenital Heart Disease was established [47, 48, 53]. This committee eventually evolved into the International Society for Nomenclature of Paediatric and Congenital Heart Disease (ISNPCHD). The working component of the ISNPCHD has been The International Working Group for Mapping and Coding

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of Nomenclatures for Paediatric and Congenital Heart Disease, also known as the Nomenclature Working Group (NWG). By 2005, the NWG crossmapped the nomenclature of the International Congenital Heart Surgery Nomenclature and Database Project of The EACTS and The STS with the European Paediatric Cardiac Code (EPCC) of the Association for European Paediatric Cardiology (AEPC), and therefore, created the International Paediatric and Congenital Cardiac Code (IPCCC), which is available for free download from the internet at [<http://www.IPCCC.NET>]. The NWG has also crossmapped separate coding systems and provided unified nomenclature and definitions for several complex congenital cardiac malformations including the functionally univentricular heart [68], hypoplastic left heart syndrome [71], congenitally corrected transposition [72], and heterotaxy [80].

On Monday July 9, 2007, the International Society for Nomenclature of Paediatric and Congenital Heart Disease created two new committees, so that the Society now has the following three committees:

1. The International Working Group for Mapping and Coding of Nomenclatures for Paediatric and Congenital Heart Disease, also known as the NWG
2. The International Working Group for Defining the Nomenclatures for Paediatric and Congenital Heart Disease, also known as the Definitions Working Group (DWG)
3. The International Working Group for Archiving and Cataloging the Images and Videos of the Nomenclatures for Paediatric and Congenital Heart Disease, also known as the Archiving Working Group (AWG), and the Congenital Heart Archiving Research Team (CHART).

The NWG continues to maintain, preserve, and update the IPCCC, as well as provide ready access to it for the international paediatric and congenital cardiology and cardiac surgery communities, related disciplines, the healthcare industry, and governmental agencies, both electronically and in published form. The DWG writes definitions for the terms in the IPCCC, building on the previously published definitions from the NWG [68, 71, 72, 80]. The AWG (or CHART) links images and videos to the IPCCC. These images and videos will come from cardiac morphologic specimens, echocardiography, angiography, and additional imaging modalities such as computerized axial tomography and magnetic resonance imaging, as well as intraoperative images and videos. An image and video archive will be created, based on the IPCCC, and this archive will be linked to the CTSNet Congenital Portal.

13.3 Database Standards

The IPCCC and the common minimum database dataset created by The International Congenital Heart Surgery Nomenclature and Database Project, are now utilized by both The STS and The EACTS [56, 61, 67, 85]. Between 1998 and 2007, this nomenclature and database was used by both these two organizations to analyze outcomes of over 114,000 patients undergoing surgery as treatment for congenital heart disease [75, 81]. Table 13.1 presents data from an analysis of over 40,000 patients published in 2005 [67].

Table 13.1 The European Association for Cardio–Thoracic Surgery (EACTS) and The Society of Thoracic Surgeons (STS) aggregate data [67]

	All	0–28 days	29 days to 1 year	Other
STS				
Eligible patients	18,928	3,988	6,152	8,788
Discharge mortality	825	487	202	136
Discharge mortality %	4.4%	12.2%	3.3%	1.5%
Aristotle basic complexity score	7.1	8.6	7.0	6.5
EACTS				
Eligible patients	21,916	4,273	7,316	10,327
Discharge mortality	1,097	514	377	206
Discharge mortality %	5.4%	13.3%	5.56%	2.1%
Aristotle basic complexity score	6.5	7.6	6.6	5.9

These data represent surgical operations performed between 1998 and 2004 inclusive [39, 50, 51, 67]

During the 2007 STS Congenital Database Harvest, 57 participating programs submitted data: 55 from the United States of America, 1 from Canada, and 1 from Japan [77]. The Report of the 2005 STS Congenital Heart Surgery Practice and Manpower Survey, undertaken by the STS Workforce on Congenital Heart Surgery, documented that 122 centers in the United States of America and eight centers in Canada perform pediatric and congenital heart surgery [86]. The 2007 STS Congenital Heart Surgery Database Report contains data from 58 of these 130 centers from North America (56 of whom submitted data in the 2007 Harvest, and two of whom submitted data previously, but did not participate in the 2007 Harvest) [77].

The STS Congenital Heart Surgery Database is the largest database in North America dealing with congenital cardiac malformations [77]. It has grown annually since its inception, both in terms of the number of participating centers submitting data, and the number of operations analyzed [2, 4, 39, 50, 51, 57, 70, 77]. Figures 13.1 and 13.2 document the annual growth in the STS Heart Surgery Database by both number of participating centers submitting data and the number of operations [77]. The 2007 STS Congenital Heart Surgery Database Report includes 61,014 operations performed in 58 centers in North America, 57 from the United States of America, and one from Canada. One

Japanese center also submits data; however, these Japanese data are not included in the aggregate report produced by the Society of Thoracic Surgeons [77]. The EACTS Congenital Heart Surgery Database now includes data from 103 active centers from 30 countries. As of May 2007, this database contained data on 52,172 operations (Fig. 13.3). Multiple publications generated from these two databases have reported outcomes after treatment for congenital heart disease in general, as well as specific lesion based outcomes [56, 61, 67, 85].

13.4 Complexity Stratification

The importance of the quantitation of case complexity centers on the fact that in the field of pediatric cardiac surgery, outcomes analysis using raw mortality measurements without complexity adjustment is inadequate. Case mix can vary greatly from program to program. Without complexity stratification, outcomes analysis for congenital heart surgery will be flawed. Two major multi-institutional efforts have attempted to measure congenital heart surgery case complexity: the Risk Adjustment in Congenital Heart Surgery-1 (RACHS-1) system [1, 3, 44, 52, 58, 74, 85, 87, 88] and the Aristotle Complexity Score [41, 54, 55, 58, 61–63, 85]

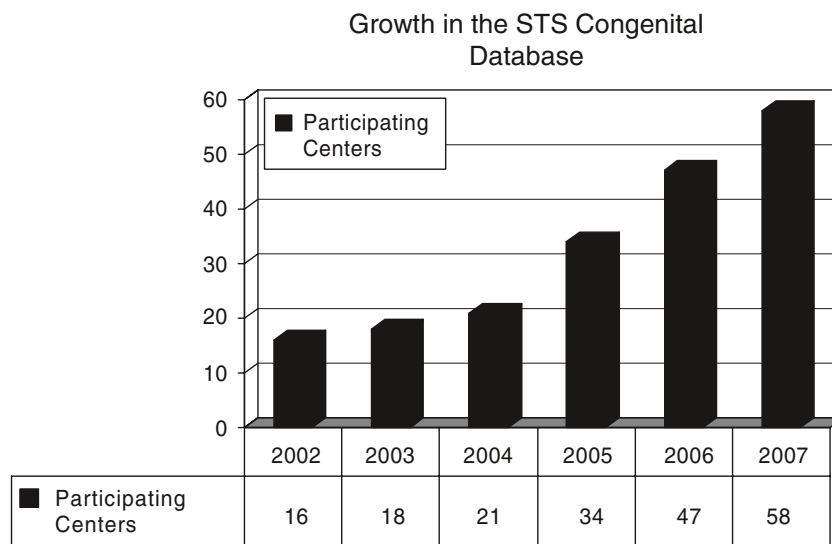
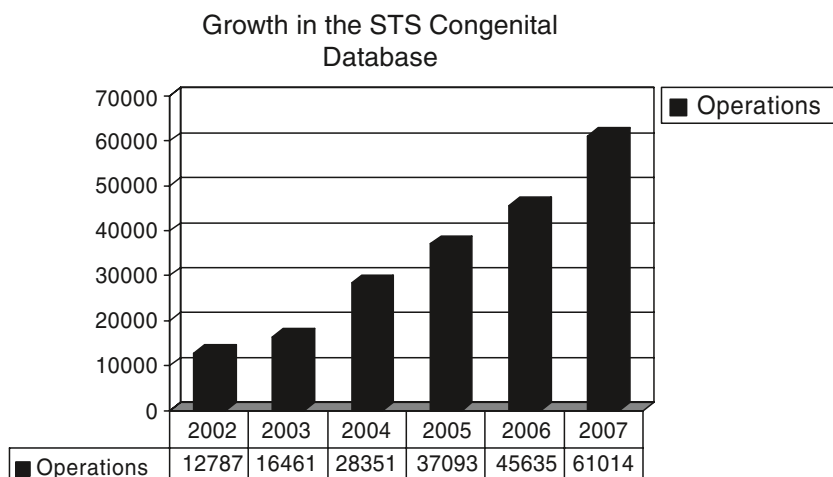


Fig. 13.1 The graph documents the annual growth in the Society of Thoracic Surgeons Congenital Database by number of participating centers submitting data. The aggregate report from 2007 of the Society of Thoracic Surgeons Congenital Heart Surgery Database includes data from 58 Congenital Heart

Surgery Centers from the United States of America and Canada. One Japanese center also submits data; however, these Japanese data are not included in the aggregate report produced by the Society of Thoracic Surgeons



Operations per averaged 4 year data collection cycle

Fig. 13.2 The graph documents the annual growth in the Society of Thoracic Surgeons Congenital Heart Surgery Database by the number of operations. The aggregate report from 2007 of the Society of Thoracic Surgeons Congenital Heart Surgery Database included 61,014 operations submitted

from 58 centers from North America, 57 from the United States of America and one from Canada. One Japanese center also submits data; however, these Japanese data are not included in the aggregate report produced by the Society of Thoracic Surgeons

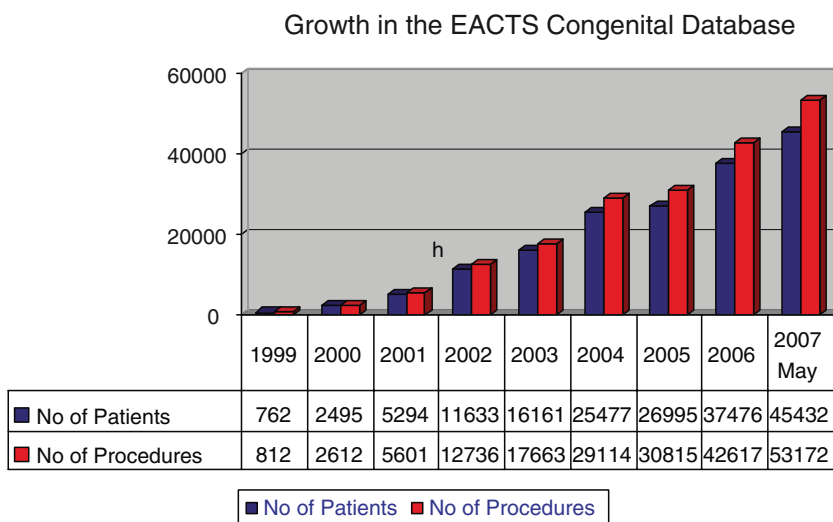


Fig. 13.3 This graph documents the annual growth in The European Association for Cardio-Thoracic Surgery (EACTS) Congenital Heart Surgery Database by both number of participating centers submitting data and the number of operations. Between 2004 and 2005, database specifications were updated,

possibly accounting for the lag in growth seen at that time. This graph is provided courtesy of Bohdan Maruszewski, MD of the Children's Memorial Health Institute in Warsaw, Poland and Director of The EACTS Congenital Heart Surgery Database

The STS and the EACTS have included the Aristotle Basic Complexity (ABC) score in their database reports since 2002 [39, 50, 51, 57, 70, 77]. Starting in 2006, both organizations incorporated the RACHS-1 method into their database reports as well [70, 77].

The ABC Score and the ABC Level are measures of procedural complexity that were developed by the

EACTS–STS Aristotle Committee and are based on mortality potential, morbidity potential, and technical difficulty [41, 54, 55, 61]. The initial panel of experts who created the ABC Score was made up of 50 congenital heart surgeons in 23 countries, and representing multiple societies, including the Congenital Heart Surgeons' Society (CHSS), the EACTS, the European Congenital

Heart Surgeons Association [ECHSA – formerly known as the European Congenital Heart Surgeons Foundation (ECHSF)], and STS. The ABC score allocates a basic score to each operation, varying from 1.5 to 15, with 15 being the most complex, based on the primary procedure of a given operation as selected from the Short List of the nomenclature of the version of the IPCCC derived from the International Congenital Heart Surgery Nomenclature and Database Project of The EACTS and The STS [5–37]. The ABC score was calculated using the three factors of the potential for mortality, the potential for morbidity, and the technical difficulty of the operation. In addition to assigning each procedure an ABC Score ranging from 1.5 to 15, each procedure was next assigned an ABC Level, which is an integer ranging from 1 to 4 based on the ABC Score (ABC Score of 1.5–5.9=ABC Level of 1, ABC Score of 6.0–7.9=ABC Level of 2, ABC Score of 8.0–9.9=ABC Level of 3, and ABC Score of 10.0–15.0=ABC Level of 4) [41, 54, 55]. Of the 162 procedures from the EACTS–STS Procedure Short List that are currently given an ABC Score, 30 are in ABC Level 1, 48 are in ABC Level 2, 51 are in ABC Level 3, and 33 procedures are in ABC Level 4 [77]. The ABC Level provides a broad generalization of complexity by dividing surgical procedures into four complexity levels [61]. Meanwhile, the ABC score can provide more precise complexity stratification [61]. Both the score and the level are useful tools; the appropriate tool can be chosen to match the required analysis [61].

The RACHS-1 methodology is also procedure driven [1, 3, 44, 52]. The RACHS-1 method was developed to adjust for baseline case mix differences when comparing

the discharge mortality for groups of patients undergoing pediatric congenital heart surgery. RACHS-1 was created using a combination of judgment-based and empirical methodology. To begin, an 11-member nationally representative panel of pediatric cardiologists and cardiac surgeons grouped cardiac surgical procedures into six risk categories, based on expected discharge mortality, with category 1 representing the lowest risk and category 6 representing the highest risk [44, 52]. (Functionally, category 5 has been shown to include too few cases to accurately estimate mortality rates.) Categories were then refined using empirical data from two large datasets, one from the Pediatric Cardiac Care Consortium (PCCC) and the other generated from statewide hospital discharge databases. In addition to risk group, the RACHS-1 method incorporates age at surgery, prematurity, presence of a major noncardiac structural anomaly, and whether multiple surgical procedures were performed simultaneously [44, 52, 58, 74, 87, 88]. The RACHS-1 method has been demonstrated to be a useful tool in several studies in both Europe and North America [44, 52, 58, 74, 75, 85, 87, 88] and represents one of the first widely accepted complexity adjustment tools developed in our field.

Data from The EACTS and The STS multi-institutional databases indicates that the ABC Score correlates well with mortality prior to discharge from the hospital after congenital heart surgery as well as prolonged post-operative length of stay [61, 75, 79, 85]. Figure 13.4 plots the ABC Level against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2002

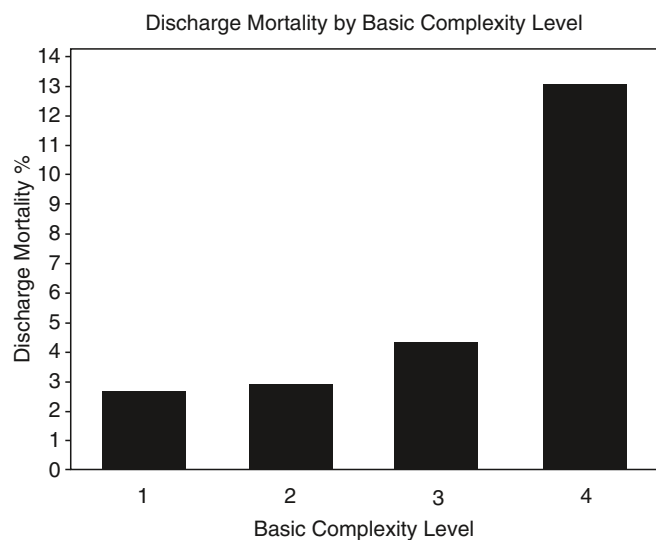
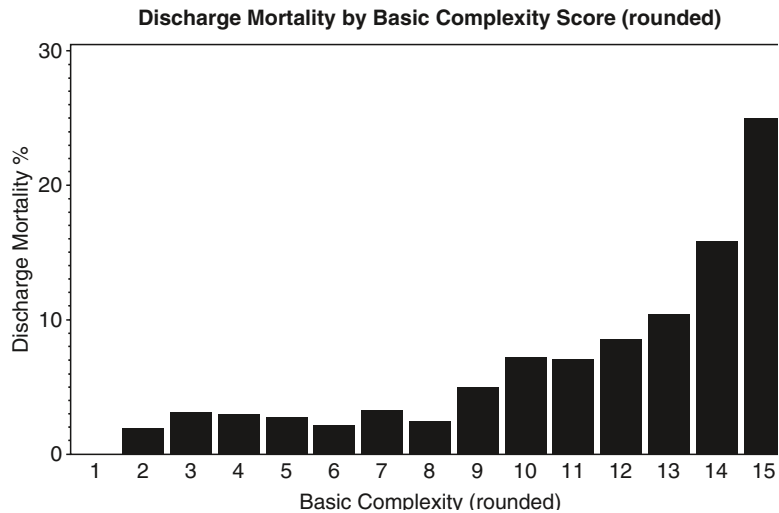


Fig. 13.4 The graph plots the Aristotle Basic Complexity Level against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2002 Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database data harvest utilizing data from 16 centers (12,787 total cases, 2,881 neonatal cases, and 4,124 infant cases). These data represent surgical operations performed between 1998 and 2001 inclusive [39, 56]

Fig. 13.5 The graph plots the rounded Aristotle Basic Complexity Score against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2005 STS Congenital Heart Surgery Database data harvest utilizing data from 34 centers (27,820 total cases). These data represent surgical operations performed between 2002 and 2004 inclusive [57]



STS Congenital Heart Surgery Database data harvest utilizing data from 16 centers. These data include 12,787 total cases, 2,881 neonatal cases, and 4,124 infant cases, and represent surgical operations performed between 1998 and 2001 inclusive [39, 56]. Figure 13.5 plots the rounded ABC Score against discharge mortality and also demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2005 STS Congenital Heart Surgery Database data harvest utilizing data from 34 centers. These data include 27,820 total cases and represent surgical operations performed between 2002 and 2004 inclusive [57].

In an analysis from the 2006 STS Congenital Heart Surgery Database Report [77, 85], overall discharge mortality was 3.9% (1,222/31,719 eligible cardiac index operations). 85.8% (27,202/31,719) of operations were eligible for analysis by the RACHS-1 system and 94.0% (29,813/31,719) were eligible for analysis by the ABCS. Figure 13.6, [85] demonstrates an analysis of discharge mortality stratified by ABC Level in data taken from the 2006 STS Congenital Heart Surgery Database Report which contained 45, 635 operations. Figure 13.7, [85] and Table 13.2, [85] use the same dataset from the 2006 STS Congenital Heart Surgery Database Report and present the relationship between discharge mortality and the rounded ABC Score. One has the opportunity to further stratify operations into additional complexity groupings when the scope of the analysis is expanded beyond ABC Level to incorporate ABC Score. Data from The EACTS and The STS multi-institutional databases also indicate that the RACHS-1 methodology correlates well with mortality prior to discharge from the

STS 2006 Congenital Database
45,635 cases

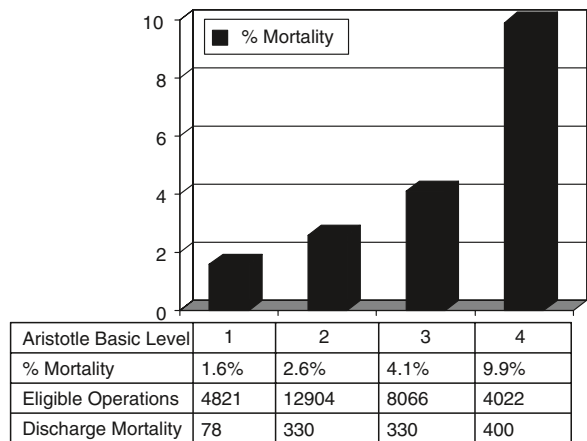


Fig. 13.6 The graph plots the Aristotle Basic Complexity Level against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2006 STS Congenital Heart Surgery Database Report, which contained 45,635 operations. These data represent surgical operations performed between 2003 and 2006 inclusive [77, 85]

hospital after congenital heart surgery. Figure 13.8, [85] demonstrates an analysis of discharge mortality stratified by RACHS-1 Category in data taken from the 2006 STS Congenital Database Report which contained 45,635 operations. With both RACHS-1 and Aristotle, as complexity increases, discharge mortality also increases. The ABC methodology allows classification of more operations, while the five RACHS-1 Categories discriminate better at the higher end of complexity when compared to the four ABC Levels [77, 85].

Fig. 13.7 The graph plots the rounded Aristotle Basic Complexity Score against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2006 STS Congenital Heart Surgery Database Report, which contained 45,635 operations. These data represent surgical operations performed between 2003 and 2006 inclusive [77, 85]

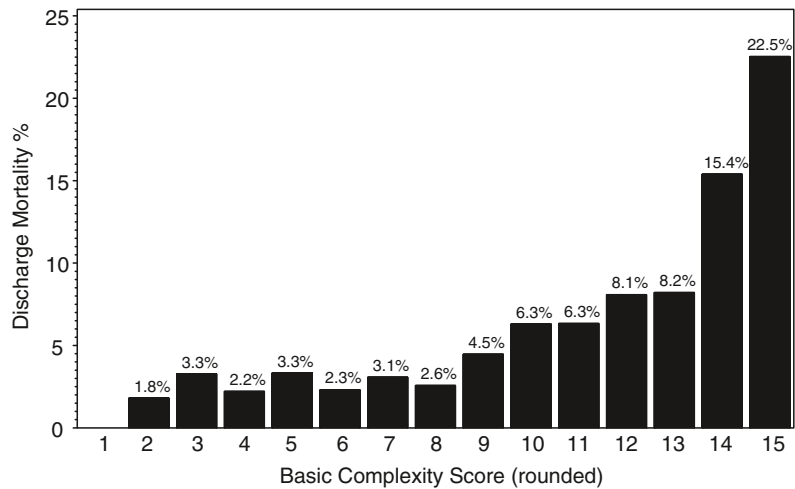


Table 13.2 STS congenital cardiac surgery database

Aristotle basic complexity score (rounded)	Number of records	Discharge mortality ^a
2	1,332	1.8%
3	8,879	3.3%
4	995	2.2%
5	451	3.3%
6	7,112	2.3%
7	7,555	3.1%
8	7,770	2.6%
9	4,393	4.5%
10	2,286	6.3%
11	2,228	6.3%
12	260	8.1%
13	134	8.2%
14	26	15.4%
15	1,576	22.5%

The table documents the rounded Aristotle Basic Complexity Score against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2006 STS Congenital Heart Surgery Database Report, which contained 45,635 operations. These data represent surgical operations performed between 2003 and 2006 inclusive [77, 85]

^aExcludes records with missing discharge mortality

Both RACHS-1 and the ABC Score allow stratification of operations based on the operation performed, without considering detailed patient-specific variables. The Aristotle Comprehensive Complexity (ACC) score adds to the ABC score by adding detailed patient-specific variables, with the addition of two sorts of complexity modifiers: procedure-dependent factors (including anatomical factors, associated procedures, and age at procedure) and procedure independent factors (including general factors, clinical factors,

STS 2006 Congenital Database
45,635 cases

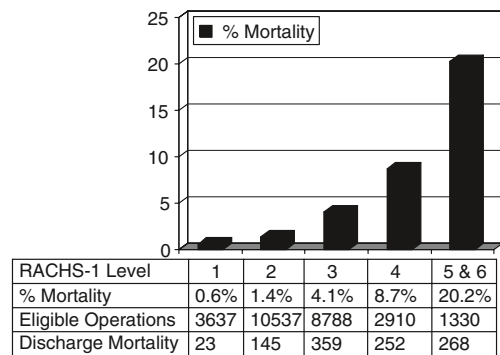


Fig. 13.8 The graph plots the RACHS-1 Level against discharge mortality and demonstrates the expected relationship of increasing mortality with increasing complexity based on data from the 2006 STS Congenital Heart Surgery Database Report, which contained 45,635 operations. These data represent surgical operations performed between 2003 and 2006 inclusive [77, 85]

extracardiac factors, and surgical factors). The ACC Score allows for the addition of ten points to the ABC Score; therefore, the ACC Score is calculated on a total of 25. The additional ten points were also determined by the opinion of experts, adding potentially five points for procedure-dependent factors and five points for procedures-independent factors. Each factor has been scored for its contribution to mortality, morbidity, and technical difficulty. All complexity factors meet the following requirements: precisely quantifiable, easily available, admitted by a majority, and verifiable [54, 55, 61]. The ACC Score Procedure Independent Factors are presented and defined in Table 13.3.

Table 13.3 The Aristotle Comprehensive Complexity (ACC) Score adds to the ABC Score by adding detailed patient-specific variables, with the addition of two sorts of complexity modifiers: procedure-dependent factors (including anatomical factors, associated procedures, and age at procedure) and procedure independent factors (including general factors, clinical factors, extracardiac factors, and surgical factors). This table lists and defines the ACC Score Procedure Independent Factors

Procedure independent factors			
General factors		Score	
	Weight <2.5 kg	2	
	Prematurity 32–35 weeks	2	
	Extreme Prematurity <32 weeks	4	
Clinical factors		Score	
Cardiac	Mechanical Cardio–Pulmonary Support	Excluding ECMO as a primary procedure	4
	Shock – persistent at time of surgery	Metabolic acidosis with pH <7.2 and/or Lactate >4 mmol/l	3
	Myocardial dysfunction	LVSF <25%, moderate to severe for RV	2
	Cardio–pulmonary resuscitation	Chest compression with medications within 48 h prior to surgery	2
	Shock – resolved at time of surgery	Metabolic acidosis with pH <7.2 and/or Lactate >4 mmol/l	1
	Supraventricular tachycardia	>160 ventricular beats/min (JET, AET, IART, WPW)	0.5
	Ventricular tachycardia		0.5
Pulmonary	Mechanical ventilation to treat cardiorespiratory failure		2
	Respiratory Syncytial Virus	“During same hospital admission”	3
	Elevated lung resistances. Biventricular repair	>6 Wood Units	2
	Elevated lung resistances. Heart transplant	>4 Wood Units	2
	Elevated lung resistances. Univentricular repair	>2 Woods Units	2
	Single lung	Only one lung present	3
	Tracheostomy	Tracheostomy present	1
Infectious	Septicemia	Positive blood culture	2
	Endocarditis	Vegetation or new regurgitation at echocardiography	3
	Necrotizing enterocolitis treated medically	“During same hospital admission” extraluminal air on xray	1
Gastrointestinal	Necrotizing enterocolitis treated surgically	“During same hospital admission” extraluminal air on xray	2
	Hepatic dysfunction	prothrombin time >2×normal	1
	Enterostomy present	Enterostomy present includes esophagostomy, gastrostomy, enterostomy, colostomy	0.5
	Hematologic	Coagulation disorder – Acquired	PT/PTT above normal, Thrombopenia <100,000 Fibrinogen split products positive (>10%)
Coagulation disorder – Congenital		PT/PTT above normal, Thrombopenia <100,000 Fibrinogen split products positive (>10%)	0.5
Renal	Renal dysfunction	Creatinine >1 mg/dl in neonate or Creatinine >2 mg/dl in older child	1
	Renal failure requiring dialysis	Renal failure requiring dialysis	3
Neurologic	Stroke, CVA, or Intracranial hemorrhage >Grade 2	During lifetime	1
	Stroke, CVA, or Intracranial hemorrhage >Grade 2	Within 48 h prior to surgery	2
	Seizure during lifetime	During lifetime	0.5
	Seizure within 48 h prior to surgery	Within 48 h prior to surgery	1
Endocrine	Hypothyroidism	TSH >20 mU/l	1
	Diabetes mellitus – insulin dependent		1
	Diabetes mellitus – noninsulin dependent		0.5

(continued)

Table 13.3 (continued)

Procedure independent factors		Score
Extra cardiac factors		
Central Nervous System	Hydrocephalus	0.5
	Spina Bifida	0.5
Respiratory	Laryngomalacia	3
	Broncho-tracheal Malacia	3
	Cystic fibrosis	2
	Tracheo-oesophageal Fistula	1
	Pulmonary lymphangectasis	1
	Choanal atresia	0.5
	Cleft Palate	0.5
	Congenital lobar emphysema	0.5
	Congenital cystic adenomatoid malformation	0.5
	Sequestration	0.5
	Chest wall deformity including pectus	0.5
Gastrointestinal	Biliary atresia	4
	Gastroschises	2
	Omphalocele	1
	Duodenal atresia	1
	Imperforate anus	0.5
	Hirshsprungs disease	0.5
	Inflammatory bowel disease – Crohn’s, Ulcerative colitis	0.5
Renal	Polycystic disease	0.5
	Vesicouteric reflux	0.5
	Hydronephrosis (PUJ and VUJ obstruction)	0.5
Chromosomal anomalies	Marfan’s syndrome	2
	Down’s syndrome	1
	Di George	1
	22q11 deletion	1
	William Beuren’s syndrome	1
	Alagille’s syndrome	0.5
	Turner’s syndrome	0.5
	Genetic + Chromosomal Other	0.5
Spatial anomalies	Heterotaxia	1
	Situs inversus	0.5
	Criss-cross heart	0.5
	Dextrocardia	0.5
	Ectopia cordis	4
Other	Diabetic mother	1
	Muscular dystrophy	0.5
	Currently taking steroids	0.5
Surgical technique factors		Score
	Redosternotomy: Redo # 1, 2, or 3	2
	Redosternotomy: Redo # 4 or more	3
	Redothoracotomy	1
	Minimal invasive sternotomy	Open heart surgery with skin incision <50% manubrial-xiphoid distance
	Minimal invasive AL thoracotomy	Open heart surgery through antero lateral thoracotomy
	Minimal invasive PL thoracotomy	Open heart surgery through postero lateral thoracotomy
	Robot surgery	0.5
	Video assisted thoracic surgery (VATS)	0.5

The Aristotle Committee is currently involved in ongoing research to validate the ACC score on a multi-institutional basis. The ACC score has been used in several publications to score complex procedures [89–93].

The STS Congenital Heart Surgery Database Task Force and the Joint EACTS–STS Congenital Heart Surgery Database Committee continue to study improved methodologies of case mix complexity adjustment in pediatric and Congenital Heart Surgery. The ABC Score has been analyzed to assess its validity, and initial analysis confirms this tool as a useful and valid metric for expression of case mix complexity [79, 85]. Analysis of data in the STS Congenital Heart Surgery Database also confirms that the RACHS-1 methodology is a useful and valid metric for expression of case mix complexity [85]. Collaborative research efforts involving the STS Congenital Heart Surgery Database Task Force along with the developers of both the ABC Score and the RACHS-1 methodology eventually aim to unify these two systems and create a complexity stratification methodology based more on objective data, with subjective probability and expert opinion utilized where objective data is lacking [94]. Current efforts to unify the RACHS-1 system and the ABC Score are in their early stages, but encouraging.

13.5 Data Verification

The accuracy and completeness of our data are critical to the success of the STS Congenital Heart Surgery Database. Our patients and their families as well as third party payers and other providers all expect verification of that accuracy and completeness. Moreover, governmental agencies may soon require such verification. Internal data analysis can identify missing data elements and data inconsistencies, but cannot verify whether the data are accurate and complete. The need exists for a common methodology for data verification to be developed and implemented in all congenital heart disease outcomes registries worldwide. Furthermore, common definitions for fields such as mortality will need to be implemented into all congenital heart disease outcomes registries worldwide [69, 82, 83]. Verification of the completeness of the data is crucial because it has been previously shown that patients not included in medical audit have a worse outcome than those included [95]. The importance

of the verification of the accuracy of the data is demonstrated in a recent prospective, longitudinal, observational, national cohort survival study from the United Kingdom Central Cardiac Audit Database [96]. The United Kingdom Central Cardiac Audit Database analyzed 3,666 surgical procedures and 1,828 therapeutic catheterizations performed from 2000 and 2001, from all 13 United Kingdom tertiary centers performing cardiac surgery or therapeutic cardiac catheterization in children with congenital heart disease. Thirty day mortality was identified both by volunteered life status from the hospital databases and by independently validated life status through the Office for National Statistics, using the patient's unique National Health Service number, or the general register offices of Scotland and Northern Ireland. Central tracking of mortality identified 469 deaths, with 194 occurring within 30 days and 275 later. Forty two of the 194 deaths within 30 days (21.6% of the 30-day mortality) were detected by central tracking but not by volunteered data. In other words, hospital-based databases underreported 30-day mortality by 21.6% even though the hospitals were aware that the data would be independently verified. The authors conclude that “independent data validation is essential for accurate survival analysis” and that “one-year survival gives a more realistic view of outcome than traditional peri-operative mortality” [96]. These two publications [95, 96] clearly demonstrate the importance of data verification for both completeness and accuracy.

Collaborative efforts involving The EACTS and The STS are under way to develop mechanisms to verify the completeness and accuracy of the data in the databases. The European Association for Cardiothoracic Surgery Congenital Heart Surgery Database [64] attempted to verify the data within the databases of five European Congenital Heart Surgery Centres using Source Data Verification (SDV). Pre and post verification mortalities in all groups showed no significant differences, although 7 deaths out of 68 (10.27%) were missed. None of the other verified fields showed significant differences after verification. The authors state that SDV showed no statistically significant differences between verified and nonverified data on 30-day mortality, length of stay, age, body weight, cardio-pulmonary bypass time, aortic cross-clamp time, and circulatory arrest time. The authors also state that “an international committee of experts is needed to define common data verification

methodology and to apply it in future works on outcome analysis in congenital heart surgery (CHS).” This well done study by Maruszewski et al [64] analyzes the data properly and appropriately discusses the limitations of the analysis [65]. The authors honestly report that 7 deaths out of 68, or 10.27%, were missed. This presentation of the “missed mortality” data is more honest than stating that 7 deaths out of 1,895 operations, or 0.37%, were missed. Although, the authors state that source data verification showed no statistically significant differences between verified and nonverified data in the 30-day mortality fields, it is troubling that more than 10% of the 30-day mortality was not reported.

A new cycle of STS Congenital Heart Surgery Database audits began in June of 2007 following the annual Spring Congenital Heart Surgery Database data harvest. Five participating sites will be audited each year. All audits are being conducted by the Iowa Foundation for Medical Care (IFMC), the quality improvement organization for Iowa and Illinois. (Since 2006, STS has contracted with IFMC to conduct their Adult Cardiac Surgery Database audits.) As part of the audit team, a Congenital Heart Surgeon will participate in the audit site visit. Participating sites will be randomly selected and each site will be notified no less than 6 weeks before an audit is to be scheduled. The onsite audit will consist of pre- and post-audit meetings with the site data manager and surgeon leadership, hospital case log comparison, and data abstraction from 20 randomly selected surgical procedures. Additionally, mortality cases will also be reviewed. Twenty one data elements will be audited. Each site will receive an individual audit report within 30 days after conclusion of the audit. It should be emphasized that these audits are primarily for the purpose of identifying and helping to solve problems related to data collection and submission and, therefore, helping to improve the quality of the Database. Insuring good data quality is ultimately the only way we can achieve equitable evaluation of our performance.

Collaborative efforts continue, with the goal of improving and standardizing the methodology of data verification. The EACTS [64] and The STS now both have programs in place for site visits for onsite data verification. A combination of site visits with Source Data Verification and external data verification from independent databases or registries, such as

governmental death registries, may ultimately be required to allow for optimum data verification. Obviously, further research in the area of data verification is necessary. Data must be verified for both completeness and accuracy.

13.6 Collaboration Between Medical and Surgical Subspecialties

Further collaborative efforts are also ongoing between pediatric and congenital heart surgeons other subspecialties including pediatric cardiac anesthesiologists, via The Congenital Cardiac Anesthesia Society, and pediatric cardiac intensivists, via The Pediatric Cardiac Intensive Care Society, and pediatric cardiologists, via the Joint Council on Congenital Heart Disease and The Association of European Pediatric Cardiology.

The MultiSocietal Database Committee for Pediatric and Congenital Heart Disease has been created to foster these collaborative efforts and is composed of members of the following organizations [75, 81]:

- a. The STS Congenital Heart Surgery Database Taskforce
- b. The STS Congenital Heart Surgery Database Taskforce Core Users Group
- c. The STS Congenital Heart Surgery Database Data Verification Subcommittee
- d. The EACTS Congenital Heart Committee
- e. The Aristotle Institute, developers of the Aristotle Complexity Score
- f. The Multi-Center Panel of Experts for Cardiac Surgical Outcomes, developers of the Risk Adjustment in Congenital Heart Surgery-1 system
- g. The Pediatric Cardiac Intensive Care Society and the Virtual Pediatric Intensive Care Unit Performance System (VPS) Database
- h. The Congenital Cardiac Anesthesia Society
- i. The Joint Council on Congenital Heart Disease
- j. The Association of European Pediatric Cardiology
- k. The Pediatric Committee of the International Consortium of Evidence Based Perfusion
- l. The International Working Group for Mapping and Coding of Nomenclatures for Paediatric and Congenital Heart Disease, otherwise known as the Nomenclature Working Group

- m. The World Society for Pediatric and Congenital Heart Surgery
- n. The Center for Quality Improvement and Patient Safety of Agency for Healthcare Research and Quality of the United States Department of Health and Human Services
- o. The Birth Defect Branch of the Centers for Disease Control and Prevention

Under the leadership of The MultiSocietal Database Committee for Pediatric and Congenital Heart Disease, multiple ongoing collaborative initiatives exist:

- a. Developing regional outcomes reporting initiatives
- b. Developing improved methodologies of data verification, utilizing site visits with Source Data Verification and perhaps linking to the National Death Index in the United States
- c. Validating the Aristotle Basic Complexity Score
- d. Unifying the Aristotle Basic Complexity Score and the Risk Adjustment for Congenital Heart Surgery methodology
- e. Developing improved methodologies to assess and measure morbidity
- f. Developing improved methodologies of long-term follow-up
- g. Improving the level of national and international database participation
- h. Increasing the involvement from Africa, Asia, Australia, and South America

13.7 Long-Term FollowUp

The ultimate goal of the databases of The STS and The EACTS is the capture of all of the pediatric and congenital cardiac surgery operations in the United States, Canada, and Europe. Through collaboration with other international societies, the goal becomes the eventual capture of all of the pediatric and congenital cardiac surgery operations in the world.

Methodologies must be implemented in these databases to allow uniform, protocol driven, and meaningful, long-term followup [73, 81]. Unique patient identifier information needs to be included in multi-institutional databases to achieve meaningful long-term followup. Regulations designed to protect patient privacy, such as the Health Insurance Portability and Accountability Act in the United States of America, must be respected. We must solve the legal, technical, financial,

and ethical issues using methodology that respects patient privacy and these regulations. Congenital heart disease outcomes analysis must move beyond mortality, and encompass longer-term followup, including cardiac and noncardiac morbidities, and importantly, those morbidities impacting health related quality of life.

Methods of congenital heart disease outcomes analysis continue to evolve, with continued advances in the areas of nomenclature, database, stratification of case complexity, verification of data, subspecialty collaboration, and the development of standardized protocols for lifelong followup. Although much has been accomplished, we can do better!! We should eventually create a multi-institutional outcomes database for congenital heart disease that spans geographic, subspecialty, and temporal boundaries.

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Part II

Specific Cardiac Lesions

Chapter 14

Patent Ductus Arteriosus

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The ductus arteriosus is a normal and vital fetal structure that arises from the left sixth aortic arch. It connects the main pulmonary artery to the descending thoracic aorta just distal and opposite to the origin of the left subclavian artery (Fig. 14.1). The pulmonary end usually tapers and is narrower than the aortic end.

The histology of the ductus differs from that of arteries in that the media is deficient in elastic fibers and is instead composed of poorly arranged smooth muscle cells in a spiral configuration. This smooth muscle is especially sensitive to prostaglandin-mediated relaxation and oxygen-induced constriction.

During fetal life, approximately 60% of the right ventricular outflow is shunted across the ductus arteriosus and away from the high pressure pulmonary vascular bed. Circulating prostaglandins produced by the placenta actively keep the ductus patent during fetal life.

After birth, with the removal of the placenta and with active breathing that causes an increase in the arterial oxygen tension that inhibits prostaglandin synthetase, there is an abrupt decrease in prostaglandin levels, which then leads to ductal constriction [1]. Contraction of the medial muscle causes shortening of the ductus and its functional closure. Lately, folding of the endothelium and proliferation of subintimal layers causes permanent closure, usually during the first several weeks of life [2].

14.1 Natural History

PDA accounts for 5–10% of all congenital heart defects. The overall incidence in preterm infants is 20–30%, with the incidence arising sharply with earlier gestational age and lower birth weight (>32 weeks: 20%; <28 weeks: 60%). In preterm infants, immature ductal tissue is less sensitive to oxygen-mediated constriction and more sensitive to prostaglandin vasodilation [3].

In preterm infants, a PDA can contribute to morbidity secondary to decreased systemic flow due to the diastolic steal induced by the left-to-right shunt: renal failure, intracranial hemorrhage, necrotizing enterocolitis, abnormal cerebral blood flow, respiratory distress syndrome, and chronic lung disease (Fig. 14.2).

When left untreated, a large PDA can lead to irreversible pulmonary hypertension with the development in the mid- to long-term of a right-to-left shunt and Eisenmenger's syndrome. Supra-systemic pulmonary artery pressure can develop as early as 6 months of life.

Functional closure of the ductus arteriosus usually occurs within the first 48 h of life in most newborns of more than 36 weeks of gestation, with complete anatomic closure within 6 weeks [4–7]:

24 h	42%
40 h	78%
48 h	90%
96 h	100%

However, closure may occur later in life. It has been estimated that the percentage of PDA closing after one year of age is 0.6% per year [8].

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Prior to the antibiotic era, the average age of death in patients with a PDA who survived infancy was 36 years, with infective endocarditis being the most common cause of death.

The risk of pulmonary hypertension with moderate or large ducts, as well as the small but definite risk of endocarditis with even small ducts justifies the

current recommendation for duct closure in all clinically audible PDA.

14.2 Pathophysiology

PDA may be the source of a significant left-to-right shunt between the aorta and the pulmonary artery. Depending on the degree of shunting and the ratio of systemic and pulmonary resistances, this increased shunt may coexist with various degrees of pulmonary arterial hypertension.

The hemodynamic impact depends on the following factors:

- The size and length of the PDA* (directly proportional to the diameter, inversely proportional to the length)
- The ratio between systemic resistance (SVR) and pulmonary resistances (PVR)*
- The blood viscosity* (low viscosity increases the severity of the shunt)

Five pathophysiological scenarios may be documented as defined in Figs. 14.3–14.7.

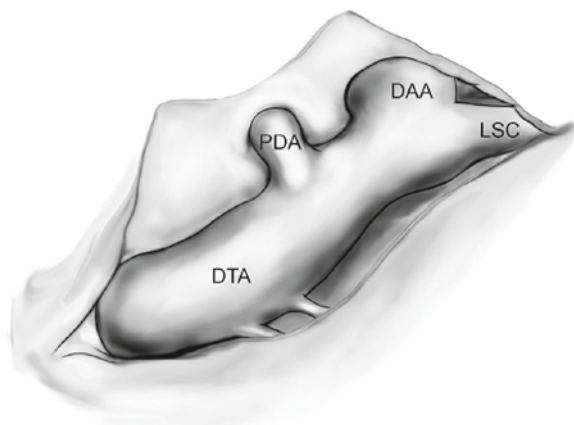


Fig. 14.1 PDA anatomy as seen through a left thoracotomy (DAA distal aortic arch; LSC left subclavian artery; PDA patent ductus arteriosus; DTA descending thoracic aorta)

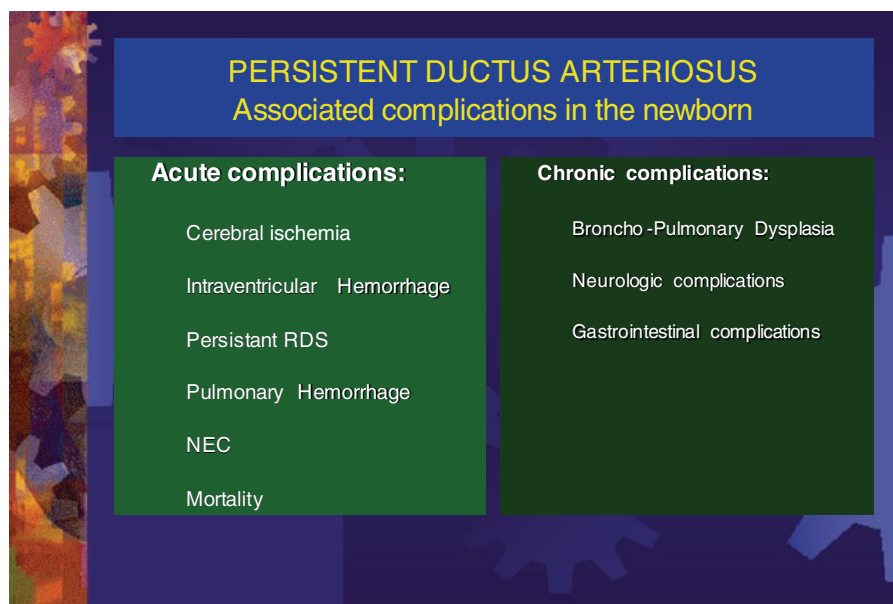


Fig. 14.2 Acute and chronic neonatal complications associated with a Persistent Ductus Arteriosus

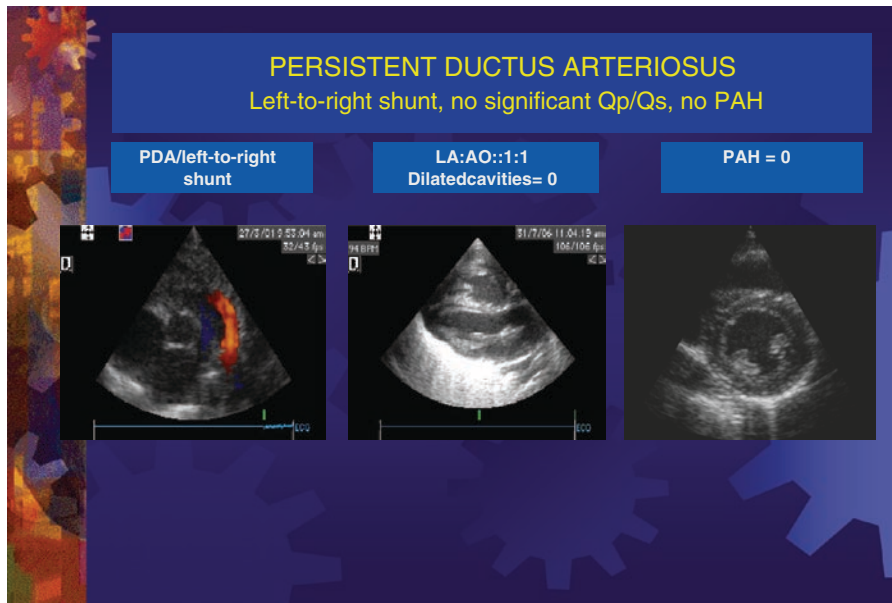


Fig. 14.3 Pathophysiological scenario 1: Left-to-right shunt through a restrictive ductus arteriosus, thus with normal Qp/Qs and pulmonary pressures (normal PVR)

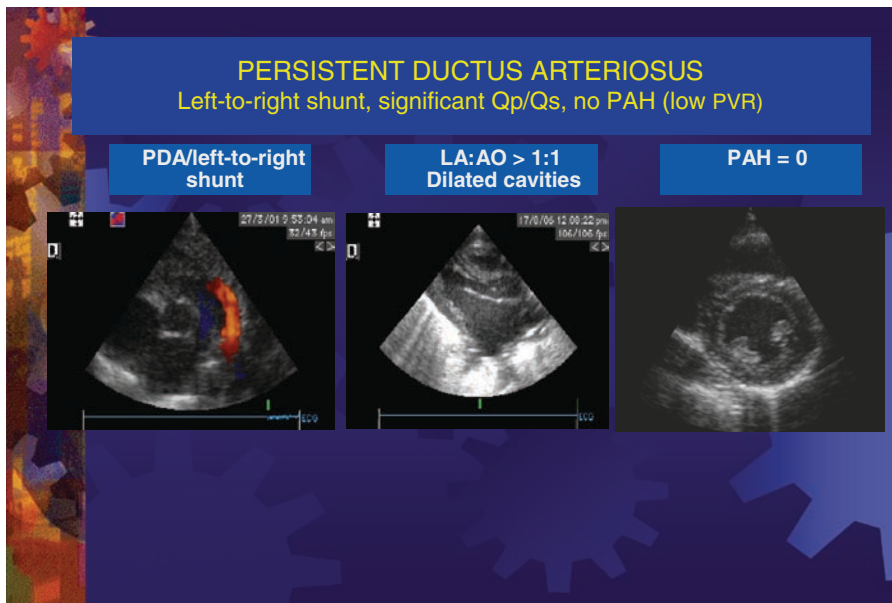


Fig. 14.4 Pathophysiological scenario 2: Left-to-right shunt through a non-restrictive ductus arteriosus, with high Qp/Qs but normal pulmonary pressures (normal PVR)

When PAH is severe and supra-systemic, there may be an inversion of both the intra-cardiac shunt (right-to-left shunt through the foramen ovale) and the extra-cardiac shunt (right-to-left shunt through the ductus arteriosus).

Once treated and when pulmonary resistances drop below systemic levels both shunts might become left-to-right this being an appeal to caution in patients with poor left ventricular function (Figs. 14.8–14.10).

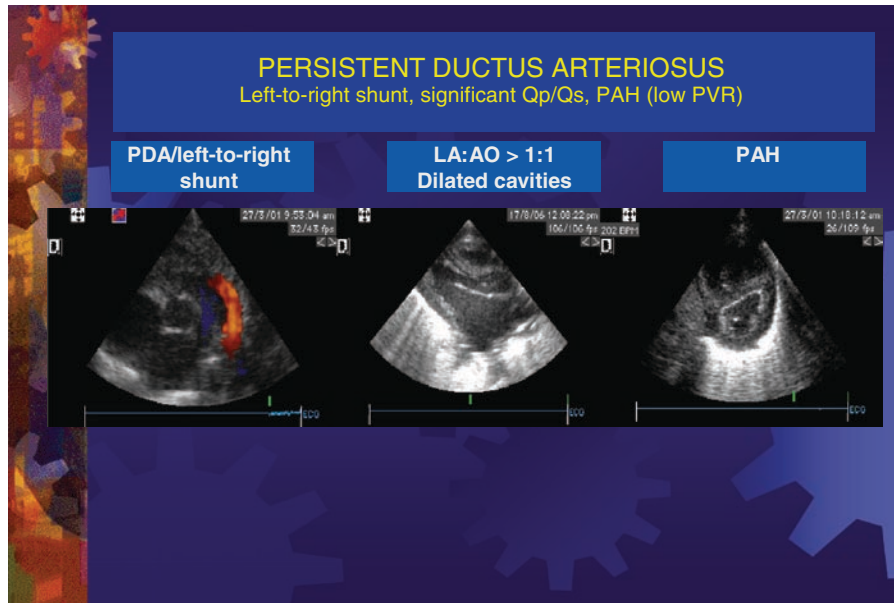


Fig. 14.5 Pathophysiological scenario 3: Left-to-right shunt through a non-restrictive ductus arteriosus, with high Qp/Qs and pulmonary arterial hypertension (low PVR)

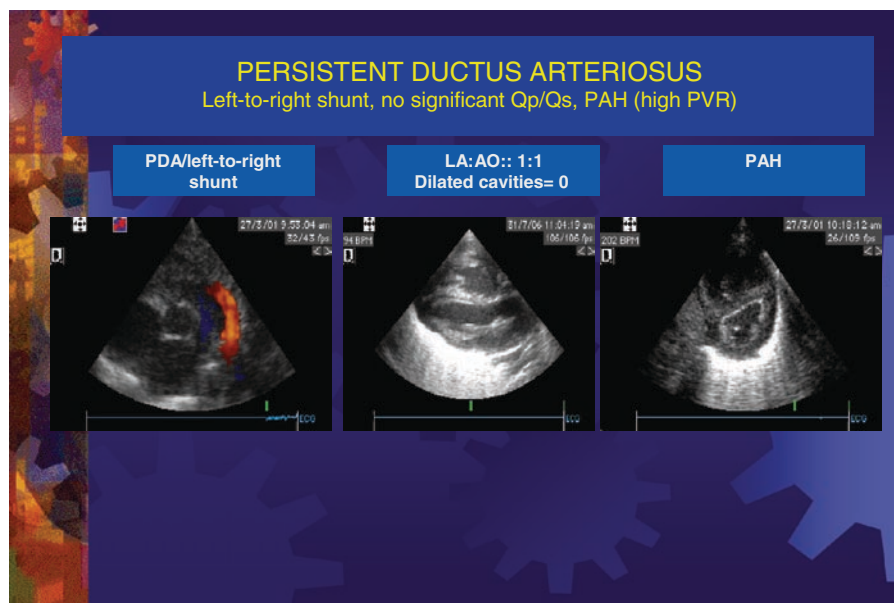


Fig. 14.6 Pathophysiological scenario 4: Left-to-right shunt through a non-restrictive ductus arteriosus, non-significant Qp/Qs and yet with pulmonary arterial hypertension (high PVR)

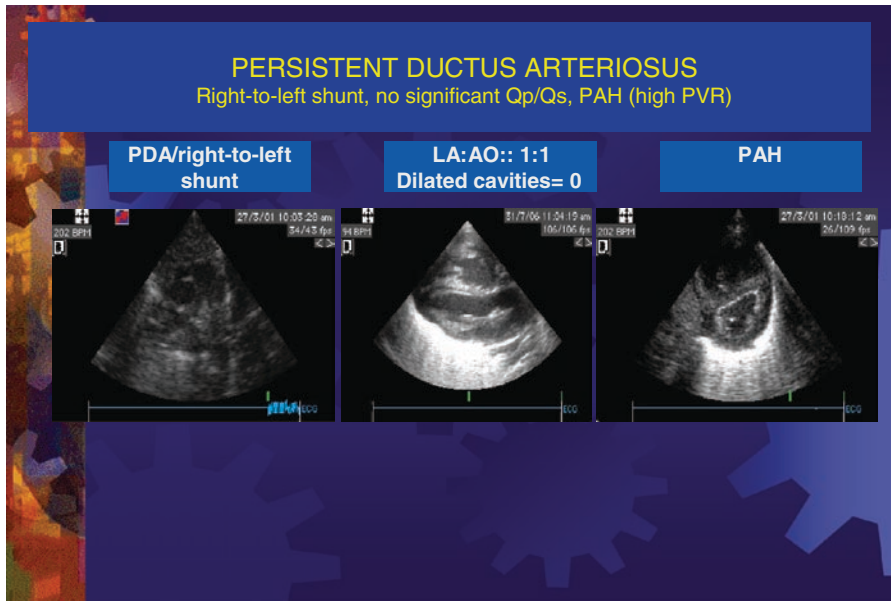


Fig. 14.7 Pathophysiological scenario 5: Right-to-left shunt through a non-restrictive ductus arteriosus, low Qp/Qs and supra-systemic pulmonary arterial hypertension (high PVR)

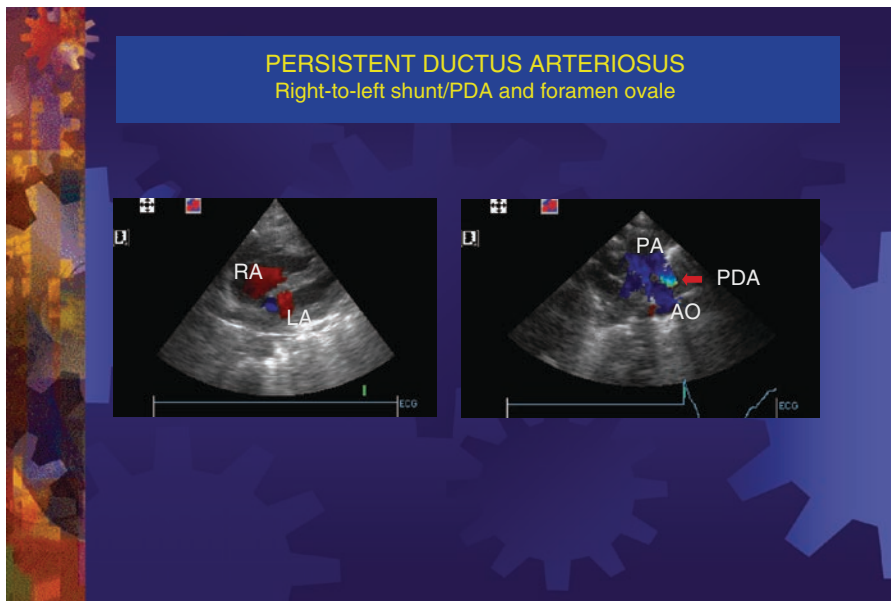


Fig. 14.8 Severe PAH with right-to-left shunt through the foramen ovale and the ductus arteriosus

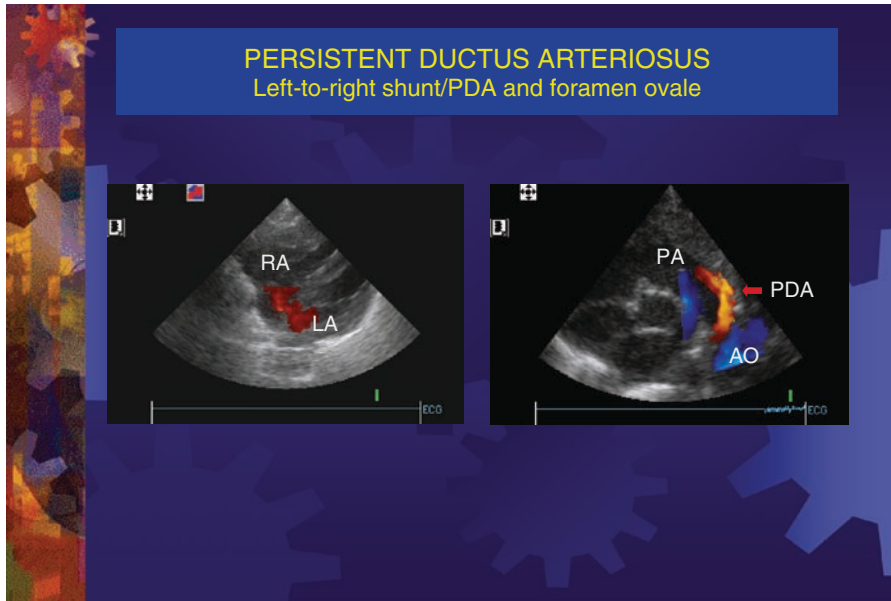


Fig. 14.9 Once treated, pulmonary hypertension becomes infra-systemic and there is an inversion of the shunt from right-to-left to left-to-right, across both the foramen ovale and the ductus arteriosus

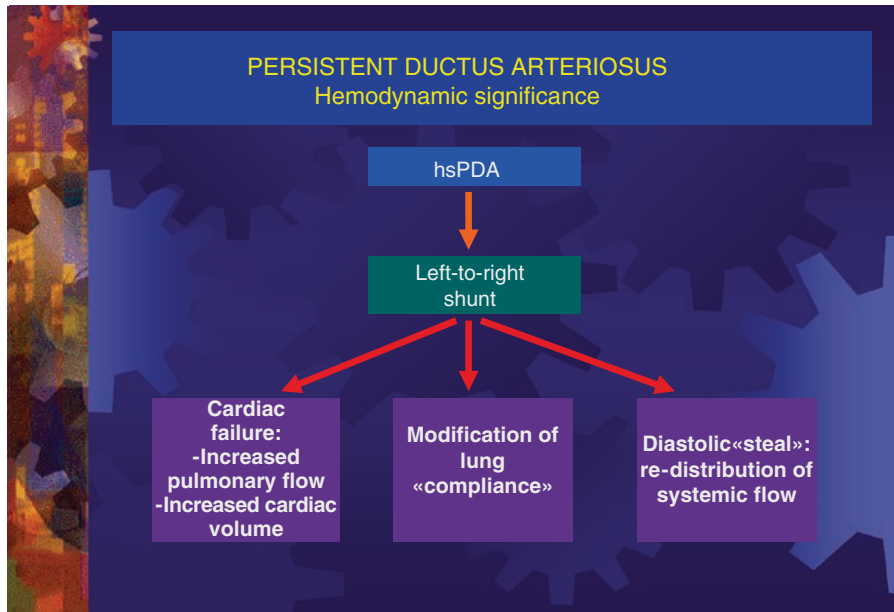


Fig. 14.10 Brief summary of the pathophysiology of the hemodynamically significant PDA (hsPDA)

14.3 Diagnosis

14.3.1 Clinical

A PDA may be symptomatic in 55–70% of premature babies with less than 1000 g or 28 weeks [9, 10]. Hemodynamically significant ductus arteriosus (hsPDA) concern 60% of premature babies less than a week-old (Fig. 14.10) [11].

Symptoms and physical findings depend on the size and length of the ductus as well as the degree of shunt, the ratio between systemic and pulmonary resistances, blood viscosity (Poussuille's law), and associated cardiac or extra-cardiac defects.

Premature babies should be screened for hsPDA in the presence of persistent dependence of the mechanical ventilation, feeding intolerance, or any complication as described above.

Clinically, the main signs (Fig. 14.11) to be explored concern cardiac murmurs, the presence of a significant systolic–diastolic gradient, precordial hyperactivity, and the anomalous peripheral pulses. Signs of cardiac failure are usually very unspecific in this patient population [32, 33].

The murmur of the PDA may be systolic, but with the increase in the size of the shunt, it becomes louder, more prolonged, and finally continuous, usually heard in the second and third intercostal space.

Pulses are bounding and reflect the degree of diastolic steal.

Clinical PDA scores (Fig. 14.12) may be useful to assess the hemodynamic impact of the PDA.

14.3.2 ECG

The electrocardiogram may be normal in small PDAs, but on increasing size of the shunt, the electrocardiogram may show moderate to severe left ventricular hypertrophy, as well as left atrial enlargement.

14.3.3 Chest X-ray

Chest X-ray findings are variable and may be normal. Classical signs of a hsPDA are mild to moderate cardiomegaly, increased pulmonary vascularization, the presence of a dilated left atrium, and of a horizontalized left main bronchi.

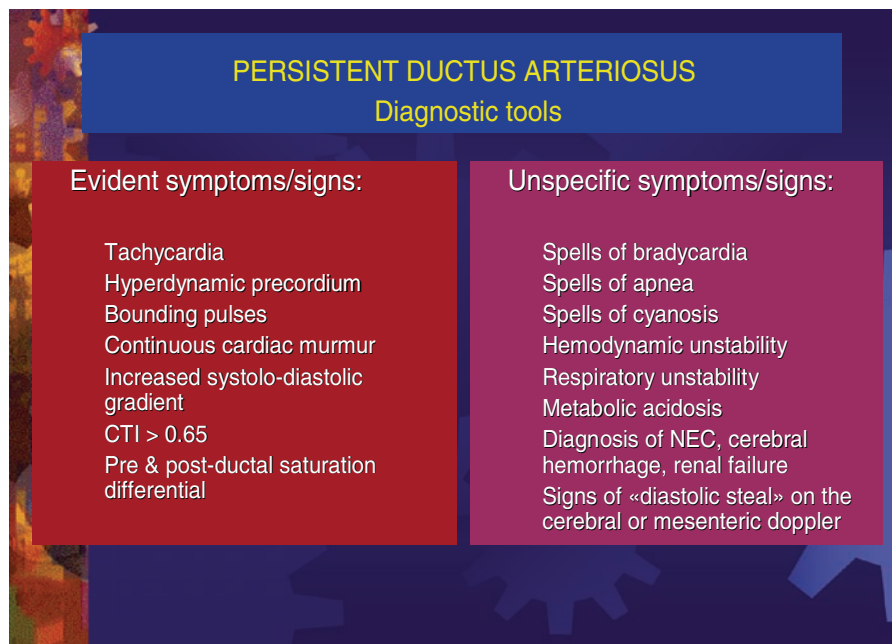


Fig. 14.11 Clinical symptoms and signs of hsPDA

PERSISTENT DUCTUS ARTERIOSUS PDA Score			
Data\Score	0	1	2
HR	<150	150-170	>170
Precordium	normal	dynamic palpation	dynamic inspection
Murmur	absent	systolic	continuous
Pulses	normal	increased SsLs	increased IsLs
CTI	<0.60	0.60-0.75	>0.75

Fig. 14.12 PDA score: a total of more than 3 points suggests the presence of a hsPDA (modified from Yeh TF et al. [35].)

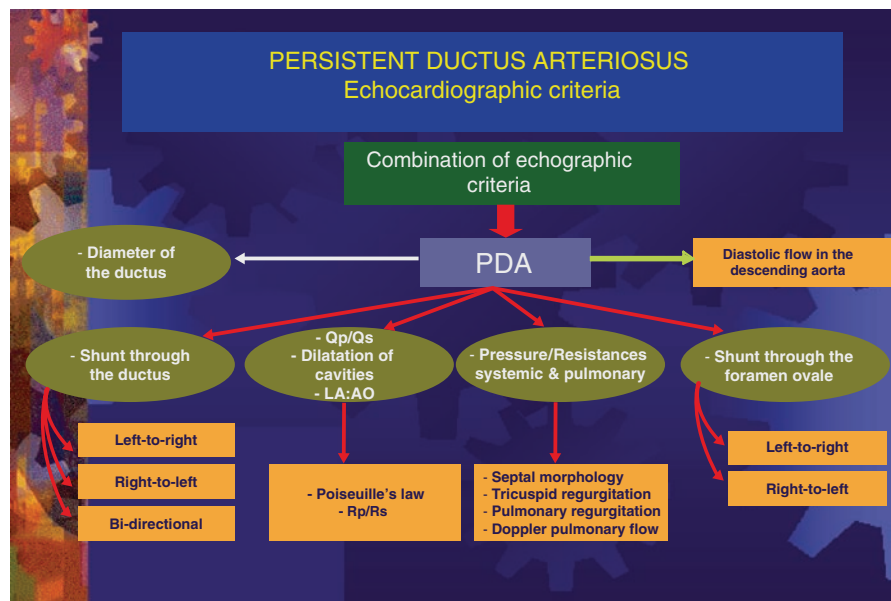


Fig. 14.13 Echocardiographic criteria in the diagnosis of Persistent Ductus Arteriosus

14.3.4 Echocardiography

Echocardiography with Doppler flow studies remains the gold standard for diagnosis of PDA (Fig. 14.13). It allows the diagnosis of the ductal patency as well as the assessment of associated intracardiac defects,

ventricular function, the degree of shunt (Qp/Qs) [34], presence and severity of pulmonary arterial hypertension (PAH). The evaluation of the shunt across the foramen ovale is also crucial. As PAH increases, a reversal of flow (becoming right-to-left) across the foramen will be observed.

Echocardiography is also fundamental in the appraisal of therapeutic efficiency.

14.3.5 Cardiac Catheterization

Diagnostic cardiac catheterization is seldom required for isolated PDA in the young infant. In grown-up untreated individuals with significant pulmonary hypertension, a cardiac catheterization should be performed prior to ductal closure.

Interventional catheterization is an outstanding tool for PDA closure but not in neonates. Currently, most persistent ductus in toddlers, infants, and children may be closed with very low associated morbidity by percutaneous techniques including coils (A) and devices (B).

14.4 Medical Management

14.4.1 Preterm and Term Neonates

When and how to treat PDA in neonates are still a controversial matter. Main principles of the medical treatment include:

- a. The use of NSAID's
- b. Fluid restriction
- c. Maintenance of a high viscosity
- d. Probably the use of loop-diuretics
- e. Phototherapy

The most commonly used NSAID's are indomethacin and ibuprofen. Indomethacin was introduced in 1976 as a method of PDA closure in preterm infants. It has since become the standard of management in preterm infants with a significant ductus. Multiple protocols have been proposed. A dose of 0.1–0.2 mg/kg is given intravenously for 3 doses, 12–24 h apart, before the infant is considered for surgical closure. A scheme of 0.1 mg/kg every 24 h for 6 days may be used in stable premature babies.

Whatever protocol is chosen (Fig. 14.14), caregivers should keep in mind that there are no medications without side-effects.

Some authors have described that the use of medical treatment with NSAID's is useless in up to 64% of treated premature babies [12]. Early treatment of hsPDA reduces symptoms, need for surgical ligation and duration of ventilatory support, and hospitalization in premature neonates [13–15]. Treatment seems to be more efficient on the first day of life and efficacy is inversely proportional to age. Late use of NSAID's might be inefficient.

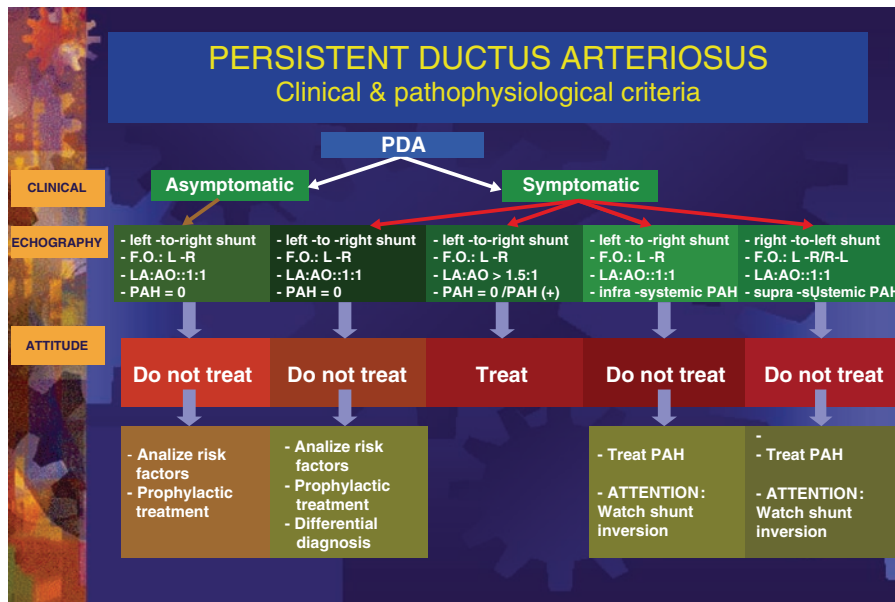


Fig. 14.14 Algorithm for the treatment of hemodynamically significant PDA in the neonate

Prophylactic use on Indomethacin is also controversial. In premature newborns <28 weeks, prophylaxis between 6 and 15 h of life may decrease the incidence of intra-cranial and pulmonary hemorrhage and the need for surgical ligation. Still, there is no evidence-based data demonstrating significant differences in mortality and complications. Further randomized, double-blind, placebo-controlled studies are required to elucidate the potential benefits of this practice.

Contraindications to the use of indomethacin include:

- a. Active hemorrhage
- b. Suspicion of NEC
- c. Diuresis < 0.6 ml/kg/h
- d. Creatinin >2 mg/dl
- e. Platelets <50,000/mm³
- f. Coagulopathy
- g. Sepsis
- h. Hyperbilirubinemia
- i. Duct-dependant cardiac defect
- j. Renal or intestinal congenital abnormality (relative)

Potential *adverse effects* are as follows.

- a. Decreased gastrointestinal perfusion
- b. Decreased renal blood flow
- c. Interference with platelet function with the potential for bleeding
- d. Possible reduction of renal blood flow
- e. Hypertension on intravenous administration [16].

Therefore, a number of recommendations should be followed prior and during indomethacin administration:

- a. Check coagulation profile prior to treatment
- b. Control diuresis before and throughout the treatment
- c. Check platelet count before and throughout the treatment
- d. Check renal function before and throughout the treatment
- e. Fasting for 48 h
- f. Echocardiography before and after the treatment

Ibuprofen has a similar effect to Indomethacin, is to be administered at 5 mg/kg/day, for 5 days and supposedly has less side effects. However, there is no evidence-based data to recommend its use over indomethacin, all the more that it is more expensive [17–25].

14.4.2 Toddler and Children

In patients beyond the neonatal period, medical treatment is seldom indicated since once diagnosed and if a murmur or symptoms are present, the PDA should be promptly closed by interventional catheterization or surgically. In case of contraindication in symptomatic patients, treatment is similar to that of any other left-to-right shunt including diuretics, systemic vasodilators and prevention of anemia. The use of digoxin is controversial.

14.5 Interventional Management

14.5.1 Cardiac Catheterization

As described earlier, most PDA, except in neonates, are closed by interventional catheterization. Please see the chapter on cardiac catheterization for further details.

14.5.2 Surgery

Surgical treatment of the PDA is indicated in the following circumstances;

- a. Therapeutic failure of the NSAID's
- b. Complications of the NSAID's
- c. Contraindication to the NSAID's
- d. PDA after treatment in an unstable premature baby

Surgery may be performed by thoracoscopy [25–28] or by mini-thoracotomy (Fig. 14.15).

14.6 Postoperative Management

14.6.1 Monitoring

Monitoring of these patients is simple and includes continuous ECG, cardiac and respiratory rate, and peripheral oxygen saturation. Central and arterial lines are seldom required unless patients have supplementary risks or associated defects.

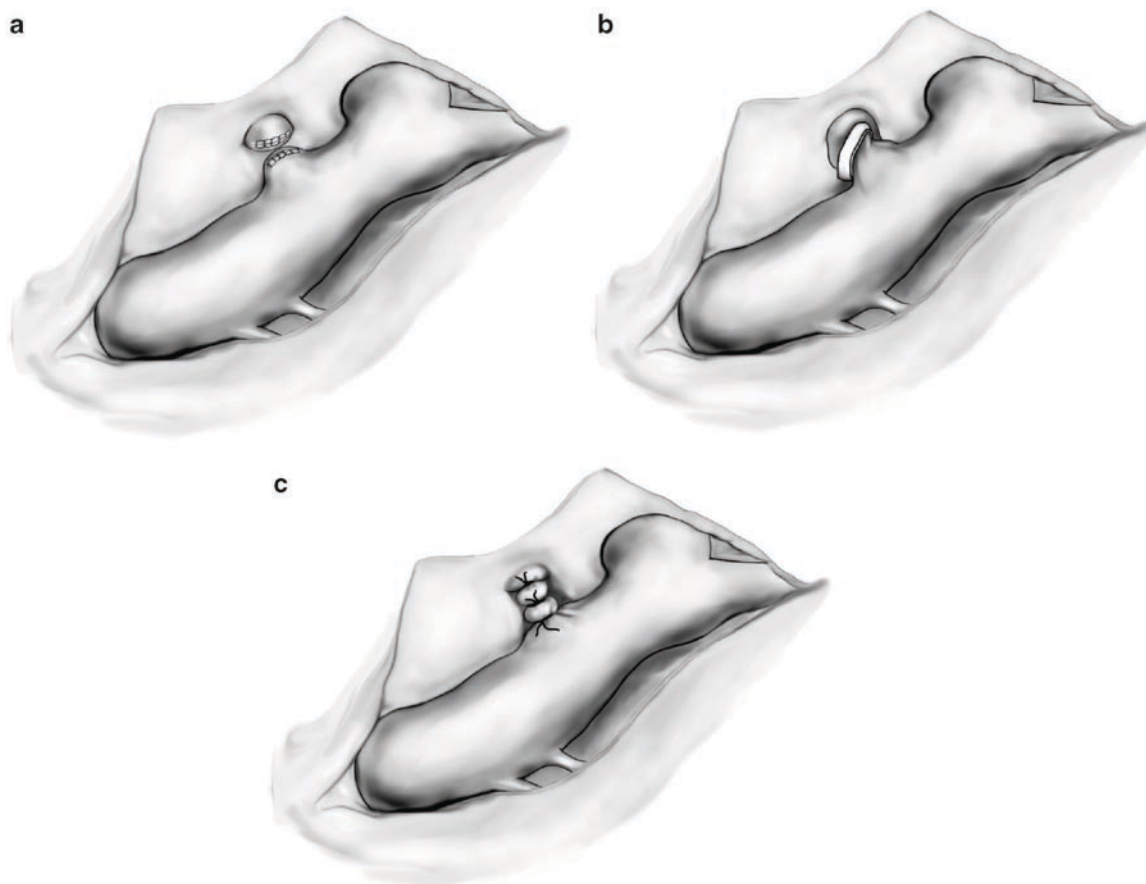


Fig. 14.15 Surgical options for repair of a PDA. Via a left posterolateral thoracotomy, or with thoracoscopy, the PDA is visualized and carefully dissected. Surgical options include (a) ligation and division, (b) hemoclip occlusion or (c) ligation

14.6.2 Fluid Management

PDA closure is a close heart intervention and therefore fluids are to be administered at the physiological rate, except in patients with severe cardiac failure or volume overload in whom fluid administration ought to be individualized.

14.6.3 Sedation and Analgesia

Thoracotomies are potentially painful. Sedation and analgesia should be provided in order to keep patients comfortable and free of pain and yet with spontaneous breathing allowing rapid extubation. The use of

nonopioid medications decreases the required doses of opioids (morphine or fentanyl) that are usually administered with low dose of benzodiazepines for the amnestic effect. In patients above 5 years of age, concomitant use of NSAID's, PCA opioid administration, or epidural analgesia may be considered.

14.6.4 Respiratory Management

After PDA closure, patients may be rapidly extubated in the operating room or else during the first six post-operative hours. Careful attention should be taken with premature babies who often require more prolonged ventilatory times, particularly in the presence of associated respiratory or other extra-cardiac problems.

Immediate failure of extubation should raise suspicion of phrenic or recurrent laryngeal nerve insult.

14.6.5 Inotropic and Vasodilator Management

After this intervention patients exceptionally need inotropic and vasodilator support. If required, dopamine should be the elective option.

14.6.6 Anticipated complications [29–31]

- a. Horner's syndrome
- b. Diaphragmatic paresis and palsy (phrenic nerve lesion)
- c. Vocal chordae palsy (laryngeal-recurrent nerve lesion)
- d. Residual shunt
- e. Repermeabilization
- f. Ligation of the aorta/pulmonary artery
- g. Aortic coarctation

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Chapter 15

Atrial Septal Defects

Steven P. Goldberg, Deborah Kozik, Lisa B. Willis, and Eduardo M. da Cruz

15.1 Introduction

Atrial septal defects (ASDs) represent a varied spectrum of deficiencies in the interatrial septum ranging from common forms existing in as many as 1 in 1,500 births (even higher if considering a pathologically patent foramen ovale under the same umbrella) to relatively uncommon ones, such as the vestibular type ASD's [1, 2]. The ASD holds a unique position in the story of congenital heart defects, as it was the subject of the very first open cardiac operation in history, as well as being the vanguard of the modern revolution in catheter-based correction of intracardiac defects.

ASD may be diagnosed as isolated anomalies or associated with other cardiac defects or with syndromes (i.e., Lutembacher syndrome when associated with mitral stenosis), sometimes linked to familiar traits (i.e., the Holt–Oram syndrome).

15.2 Embryology

The complete atrial septum actually represents the culmination of a complex interplay between formation and resorption of various parts of two individual septa. Beginning around the fourth week of gestation, the *septum primum* begins to descend from the roof of the primitive common atrium, dividing it into two on its way to meet the endocardial cushions arising from below, which partition the ventricles (Fig. 15.1a).

The *ostium primum* is the gap that remains between the inferior rim of the septum primum and the endocardial cushions. As this gap closes, in order to continue to allow interatrial mixing, the superior portion of the septum primum begins to resorb, leaving behind the *ostium secundum*. Contemporaneously with this, by the sixth week of gestation, the *septum secundum* likewise descends, curtain-like, from the atrial roof, on the “right atrial” side, finally closing off the remaining ostium primum. As it does this, however, it courses around the ostium secundum, leaving behind the flap-valve mechanism of the *fossa ovalis* (Fig. 15.1b). Save for this offset valve-like apparatus, the mature septum is a fusion of the two parallel primitive septa [3]. The common forms of an atrial septal defect, then, depend on failures at different points in this stepwise process.

15.3 Anatomy

The most common morphological subtype of ASD (80%) is the *ostium secundum defect* (Fig. 15.2a), which sits relatively centrally within the atrial septum, and can form either as a failure of septum secundum tissue to cover the ostium secundum, or as a result of excessive resorption of septum primum tissue, leaving too large a gap.

Ten percent of ASDs are an *ostium primum defect* (Fig. 15.2b), representing failure to close off the ostium primum at the base of the septum. This defect, with its nearly ubiquitously associated cleft in the mitral valve, constitutes the *partial* form of *atrioventricular septal defects*, as the absence of a ventricular septal defect, as well as the existence of anatomically separate right and left atrioventricular valves, distinguish it from its cousin, the complete atrioventricular septal defect (CAVSD), which is covered elsewhere in the text.

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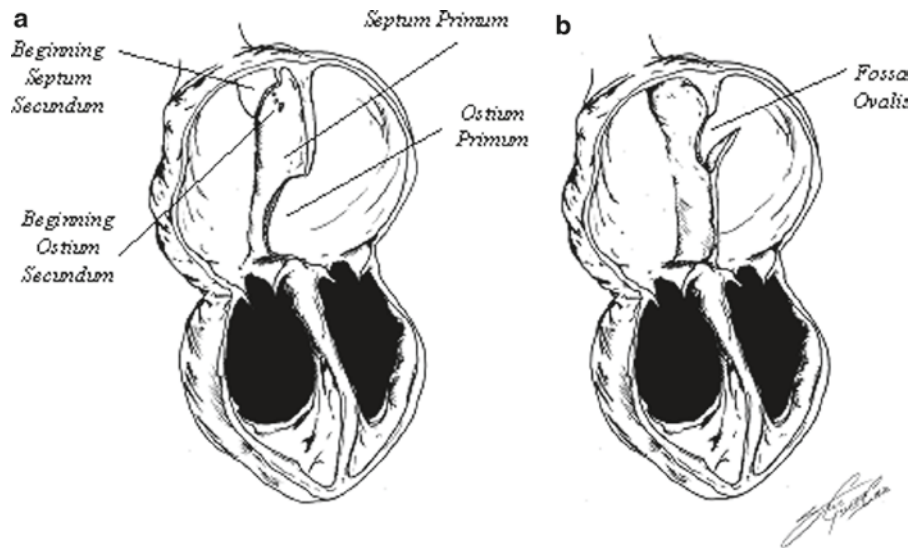


Fig. 15.1 (a): The septum primum partitions the common atrium. As the septum secundum forms, the ostium secundum begins as a vacuolization of the septum primum; (b): Fusion of both septa, except for the flap-valve mechanism of the fossa ovalis

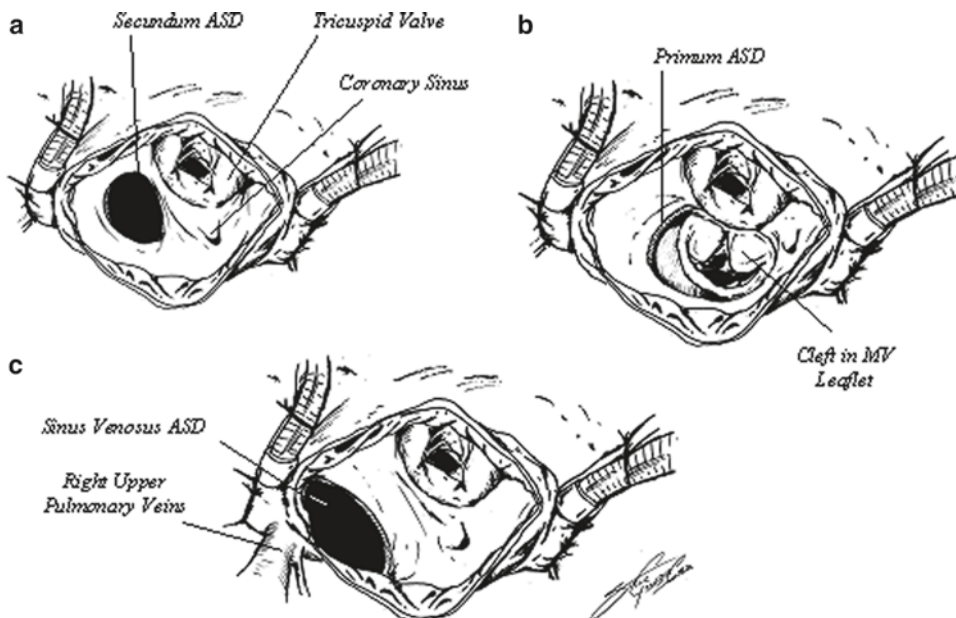


Fig. 15.2 The three major types of atrial septal defect (ASD). All views are in surgical orientation, viewed through a right atriotomy. Venous cannulas are shown in the superior and inferior vena cavae

(IVC): (a): Secundum ASD; (b): Primum ASD (showing cleft in mitral valve leaflet); (c): Sinus Venosus ASD (showing anomalous drainage of right upper lobe pulmonary veins)

An additional nearly 10% fall under *sinus venosus defects* (Fig. 15.2c), which lie high in the superior-posterior aspect of the atrium, and as such are almost invariably associated with some form of partial anomalous pulmonary venous connection (PAPVC). In the commonest configuration, one or more right upper

lobe pulmonary veins enter the right atrium (RA), either at the junction of the superior vena cava (SVC) with the RA, or more cephalad in the SVC itself.

The rarest ASD forms are the *unroofed coronary sinus*, in which the wall separating the left atrium from the posteriorly coursing coronary sinus is obliterated,

and the markedly desaturated venous effluent from the coronary sinus empties directly into the left atrium, making its way to the RA by way of the septal orifice of the coronary sinus itself [4, 5] and the *vestibular ASD*, seldom described in literature [6–8].

15.4 Pathophysiology

The main pathophysiological consequence of ASD's is the presence of an intracardiac shunt. This shunt flow is overwhelmingly left-to-right owing to the differential pressures and compliance in the two sides of the heart, yielding excessive pulmonary blood flow, and an elevated $Q_p:Q_s$ ratio. The magnitude of the shunt is only accentuated with the usual postneonatal fall in pulmonary vascular resistance (PVR). The right ventricle (RV) is volume overloaded, and becomes both dilated and hypertrophic. The enlargement of the RV bulges the ventricular septum leftward, impinging upon the left ventricular cavity, and eventually impairing the left heart function. Additionally, the RV hypertrophy increases the wall stress and diastolic pressure, impeding the filling of the subendocardial coronary vasculature in diastole. In the long-term, right atrial distension is a substrate for dysrhythmias such as atrial fibrillation and flutter. The excessive pulmonary blood flow, over time, does lead to pulmonary vascular disease and an elevated PVR if the ASD is not corrected in adulthood, but to a lesser degree than in unrestrictive ventricular septal defects [1, 5, 9].

When associated with mitral cleft or other forms of endocardial cushion defects, there may also coexist crossed shunts (i.e., left ventricle to right atrial shunt) and various degrees of mitral regurgitation leading to postcapillary pulmonary hypertension.

15.5 Diagnosis

15.5.1 Clinical

Clinically, children presenting with an ASD may be asymptomatic or discretely symptomatic on exertion, with easy breathlessness, tachypnea, and sinus tachycardia.

Clinical examination will reveal a fixed split second sound, made evident on sustained inspiration and

explained by the volume overload of the pulmonary circulation delaying closure of the pulmonary valve. Auscultation will also document a functional pulmonary systolic murmur due to the excessive $Q_p:Q_s$, and possibly a diastolic rumble across the tricuspid valve mimicking that of tricuspid stenosis.

15.5.2 ECG

Electrocardiographic features of an ASD are essentially those of right atrial enlargement and RV hypertrophy and right deviation of the electrical axis ($+100^\circ$). A first degree AV block and an rSR' pattern may also be identified. The background rhythm is usually sinus. In the presence of endocardial cushion defects, the QRS axis will vary between -30° and -120° .

15.5.3 Chest X-ray

Chest roentgenography demonstrates cardiomegaly, and possibly plethoric pulmonary hilar vessels, right atrial enlargement, and right ventricular dilatation.

15.5.4 Echocardiography

The essential mainstay of diagnostic evaluation is echocardiography (Figs. 15.3–15.6). Two-dimensional imaging is excellent at:

- Delineating the anatomic features of ASD's, the exact diameter and shape as well as the characteristics of the surrounding septum, aortic roof, coronary sinus, mitral valve, and pulmonary veins (fundamental for the assessment during the percutaneous closure)
- Following the course of pulmonary venous drainage
- Determining the degree of diastolic overload, degree of right-sided dilatation, and the presence of a paradoxical motion of the interventricular septum that is usually present.
- Evaluating for associated defects.

Color-flow Doppler interrogation is indispensable in quantifying the magnitude of the shunt, as well as

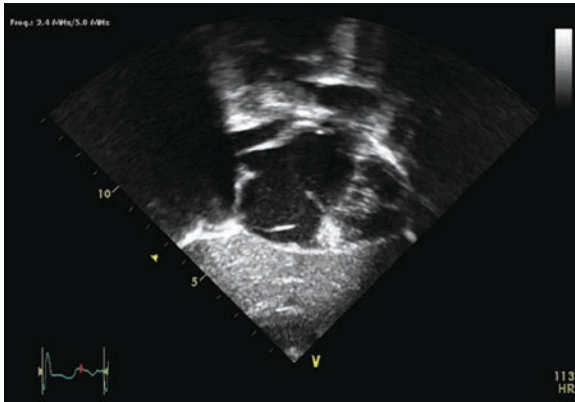


Fig. 15.3 Transthoracic 2D Echocardiography showing a large Ostium Secundum type ASD

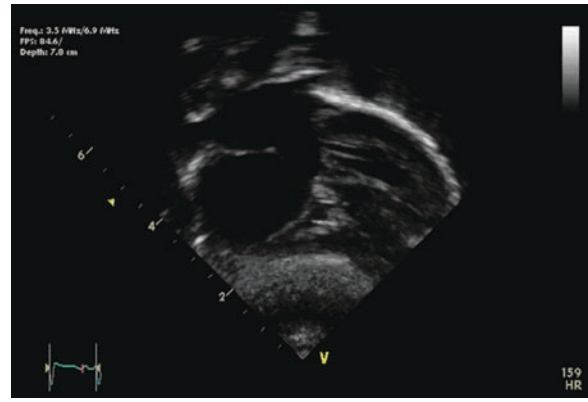


Fig. 15.4 Transthoracic 2D echocardiography showing a large Ostium Primum type ASD

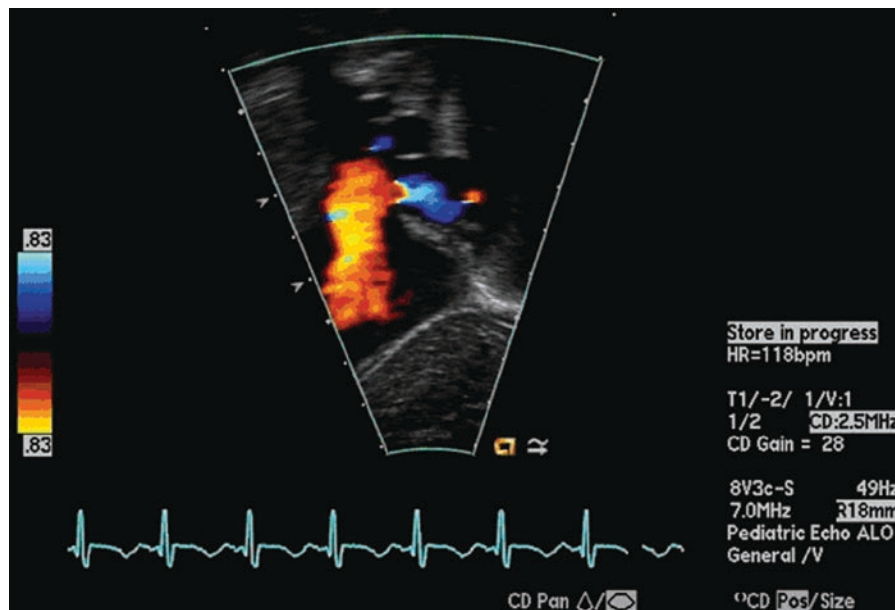


Fig. 15.5 Transthoracic Color-Doppler echocardiography showing a large Sinus Venosus type ASD

examining the degree of mitral incompetence in ostium primum defects or other anomalies with cleft anterior mitral leaflets.

Transesophageal echocardiography (Fig. 15.7) is useful to assess the immediate surgical defect and to follow the percutaneous closure of ASD and may be essential to visualize the anatomy in large-sized individuals in whom the transthoracic imaging is technically limited.

3D Echocardiography may also offer a number of useful anatomic information instrumental in taking

therapeutic decisions and in following percutaneous or surgical closure of the defect.

For the same purpose, intravascular echocardiography may also be useful in grown-up patients.

15.5.5 Cardiac Catheterization

With the quality of echocardiographic imaging in the modern era, there is limited role for cardiac

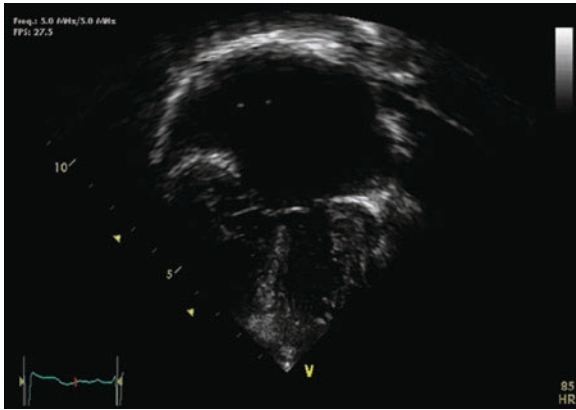


Fig. 15.6 Transsthoracic 2D echocardiography showing a single atrium

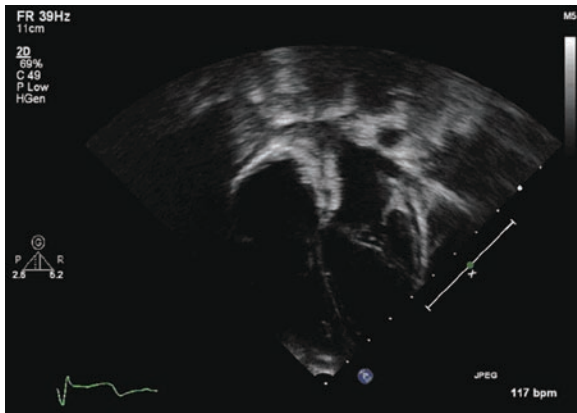


Fig. 15.7 Transesophageal echocardiography documenting the adequate position of an Amplatzer® device after delivery. Note that pulmonary veins, the mitral valve and the coronary sinus are unobstructed by the device

catheterization in the routine diagnostic evaluation of an ASD (Fig. 15.8). Indications for catheterization currently are:

- Complementary in the diagnosis of ASD with suspected pulmonary hypertension or reactivity
- Evaluation of other associated defects
- Transcatheter or percutaneous closure of the ASD itself [1, 5, 9].

15.5.6 Other

MRI does not add significantly to the findings of echocardiography.

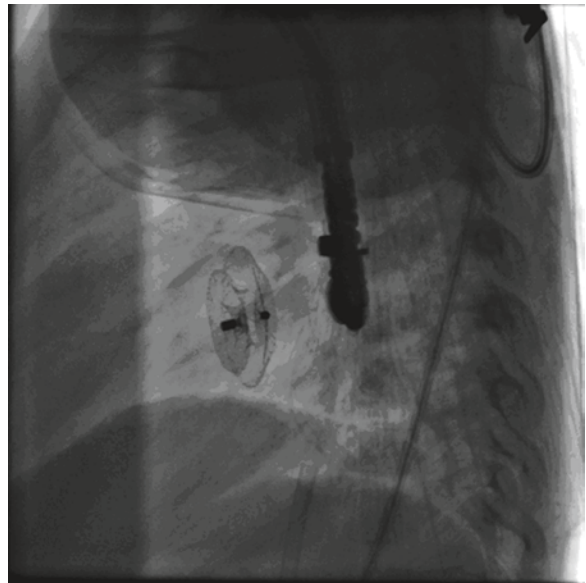


Fig. 15.8 Percutaneous Ostium Secundum ASD closure: fluoroscopy shows the Amplatzer device in situ immediately after delivery

15.6 Indications for ASD Closure

ASD's that are smaller than 4 mm have been known to undergo spontaneous closure, whereas those larger than 8 mm are far less likely to close on their own [10]. Generally accepted indications for intervention are uncomplicated defects with a $Q_p:Q_s$ of 1.5:1 or greater, or echocardiographic evidence of right heart volume overload.

Most children are repaired by 1–5 years of age, ideally before they begin school. Earlier repair definitely correlates with improved long-term survival, compared with those corrected in adulthood.

Contraindications to closure are few, but irreversible pulmonary hypertension, defined as a PVR of 8–12 Wood units/m² that does not decrease to at least seven with pulmonary vasodilatory maneuvers (e.g., 100% oxygen, inhaled nitric oxide) is the principal one, as the right heart would lose its mechanism to decompress elevated pulmonary pressures [9].

Closure may be achieved by *percutaneous* or *transcatheter procedures* or by *open heart surgery*. Ostium secundum ASDs are the main anatomic forms eligible for percutaneous closure. Ostium primum and sinus venosus ASDs or forms with significant associated cardiac defects require a mandatory surgical approach.

15.7 Percutaneous Closure

There has been a paradigm shift in recent years in the management of uncomplicated secundum ASDs, with a greater number of children able to have their defects closed in the catheterization laboratory with an increasing array of available occlusion devices. One of the more commonly used devices is the Amplatzer (AGA Medical, Golden Valley, Minnesota), which consists of two disks (the larger of the two rests on the left atrial (LA) side to hold it in place with higher LA pressure) connected by a central stalk that bridges the defect (Fig. 15.9). Success with devices such as these ranges from 80–95%, but there is a size limit to industry-made devices, and there must be a sufficient rim of atrial tissue on which to land the disks [13]. Case reports appear periodically of dislodgement and embolization of occluder devices, to either side of the circulation [13, 14]. As mentioned above, because of the anatomical features associated with ostium primum and sinus venosus defects, transcatheter closure is not used for these defects.

15.8 Surgical Management

ASD were the first intracardiac conditions to be addressed surgically. Correction of ASDs in the pre-cardiopulmonary bypass era was challenging, and included creative solutions by way of a mostly closed atrium. In 1952,



Fig. 15.9 Amplatzer occluder device closure of a secundum ASD

Floyd Lewis and Mansour Taufic at the University of Minnesota used surface hypothermia and inflow occlusion to rapidly (5.5 min) suture closed as ASD in a young girl, the first time anyone had operated inside a human heart [11]. With the advent of cardiopulmonary bypass in 1955 by John Kirklin, the modern era of closure of all manner of ASDs had finally arrived [12].

Of those secundum defects that are referred for surgical rather than percutaneous closure, many can be closed primarily by suturing the rims of the defect together. There is usually enough laxity in the tissues to allow for secure closure without tension. The other extremely common technique is patch closure with a segment of autologous pericardium that is harvested promptly after opening the chest (Fig. 15.10). Care is taken in excising the pericardial patch to avoid injury to either phrenic nerve. The operation is conducted on full cardiopulmonary bypass, usually cooling to only mild hypothermia (28–32°C), with cardioplegic arrest of the heart. There is usually enough distance between the inferior rim of the defect and the atrioventricular node as to make iatrogenic heart block an exceedingly rare occurrence. One important potential complication is inadvertent incorporation of the eustachian valve of the inferior vena cava (IVC) into the inferior lip of the patch (an area that can be difficult to see due to traction from the IVC cannula), which diverts systemic venous blood from the IVC into the left atrium, causing marked desaturation. Prompt recognition of this is vital, and the only treatment is a return to cardiopulmonary bypass and revision of the patch.

Repair of ostium primum ASDs mandates a patch, as the size and location of these defects are not amenable to primary closure. The cleft in the anterior leaflet of the



Fig. 15.10 Pericardial patch closure of a secundum ASD

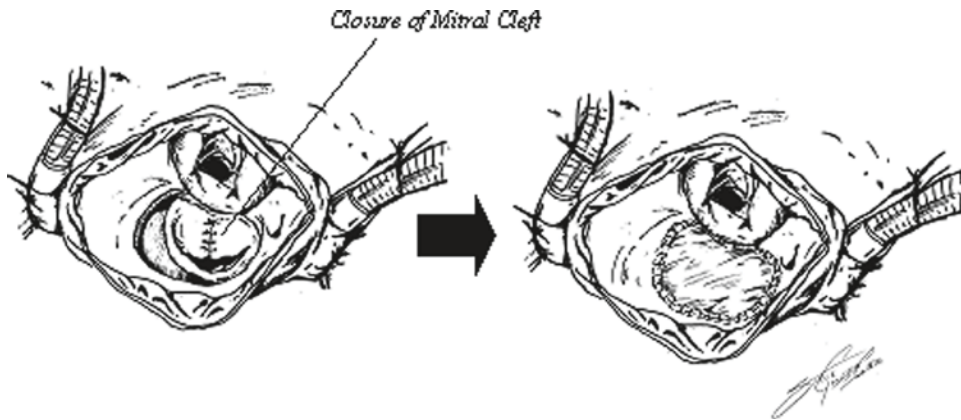


Fig. 15.11 Closure of mitral valve cleft, followed by pericardial patch closure of a primum ASD

mitral valve is sutured closed to restore competency to the valve, prior to closing the atrial septum (Fig. 15.11). Pericardium is favored in these cases over prosthetic material, as a regurgitant jet from the mitral valve striking artificial material has a higher risk of serious hemolysis. The atrioventricular node in ostium primum defects is displaced inferiorly and posteriorly (as the triangle of Koch no longer exists), and great care is taken when carrying the suture line around the region of the coronary sinus. As complete heart block is a legitimate concern, some surgeons favor carrying the patch way laterally around the coronary sinus, which would then be put inside the left atrium. The resultant right-to-left shunt is usually well tolerated.

Sinus venosus defects require a patch as well, in order to redirect, or “baffle” the anomalous pulmonary veins back into the left atrium. If the entry of the veins is relatively close to the SVC–RA junction, the patch can be carried superiorly into the lumen of the SVC (Fig. 15.12), capturing the anomalous veins within the pericardial baffle and allowing the SVC to drain normally into the RA. Two anatomical considerations mandate a change in strategy however: (a) potential luminal compromise of SVC drainage by a protruding patch, and (b) entry of the anomalous veins high in the SVC. One alternate plan is to use a second patch to augment the SVC; the other is to perform a *Warden procedure* (Fig. 15.13) [15]. The SVC is divided above the level of entry of the anomalous pulmonary veins. The ASD is then patched to include the native orifice of the SVC, which now is simply the point of entry of the pulmonary veins into the LA. The cephalad SVC, still responsible for systemic venous drainage, is then



Fig. 15.12 Patch closure of a sinus venosus ASD, redirecting the pulmonary veins to the left atrium

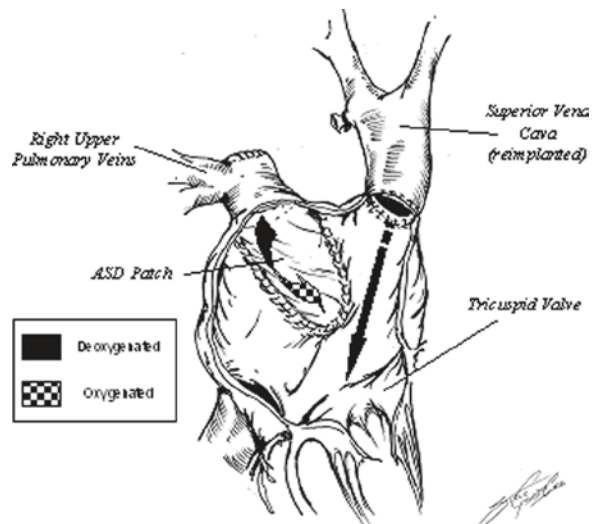


Fig. 15.13 The Warden procedure: the ASD is patched, baffling the anomalous pulmonary veins to the left, while the divided superior vena cava (SVC) is reimplanted in the right atrial appendage

reanastomosed to the RA appendage, restoring normal return to the right atrium.

15.9 Postoperative Care

After percutaneous ASD closure, patients seldom require ICU admission. Their postinterventional management consists essentially of pain control and anticoagulation with intravenous heparin until resuming enteral feeding and initiating oral antiplatelet therapy.

15.9.1 Monitoring

Monitoring is customarily by continuous ECG, cardiac, and respiratory rate and oxygen saturation, an arterial line, a central venous line and occasionally a pulmonary artery line, or a Swan–Ganz catheter if there are concerns about elevated pulmonary pressures.

15.9.2 Fluid Management

Postoperative fluid management is the same as for any case involving cardiopulmonary bypass – one-half of the age- and weight-appropriate amount of maintenance fluids because of the obligatory total body volume overload from the pump oxygenator. So, immediately upon return from the operating room it is recommended to set a goal of total fluid administration at 30–50% of maintenance requirements calculated by weight, to be increased to 75% on day 1 and to 100% on day 2.

In older children, ASD closure may be performed with hemodilution techniques. These patients remain relatively anemic and a careful control of fluid intake is required in order to avoid the need for transfusion of blood products.

15.9.3 Sedation and Analgesia

After an ASD closure the objective is to maintain patients comfortable, free of pain and anxiety, and yet with spontaneous breathing and efficient cough. Nonopioid pain

control should be promptly started and associated either NSAIDs as soon as surgical bleeding has been ruled-out. The use of low dose opioids (morphine or fentanyl) associated with benzodiazepines has proved useful during the first 48 h of postoperative course and as required. In patients beyond 5 years of age, Patient Controlled Analgesia opioid infusions are very useful. Epidural analgesia is also an interesting option to be considered in this group of patients.

15.9.4 Inotropic and Vasodilator Management

Inotropic support is seldom required. Whenever necessary, a low dose of Dopamine (2–5 $\mu\text{g}/\text{kg}/\text{min}$) and/or Milrinone (0.5–0.75 $\mu\text{g}/\text{kg}/\text{min}$) is the most common indication.

15.9.5 Respiratory Management

Most children undergoing repair of uncomplicated ASDs can often be extubated in the operating room or shortly after arrival to the intensive care unit. For this purpose, it is essential to use sedation protocols that allow spontaneous breathing.

Chest tube drainage is observed closely. The mediastinum is drained postoperatively, but the presence or absence of tubes in the pleural cavities is dependent upon whether either pleural space was entered at the time of surgery (e.g., during sternotomy, pericardial patch harvest, etc.). There are no set standards for what amount of chest drainage necessitates a return to the operating room, but a generally agreed upon guideline for acceptable drainage is <1 cc/kg/h.

15.9.6 Other

Temporary epicardial pacing wires are often not necessary in routine secundum or sinus venosus ASDs, but are often left if there were intraoperative arrhythmias encountered when coming off cardiopulmonary bypass. Because of the suture lines for a primum ASD that

course along the vicinity of the conduction bundle, pacing wires are usually included in those cases.

Routine anticoagulation is not necessary in children, but adults (particularly over 40) are more susceptible to atrial arrhythmias and thromboembolic events, and should be fully anticoagulated with warfarin for approximately 3 months.

15.9.7 Anticipated Complications

Postoperative complications are exceptional after an ASD closure. Some arrhythmias such as sinus node dysfunction, junctional ectopic tachycardia, or complete AV block may occur after sinus venosus repair or in the context of more complex endocardial cushion defects. Systemic or pulmonary venous obstructions, also more likely to happen after repair of sinus venosus type ASDs may require interventional catheterization procedures or reoperation to be rectified. In grown-up patients with borderline pulmonary pressures and resistances may also require support for pulmonary hypertension and ventricular systolic or diastolic dysfunction. Hypoxemia should motivate the search of undiagnosed systemic venous returns onto the left atrium.

Another potentially worth mentioning complication is the postpericardiotomy syndrome (PPS) that curiously occurs in a significant number of cases, throughout the first postoperative month. Patients may have discrete symptoms such as asthenia, fever, and chest pain and may develop a pericardial rub. They may also accumulate fluid in the pericardial sac and progress toward a cardiac tamponade physiology. Treatment is based on analgesia and NSAIDs. In refractory cases, steroids may be considered. Pericardiocentesis is required in case of tamponade or in cases refractory to medical treatment.

15.10 Results

In the current era, surgical mortality is 1% or less. In infants and children, long-term survival is essentially no different from the general population [9].

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Chapter 16

Ventricular Septal Defects

Diego Moguillansky, Traci M. Kazmerski, Ricardo Muñoz, and Victor O. Morell

16.1 Definition

Isolated ventricular septal defects (VSDs) are the most common form of congenital heart disease (20–25% of patients with congenital malformations) and consist of defects in any portion of the ventricular septum [1, 2]. Echocardiographic studies in newborns have shown an incidence of VSDs as high as 2%, and the substantially lower incidence of VSDs in older patients is due to the spontaneous closure of some of these defects [2].

16.2 Anatomy

Several classifications have been published regarding VSDs. In this chapter, we use a combination of the Soto's and the Van Praagh's classifications. There are four major components of the interventricular septum as described by Van Praagh and associates [3]:

1. Inlet (Atrioventricular canal)
2. Muscular
3. Septal band or proximal conal septum
4. Parietal band or distal conal septum (Fig. 16.1).

Defects can be characterized by their location in relation to these structures [3, 4].

1. *Inlet (atrioventricular canal type)*: This area of the septum is formed by endocardial cushion tissue. It

is associated with abnormalities of the atrioventricular (A–V) valves. Details about this defect will be discussed separately in the respective chapter.

2. *Muscular*: Second most common defect accounting for 10–20% of VSDs. It consists of several subtypes: apical, central, marginal, and “Swiss cheese” when multiple defects are present.
3. *Conoventricular*: These defects are located between the conal septum and the muscular – septal band septum. Includes the following:
 - a. *Membranous*: In this variety of VSD, the conal and ventricular sinus septa are normal and the deficiency is anatomically restricted to the membranous septum.
 - b. *Perimembranous*: Most common VSD; commonly associated with abnormalities of the aortic valve. It is located superior to the division of the septal band and adjacent to the junction of the septal and anterior leaflets of the tricuspid valve. In addition, it is situated immediately under the aortic valve, and it is surrounded by fibrous tissue which can be responsible for the spontaneous closure of the defect. The Bundle of His passes near the VSD at the posterior and inferior vertices of the defect.

The Van Praagh's classification considers that “perimembranous” is a misnomer for this VSD because “peri-” is the Greek prefix meaning “around” and the defect lies beside the membranous septum. They suggest that the appropriate terminology should be “paramembranous” VSD.

- c. *Malalignment*: or hypoplasia of the conal septum is typically an anterior deviation of the septum and causes a right ventricular outflow tract obstruction (TOF). A posterior deviation causes a

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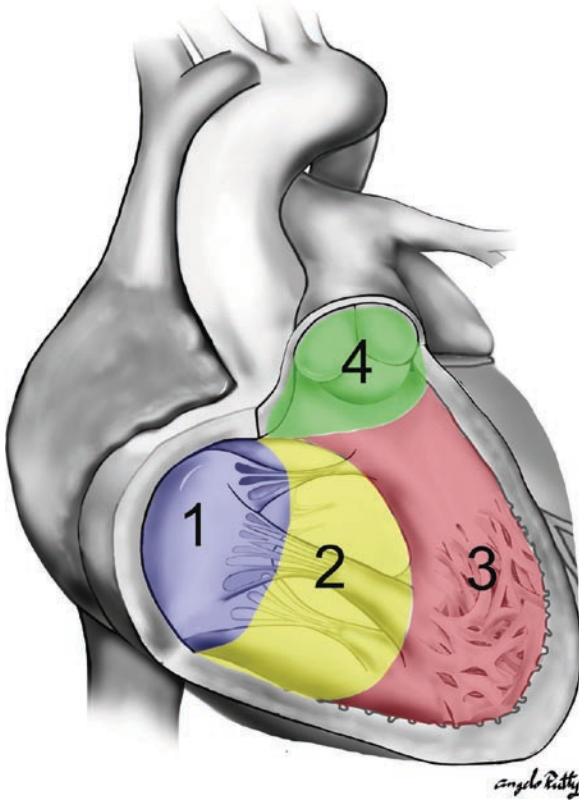


Fig. 16.1 Components of the interventricular septum: (1) inlet, (2) muscular, (3) septal band and (4) parietal band

left ventricular outflow tract obstruction (VSD associated with coarctation of the aorta and/or a hypoplastic or interrupted aortic arch).

4. *Conal septal defects (VSD of the right ventricular outlet)*: accounts for approximately 5% of defects. It overlies the conal septum and is located below the pulmonary valve. It is also called a supraceristal, conal, infundibular, or subpulmonary defect (Fig. 16.2)

16.3 Pathophysiology

The most important variables that determine the hemodynamic state in a patient with a VSD are the size of the VSD, pulmonary vascular resistance (PVR), systemic vascular resistance, and the presence of associated defects such as atrial septal defect, patent ductus arteriosus, right and left ventricular outflow tract obstruction, and arch obstruction.

In complex patients, the amount of shunting between pulmonary and systemic circulations (Q_p/Q_s) is determined by a combination of all the aforementioned factors. In the absence of other associated defects, there is initially a left-to-right shunt across the VSD causing volume overload to the left atrium and left ventricle. Depending on the amount of shunting the pulmonary artery pressure varies from normal to systemic levels. When the VSD is large, the pulmonary artery pressure is systemic and there is a significant left ventricular volume overload with the resultant congestive heart failure.

It is important to understand that high pulmonary artery pressure does not necessarily mean high PVR. When a critical level of PVR has been reached, the shunt becomes bidirectional and eventually right to left (Eisenmenger's complex).

VSDs may also be assessed and classified by the pathophysiologic features they demonstrate based on the size of the defect compared with the size of the Aortic root.

1. *Small*: Less than 1/3 of the size of the Aortic root. The size of the defect limits the left to right shunt (restrictive defect) and the degree of left ventricular (LV) volume overload is minimal. There is no tendency to develop increased pulmonary vascular resistance (PVR) and patients are usually asymptomatic.
2. *Moderate*: 1/3–2/3 of the size of the Aortic root. Patients develop moderate left to right shunts leading to LV volume overload, with subsequent development of LV dilation and hypertrophy. The left atrium (LA) also becomes dilated. The right ventricle (RV) is not dilated, and the RV pressure is only mildly to moderately elevated. The PVR is usually normal or minimally elevated.
3. *Large*: Measures more than 2/3 of the size of the Aortic root. There is no resistance to flow across the defect (unrestrictive VSD) and the degree of left to right shunt is determined by the relationship between the pulmonary and systemic vascular resistance. The LV pressure is transmitted to the RV, which becomes dilated and hypertrophied. There is a large left-to-right shunt, with significant left-sided volume overload and pulmonary edema. If left untreated, a large VSD can result in irreversible damage to the pulmonary arterial tree with development of pulmonary vascular obstructive disease (PVOD) and Eisenmenger's syndrome.

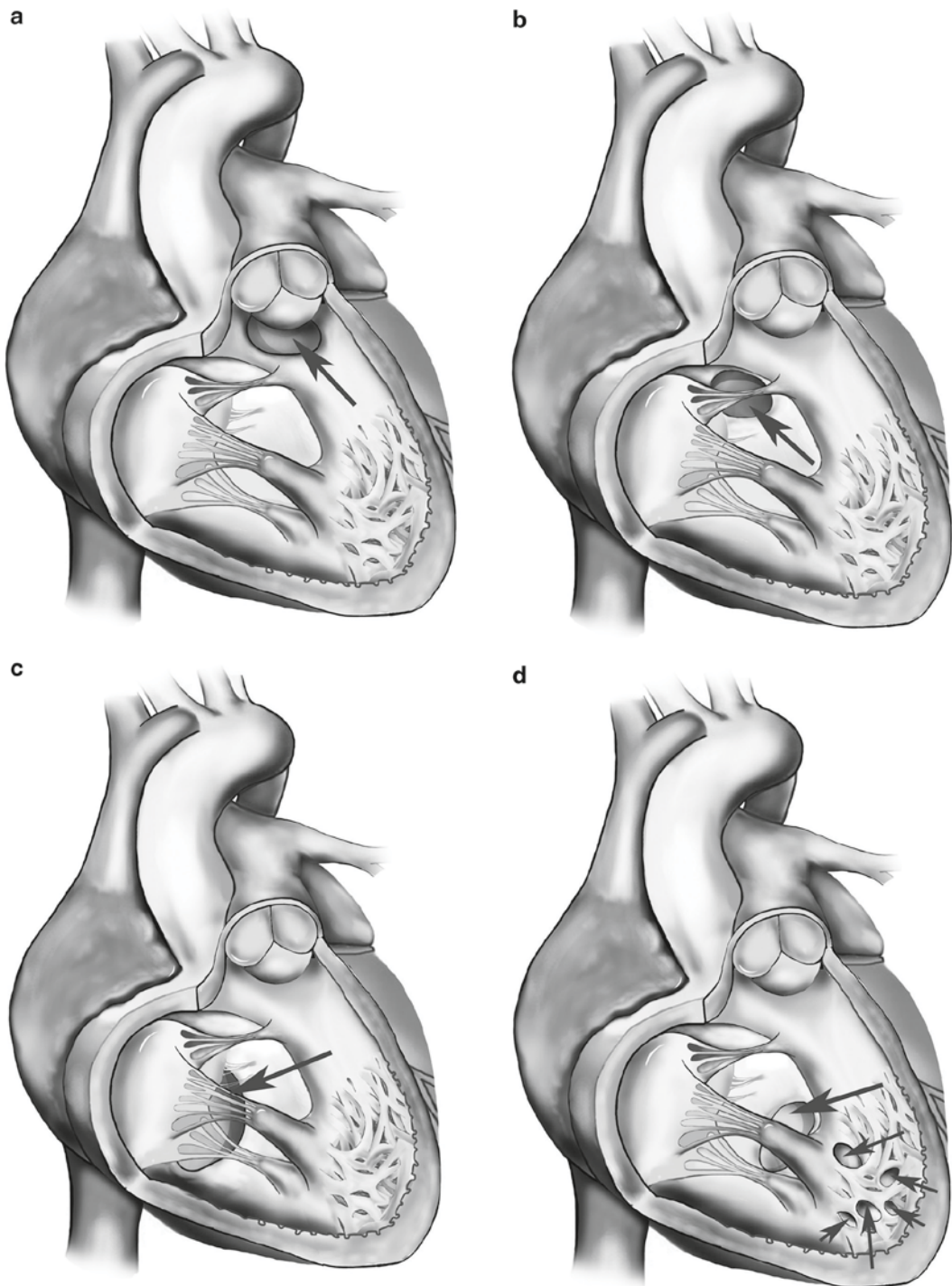


Fig. 16.2 Types of ventricular septal defects: (a) Subarterial, (b) Perimembranous (type of conoventricular defect), (c) Inlet, and (d) Muscular

16.4 Clinical Presentation

The clinical presentation of a VSD, like the pathophysiology, is determined by the size of the defect and the PVR.

1. *Small:* In neonates and infants with a small VSD, a murmur is usually noted either in the newborn nursery or during a routine examination in the first few weeks of life. There is minimal left to right shunting, and patients remain asymptomatic with normal growth and development. If the Qp/Qs is less than 1.5:1, the patient has a normal precordial impulse and normal first and second heart sounds (S1 and S2). The murmur may be low intensity holosystolic or high-pitched (reflecting a high left-to-right gradient across the septum) and mainly heard over the lower sternal area and a precordial thrill may be palpable. In conal or perimembranous VSDs the murmur may be most audible over the upper left sternal area.

The electrocardiogram (ECG) and chest X-ray (CXR) reveal no abnormalities in small VSDs.

2. *Moderate-Large:* In moderate to large defects, infants present with symptoms of heart failure as the PVR drops at 2–6 weeks of age. These may include difficulty in feeding, poor weight gain, excessive sweating, recurrent pulmonary infections, and respiratory distress due to pulmonary edema.

In *moderate defects* the physical examination yields a harsh pansystolic murmur best heard in the mid sternal border that radiates throughout the entire precordium. A soft thrill and a prominent RV impulse may be also present. In addition, an LV impulse may also be prominent. The intensity of the S2 is usually normal or increased due to pulmonary hypertension. Tachypnea and liver congestion can also be present.

ECG reveals LA dilatation and LV hypertrophy.

Cardiomegaly (due to LA and LV dilatation) and increased pulmonary vascular markings are seen on the CXR.

Large defects present with left-sided volume overload and RV dilatation and hypertrophy. The findings of the physical examination are similar to the moderate sized VSD. However, a hyperactive precordium with a prominent apical impulse as well as a prominent thrill are usually present and the intensity of the pulmonic component of the S2 is increased, reflecting elevated

RV and pulmonary artery pressures. Tachypnea and an enlarged liver are usually present, reflecting pulmonary edema and congestive heart failure.

Combined biventricular hypertrophy is seen in the ECG.

CXR shows marked cardiomegaly and pulmonary edema reflecting a larger shunt.

16.5 Preoperative Management

The preoperative management of VSDs is influenced by the natural history of the defect, which is related to size and location, and by the clinical symptoms.

Muscular and perimembranous defects, especially if they are small, close spontaneously in 80% of patients. Inlet, conoseptal, and malalignment VSDs do not close spontaneously. Conoseptal and, less frequently, perimembranous defects can be associated with prolapse of one of the coronary cusps (the right coronary or less likely the noncoronary cusp) across the VSD. Even though this event tends to decrease the left to right shunt, prolapse also causes damage to the aortic valve with the development of progressive aortic insufficiency (AI). The incidence of aortic cuspal prolapse has been shown to be as high as 73% in patients with conoseptal VSDs (with progression to AI in 52–78% of patients) and 14% in patients with perimembranous VSDs (with progression to AI in 6%) [5].

Small defects are usually asymptomatic and have a high likelihood of closing spontaneously. They do not usually require medical or surgical therapy. Moderate defects are frequently associated with symptoms of congestive heart failure (CHF) and often require medical therapy. Diuretics are commonly used and after-load reduction is achieved with ACE inhibitors.

If the patient is admitted to the intensive care unit due to severe CHF and pulmonary edema, oxygen should be administered carefully as it acts as a selective pulmonary vasodilator, which may potentially increase the Qp/Qs. Diuretic therapy should be administered intravenously and intravenous inotropic agents may be needed. The use of digoxin has become somewhat controversial, but it is also still frequently used. Anemia should be prevented and treated as required in order to maintain a normal blood viscosity. Careful monitoring to prevent the development of

electrolyte imbalances, particularly in children on digoxin, is required.

Serial echocardiograms are performed to evaluate ventricular function, monitor defect size and development of pulmonary hypertension as well as to watch for potential complications such as aortic cuspal prolapse or AI. Due to the increased caloric requirements secondary to CHF, nutritional supplementation with formulas with high caloric concentration or fortified breast milk is usually required.

Patients in whom the defect does not appear to decrease in size or that continue to have symptoms of heart failure despite medical therapy should be considered for surgery. Given the excellent surgical results in young infants, delaying surgery in clinically symptomatic patients is usually not indicated.

A small number of patients present after having developed severe PVOR and are not surgical candidates. Supplemental oxygen and partial exchange transfusions in cases of severe cyanosis as well as prevention of iron deficiency with iron supplements can be helpful. A subset of patients can be considered for lung or heart–lung transplantation. Treatment of pulmonary hypertension is indicated in patients who show response to oxygen and nitric oxide and a small number of these patients can then become candidates for surgical repair, usually with a fenestrated VSD patch or small atrial communication.

In the past, most patients underwent cardiac catheterization as a means of preoperative assessment for VSD repair. Currently, however, the size and location of the primary defect, additional VSDs, and other associated lesions can be assessed using echocardiogram with excellent sensitivity and specificity [2, 6]. Cardiac catheterization is only indicated for assessing PVR and test reactivity of PVR to different pulmonary vasodilators at this time. The size and cross-sectional area of the VSD in the initial echocardiogram is a good predictive factor to assess the likelihood of requiring surgical repair in the future. VSDs smaller than 5 mm or $0.5 \text{ cm}^2/\text{m}^2$ are very likely to close or become hemodynamically insignificant; defects larger than 6.5 mm or $1 \text{ cm}^2/\text{m}^2$ almost always require surgery [7, 8]. The location of the defect is also important, with muscular defects having a higher likelihood of spontaneous closure than perimembranous VSDs. Restrictive defects are also more likely to close [7, 9].

Conflicting evidence exists about the value of the presence of aneurismal tissue formation from the

tricuspid valve to predict the closure of perimembranous VSDs with one study finding significant association with spontaneous closure [10] and another finding no association after correcting for defect size [7]. Recently, some selected groups of patients are considered for transcatheter VSD closure [11–13].

16.5.1 Surgical Management

16.5.1.1 Indications for Surgical Intervention

Commonly accepted indications for surgical closure of a ventricular septal defect include [14]:

1. Refractory heart failure and/or failure to thrive
2. Large defects that are unlikely to close, with or without symptoms
3. Development of AI or aortic cuspal prolapse
4. Asymptomatic older children with Q_p/Q_s greater than 2.

The development of LV dilation alone as an indication for surgery has become controversial after a natural history study showed that most patients with pressure restrictive VSDs, moderate-to-severe LV dilation, and no evidence of heart failure or pulmonary hypertension will experience spontaneous resolution of LV dilation and can avoid cardiac surgery [14, 15]. The development of infective endocarditis is also no longer considered a clear surgical indication if the infection can be treated successfully and leaves no hemodynamic disturbances as long-term studies have shown that the risk of recurrence of endocarditis is very low [14–16].

16.5.1.2 Surgical Technique

Surgical patch closure of the VSD has largely become the technique of choice in most centers; it requires cardiopulmonary bypass, cardioplegic arrest, and is usually performed with mild hypothermia. The majority of conoventricular, inlet, and muscular defects can be repaired with a transatrial approach (Fig. 16.3). Conoseptal defects can be closed through the pulmonary valve and/or a transverse infundibulotomy. Apical defects frequently require closure via a right (or left)

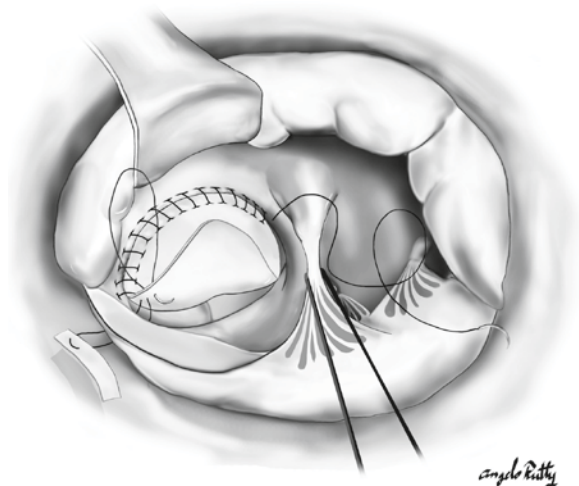


Fig. 16.3 *VSD Closure.* Via a right atriotomy, the tricuspid valve leaflets are retracted exposing the VSD. The perimembranous VSD is closed with a prosthetic patch using a running suture technique

apical ventriculotomy or via a transventricular hybrid approach. The surgical closure of VSDs can be performed with a very low mortality rate (<2%) and minimal sequelae. Injury to the conduction system causing irreversible complete heart block occurs in approximately 2% of patients.

Pulmonary artery banding (Fig. 16.4), as part of a two-stage repair, has been relegated to patients that are critically ill, have multiple VSDs, or present with associated anomalies.

16.6 Postoperative Management

16.6.1 Monitoring

Patients are monitored in an intensive care unit (ICU) setting, with an arterial line and a central venous line to provide intra-arterial pressures and facilitate frequent arterial blood gases, mix venous saturations, lactate levels, and monitoring of central venous pressures. These measurements assist in the rapid assessment of the current hemodynamic state of patients and provide valuable information on continued trends over time. Atrial and ventricular epicardial wires are also routinely used, and can be extremely helpful in the

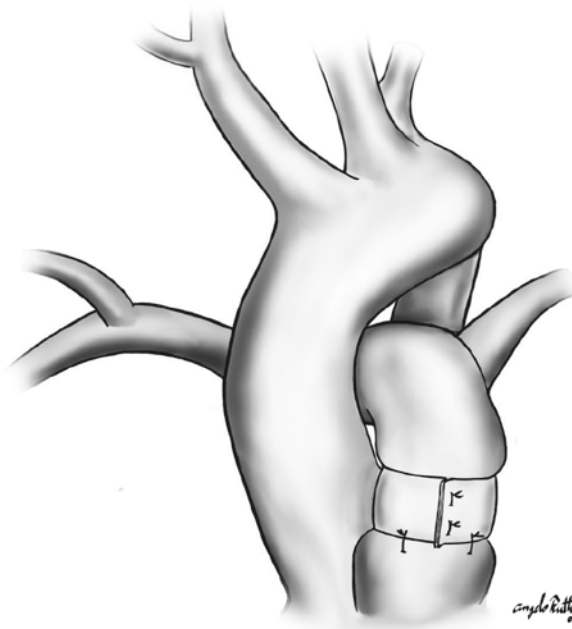


Fig. 16.4 *Pulmonary artery band.* Via a left thoracotomy or a median sternotomy the “band” is placed around the main pulmonary artery, restricting the pulmonary flow

diagnosis and treatment of postoperative arrhythmias and conduction abnormalities.

16.6.2 Cardiovascular Management

Low cardiac output syndrome is expected and inotropic support is routinely started in the operating room, echocardiographic assessment of ventricular function will determine the selection of the inotropic agent and the duration of therapy.

In our practice, at Children’s Hospital of Pittsburgh, milrinone is usually started in the operating room and is maintained for the first 12–24 h and then discontinued. Administration of milrinone in neonates and infants with low cardiac output after surgery lowers filling pressures, systemic and pulmonary arterial pressures, and vascular resistances, improves cardiac index, and increases heart rate without significantly altering myocardial oxygen consumption [17].

Arrhythmias, transient or permanent complete heart block, and junctional ectopic tachycardia may be seen in the immediate postoperative period. In the event of complete heart block upon arrival to the ICU, patients

are A-V sequentially paced (DDD mode) and pacemaker wires should be periodically tested to determine threshold and sensitivities. If the patient remains in complete heart block after 10 days, permanent pacemaker placement should be planned.

16.6.3 Respiratory Management

Young infants may arrive to the ICU intubated and extubation is usually achieved within 24–72 h after surgery, older infants and children are frequently admitted extubated. The ventilatory management of the child at risk of pulmonary hypertension is more challenging, cardiac catheterization data is critical to determine the most appropriate therapy; the combination of oxygen and inhaled nitric oxide is greatly beneficial to this subset of patients. Increase in FIO_2 and instillation of lidocaine 1% diluted to 0.25% (50 mg in 5 ml, dilution 1 ml=10 mg in 3 ml of normal saline) prior to endotracheal tube suctioning is recommended to prevent pulmonary hypertensive crisis.

16.6.4 Fluid Management

Negative fluid management is advisable during the initial 12 h after surgery and it is important particularly in patients who have an open chest, to facilitate sternal closure. Diuretics are routinely started 6–12 h after surgery.

16.6.5 Sedation and Analgesia

Sedation and anxiolysis are successfully achieved with narcotics, dexmedetomidine, and benzodiazepines. Pain control is crucial and may be ensured by a combination of opioids and nonopioid therapy. Morphine and fentanyl are the most commonly used opioids, both as boluses, PCA, or as a continuous infusion. Nonopioid therapy may be achieved with dexmedetomidine or acetaminophen or acetaminophen, eventually associated with NSAIDs once patients are deemed free of bleeding.

16.7 Postoperative Complications

Postoperative complications and sequelae of VSD repair are uncommon and include RV or LV dysfunction, cardiac arrhythmias, residual VSDs, and/or pericardial effusions. The use of intraoperative transesophageal echocardiography has become routine in most centers and enables early recognition and immediate postoperative care of some of these surgical complications [18]. Most residual VSDs do not usually warrant reoperation. The presence of RV or LV dysfunction is rare and can be associated with poor myocardial protection during the surgery. If a ventriculotomy was performed, it may also cause RV or LV dysfunction as well as the late development of ventricular arrhythmias.

16.8 Long-Term Outcomes

In general, patients with isolated VSDs have good long-term outcomes. Patients with small defects usually have an excellent prognosis, as the majority of these defects spontaneously close in the first 2 years of life and, even if they do not, have minimal hemodynamic implications. A small risk of endocarditis exists for perimembranous and outlet defects. Aortic cuspal prolapse and AI may also occur. Patients with moderate to large defects are often symptomatic and usually require anti-congestive therapy and repair. Most of these patients undergo surgery with very low morbidity and mortality and experience good long-term results.

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Chapter 17

Complete Atrioventricular Septal Defects

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17.1 Introduction

Complete atrioventricular septal defect (CAVSD) refers to a complex malformation of the atrial and ventricular septum and is defined by an abnormal embryological development of the endocardial cushions in the atrioventricular canal resulting in maldevelopment of the atrial–ventricular valves [1].

CAVSD represents around 3% of congenital cardiac defects and it is a frequent anomaly in the context of autosomic trisomic anomalies, particularly in patients with Down’s syndrome (trisomy 21) and Edward’s syndrome (Trisomy 18). Fifty percent of atrioventricular septal defects are diagnosed in patients with Down’s syndrome and 30% of these have a CAVSD [2].

The pathophysiology of this defect, and the course from diagnosis through repair, extending into the post-operative period, may be predicated upon the degree of atrial and ventricular level shunting and atrioventricular valvar dysfunction.

The term “atrioventricular defects” encompass a wide spectrum of anatomic variants and there is an overabundance of terms for this congenital cardiac defect: complete atrioventricular defect, atrioventricular canal defect, endocardial cushion defect, and there have also been many subclassifications within this defect: defects are described as partial, incomplete or intermediate, complete, and common. Partial AVSDs, with no ventricular component may behave physiologically as a primum atrial septal defect.

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An unbalanced atrioventricular septal defect should be considered as a physiologic variant of a single ventricle.

This chapter deals with the complete atrioventricular defect which we understand as characterized by the failure of development of the atrial and ventricular septum and a single orifice AV valve. For the CAVSD the results are a balanced pair of ventricles and atria that are essentially equal in size and dimensions.

17.2 Anatomy

CAVSDs are characterized by the failure of the central portions of the anterior and posterior cushions to fuse. This results in the underdevelopment of the tricuspid and mitral valves [2–5]. The anatomic expression of this deficit is quite variable, however, in most patients with this CAVSD, the endocardial cushion defect is positioned so that there is relatively equal opening into the right and left ventricles. When this is not the case and there is a left or right ventricular dominance with regard to flow through the orifice, the result is functional single ventricle physiology.

The main components of the CAVSD are as follows (Fig. 17.1):

1. *A ventricular septal defect*: in the inlet area, that is unrestrictive in the case of the CAVSD or restrictive in the case of an intermediate or incomplete atrioventricular septal defect.
2. *An atrial septal defect*: most commonly an Ostium Primum type atrial defect or a common atrium, almost always associated with a mitral cleft; an Ostium Secundum atrial septal defect may also be associated.
3. *Anomalous atrioventricular valves*: the atrioventricular annulus is shared by both the ventricles and

there are usually five components with different degrees of dysplasia, a left-sided “mitral” cleft and an abnormal sub-valvular apparatus with different types of insertions. This anatomic feature has been classified by Rastelli (Fig. 17.2). In 4–10% of cases, there may be an accessory mitral orifice.

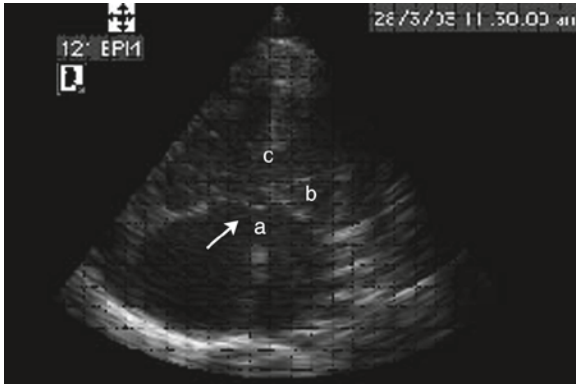


Fig. 17.1 Echocardiographic four-chamber view showing the main components of the complete atrio-ventricular canal: Ostium Primum atrial septal defect, (a) single atrioventricular valve, (b) and ventricular septal defect, (c) with a mitral cleft (arrow)

4. Various degrees of *left ventricular outflow tract obstruction*: often described as a “swan-neck” obstruction.

The CAVSD may be associated with other cardiac or extra-cardiac malformations:

1. Cardiac defects:
 - a) Persistent ductus arteriosus
 - b) Conotruncal anomalies (Tetralogy of Fallot, Truncus Arteriosus)
 - c) Aortic coarctation
 - d) Left Superior Vena Cava (LSVC)
 - e) Heterotaxy
2. Extra-cardiac defects:
 - a) Renal
 - b) Osteo-articular
 - c) Intestinal

Some malformative associations contra-indicate a surgical total repair and confine the indications to palliation and eventually to a univentricular type repair:

1. multiple ventricular septal defects
2. unbalanced ventricular mass
3. extra-cardiac contra-indications

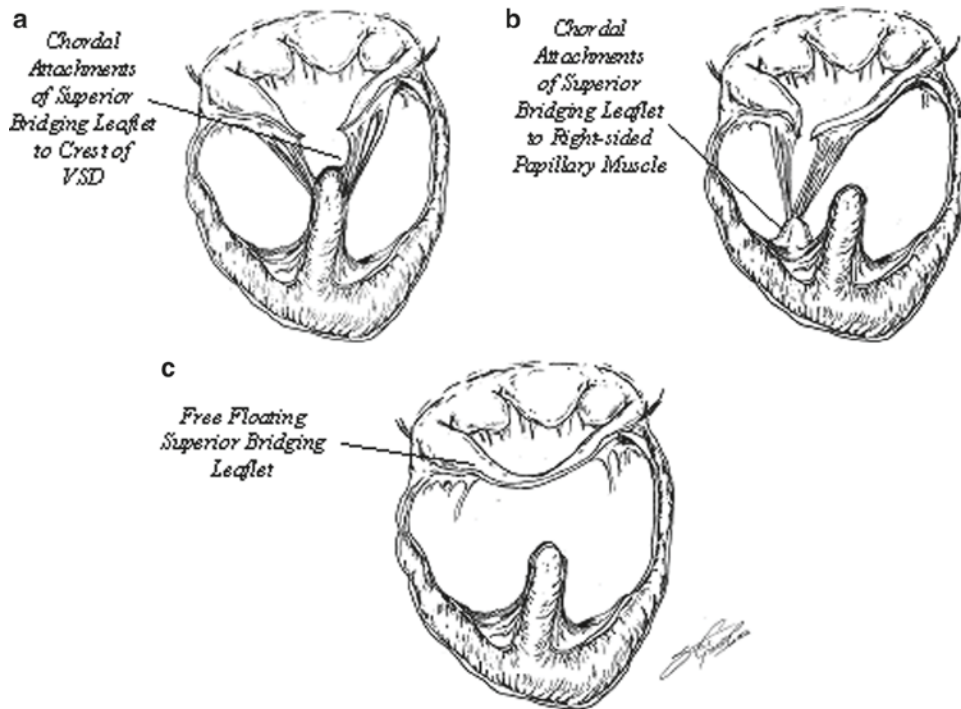


Fig. 17.2 Rastelli's classification of CAVSD

17.3 Pathophysiology

The newborn with CAVSD can be expected to rapidly develop signs and symptoms of congestive heart failure within 6–8 weeks of life as the pulmonary vascular resistance falls [6, 7]. In cases of persistently elevated PVR or commonly in infants with CAVSD and Trisomy 21, CHF may develop more slowly; however, these infants may be more profoundly cyanotic.

The main pathophysiological characteristics are described as follows:

1. Shunts
 - a) Left-to-right at the ventricular level
 - b) Left-to-right at the atrial level
 - c) “Crossed” LV–RA and/or RV–LA shunts
 - d) Right-to-left in the setting of Eisenmenger’s complex
2. Valvular Regurgitation:
 - a) Left sided AV valve regurgitation: central and/or by the cleft
 - b) Right sided AV valve regurgitation

As a consequence of these characteristics, there is a severe left-to-right shunt (Figs. 17.3a, b) with high Q_p/Q_s , unless pulmonary resistances are high. If the VSD is unrestrictive, there will be an iso-systemic, precapil-

lary pulmonary hypertension that can be worsened by a postcapillary component when the AV valve regurgitation is severe. It is important to remember that patients with Down’s syndrome may have an exquisite pulmonary vascular reactivity adding a capillary factor to the pulmonary hypertension. This, in combination with the pre and postcapillary components, can promote fixed pulmonary resistances which can progress towards an Eisenmenger’s complex early in life. Hence, there is currently a clear trend to repair this cardiac malformation around 3–4 months of age.

17.4 Clinical Presentation

As this is a mixing lesion, most infants with CAVSD’s are symptomatic soon after birth and exhibit some degree of cyanosis until the pulmonary vascular resistances decrease. As pulmonary vascular resistance falls the effects of a large left-to-right shunt become more apparent. However, the clinical presentation of a CAVSD may be determined by the characteristic of the anatomic defect [7]. Usually, the atrial septal defect is quite large, whereas, the ventricular septal defect can be of variable size. Such a patient with a large atrial level component and small ventricular component may present identical to an ostium primum defect with a large left-to-right

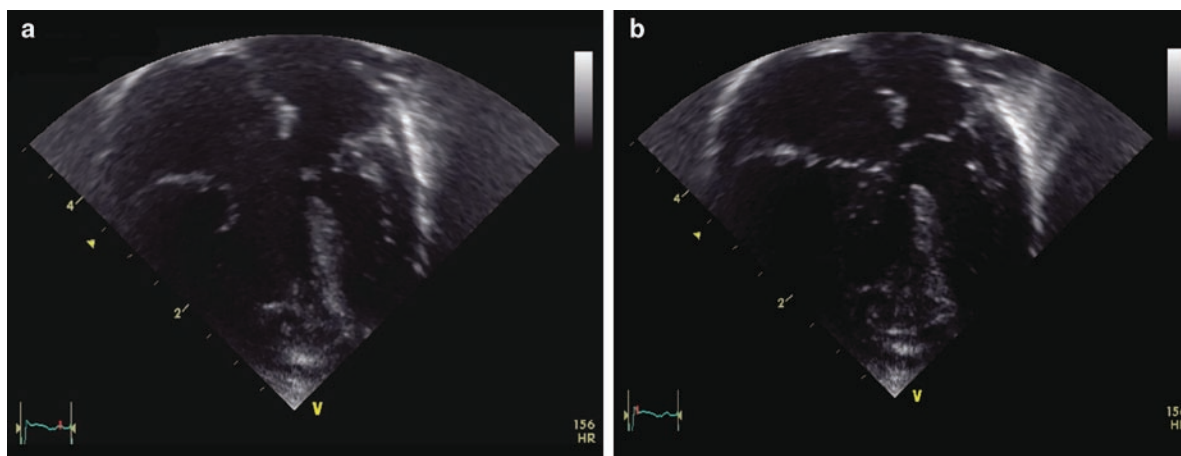


Fig. 17.3 (a) Echocardiographic 2-D four-chamber view showing a complete Atrioventricular Septal Defect with an open AV valve. When opened, this valve allows massive left-to-right shunts at the ventricular and the atrial level, as well as crossed

shunts (left ventricular to right atrial and/or right ventricular to left atrium) (b) Echocardiographic 2-D four-chamber view showing a complete Atrioventricular Septal Defect with a closed AV valve.

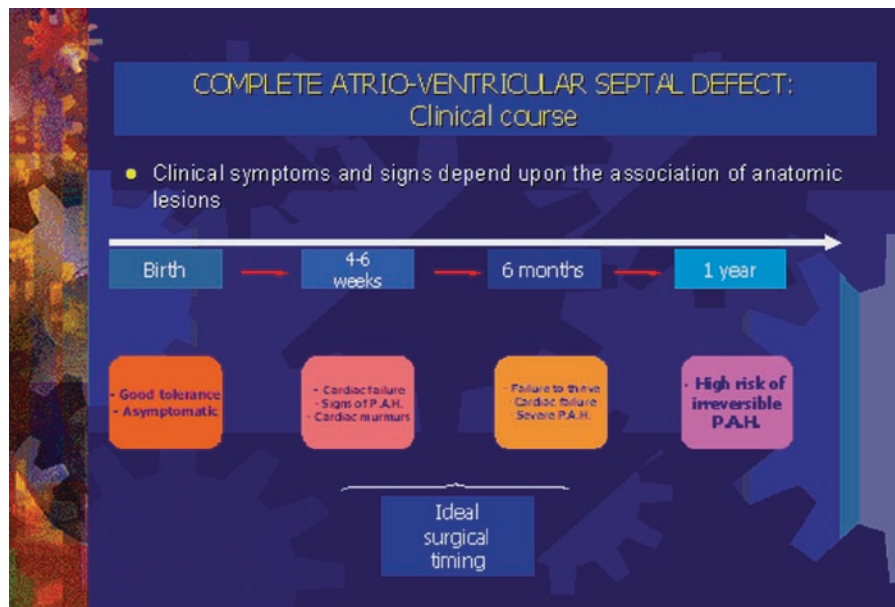


Fig. 17.4 Clinical course of complete Atrioventricular Septal Defects

atrial level shunt and a predominant right-sided diastolic volume overload. In the case of a large ventricular defect and a large left-to-right shunt at the ventricular level, the presentation is likely that of left-sided or global congestive heart failure (Fig. 17.4). Signs such as cardiomegaly, pulmonary over circulation and pulmonary edema, and evidence of end organ hypoperfusion may be present in patients who have symptoms of moderate to severe failure to thrive, breathlessness on feeding, tachypnea, and tachycardia. Over time this can progress to right-sided heart failure with elevated central venous pressures, hepatic congestion, and peripheral edema. Many of these patients are prone to recurrent airway intercurrent infections. In fact, viral infections like respiratory syncytial virus (RSV) or influenza may be poorly tolerated.

17.5 Radiology

The chest X-ray remains as an important tool in the assessment of patients with CAVSD. The classical radiological findings consistent with the left-to-right shunt are: moderate to severe cardiomegaly and increased pulmonary vascularization. In patients with severe pulmonary hypertension, the vascular markings may become normal and there may even be hypoperfusion in the case of Eisenmenger's.

17.6 Echocardiography

Echocardiography provides a complete understanding and evaluation of the CAVSD [8]. The main anatomic and physiological features to be assessed are:

1. The clear definition of the main lesions as described above
2. The degree of AV valve regurgitation
3. The ventricular balance and global function
4. The degree of shunting
5. The degree of pulmonary hypertension
6. A careful assessment of other associated cardiac malformations.

Rarely, it is necessary to employ any other modalities prior to surgical intervention, unless there is an indication for interventional catheterization.

17.7 Cardiac Catheterization

Cardiac catheterization is rarely required in the presurgical evaluation of CAVSD, particularly, if surgical correction is performed in infancy between 2 and 4 months of age in which case it will likely not yield much to the diagnosis. It should be assumed that there is likely to be elevated but not fixed pulmonary artery

pressures and this can be managed expectantly in the postoperative period.

Nevertheless, in patients who display a doubtful physiological status, cardiac catheterization may be of benefit to perform functional tests to appraise pulmonary vascular resistances and responsiveness to therapy (i.e., oxygen, nitric oxide, prostacyclin, calcium inhibitors etc.).

17.8 Preoperative ICU Management

The diagnosis of CAVSD is usually made by fetal echocardiography or soon after birth in the neonatal period. It is therefore, uncommon for the infant with a complete AVSD to present undiagnosed in severe congestive heart failure. However, the lability of neonatal and infant PVR can affect the severity of congestive heart failure and it is possible that an infant can become rapidly ill to the point of requiring critical care. A more common scenario would be the infant who requires hospitalization prior to surgical correction for failure to thrive and poor weight gain. Presurgery, these infants are also at a greater risk for respiratory failure due to pneumonias, both viral and bacterial. This justifies preventive protocols that include the administration of palivizumab for RSV and the influenza vaccine during the endemic periods.

The most common symptoms upon presentation for surgical correction are congestive heart failure based upon the degree of left-to-right shunting. At conditions of elevated altitude and/or in the presence of an elevation of the pulmonary artery pressures, these patients may need to be placed, seemingly paradoxically, on oxygen, with the recognition that under normal conditions; this would increase the left-to-right shunt and possibly exacerbate symptoms of congestive heart failure.

Surgical correction is the definitive treatment for this lesion, thus if a child presents in extremis, due to either severe congestive heart failure or elevated pulmonary artery pressures, every effort should be undertaken to ensure that he or she is an acceptable candidate and can progress to the operating room. Diuretics and afterload reduction are the mainstay of congestive heart failure treatment for these infants and children. Evaluation of end organ function prior to cardiopulmonary bypass may be needed, if these patients do present critically ill.

Preoperative management may depend upon the degree of congestive heart failure as well as the degree

of atrioventricular valve insufficiency. In the setting of severe right- or left-sided atrioventricular valve regurgitation, right- or left-sided heart failure symptoms may be quite apparent. In very symptomatic patients, early mechanical ventilation and the use of inotropic and vasodilators associated with loop-diuretics may be instrumental in optimizing the condition of the patient prior to the surgical intervention.

More often than not, the preoperative management of the infant with complete AVSD is managed by the outpatient cardiologist and general pediatrician, and care centers around managing congestive heart failure and perhaps the underlying pathologies related to chromosomal abnormalities specifically trisomy 21. Classical management includes the use of diuretics, oral vasodilators, and often digoxin, (although the usefulness of digoxin is controversial). Avoiding anemia is also an important factor in the medical management of these patients.

Failure to thrive may encompass many etiologies, including genetic abnormalities and it is important to remember that moving ahead with surgical correction may improve some, but by no means all, the symptoms of failure to thrive.

17.9 Surgical Management

There are three main objectives in the surgical management of patients with a complete atrioventricular canal defect and they consist of the elimination of the intra-cardiac shunting by closing the ASD and the VSD, the creation of two AV valves from the common valve, and the repair the left-sided cleft [9–11]. Three surgical repairs are commonly used for this lesion, the one-patch technique (Fig. 17.5), the two-patch technique (Fig. 17.6), and the Australian technique (Fig. 17.7). They are all performed via a median sternotomy incision, with cardiopulmonary bypass and the administration of cardioplegia.

Right or left ventricular hypoplasia is frequently seen in patients with unbalanced atrioventricular valve anatomy, often requiring a single ventricle repair. Occasionally, surgical palliation (pulmonary artery banding) is indicated as the initial form of surgical therapy for the management of high-risk patients, including those with significant prematurity and/or multiple other congenital anomalies.

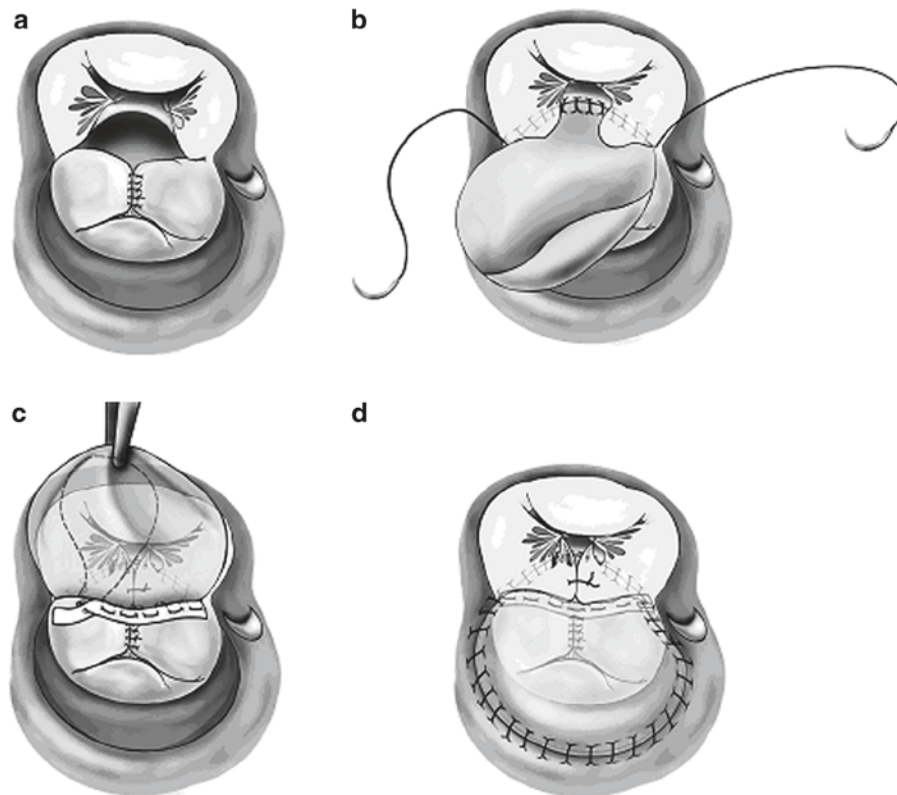


Fig. 17.5 One Patch Technique (a) First, the cleft in the left-sided atrioventricular valve is closed with interrupted sutures, (b) the VSD is closed with the patch; the sutures are placed on the right side of the crest of the ventricular septum to avoid injuring the conduction system, (c) the medial edge of both

valves is sutured to the VSD patch; a strip of autologous pericardium is used along the left AV valve sutureline for reinforcement, (d) The atrial segment of the patch is used to close the interatrial communication, leaving the coronary sinus draining into the right atrium

17.10 Postoperative Management

17.10.1 Monitoring

Postoperative management of the patient with CAVSD may be assisted by the placement of a pulmonary artery catheter (Swan-Ganz or trans-thoracic catheter) or left atrial line to monitor pulmonary artery or left sided pressures, in addition to arterial and venous lines. It should be expected that many of these children will experience some elevation of their pulmonary artery pressures due to preoperative elevated pulmonary vascular reactivity perhaps exacerbated by exposure to the inflammatory insult of cardiopulmonary bypass.

In addition the standard hemodynamics parameters are carefully monitored. Recent modalities are used to

assess cerebral and somatic perfusion and regional oxygen delivery and utilization. These include acid-base status, serum lactate and SvO₂. Near-Infrared Spectroscopy is also becoming a very useful technology to assess regional perfusion in these patients.

Important premises that need to be taken into account when managing the postoperative course of a CAVSD are:

1. Even after a good surgical repair, AV valves remain abnormal. It is therefore essential to protect the AV valvular plasty, by avoiding volume overload and systolic hypertension that would reflect the inter-ventricular pressure during systole.
2. Patients, particularly those with Down's syndrome, are predisposed to and at risk for pulmonary arterial hypertensive (P.A.H.) crisis.

Fig. 17.6 *The Two Patch Technique* (a) The cleft of the left-sided atrioventricular valve is closed with interrupted sutures, (b) The VSD patch is sutured on the right side of the crest of the ventricular septum to avoid injuring the conduction system, (c) the medial edge of both atrioventricular valves is sutured to the VSD patch; the same sutures are used to secure the medial aspect of the ASD patch, (d) The ASD patch suture line is completed

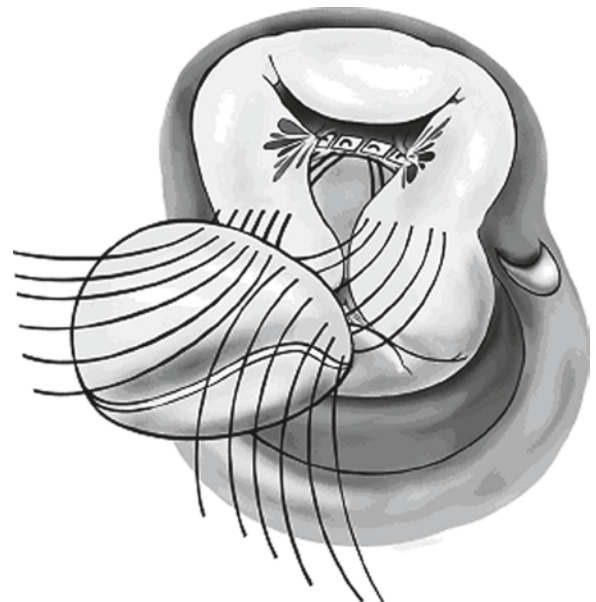
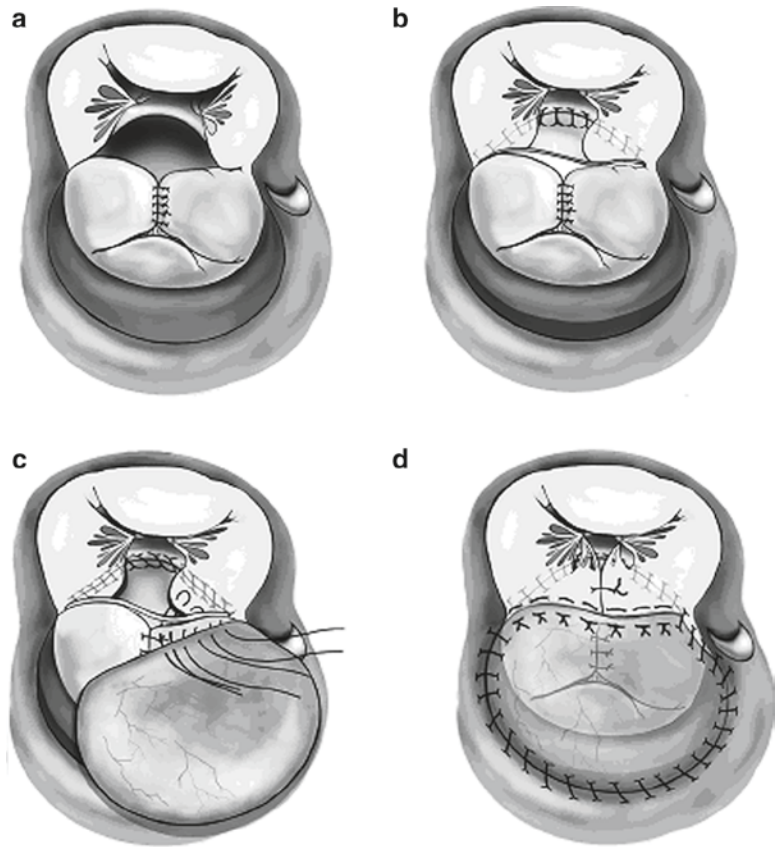


Fig. 17.7 *Australian Technique*. This technique requires multiple pledgetted sutures to be placed along the right side of the crest of the ventricular septum and passed through the common atrioventricular valve and then the atrial septal defect patch. Once all the sutures are tied, the atrioventricular tissue is brought down to the level of the crest of the ventricular septum, obliterating the ventricular septal defect. The cleft is repaired in the usual fashion

The postoperative strategy for the child with CAVSD should include and target the following specific aspects of support:

- a) Anticipation of and aggressive treatment of P.A.H. crisis
- b) Attempt to maintain low filling pressures (preload)
- c) Providing appropriate inotropic support and systemic vasodilation
- d) Vigilance for arrhythmias and heart block
- e) Prevention and treatment of specific problems and anticipated complications as specified below

General intensive care measures that are also crucial in the management of these patients, are:

- a) Careful assessment of extra-cardiac abnormalities
- b) Maintenance of physiological body temperature
- c) Maintenance of anabolic status (aggressive enteral and parenteral nutrition)
- d) *Ad minimum* handling
- e) Providing gastric protection
- f) Treatment with anti-coagulation/anti-fibrinolytic agents as required

17.10.2 Mechanical Ventilation

After surgical correction, rapid extubation may be possible. However, the underlying preoperative physiology may dictate attention to particular potential complications in the postoperative period. Though, these complications can be anticipated and treated, they also may delay extubation and progression of care.

Ventilation around the expected functional residual capacity (FRC) can prove difficult. In many cases this translates into providing adequate support to prevent atelectasis and limit overdistention and the maintenance of a normal or even alkalotic arterial pH via hyperventilation. Care must also be taken to avoid barotrauma and volutrauma as these can cause alveolar damage and further increase pro-inflammatory cytokines and further agitate an already reactive pulmonary vascular bed.

General considerations regarding mechanical ventilation:

1. Positive end expiratory pressure (PEEP)

With normal lungs PEEP should remain around 5 cm H₂O

In case of interstitial edema or hypoxemia, cautious increments as required

With such adjustments, cardio-pulmonary interactions must be considered

2. Acid-base Status

This factor exerts a strong influence on pulmonary vascular resistances.

It is recommended to target a relative alkalosis, with a pH between 7.45 and 7.55, this being particularly useful in case of elevated PVR.

Some groups discuss the use of ventilation versus HCO₃⁻ or THAM infusions to ensure such alkalosis with less barotrauma.

3. Hyperventilation may be useful during the acute PAH crisis
4. Permissive hypercapnia is a useful tool as a pulmonary reactivity test, prior to weaning ventilation
5. HFOV may be considered in patients with significant parenchymal involvement or requiring high ventilatory parameters in conventional ventilation.

17.10.3 Fluid Management

Immediately upon return from the operating room it is recommended to set a goal of total fluid administration at 30–50% of maintenance requirements calculated by weight. Volume administration and resuscitation depends upon the clinical situation and it is not uncommon that the child status post CAVSD repair requires hemodynamic support in the form of intravascular volume. However, it is important to remember the specifics of surgical repair and that in the immediate postoperative the reconstructed right- and left-sided AV valves may be vulnerable to injury and even disruption if volume is given too aggressively.

17.10.4 Sedation and Analgesia

The strategy for sedation and analgesia in the postoperative CAVSD repair depends in part upon the pre-morbid and co-morbid state of the child in the intensive care unit. Stable hemodynamics, low ventilator requirements, the absence of serious arrhythmias, minimal postoperative bleeding, and low pulmonary artery or

left atrial pressures may dictate early and rapid extubation, and therefore, intermittent administration of analgesics and sedatives until the child is deemed ready for this. In this case, the shorter acting opioids such as fentanyl and shorter acting sedatives such as midazolam may be preferred, all the more that it has been shown that fentanyl is more efficient and better tolerated in patients with pulmonary hypertension, when compared with morphine.

However, if the postoperative CAVSD exhibits hemodynamic instability, abnormal lung mechanics, malignant arrhythmias such as Junctional Ectopic Tachycardia, or elevated PA or left atrial pressures, it may be prudent and in fact necessary to keep the child sedated, eventually on muscle relaxants and mechanically ventilated until the time that these issues improve and/or resolve. In this case a continuous infusion of analgesia and a sedative is recommended.

The child with trisomy 21 and CAVSD may present particular obstacles for an effective sedation strategy. As mentioned earlier these are the children who carry the biggest risk of PAH. They are also known to suffer from decreased muscle tone, redundant pharyngeal tissue, and airway obstruction. They are often difficult to effectively sedate and require rapidly escalating doses of sedatives and analgesics. It is our experience with these children that we often adopt a strategy of a “gentle and deep extubation” in the intensive care unit. In these circumstances avoiding peri-extubation agitation that can exacerbate PVR lability or airway compromise, or both is desired. Sedation may be provided with propofol or dexmetomidine: since, either drug may allow for spontaneous breathing during endotracheal tube removal and both share the pharmacologic properties of rapid onset and rapid metabolism with short half-lives.

17.10.5 Inotropic and Vasodilator Support

Inotropic and vasoactive support for the CAVSD in the postoperative period is not so different from many of the other congenital lesions. Afterload reduction is the mainstay of treatment to facilitate postsurgical left-sided AV valve competency and to optimize cardiac output [12, 13]. This is achieved with milrinone and if necessary with agents such as sodium nitroprusside,

nitroglycerin, or esmolol. In the setting of overall low cardiac output, vasopressor support with dopamine and low dose epinephrine is not uncommon.

Concern must be paid to the proarrhythmic properties of these vasopressors and the potential for postoperative junctional ectopic tachycardia or JET. However, depending upon the complexity of the repair, the myocardium may require such support. It is our approach, to be generous in the support of the struggling postoperative myocardium with vasoactive agents and attempt to limit the aggressive administration of fluids, that can result in valvar and left atrial distention.

17.11 Postoperative Complications

The *main anticipated postoperative complications* related to this malformation are as follows:

1. Valvar regurgitation and stenosis
2. Elevated pulmonary artery pressure
3. Arrhythmias and conductive disorders
4. Low Cardiac Output Syndrome (LCOS)
5. Residual intra-cardiac shunt

17.11.1 Valvar Regurgitation and Stenosis

It is important to remember that even after a successful repair of complete atrio-ventricular septal defect, the atrioventricular valves are not normal, nor will they ever be normal. This reality may guide postoperative management and determine strategy, insofar as aggressive volume administration must be avoided to prevent distention of the left atrium, elevation of left atrial pressure, and contribute towards valvar regurgitation and elevation of left atrial pressures.

Severe left AV valve regurgitation is likely to be poorly tolerated even in the immediate postoperative period as this can lead to annular dilation and consequently worsening valvar regurgitation. Echocardiography both transesophageal and transthoracic can determine the degree of valvar dysfunction. In some cases prompt return to the operating room is the only solution.

Similarly, the provider should be cognizant of potential left-sided valvar regurgitation or stenosis as

recognized by the development of a diastolic (valvar stenosis) or a systolic (valvar regurgitation) murmur, sudden increase of the left atrial and pulmonary pressures, decrease of systemic pressures, concomitant with a progressive metabolic acidosis. These can be detected on physical exam by the astute provider as well as with echocardiography. Left-sided AV valve disease is less tolerated than right-sided AV valve disease.

17.11.2 Elevated Pulmonary Artery Pressure

A specific chapter on pulmonary hypertension may be consulted elsewhere in this book.

The degree of pulmonary hypertension may be predicted based upon their preoperative condition. Again, a child with complete AVSD and trisomy 21 has usually a different postoperative course than a child with normal chromosomes. The child with Down's syndrome may have a predilection to pulmonary vascular reactivity. Causes of elevated pulmonary artery pressures must be distinguished between obstructive anatomic lesions such left-sided valvar obstruction or insufficiency (post-capillary), residual lesion such as a VSD (pre-capillary), pulmonary vascular reactivity (capillary), or a combination of these. If the pre- and postcapillary causes are ruled out by exam and echocardiography, the intensivist is left with treating intrinsic elevated pulmonary artery pressure that may have been exacerbated by exposure of the pulmonary vasculature to the pro-inflammatory effects of cardiopulmonary bypass.

In fact, pulmonary hypertension should be anticipated as a likely postoperative entity and steps should be taken in place that can effectively mitigate this. Factors that contribute to the occurrence and severity of pulmonary hypertension are age of repair, underlying chromosomal abnormality, and even the time period the lungs have been exposed to cardiopulmonary bypass. Potentially malignant and life-threatening PAH crisis are those that become iso or supra-systemic or those that are associated with LCOS, hypoxia, arrhythmia, or acidosis.

Prevention of PAH should be the main goal of the intensivist caring for these patients. Many factors, discussed above may be considered as predisposing or triggering PAH, and prevention starts in the preoperative period.

17.11.2.1 General Measures to Prevent PAH in the Peri-operative Period

1. Adequate surgical indications and timing
2. Minimizing peri-operative risks:
 - a) CPBP conditions
 - b) Surgical technique
 - c) Myocardial protection
 - d) Ultrafiltration
 - e) Systemic steroids
 - f) Controlled re-oxygenation
 - g) Leucocyte depletion
3. Ventilation strategy to target the expect FRC
4. Early use of iNO in labile patients
5. Ensuring metabolic and acid-basic balance
6. Avoid/anticipate/treat:
 - a) Fever
 - b) Hypothermia
 - c) Anemia
 - d) Acidosis
 - e) Dehydration
 - f) Volume overload
 - g) Hypoxia
 - h) Hypercapnia
 - i) Sepsis
 - j) Agitation
 - k) Pain

In some cases, in patients with borderline indications for surgery because of high pulmonary resistances, the use of preoperative pulmonary vasodilators (i.e., iNO, sildenafil, endothelin-blockers, etc.) should be seriously considered. However, this practice thus far, lacks evidence based data.

17.11.2.2 Management of PAH Crisis

Approach to patients with postoperative acute PAH should be individualized since all therapies carry risks. In some circumstances, moderate and well tolerated PAH should be treated conservatively rather than aggressively (Fig. 17.8).

An important premise in such patients is that it is crucial to rule-out residual lesions that might explain such severe PAH crisis (i.e., mitral valve incompetence, residual or recurrent ventricular shunt, left ventricular dysfunction).

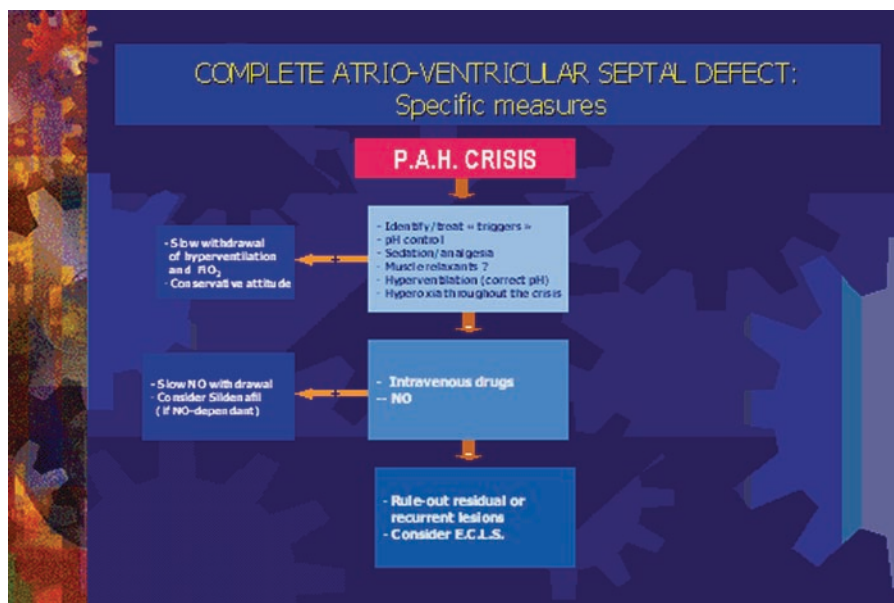


Fig. 17.8 A simple algorithm for the management of acute PAH

Ventilation should be provided as described above. It is important to ensure adequate arterial oxygen content, provide sedation and analgesia, limit noxious stimuli for the immediate postoperative period, and avoid acidosis. Not uncommonly, despite enacting all these measures, it is necessary to initiate pulmonary vasodilator therapy with inhaled nitric oxide.

Patients without pain and relaxed are better controlled in these circumstances. The association of opioids (fentanyl), hypnotics (benzodiazepines), and muscle relaxants as required is recommended in labile patients with recurrent PAH crisis.

Intravenous vasodilator drugs are not selective to the pulmonary vascular bed and are inconsistently efficient. Nevertheless, lusitropic drugs, such as Milrinone, may need to be increased. Nitroprusside and nitroglycerine have some pulmonary vasodilator effect, but with a significant and disproportioned systemic vasodilator effect.

Inhaled NO is the cornerstone of therapy nowadays [14, 15]. Patients requiring iNO, who show evidence of NO-dependent pulmonary vascular resistances, should promptly be started on sildenafil to facilitate the eventual weaning of the latest.

Patients with “malignant” or refractory PAH crisis may benefit from:

- The creation of a calibrated atrial or ventricular septal defect (on the patch) that will function as a decompressing mechanism
- Extracorporeal life support (ECLS) for 48–72 h, while the inflammatory “storm” is controlled or self-limited.

17.11.3 Arrhythmias

Arrhythmias following surgical repair of CAVSD defect are not uncommon [16]. Much of the surgical repair of the AV valves in particular occurs in the region of the AV node, thus A-V synchrony may be disrupted and require temporary pacing. Atrial and ventricular pacing wires are therefore mandatory.

Junctional ectopic tachycardia (JET) is a rare but potentially dangerous occurrence. This is a tachycardia originated at the AV node, with rates usually below 200 bpm and associated with periods of atrioventricular asynchrony in which the ventricular rate is higher than the atrial rate. JET may be poorly tolerated even for a short while and multiple treatments may be instituted simultaneously. Treatment of JET has been extensively described elsewhere, however, mild to moderate body surface cooling in the range of

33–36°C is often the first course of action. This might necessitate using paralytics to prevent shivering. The main objective of therapy is to reduce the ventricular rate and to reestablish the atrio-ventricular synchrony. Amiodarone is currently the first line pharmacotherapy. We recommend a bolus dose of 5 mg/kg over 1 h, and this can be repeated up to 15 mg/kg total IV load. A continuous amiodarone infusion is often required and the usual dose ranges between 5 and 15 µg/kg/min. It is also very important to reduce vasoactive drugs as much as possible since this is an autonomic-driven tachycardia (please refer to the chapter on arrhythmias for further details). Although, JET can be a catastrophic postoperative complication requiring in the most extreme circumstance mechanical support, it is often quite transient and resolves within the first 24 h.

17.11.4 Low Cardiac Output Syndrome

As in most congenital heart lesions that undergo surgical repair, low cardiac output syndrome is often a ubiquitous term applied to impaired cardiac function and systemic output, vasopressor and inotrope dependence, and evidence of end organ hypoperfusion. For the infant with CAVSD, there are specific considerations that may make a patient with this lesion particularly vulnerable to LCOS. As stated earlier, the neo left and right AV valves will never be normal, and the surgery of CAVSD can involve extensive repair and manipulation of the atrioventricular valves, and in fact, requires the creation of two competent valves from one common valve. Thus, in the postoperative period, if the patient is in a low cardiac output state, investigation must be undertaken to ensure that the AV valves are functional. This is best done by echocardiography, however, if the patient is unstable in spite of an optimized medical therapy with inotropic drugs, systemic vasodilators, and diuretics, reoperation should be carried out.

Echocardiographic assessment is mandatory to rule out valvar regurgitation or stenosis, as well as evaluation of ventricular performance, residual intra-cardiac shunts, or evidence of malignant pulmonary hypertension.

The length of aortic cross clamp time can contribute to postoperative diastolic dysfunction as can the adequacy of myocardial protection particularly with right ventricular hypertrophy.

Steps to limit AV valve regurgitation should be instituted, thus avoiding rapid large volume infusions which could cause sudden atrial distention and worsening valvar regurgitation. In our experience, afterload reduction with milrinone can also provide inotropic support without a significant risk of tachycardia. Milrinone is also one of the few available medications that may provide lusotropy in the setting of postoperative diastolic dysfunction [12, 13].

Anticipation of LCOS and follow up of the adopted medical strategies require the use of serial assessment of arterial blood gases, blood lactate levels, sVO₂ if possible, as well as cerebral and somatic NIRS. In patients with a Swan-Ganz catheter, information regarding cardiac output and index is instrumental in steering the therapy.

Patients with persistent LCOS might be candidates for extracorporeal support. In cases of refractory conductive disorders, with conductive disorders, interventricular re-synchronization might significantly optimize cardiac output.

17.12 Long Term Outcomes

The perioperative mortality associated with a CAVC repair is between 2 and 5%. Residual lesions such as mitral and/or tricuspid regurgitation have been described in as many as 50% of operated patients. These patients remain at risk for re-intervention on the AV valves.

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Chapter 18

Aortopulmonary Window

Diego Moguillansky, Ricardo Muñoz, and Víctor O. Morell

18.1 Definition

Aortopulmonary (AP) window, a communication between the ascending aorta and the pulmonary trunk in the presence of two separate arterial valves, is a relatively rare cardiac malformation, accounting for 0.1–0.6% of all cases of congenital heart disease [1–6]. As the natural history of AP window is similar to that of a large ventricular septal defect (VSD) or a patent ductus arteriosus (PDA), early recognition is particularly important to allow for surgical closure before the development of pulmonary vascular obstructive disease (PVOD) [1, 3–6, 7–9]. AP windows do not close spontaneously, nor do they show diminution of size with time and growth [1, 3]. It is frequently (47–77% of cases) associated with other cardiac defects [1, 3, 4, 7, 9, 10]; including aortic origin of the right pulmonary artery, type A interruption of the aortic arch, right and double aortic arch, Tetralogy of Fallot, anomalous origin of the coronary arteries from the pulmonary artery, VSD, pulmonary or aortic atresia, transposition of the great arteries, and tricuspid atresia [1–3, 7, 8, 11–13].

AP window consists of a defect in the AP septum, formed by the two opposing truncal cushions which, under the influence of migrating cells from the neural crest, divide the embryologic truncus arteriosus into separate aortic and pulmonary arteries [7, 14]. Interestingly, unlike other conotruncal malformations such as truncus arteriosus, AP window is not frequently associated with 22q11 deletions and/or DiGeorge syndrome, and

studies involving removal of premigratory neural crest cells have not resulted in the development of AP window, suggesting that AP window may have an altogether different embryologic origin compared with truncus arteriosus or PDA [7, 10, 14–16].

18.2 Anatomy

AP window can be classified (Figs. 18.1 and 18.2) according to the position of the defect in the AP septum [3, 5, 7, 8, 10, 13, 17–19]:

- *Type I*: The most common type, involves proximal defects between the semilunar valves and the pulmonary bifurcation.
- *Type II*: Distal defects located in the uppermost position of the ascending aorta, with the posterior border of the defect formed by the pulmonary bifurcation.
- *Type III*: The defect is posterior in the aorta, creating a communication with the right pulmonary artery.

18.3 Pathophysiology

The defect in the AP septum can be variable in size but invariably results in a large left-to-right shunt when the pulmonary resistance falls, similar to other interarterial shunts like PDA or truncus arteriosus.

The left-to-right shunting results in cardiomegaly due to volume load and dilatation of the left atrium and left ventricle. The main pulmonary arteries and branch pulmonary arteries are usually dilated reflecting increased pulmonary blood flow. The ascending aorta can be small

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in patients with proximal defects or with associated arch anomalies.

The most important variables to determine the clinical presentation are the size of the defect, the relationship

between systemic and pulmonary vascular resistance, and the presence of associated defects [1].

18.4 Clinical Presentation

In the absence of associated cardiac lesions, the clinical features of AP window are those of a large left-to-right shunt and are, therefore, similar to a large VSD or a large PDA [4, 5].

The diagnosis can be made in utero using fetal echocardiography, after a murmur is noted after the delivery prior to hospital discharge, or after signs of congestive heart failure with tachypnea, respiratory distress, difficulty in feeding, and failure to thrive appear in the first weeks of life [4, 5]. Cyanosis is usually not present, except with associated lesions or with very large defects that lead to bidirectional shunting [1, 2, 4, 5, 7]. When associated malformations are present, the clinical presentation can change to reflect the combined hemodynamic features, with interrupted aortic arch usually presenting with metabolic acidosis and poor perfusion after PDA closure, making the clinical diagnosis of AP window more challenging [4, 5].

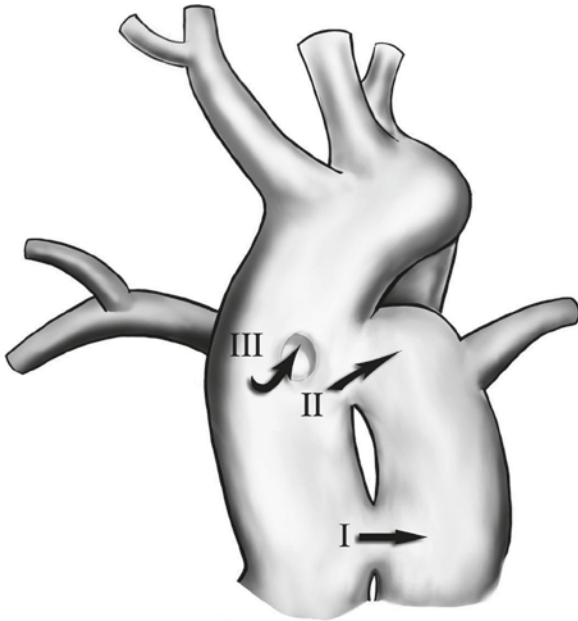


Fig. 18.1 Classification of aortopulmonary window

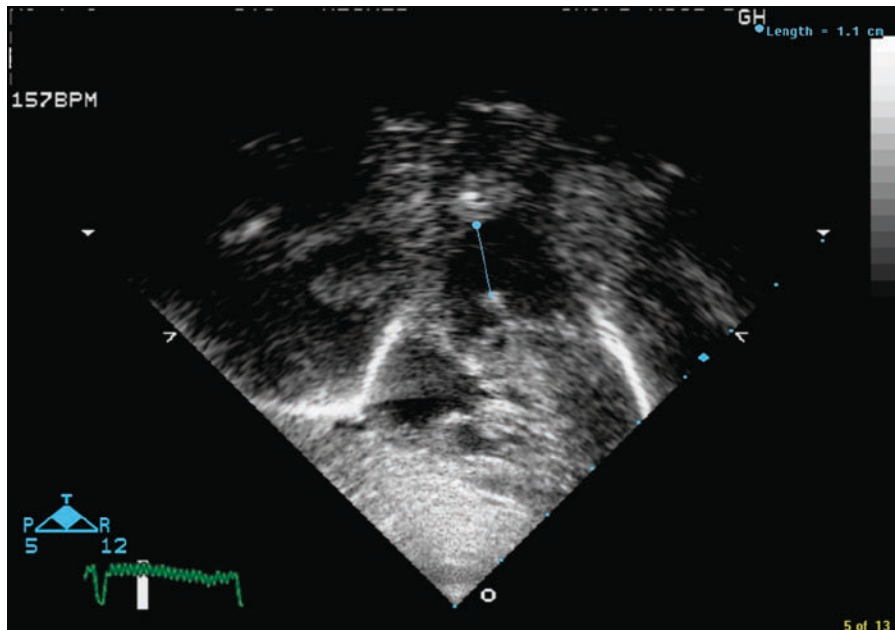


Fig. 18.2 2D echocardiogram. Subcostal view of a large proximal (type 1) Aortopulmonary (AP) window

Physical examination demonstrates tachypnea, respiratory distress, and bounding pulses due to widened pulse pressure. The second heart sound is accentuated and narrowly split, consistent with pulmonary hypertension. There is a loud systolic ejection murmur at the left upper sternal border, or a continuous machinery-like murmur that can be difficult to differentiate from that of a PDA. There is usually a mid-diastolic rumble at the apex of relative functional mitral stenosis [5].

18.5 ECG

The ECG usually demonstrates left ventricular hypertrophy, or biventricular hypertrophy in larger or longer standing defects [5].

18.6 Chest Radiography

The chest roentgenogram shows cardiomegaly due to left atrial and ventricular enlargement, as well as increased pulmonary vasculature. A prominent main pulmonary artery can sometimes be seen [5].

18.7 Echocardiography

Echocardiography can demonstrate the AP window defect, as well as most associated cardiac malformations in the majority of the patients [2–4, 6, 20]. The left atrium, left ventricle, and pulmonary arteries are dilated due to the large left-to-right shunt. The semilunar valves are usually normal, unless associated defects are present. The defect in the AP septum can be visualized by 2D imaging, and flow across the defect can be demonstrated by color Doppler, with abnormal, continuous forward flow in the pulmonary arteries being a hallmark of this defect. The forward direction of the flow in the pulmonary arteries helps differentiate AP window from a PDA (retrograde in the distal pulmonary arteries). When tricuspid regurgitation is present, echocardiography is also helpful to assess right ventricular (RV) and pulmonary artery (PA) pressure [6, 20].

18.8 Cardiac Catheterization

Cardiac catheterization is usually not needed, unless significant associated defects are present that cannot be reliably assessed by echocardiography and other noninvasive imaging methods like cardiac CT or cardiac MRI–MRA [2–4, 6]. When performed, it usually demonstrates systemic RV and PA pressures, elevated left atrial pressures and increased pulmonary venous return [3, 5, 7]. When large defects are present causing significant aortic runoff, the diastolic aortic pressure can be low, with a widened pulse pressure. The size and position of the defect can also be demonstrated by angiography, as well as the presence of any associated defects.

18.9 Other Imaging Studies

Cardiac CT and cardiac MRI are sometimes used to further define the anatomy of the defect, especially when there are associated defects. They allow for 3D reconstructions and can often be performed instead of a cardiac catheterization when echocardiography is unable to completely define the anatomy [12, 21].

18.10 Preoperative Management

The preoperative medical management is relatively limited, as essentially all patients with AP window require surgery in the first few months of life to avoid the development of PVOD; often at the time of, or soon after initial diagnosis [3, 4, 6, 7, 9]. Based on the age at presentation, as well as the severity of the heart failure, patients may be referred for surgery immediately, or treated medically for a very brief period of time with diuretics and afterload reduction with ACE inhibitors [4]. The use of digoxin has become somewhat controversial, but it is still sometimes prescribed [4].

The author's approach usually involves surgical repair as soon as the lesion is diagnosed. These patients usually have significant left-to-right shunt, and demonstrate peripheral signs of rapid diastolic aortic run off. The key aspect of preoperative management is optimization of the QP/QS to avoid low systemic blood flow.

In the inpatient setting, manipulation of pulmonary vascular resistance with inhaled CO₂ or hypoxic mixture with nitrogen (via oxyhood and high flow nasal cannula) can be also used for a brief period of time in patients with large left-to-right shunts, to optimize the hemodynamic status prior to undergoing surgery. In addition, we aim to decrease (within physiologic limits) the systemic vascular resistance with phosphodiesterase inhibitors and sodium nitroprusside.

Lactate levels, mixed venous saturation and arterial blood gases, and NIRS values are frequently monitored to assess the distribution of cardiac output.

Mechanical ventilation is often necessary when patients are in decompensated heart failure due to increased pulmonary blood flow [22]. Alternatively, patients may be “electively” intubated to better control the excessive pulmonary blood flow.

Careful monitoring to prevent development of electrolyte imbalances, particularly in children on digoxin, is required.

Due to the increased caloric requirements secondary to heart failure, nutritional supplementation must be carefully planned. Enteral feeds during the neonatal period may be withheld due to the significant diastolic aortic run off and potential risk of necrotizing enterocolitis (NEC). In selected cases, enteral feeds can be carefully initiated and formulas with relatively high caloric concentration or fortified breast milk may be considered [22].

Given the excellent surgical results in young infants, especially in the absence of associated lesions, delaying surgery in clinically symptomatic patients is usually not indicated, even in symptomatic low birth-weight infants and neonates [3, 7, 22].

A small number of patients present after having developed severe PVOD and are not surgical candidates.

Supplemental oxygen and partial exchange transfusions in cases of severe cyanosis, as well as prevention of iron deficiency with iron supplements can be helpful.

A subset of patients can be considered for lung or heart–lung transplantation.

Treatment of pulmonary hypertension is sometimes indicated in patients that show some response to 100% FiO₂ and Nitric Oxide, and a small number of these patients can then become candidates for surgical repair, usually with a fenestrated patch [7].

In the past, most patients used to undergo cardiac catheterization, but currently the preoperative assessment

of most patients can be performed with an echocardiogram with excellent sensitivity and specificity, accurately identifying the size and location of the defect, as well as additional associated lesions.

18.11 Surgical Management

The surgical repair is performed via a median sternotomy incision with the use of cardiopulmonary bypass and mild to moderate hypothermia. Both branch pulmonary arteries need to be controlled with tourniquets as soon as cardiopulmonary bypass is established in order to prevent excessive pulmonary runoff. Under cardioplegic arrest the AP window is opened and occluded with a patch (Fig. 18.3). Another option is to completely divide the AP window, separating the aorta from the pulmonary artery, and repairing both great vessels with separate patches (Fig. 18.4).

18.12 Postoperative Management

18.12.1 Cardiovascular Management

Patients are monitored with an arterial line and central venous line to allow a rapid assessment of the hemodynamic state of the patients, which then can be followed over time and provide valuable trends to anticipate problems and hemodynamic changes or complications. The occurrence of postoperative pulmonary hypertensive crises is well documented, and should be treated rapidly with oxygen and nitric oxide [7]. Atrial and ventricular epicardial wires are also routinely used, and can be extremely helpful in the diagnosis and treatment of postoperative arrhythmias and conduction abnormalities.

Inotropic support with milrinone is usually recommended, and is maintained for the first 12–24 hours and then discontinued, unless the patient has developed LV dysfunction, is clinically in heart failure, or shows evidence of low cardiac output syndrome, in which case milrinone can be continued until there are signs of improvement. Administration of milrinone in neonates and infants with low cardiac output

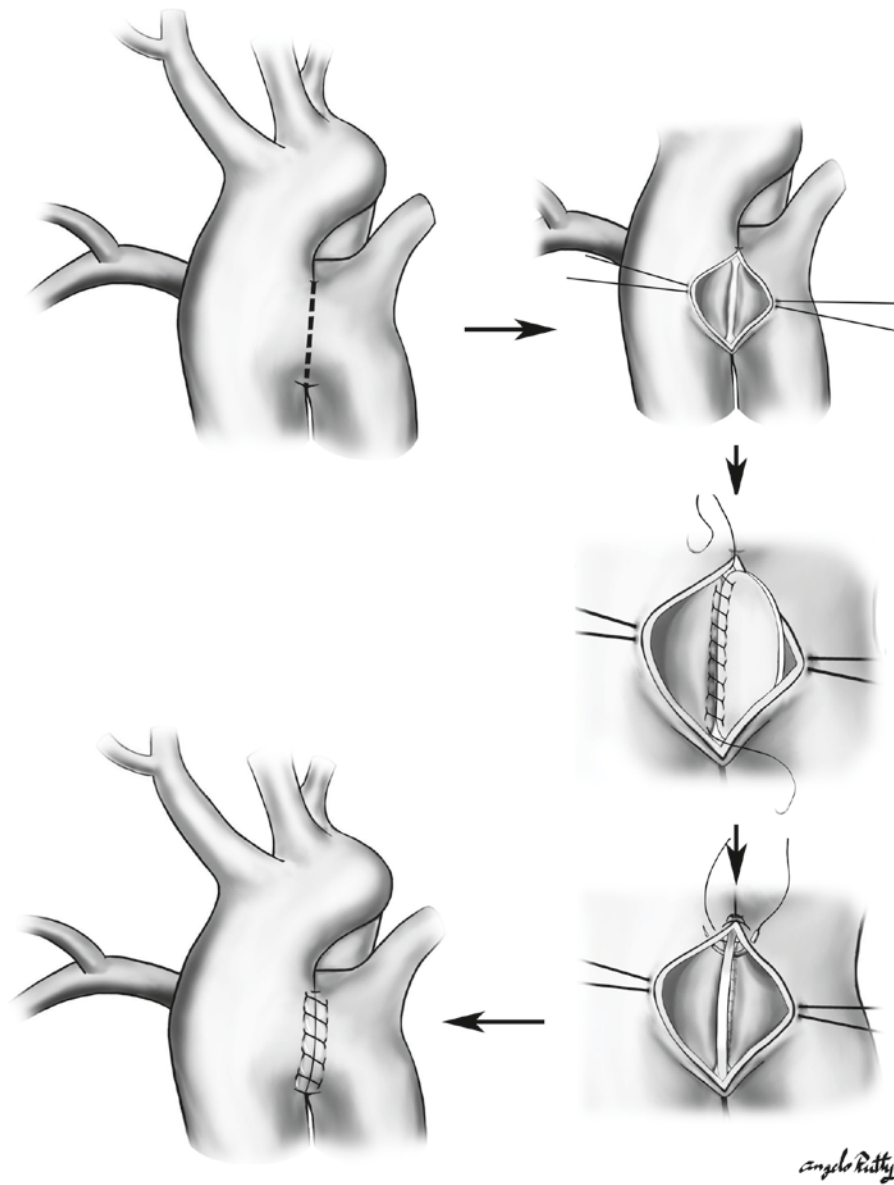


Fig. 18.3 Repair of Aortopulmonary window with a prosthetic patch. The anterior wall of the “window” is opened and the patch is sutured to the edges of the defect

after cardiac surgery lowers filling pressures, systemic and pulmonary arterial pressures and vascular resistances, improves cardiac index, and increases heart rate without significantly altering myocardial oxygen consumption [23].

The use of intraoperative transesophageal echocardiography has become routine in most centers, and enables early recognition of some of the most common postoperative complications such as RV or LV dysfunction,

residual defects or pericardial effusions, facilitating the immediate postoperative care.

18.13 Respiratory Management

Patients with AP window, especially those with associated defects, usually arrive to the ICU intubated;

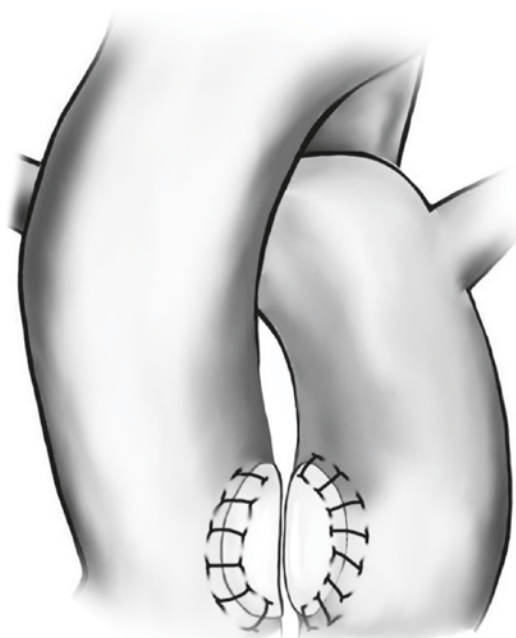


Fig. 18.4 After completely dividing the aortopulmonary window, both great vessels are repaired with separate patches

patients with simple defects are commonly extubated on admission. The chest is usually closed but in some complex defects it may be left open. After effective negative balance chest closure usually occurs 24–48 hours after surgery. Likewise, extubation should be planned soon after chest closure following standard ICU extubation protocols.

18.13.1 Fluids, Electrolytes, and Nutrition

Electrolytes are closely monitored and replaced according to specific protocols. Parenteral nutrition is routinely started 24 hours after surgery. It is important to emphasize that as soon as the infant is hemodynamically stable, enteral feeds must be carefully started.

18.13.2 Gastrointestinal Management

It is advisable to monitor liver function tests, amylase and lipase after cardiopulmonary bypass at least upon

arrival to the ICU. As previously mentioned enteral feeds should be started when the infant is hemodynamically stable.

18.13.3 Renal Management

Fluid management is critical in the initial 12 hours after surgery, and achieving a negative fluid balance is very important, particularly in patients who have an open chest, to facilitate sternal closure in the first 12–48 hours after surgery.

Furosemide (bolus or continuous infusion), thiazide diuretics, and ethacrynic acid may be used to achieve negative balance post CPB.

18.13.4 Neurologic Management, Sedation and Analgesia

Analgesia is usually managed with morphine or fentanyl, associated with nonopioid pain control. Sedation is supported with benzodiazepines as required or as an infusion. Lately, the use of dexmedetomidine has proven very helpful in managing sedation in the immediate postoperative period significantly decreasing the requirements for opioids.

18.14 Long-Term Outcomes

The long term prognosis of isolated AP window is usually excellent in patients who undergo surgical repair early in life, before the development of significant PVOD, which generally occurs after 6 months of age [3, 4].

The outcome of patients with significant associated lesions is variable and is more determined by the severity of the associated lesions and their candidacy for surgical repair, than by the AP window that can generally be corrected easily by surgery [4, 6].

In summary, postoperative mortality depends on the age of the patient at operation, status of preoperative pulmonary vascular disease, and presence of associated intracardiac defects [1, 4, 6, 7, 24]. The hospital

4mortality is 8–25% with a higher mortality in patients with associated defects, particularly interrupted aortic arch [1, 4, 7, 17, 24].

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Chapter 19

Tetralogy of Fallot

Constantinos Chrysostomou, Yuliya A. Domnina, Traci M. Kazmerski, Ricardo Muñoz, and Victor O. Morell

19.1 Anatomy

Tetralogy of Fallot (TOF) is a relatively common congenital heart defect occurring in approximately 15% of patients with congenital heart disease. The four main anatomic features of TOF include right ventricular outflow tract (RVOT) obstruction [1, 2], ventricular septal defect (VSD), *aortic dextroposition overriding the VSD*, and *right ventricular hypertrophy* (Fig. 19.1). Current teaching postulates that the basic pathology of TOF results from underdevelopment of the right ventricular infundibulum. This underdevelopment causes an anterior malalignment of the infundibular septum which subsequently determines the degree of RVOT obstruction. The VSD that results from this malalignment is almost always large, and thus unrestrictive, permitting similar pressures between the right and left ventricles to occur. In addition to these features the pulmonary valve is frequently hypoplastic and thickened and the level of obstruction may extend to the main pulmonary artery and right and left pulmonary arteries.

Associated defects in TOF include coronary artery anomalies (10%), right aortic arch (25%), atrial septal defect or patent foramen ovale, patent ductus arteriosus (PDA, 4%), multiple VSDs, and atrioventricular septal defect [3]. The most important of these conditions is the occurrence of an aberrant coronary artery coursing across the RVOT. The aberrant vessel could be the result of a left anterior descending coronary (LAD) arising from the right coronary artery (RCA), an

RCA arising from the left coronary artery, or a large branch of the RCA supplying the conus region. A single right or left coronary artery could also occur [4].

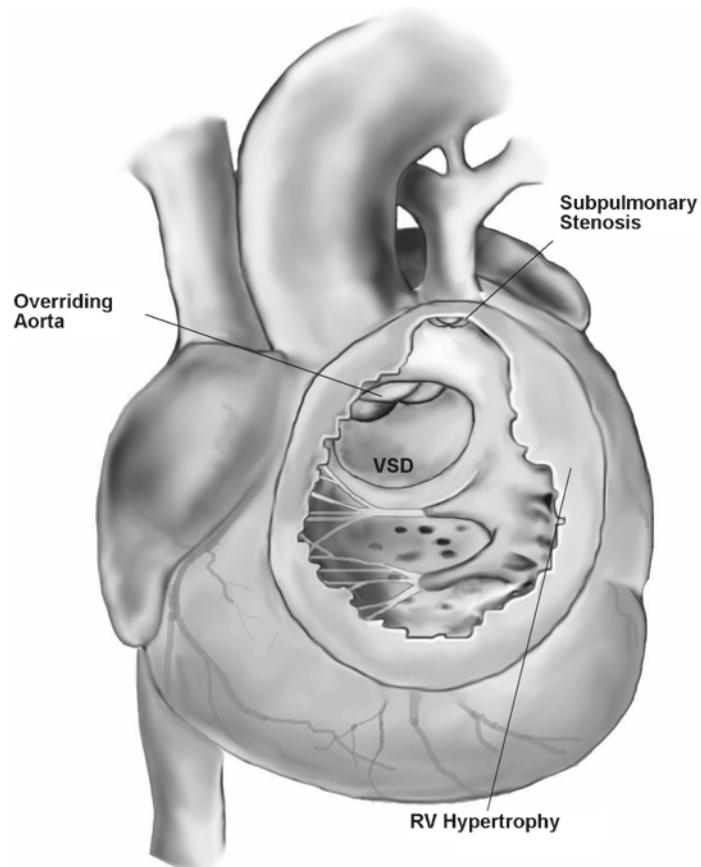
19.2 Pathophysiology

The three important features that determine the degree of hemodynamic consequences in a patient with TOF are the severity of the RVOT obstruction, the size of the VSD, and the level of systemic vascular resistance (SVR). While the degree of obstruction at the level of the pulmonic valve is unchanging, the infundibular obstruction, due to its muscular component can be quite dynamic. Usually the VSD is large and unrestrictive and will allow desaturated venous blood to be shunted to the left ventricle and aorta. Patients with TOF may present with various degrees of desaturation, from none or mild cyanosis to profound cyanosis. In cases of severe cyanosis, patients usually need an alternative source of pulmonary blood flow, either through a PDA or major aorta–pulmonary collateral arteries (MAPCAs). In general, pulmonary artery pressure and vascular resistances are usually normal and, thus, pulmonary artery hypertension is rarely seen. Some patients develop episodes of severe hypoxemia with hypoxia and acidosis, associated with nearly complete obliteration at the infundibular level. These episodes are known as hypoxic or “Tet-spells.”

19.3 Clinical Presentation

The clinical features of TOF can vary greatly. Most patients present with a variable degree of cyanosis with the most profound occurrences seen in infants with severe

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Fig. 19.1 Anatomy of Tetralogy of Fallot

infundibular and valvar stenosis after the PDA starts to constrict. In these cases, arterial oxygen saturation can fall to less than 60% often leaving infants irritable, tachypneic, excessively perspiring, and exhibiting poor feeding. Initially, blood pressure is well maintained, but, if acidosis persists, the infant can develop poor pulses and become pale and mottled.

The physical exam of most TOF patients reveals a prominent RV impulse, single second heart sound, and a 2–3/6 harsh systolic ejection murmur. The liver is usually 2–3 cm below the costal margin.

19.4 Hypoxic Spells or “Tet-spells”

As mentioned above, patients with a dynamic and hypertrophic infundibulum can develop “Tet-spells” or “hypercyanotic spells” which are believed to be episodes of exacerbated infundibular hypercontractility and increased intracardiac right to left shunting associated with abrupt and dramatic decrease of pulmonary blood flow. They are frequently precipitated by activity, straining, crying or

concomitant illnesses such as respiratory infections and dehydration. Peak frequency is observed at 2–3 months of age. Patients are frequently found hyperventilating and profoundly cyanotic. Older children may be found squatting in an attempt to improve their condition by increasing systemic venous return and SVR. As the severity of the RVOT obstruction progresses, patients become pale, gray and even comatose during a spell. Auscultation may reveal diminishing or absent murmur over the obstructed infundibulum. These episodes may be life-threatening and require prompt recognition and intervention.

19.5 Preoperative Assessment and Management

The following should be sought in all patients with TOF during the preoperative assessment:

- A. *Chest X-ray*: Often reveals normal heart size with a typical contour commonly described as “boot-shaped” This shape is created by an upturned apex and a small main pulmonary artery segment.

- B. *Electrocardiogram*: Right axis deviation and RV hypertrophy with persistent upright T wave in the precordial leads.
- C. *Echocardiography*: Usually sufficient to delineate and characterize the cardiac and the great vessel anatomy in TOF. The following need to be identified prior to surgical intervention:
- Degree and morphology of subpulmonary and pulmonary valve obstruction
 - Size of main and peripheral pulmonary arteries
 - Size and number of VSDs
 - Presence of PDA or MAPCAs
 - Origin and proximal course of coronary arteries; exclude presence of a coronary artery crossing the RVOT
 - Presence of a PFO or ASD
 - Aortic arch position
 - Exclusion other associated lesions, e.g., left superior vena cava.
- D. *Cardiac catheterization*: Usually not indicated in TOF. However, it is recommended if coronary artery anatomy cannot be delineated or if the presence of multiple VSDs cannot be excluded.
- E. *Rule-out a DiGeorge syndrome (22q11 deletion)*: Obtain chromosome and FISH probe studies in all neonates with TOF and closely follow calcium levels.
- e. If there is metabolic acidosis, administer sodium bicarbonate 1–2 meq/kg IV.
- f. If suspected hypovolemia, crystalloid fluid bolus administration 5–15 ml/kg IV.
- g. Optimize electrolytes, including ionized calcium levels.

19.6.2 “Tet-spells”

In the current era, occurrence of “Tet-spells” can be an indication for surgical repair. Prior to surgical correction, the following should be considered during an acute episode:

- a. 100% Oxygen.
 - b. Positioning- knee-chest position for infants or squatting for toddlers.
 - c. Sedation with morphine 0.1 mg/kg (IM, IV, SC), midazolam 0.05–0.1 mg/kg (IV, intranasal or intrarectal) fentanyl 1–2 µg/kg (IV), or dexmedetomidine 0.5–1 mcg/kg (IV).
 - d. Beta-blockers: Esmolol is a good choice given the possibility of titration between 50 and 200 µg/kg/min (IV). Intravenous Propranolol is a good alternative to the latter.
 - e. Phenylephrine (Neo-synephrine®) 2–5 µg/kg IV every 10–15 min, followed by a continuous infusion 0.1–5 µg/kg/min as needed. Alternatively may use vasopressin. Vasoconstrictors are indicated in spells that appear refractory to sedation, volume expansion and beta-blockers.
 - f. Crystalloid or red blood cell administration 10–15 ml/kg IV.
 - g. Sodium bicarbonate 1–2 meq/kg IV.
 - h. Intubation with sedation and muscle relaxation if persistent or refractory spell.
 - i. If all of the above fail, extracorporeal membrane oxygenation (ECMO) support and emergency Blalock-Taussig shunt (BT shunt) should be considered.
- ## 19.6 Management of Special Situations
- ### 19.6.1 Newborns and Infants with Severe Cyanosis
- Infants with severe RVOT obstruction can become significantly cyanotic when PDA closes. The following should be instituted immediately:
- a. 100% oxygen
 - b. Depending on the severity of the clinical condition, the patient likely needs to be intubated and temporarily supported with mechanical ventilation.
 - c. Intravascular access (preferably a central venous access). Appropriate sedation must be carefully planned.
 - d. Prostaglandin E₁ (alprostadil) infusion. Start at a higher dose of 0.1–0.2 µg/kg/min and once the ductus arteriosus is patent can wean to a lower dose of 0.01–0.05 µg/kg/min.

19.7 Surgical Management

19.7.1 Timing of Surgery

In general, asymptomatic patients undergo an elective one-stage surgical repair during early infancy, usually between 2 and 6 months of age. For symptomatic

patients two approaches are utilized depending on the institutional preference, complete repair vs. a two-stage repair (initial shunt placement followed by complete repair) [5, 6]. The use of a systemic to pulmonary artery shunt has been associated with the development of pulmonary artery distortion, but in patients with small pulmonary arteries, associated lesions (i.e., unbalanced ventricles, multiple VSDs) or with a contraindication to CPB [5, 6] it is a reasonable option. The author's preference is to proceed with a single stage repair.

Situations where surgical intervention needs to be planned fairly urgently include:

- a. Worsening hypoxemia, related to progressive infundibular and valvular obstruction with the saturation less than 75–80%.
- b. Severe cyanotic spell as discussed above.
- c. Dependence on prostaglandin from early neonatal period (more likely to be observed in TOF with pulmonary atresia).

19.7.2 Surgical Technique

The TOF repair is performed via a median sternotomy incision with the use of cardiopulmonary bypass. After cardioplegic arrest, the VSD is closed via a right atriotomy and the obstructive muscle bundles in the proximal aspect of the RVOT are resected. A small interatrial communication may be left open to allow for right to left shunting at the atrial level, helping preserve the cardiac output at the expense of mild cyanosis during the early postoperative period. A longitudinal arteriotomy is then made in the main pulmonary artery extending into the proximal left pulmonary artery (LPA), past the area of ductal insertion, in order to prevent proximal LPA stenosis. The distal RVOT is explored via the pulmonary valve and any residual muscular obstruction is excised. The ideal surgical repair would involve a transatrial–transpulmonary approach, avoiding a right ventriculotomy and preserving the pulmonary annulus (Fig. 19.2).

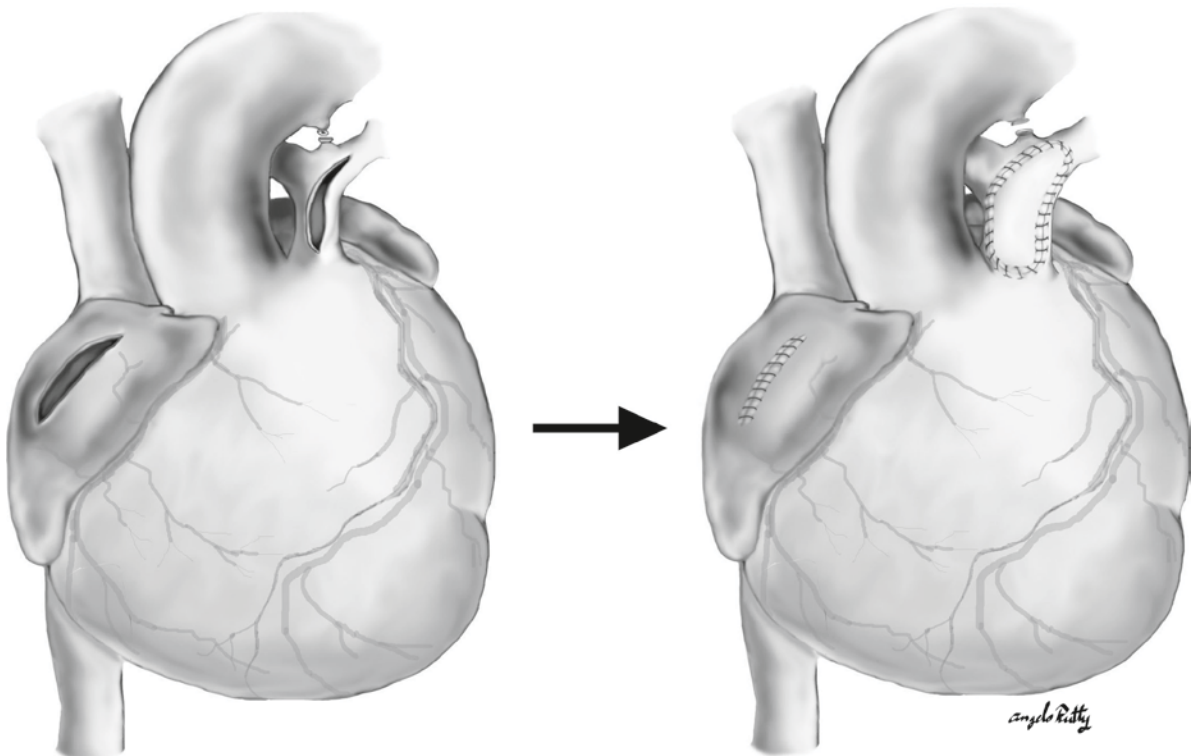


Fig. 19.2 “Transatrial–transpulmonary” repair

In the presence of severe infundibular stenosis, a right ventriculotomy might be needed; some surgeons routinely close the VSD via the ventriculotomy. In the absence of significant valvar stenosis, pericardial patches are used to close the pulmonary

arteriotomy and the right ventriculotomy (Fig. 19.3). In patients with significant pulmonary valve hypoplasia, a transannular incision is used (Fig. 19.4). The overall mortality associated with TOF repair is approximately 2–5%.

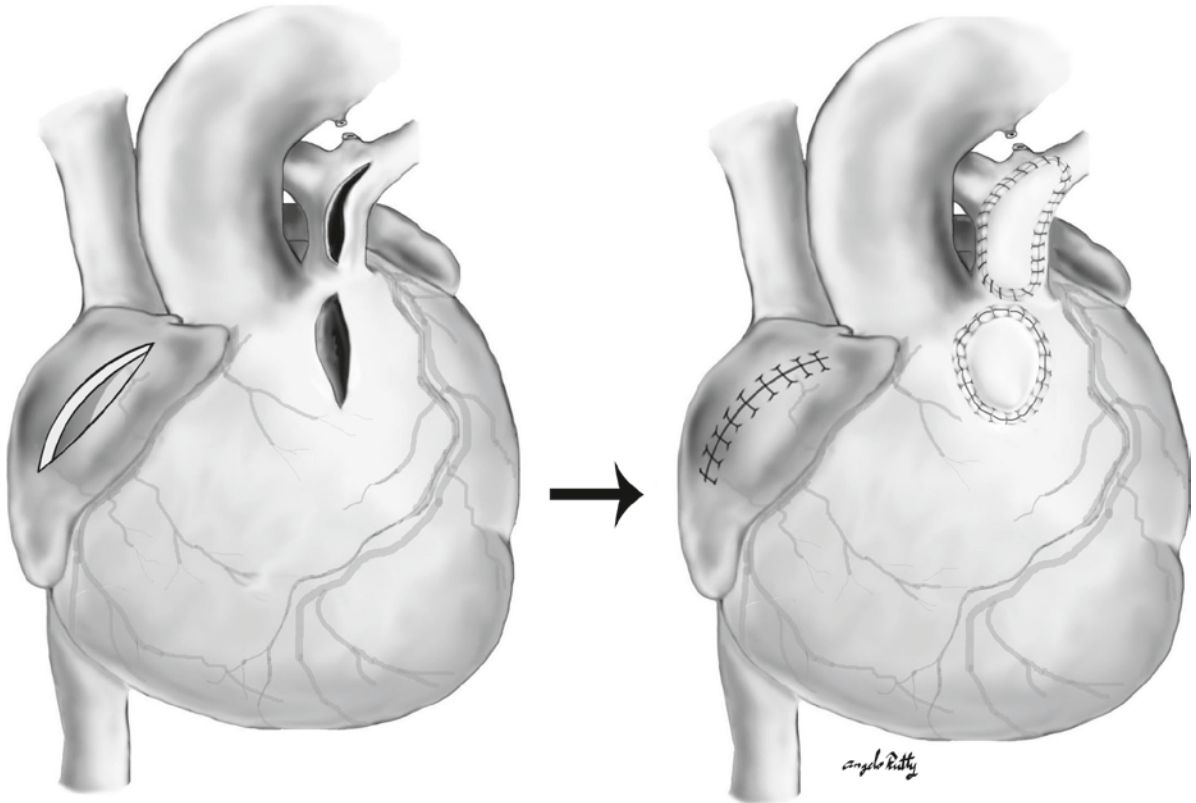


Fig. 19.3 The “two patch technique” preserves the pulmonary valve annulus

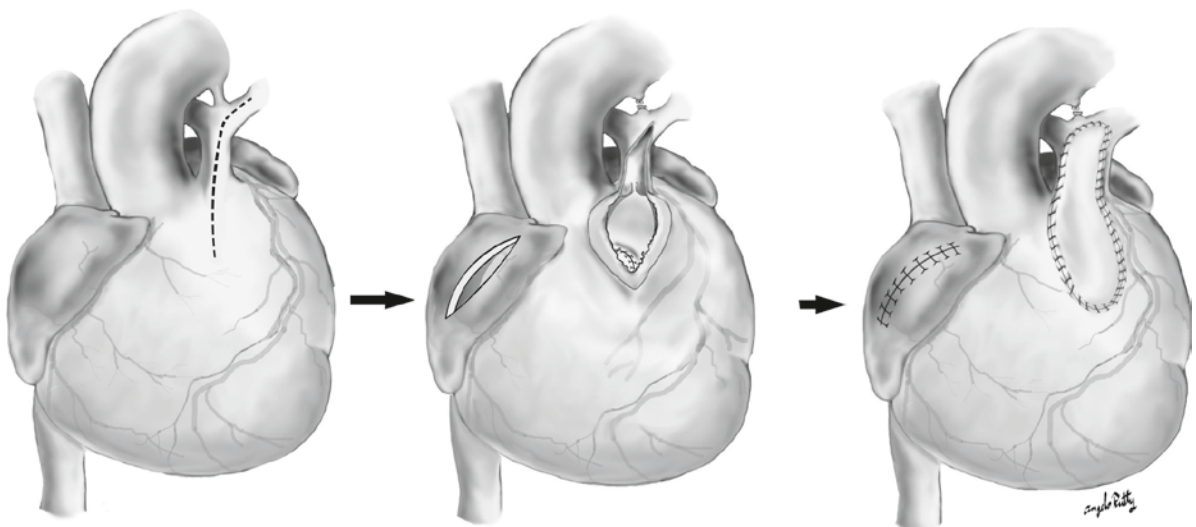


Fig. 19.4 Trans-annular repair

19.8 Postoperative Management

In some centers, most toddlers and children return to the cardiac ICU already extubated. Most patients experience a relatively uneventful postoperative course; however, some of the most frequent postoperative problems encountered during the first 12–48 h especially in neonates and infants, are the following:

- a. Low cardiac output syndrome (LCOS) due to:
 1. Right ventricular diastolic and systolic dysfunction.
 2. Left ventricular dysfunction (less frequently).
 3. Uncontrolled arrhythmias, e.g., junctional ectopic tachycardia (JET), atrial ectopic tachycardia [7, 8].
 4. Residual VSD resulting from either significant VSD patch leak or previously undiagnosed VSD.
- b. Arrhythmias. Most frequent types of hemodynamically significant arrhythmias encountered after TOF repair include:
 1. Junctional Ectopic Tachycardia (5–20%)
 2. Atrial Ectopic Tachycardia
 3. Re-entry type supraventricular tachycardia (Re-SVT) – Be aware that due to the frequent presence of postoperative right bundle branch block, Re-SVT may resemble ventricular tachycardia.
 4. Complete AV Block (<5%) – Mostly transient but occasionally permanent.

19.8.1 Monitoring

Most patients have an arterial line, central venous line (internal jugular or subclavian vein line), pleural and mediastinal chest tubes, peritoneal drainage tube, foley catheter, and temporary pacing wires. Though older patients are admitted from the operating room once extubated, infants are for the most part intubated and, in some institutions, a significant number of neonates have an open chest for 24–36 h.

19.8.2 Laboratory Work

- a. Complete blood count, electrolytes, BUN, Creatinine, immediately after surgery and every 24 h

- b. Arterial blood gases every 1–4 h, lactate and central venous saturation every 4–6 h × 24 h and then as needed
- c. Cerebral near infrared spectroscopy (NIRS, INVOS 5100 Cerebral Oximeter Somanetics Corp., Troy, MI, USA)
- d. Electrocardiogram
- e. Echocardiogram is not performed routinely, however an ECHO machine should always readily available so a quick study can be obtained by one of the cardiac intensivists at any time without delay.

19.8.3 Management of Specific Problems

19.8.3.1 Mechanical Ventilation

Time-cycled pressure limited mode is most frequently used, aiming for approximately 8–10 ml/kg tidal volumes with ideal plateau pressures of <25–28. FiO_2 is minimized to the 0.4–0.6 range to avoid potential oxygen toxicity; pO_2 levels >40 mmHg are considered acceptable (in the setting of atrial communication). It is important to be aware that nearly all patients have an intentional, residual PFO with a variable degree of intracardiac right-to-left shunt depending on the extent of right ventricular diastolic dysfunction. PEEP may also be employed at levels around five and rarely above seven to minimize right ventricular afterload.

19.8.3.2 Low Cardiac Output Syndrome (LCOS)

All patients are administered milrinone for 24–72 h at a range of 0.5–1.25 $\mu\text{g}/\text{kg}/\text{min}$. Since in most cases LCOS is due to RV dysfunction that is associated with a very hypertrophic ventricle, a higher filling pressure is needed. Many patients require a CVP of 10–15 mmHg to achieve an adequate cardiac output. Ionized calcium levels are maintained between 0.1–0.3 mmol/L. Sodium bicarbonate at 1–2 meq/kg is given as needed to achieve a base excess and a pH >7.35. If further inotropic support is needed, low dose dopamine at 3–8 $\mu\text{g}/\text{kg}/\text{min}$ or low dose epinephrine at 0.05–0.1 $\mu\text{g}/\text{kg}/\text{min}$ should be utilized. It is important to consider that both dopamine and epinephrine may initiate or exacerbate arrhythmias and specially JET.

19.8.3.3 Arrhythmias

Junctional Ectopic Tachycardia (JET)

The mainstay of managing JET is to decrease any adrenergic state with the goal of achieving adequate atrioventricular coordination, i.e., normal sinus rhythm or JET rate below 170 beats/min with AV sequential pacing. JET, though transient and lasting only up to 3–4 days, can be a major cause of increased morbidity and mortality if not treated promptly. The following algorithm represents the approach employed by the authors, at the Children's Hospital of Pittsburgh:

- a. Immediate recognition and immediate treatment
- b. Decrease or discontinue if possible, any inotropic agents that worsen JET, i.e., dopamine, epinephrine.
- c. Ensure deep sedation, i.e., through the use of fentanyl and/or dexmedetomidine.
- d. Provide adequate fluid volume to optimize RV preload.
- e. Core hypothermia 34–35°C with muscle relaxation.
- f. Amiodarone bolus 5 mg/kg IV slowly followed by an infusion of 5–15 µg/kg/min. Repeat bolus if there is no effect on heart rate within 60 min.
- g. Consider ECMO if JET cannot be controlled and LCOS worsens.

For treatment of other types of arrhythmias, please refer to the associated chapter.

19.8.3.4 Other

Sedation and analgesia are managed with fentanyl and/or dexmedetomidine.

Parenteral nutrition is started early after surgery and enteral feeds are started slowly beginning 24–48 h after hemodynamic stability has been achieved. At this time, the avoidance of opioids and the implementation of a more liberal use of dexmedetomidine may improve gut motility.

19.9 Long-term Outlook

The overall outlook for the patients with TOF is encouraging and current surgical survival is excellent.

Most patients enjoy an active life free of significant symptoms. Residual defects that reduce life expectancy in patients with TOF and increase the need for reoperation include: right ventricular dysfunction, RVOT obstruction, pulmonary artery stenosis, pulmonary regurgitation, residual VSD, ventricular arrhythmias and sudden death. Identification of patients at risk for ventricular arrhythmias and sudden death is difficult, but two suggested prognostic factors are a QRS prolongation of ≥ 180 msec and severe pulmonary regurgitation associated with a significantly dilated right ventricle [9–19].

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Chapter 20

Tetralogy of Fallot with Absent Pulmonary Valve

Constantinos Chrysostomou, Michael Tsifansky, and Victor O. Morell

20.1 Anatomy

Tetralogy of Fallot with absent pulmonary valve (TOF-APV) is a severe disease with an incidence of 0.2–0.4% among patients with congenital heart defects and 3–6% among patients with TOF. Much less frequently, APV can also occur without the features of TOF. In addition to the usual anatomic defects of TOF, i.e., anterior deviation of infundibular septum with right ventricular outflow tract (RVOT) stenosis, malaligned ventricular septal defect (VSD), overriding aorta, and right ventricular hypertrophy, patients with TOF-APV have rudimentary or absent pulmonary valve leaflets with free pulmonic insufficiency, minimally obstructed RVOT and characteristic aneurysmal dilatation of the main and branch pulmonary arteries (Fig. 20.1). Associated anomalies include atrial septal defect and the absence of the ductus arteriosus.

20.2 Pathophysiology

Patients with TOF-APV differ from those with TOF in the morphology of the RVOT, the physiology, the nature of the intrapulmonary vasculature, and the involvement of the tracheobronchial tree. Their infundibulum is wider than normal, the pulmonary valvar tissue is rudimentary, and the RVOT narrowing is minimal. Pulmonary arteries tend to be significantly dilated, and severe pulmonary regurgitation is usually

present. Typically, the symptoms are related to left-to-right shunt across the VSD and to an airway obstruction. However, many neonates with TOF-APV are cyanotic due to the combination of elevated pulmonary vascular resistances (PVR), an incompetent pulmonary valve, and a VSD. As the PVR starts to fall, cyanosis improves, the intracardiac shunt becomes left-to-right, and with the lack of significant RVOT obstruction, the Qp/Qs increases markedly. The increased flow to the lungs, in addition to the native dilation of the pulmonary arteries, may cause significant respiratory difficulties. The large airways are compressed by the dilated pulmonary arteries, and the left mainstem bronchus is further compressed by the enlarged left atrium. The pathology of the pulmonary tree is the major cause of the clinical symptoms with severe air trapping and CO₂ retention. Severely affected infants have tracheo-bronchomalacia, with abnormal bronchial arborization with arterial tufts encircling and compressing the intrapulmonary bronchi in addition to the gross airway compression by the dilated pulmonary arteries [1]. This causes air entrapment in the emphysematous lobes, which eventually compress the remaining lung tissue, causing severe respiratory compromise.

20.3 Clinical Presentation

Most patients present during the neonatal period with respiratory symptoms that result from partial bronchial obstruction. The severity of symptoms may vary from mild respiratory distress to respiratory failure requiring intubation and positive-pressure ventilation. Patients who initially appear to have only mild symptoms need to be monitored closely, as they may deteriorate when PVR start to fall and pulmonary blood

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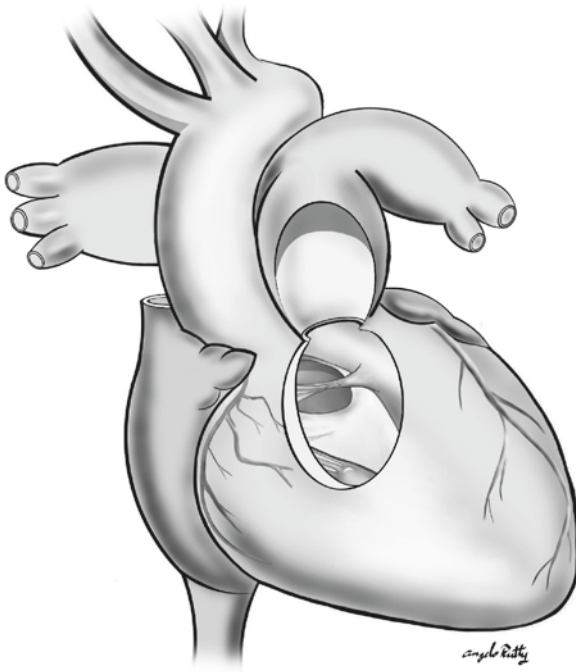


Fig. 20.1 Tetralogy of Fallot with Absent Pulmonary Valve (TOF-APV). In addition to the classic features of tetralogy of Fallot, note the dilated pulmonary arteries, which frequently result in bronchial compression

flow increases, which further enlarges the already dilated pulmonary arteries.

The physical examination of most neonates with TOF-APV reveals a variable degree of cyanosis that improves over time, increased respiratory rate, retractions, and expiratory wheezing and stridor secondary to tracheobronchial compression. There is a prominent right ventricular (RV) impulse, a single second heart sound, and the characteristic “to-and-fro” murmur of the narrowed RVOT and pulmonic insufficiency. The liver is usually palpable 3–4 cm below the costal margin due to both RV failure and to air trapping and lung overexpansion, inducing hepatic ptosis.

20.4 Preoperative Assessment and Management

20.4.1 Chest Radiography

Chest X-ray often reveals a moderately enlarged cardiac silhouette with considerably dilated main and branch

pulmonary arteries. The pulmonary vascular markings are initially normal but may increase when the PVR falls. The lung parenchyma may be overexpanded due to air entrapment, and atelectasis is frequently seen.

20.4.2 ECG

Electrocardiogram commonly shows right axis deviation and signs of RV hypertrophy. If a significant left-to-right shunt develops, biventricular hypertrophy may be present.

20.4.3 Echocardiography

Echocardiography is usually sufficient to delineate the cardiac and great vessel anatomy. The following needs to be identified:

- a. Degree and morphology of the subpulmonary and pulmonary valve area
- b. Degree of stenosis and insufficiency
- c. Size of the main and peripheral pulmonary arteries
- d. Size and number of VSDs
- e. Presence of a ductus arteriosus
- f. Origin and proximal course of coronary arteries
- g. Presence of a PFO or an ASD
- h. Aortic arch position
- i. RV function and size

20.4.4 Cardiac Catheterization

Cardiac catheterization is usually not indicated, unless distal peripheral pulmonary artery stenosis is suspected.

20.5 Other Studies

Computerized tomography may be indicated in patients with severe respiratory failure to delineate the relationship of the dilated pulmonary arteries to the tracheobronchial tree and the airway anatomy.

Because of increased prevalence of DiGeorge syndrome among patients with TOF-APV *chromosome* and *FISH studies* are recommended.

20.6 Natural History

The short- and long-term prognosis of infants with TOF-APV is strongly related to the extent of tracheobronchial compromising or obstruction. Recurrent atelectasis and obstructive emphysema, especially during respiratory infections, are the usual causes of death in patients awaiting surgery or later in life for those with severe airway disease. Neonates and infants with moderate to severe respiratory symptoms may benefit from prone positioning, which relieves the pressure on the bronchi, and from noninvasive positive-pressure ventilation. However, these measures frequently fail, necessitating intubation and mechanical ventilation. Such patients have higher perioperative mortality and morbidity compared with those repaired later in childhood.

While managing mechanical ventilation in patients with TOF-APV, it is important to provide appropriate positive end-expiratory pressure (PEEP), usually 6–7, but sometimes more, and allow for sufficient expiratory time. Intrinsic PEEP (PEEPi) should be carefully monitored and the ventilatory parameters adjusted to minimize it.

20.7 Surgical Management

The operative management is similar to that of the patients with TOF and pulmonary stenosis, consisting of closure of the VSD and the creation of an unobstructed communication between the right ventricle and the pulmonary arteries. In addition, the diameter of the dilated pulmonary arteries needs to be reduced. At Children's Hospital of Pittsburgh we prefer to perform a transannular incision with placement of a monocusp valve and a pulmonary reduction arterioplasty (Fig. 20.2). Other options for the management of the dilated pulmonary arteries include surgical resection and replacement with a pulmonary homograft or the anterior translocation of the pulmonary arteries (Lecompte's maneuver), moving them away from the bronchi [2, 3, 4, 5]. The foramen ovale is left open to allow for a right-to-left shunt to preserve the cardiac output during the early postoperative period.

20.8 Postoperative Management

The postoperative cardiac management is similar to that of TOF and is described in detail in the corresponding chapter 19. However, the significant airway pathology in patients with TOF-APV highly complicates their management and worsens their survival compared to the patients with typical TOF. Several studies have shown that preoperative need for intubation due to severe preoperative respiratory distress is a risk factor for poor outcome [6]. While the main operative goal is to restore pulmonary valve competency and reduce airway compression by the dilated pulmonary arteries, neonates and infants may continue to manifest evidence of postoperative respiratory compromise. They require careful and systematic assessment of etiology of respiratory failure and appropriate interventions to assure successful weaning from mechanical ventilation. Infants are often placed prone to reduce airway compression, and humidified high-flow nasal cannula (4–8 L/min) or nasal CPAP are often used following extubation to maintain airway patency. If patients fail extubation or continue to require noninvasive respiratory support, persistent airway compression needs to be sought.

Bronchoscopy, chest CT, echocardiography, and possibly, cardiac catheterization should be performed in a timely fashion to identify the cause of extubation failure and reduce hospitalization time. Bronchoscopy may identify significant tracheobronchomalacia or external compression by pulmonary vessels. Bronchomalacia due to previously-compressed airways may take a significant amount of time to resolve. Chest CTA can define the intrathoracic anatomy and the relationship between the airways and the vascular structures. In cases of persistent vascular compression, pulmonary artery suspension or reduction may be performed. Some centers have used intrabronchial expandable stents to treat severe airway malacia; however, these stents are limited in terms of total attainable diameter and may require subsequent removal as the child grows.

In patients who repeatedly fail extubation due to ongoing airway compression, a lobectomy of the most severely affected lung may be helpful in selected cases.

Echocardiography and cardiac catheterization can rule out obstruction of the RVOT, stenosis of the right ventricle to pulmonary artery conduit, or branch

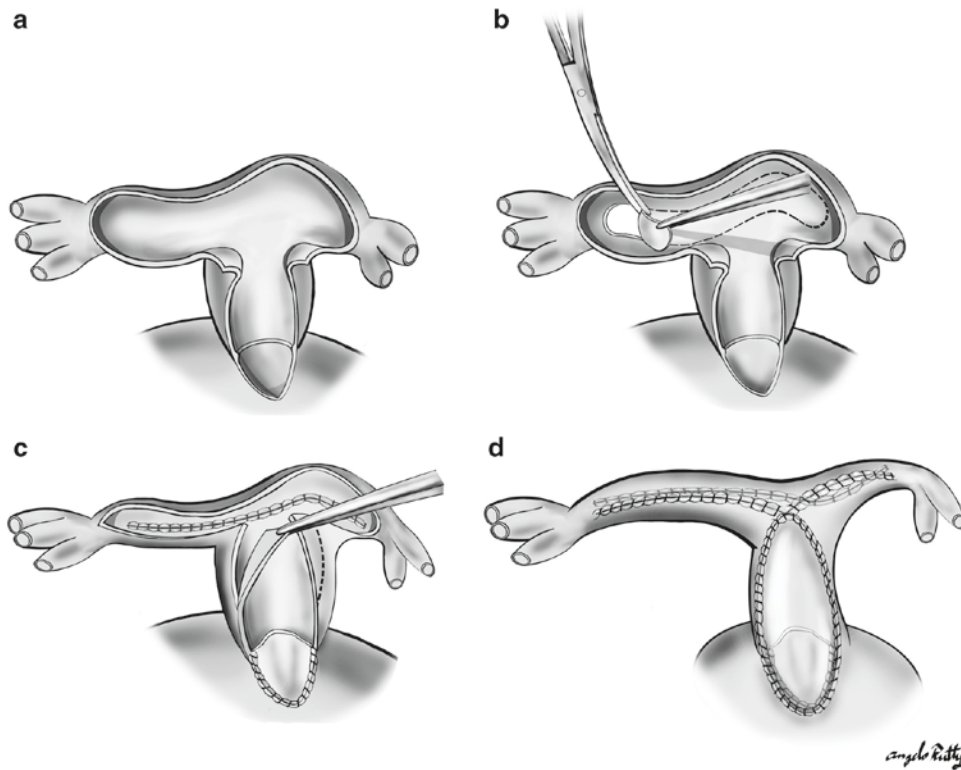


Fig. 20.2 Pulmonary Artery Reduction Arterioplasty. (a) The anterior wall of the main and branch pulmonary arteries is opened longitudinally. Note that the main pulmonary artery incision is extended across the pulmonary annulus (transannular incision). (b) A longitudinal segment of the posterior wall of the

branch pulmonary arteries is excised. (c) The posterior wall of the branch pulmonary arteries is reapproximated with a running suture. A reduction arterioplasty of the main pulmonary artery is performed, and a monocusp pulmonary valve is placed. (d) A transannular patch is used to complete the repair

pulmonary artery stenosis, which may be responsible for respiratory failure.

Diaphragmatic paresis should also be ruled out by either ultrasound or fluoroscopy, and if present, treated by diaphragmatic plication.

Tracheostomy remains an ultimate option if everything else fails.

patch, bioprosthetic valve, or valved conduit – patients may need reoperation for either stenosis or insufficiency. Echocardiography, MRI, and perfusion scans are recommended to evaluate potential pulmonary artery and RVOT stenosis, RV dimensions, and function. Many cases of distal pulmonary stenosis can be managed with interventional catheterization, but repeat surgical pulmonary arterioplasty may be necessary.

20.9 Long-term Outlook

Followup is limited in most series; nonetheless, with early repair of TOF-APV, the long-term outcome appears good, including the patients with severe airway malacia [7]. Close pulmonary followup is recommended because bronchomalacia may persist. Even mild exercise intolerance may reflect significant RV dilatation or hypertension. Depending on the RVOT repair – transannular

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Chapter 21

Tetralogy of Fallot with Pulmonary Atresia

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21.1 Anatomy

Tetralogy of Fallot with Pulmonary Atresia (TOF-PA) accounts for 1.5–3.4% of all forms of congenital heart disease and for 20% of all forms of TOF [1]. The Baltimore Washington Infant study reported an incidence of 0.07 per 1,000 live births for TOF-PA. TOF-PA is slightly more prevalent in males than in females.

The intra-cardiac anatomy of TOF-PA has all the features of classic Tetralogy of Fallot: ventricular septal defect, overriding of the aorta, right ventricular outflow obstruction, and right ventricular hypertrophy. The difference is in the membranous or complete atresia of the pulmonary valve, and extreme variability of the architecture of the main and distal pulmonary arteries [Fig. 21.1]. The central pulmonary arteries can be of good size, variably hypoplastic, discontinuous, or even absent. Blood flow to the pulmonary vasculature may be provided by a persistent ductus arteriosus (PDA), major aorto-pulmonary collaterals (MAPCAs), or both.

21.2 Pathophysiology

Pathophysiology in TOF-PA depends on the source and volume of pulmonary blood flow. Blood flow is usually provided by the PDA and/or by aorto-pulmonary collaterals. The newborn infant, in whom the PDA is the sole source of pulmonary blood flow, can present

with cyanosis and signs of hemodynamic decompensation, once the PDA starts to close, usually occurring within the first 48 h of life. Prenatal or early postnatal recognition of the diagnosis along with prompt initiation of prostaglandin E₁ (PGE₁) administration is life saving. If aorto-pulmonary collaterals are the sole source of pulmonary blood flow, the clinical presentation may vary from cyanosis with inadequate pulmonary blood flow to no cyanosis with increased pulmonary blood flow. Older infants and children commonly present with progressive cyanosis due to hypoxia. Hypoxia typically worsens as the child outgrows the source of pulmonary blood flow, or when this source becomes progressively stenotic or even atretic. Early surgical intervention associated to transcatheter pulmonary artery rehabilitation has improved survival in these patients.

21.3 Clinical Presentation

An infant with TOF-PA is often symptomatic within the first hours to days of life. Severe cyanosis becomes evident after birth as the ductus begins to close. In the presence of significant aorto-pulmonary collaterals, cyanosis may be mild to moderate. If adequate collaterals are too few to maintain sufficient pulmonary flow, closure of the ductus arteriosus may produce life-threatening hypoxemia. Occasionally, patients with well-developed aorto-pulmonary collaterals or persistent patency of the ductus may present with respiratory compromise due to pulmonary overcirculation and heart failure. Symptoms develop several weeks after birth as pulmonary vascular resistance decreases and pulmonary blood flow increases. Infants may feed poorly and fail to gain weight.

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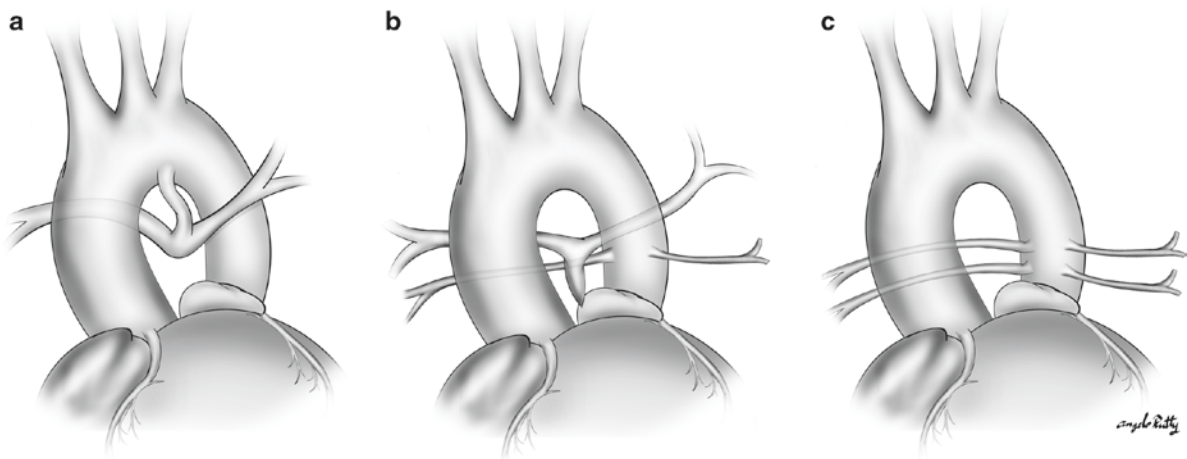


Fig. 21.1 Anatomy of the central pulmonary arteries in Tetralogy of Fallot with Pulmonary Atresia (TOF-PA) (a) Normal central pulmonary arteries, (b) hypoplastic central

pulmonary arteries with aorto-pulmonary collaterals, (c) absent central pulmonary arteries with multiple aorto-pulmonary collaterals

Growth and development are usually delayed secondary to cyanosis or congestive heart failure.

Auscultation reveals a normal first heart sound with a single loud second heart sound. A systolic murmur may be present at the left lower sternal border. A continuous murmur of PDA may occur at the left base but is uncommon beyond infancy. A continuous murmur may also originate in a systemic to pulmonary collateral artery.

In older patients, hemoptysis may occur as a result of rupture of extensive systemic-to-pulmonary collateral arteries.

DiGeorge syndrome is a common association with TOF-PA, and in this group of patients recurrent infections can occur because of immunodeficiency.

Survival to adulthood has been described in patients with well-developed collateral arteries.

21.3.1 ECG

ECG findings are similar to those of other patients with Tetralogy of Fallot (TOF). Right ventricular hypertrophy with right axis deviation is usually present.

21.3.2 Chest Radiography

Chest radiograph reveals normal heart size with variable degree of pulmonary vascularity depending

on amount of pulmonary blood flow. There is commonly the well-described “boot shaped” heart with a tilted up apex. A concave main pulmonary artery segment is typically observed.

21.4 Preoperative Management

Preoperative knowledge of all sources of pulmonary blood flow and the anatomy of central pulmonary arteries is fundamental for surgical planning.

Neonates with TOF-PA need to undergo thorough echocardiographic and angiographic evaluation for the presence and anatomy of aorto-pulmonary collaterals. Until the evaluation is completed and the presence of collaterals is ascertained, these neonates are considered to have ductal-dependent pulmonary blood flow and should be started on Prostaglandin E_1 .

As pointed out by Mackie et al [2] echocardiography is a sensitive and specific diagnostic tool for the presence of MAPCAs in infants with TOF-PA. The presence of branch pulmonary artery diameter Z score ≤ -2.5 or a PDA diameter ≤ 2 mm is the most sensitive and specific test for the presence of ≥ 1 MAPCAs. However, echocardiography alone is considered insufficient to assure the presence of collaterals [Fig. 21.2]. In addition, if collaterals are suspected, detailed definition of the anatomy and this is ensured by angiography [Fig. 21.3], MRI/A, or axial CTA. Outside the newborn period, selective angiography of

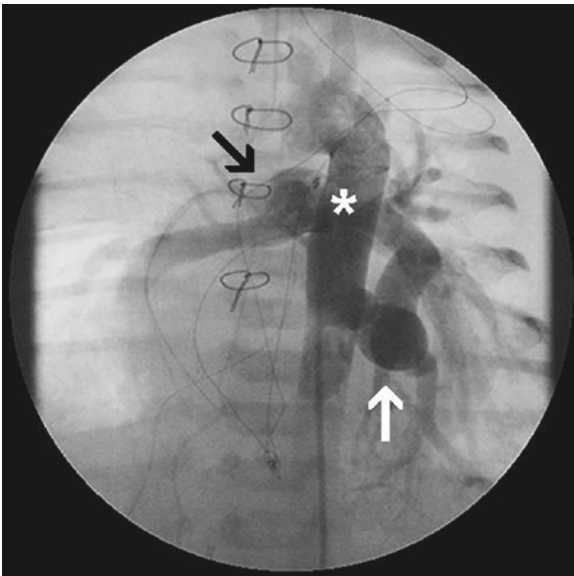


Fig. 21.2 Descending aortogram in anteroposterior projection performed in a patient after neonatal repair of (TOF) with pulmonary atresia with normal size central pulmonary arteries (*black arrow*) without a prior cardiac catheterization. A large aortopulmonary collateral from the descending aorta had been missed (*white arrow*), which lead to severe heart failure symptoms postoperatively. In this case the aortopulmonary collateral communicates with the left pulmonary artery, which is also supplied by the central pulmonary artery (*black arrow*), and thus, can be ligated or embolized safely * descending aorta

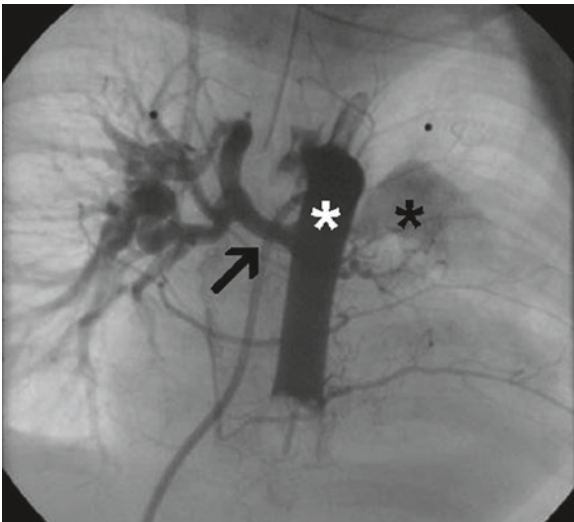


Fig. 21.3 Balloon occlusion descending aortogram (*white asterix*) performed in a newborn with TOF-PA and absent central pulmonary arteries. There is a moderate size collateral feeding the right lung (*black arrow*). The left pulmonary artery (*black asterix*) is large and fills from the aorta as well

the collateral vessels is typically performed to determine the distribution of each collateral and to define which segments are supplied solely by the collaterals, or by the central pulmonary arteries or both.

21.4.1 Surgical Management

Because of the wide variability in the native pulmonary artery development and the source of pulmonary blood flow, the surgical management of TOF-PA is more difficult than that of classic TOF. Therefore, for simplicity, these patients can be divided in three groups.

1. *Patients with normal size or minimally hypoplastic confluent central pulmonary arteries:* Most of these patients can undergo a single stage complete repair consisting of closure of the VSD and placement of a RV to PA conduit [Fig.21.4]. In these patients it is usually safe to close the VSD because of the well-developed pulmonary vasculature. Another alternative is to initially proceed with a systemic to pulmonary artery shunt followed by complete repair at a later time.

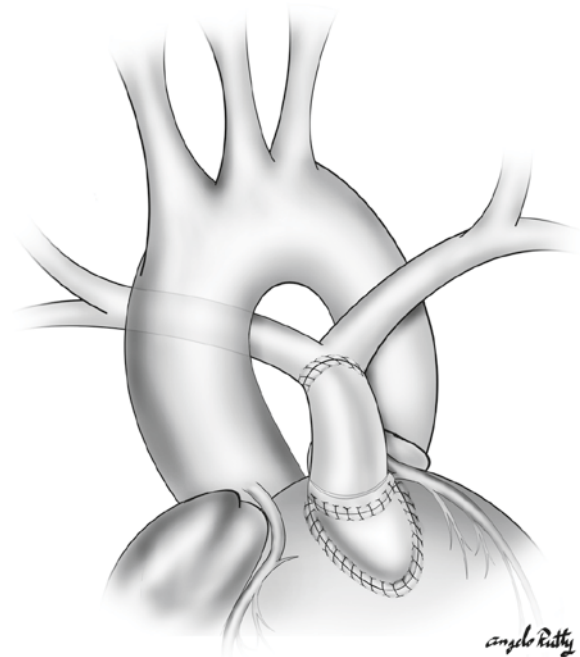


Fig. 21.4 Right ventricle to pulmonary artery conduit

2. *Patients with hypoplastic but confluent pulmonary arteries and multiple aorto-pulmonary collaterals with multiple segments of the lungs receiving dual supply:* The surgical repair is individualized to the particular anatomy. A staged approach is frequently used consisting of sequential unifocalizations and the placement of an RV to PA conduit and/or systemic to pulmonary artery shunt [Fig. 21.5]. The main goal of the initial interventions is to promote the growth of the native pulmonary arteries and of the unifocalized aorto-pulmonary collaterals. The VSD

is closed once the pulmonary artery cross-sectional area is adequate (greater than 50% of normal) so that the RV pressure would be acceptable (lesser than 75% systemic) at the end of the repair. Before VSD closure, the echocardiogram and/or catheterization should reveal primarily a left-to-right shunt across the VSD. A more aggressive approach would be a single stage repair via a median sternotomy, as suggested by the Stanford group [3].

3. *Patients with absent or severely hypoplastic nonconfluent pulmonary arteries and multiple aorto-pulmonary*

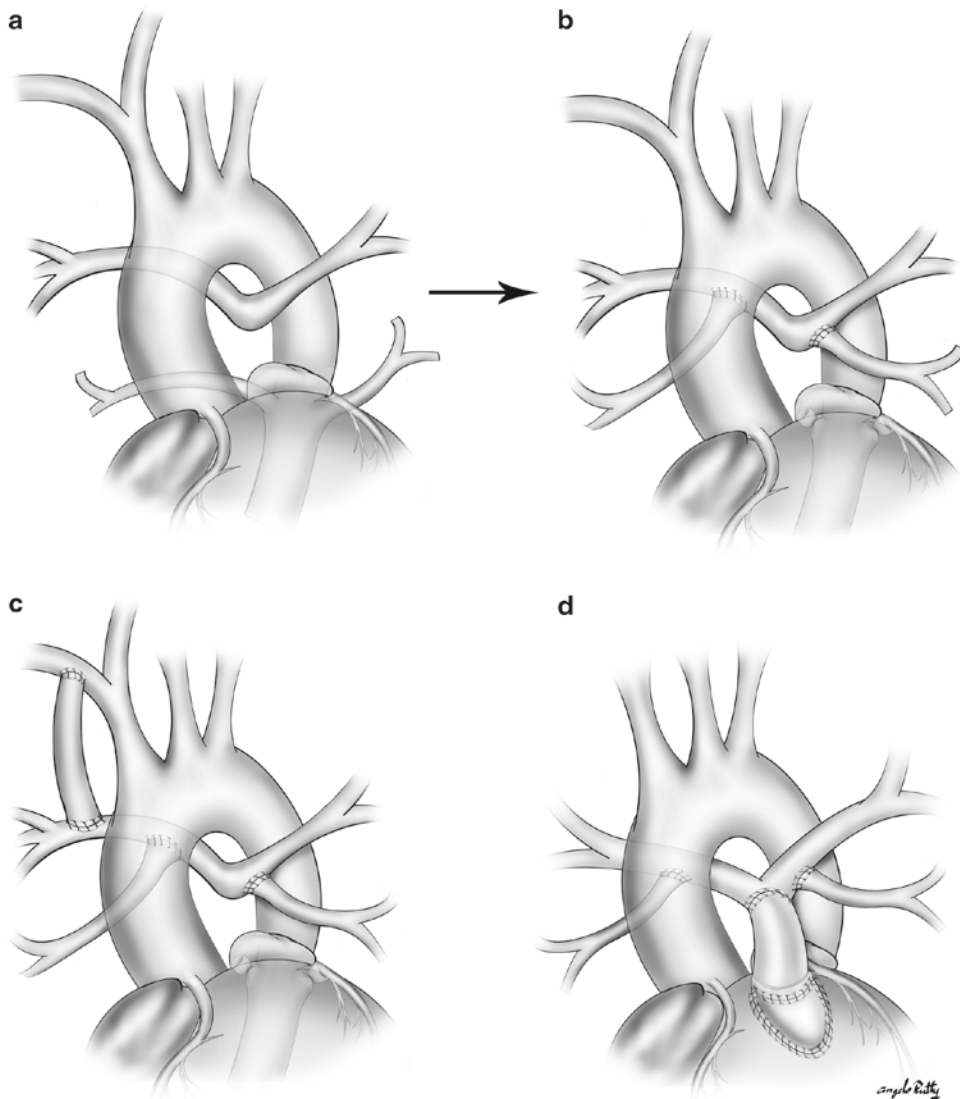


Fig. 21.5 *Unifocalization.* (a) It involves separating the aorto-pulmonary collaterals from the aorta and connecting them to the native pulmonary arteries, (b) a systemic to pulmonary artery

shunt or (c) a right ventricle to pulmonary artery conduit is usually added to augment the pulmonary blood flow and promote arterial growth

collaterals: Commonly, a staged approach is utilized consisting of unifocalizations, followed by reconstruction of the central pulmonary arteries and placement of an RV to PA conduit with or without VSD closure. The VSD patch is fenestrated or removed if the RV pressure is >75% systemic [4]. It is important to realize that some of these patients will never achieve a complete repair because of their abnormal pulmonary arterial vasculature and excessively high pulmonary vascular resistance.

21.5 Postoperative Management

The postoperative management of patients with TOF-PA with confluent pulmonary arteries and a PDA as the source of pulmonary blood flow does not differ significantly from the management of patients with TOF and pulmonary stenosis.

Patients with TOF-PA and multiple aorto-pulmonary collaterals, whether after first stage unifocalization or subsequent repair, are usually ill and present unique challenges during the immediate postoperative period.

Postoperative bleeding is common, especially in the case of extensive pulmonary arterial reconstruction.

21.5.1 Monitoring

Invasive monitoring is routine and includes central venous and arterial lines.

21.5.2 Cardiovascular Management

Vasoactive infusions are frequently employed in the patients with pulmonary hypertension and borderline right ventricular function after ventriculotomy. Patients are at risk of pulmonary hypertensive crisis due to “reactive” pulmonary vasculature. They should be properly ventilated with a goal to permit maximal afterload reduction for the right ventricle. Sufficient tidal volumes are allowed while preventing high plateau pressure and reduction in functional residual capacity. Nitric Oxide is frequently utilized in the immediate perioperative period.

Cyanosis can be present due to right-to-left shunting at the atrial level from poor RV compliance and

systolic dysfunction related to the ventriculotomy and the RV hypertrophy. In addition, in those patients palliated with an open VSD, right to left shunting can be at the ventricular level, related to high resistance or decreased distal vascular bed (remaining stenosis, kinking, or occlusion of unifocalized collaterals).

21.5.3 Sedation and Analgesia

Deep sedation, analgesia, and paralysis should be employed in the patients exhibiting signs of pulmonary vasoreactivity combined with hemodynamic instability. This goal may be achieved by combining infusions of opioids and benzodiazepines or else dexmedetomidine.

21.5.4 Respiratory Management

Patients usually arrive from the operating room intubated and remain on mechanical ventilation for 24–48 h with the goal of early extubation.

Some patients may develop severe pneumopathy secondary to reperfusion injuries.

In patients who fail to extubate, a high index of suspicion should arise for diaphragm paresis or palsy, especially in patients who underwent extensive unifocalization procedures.

21.6 Complications

If the patient has evidence of persistent pulmonary overcirculation, a residual VSD or non unifocalized aorto-pulmonary collaterals should be suspected. Many such postoperative issues can be managed in the Catheterization Laboratory, with coil embolization of residual collaterals, or with transcatheter interventions for thrombosed or stenotic unifocalized vessels. Most patients with TOF-PA and abnormal pulmonary arborizations need multiple transcatheter interventional procedures either after complete repair or following initial surgical palliation in preparation for VSD closure. The development of novel catheter techniques to deal with resistant lesions (ultra high pressure balloons, cutting balloon, stent implantation) has lead to an increased success rate of these interventions significantly in the last decade [4, 5] [Fig. 21.6].

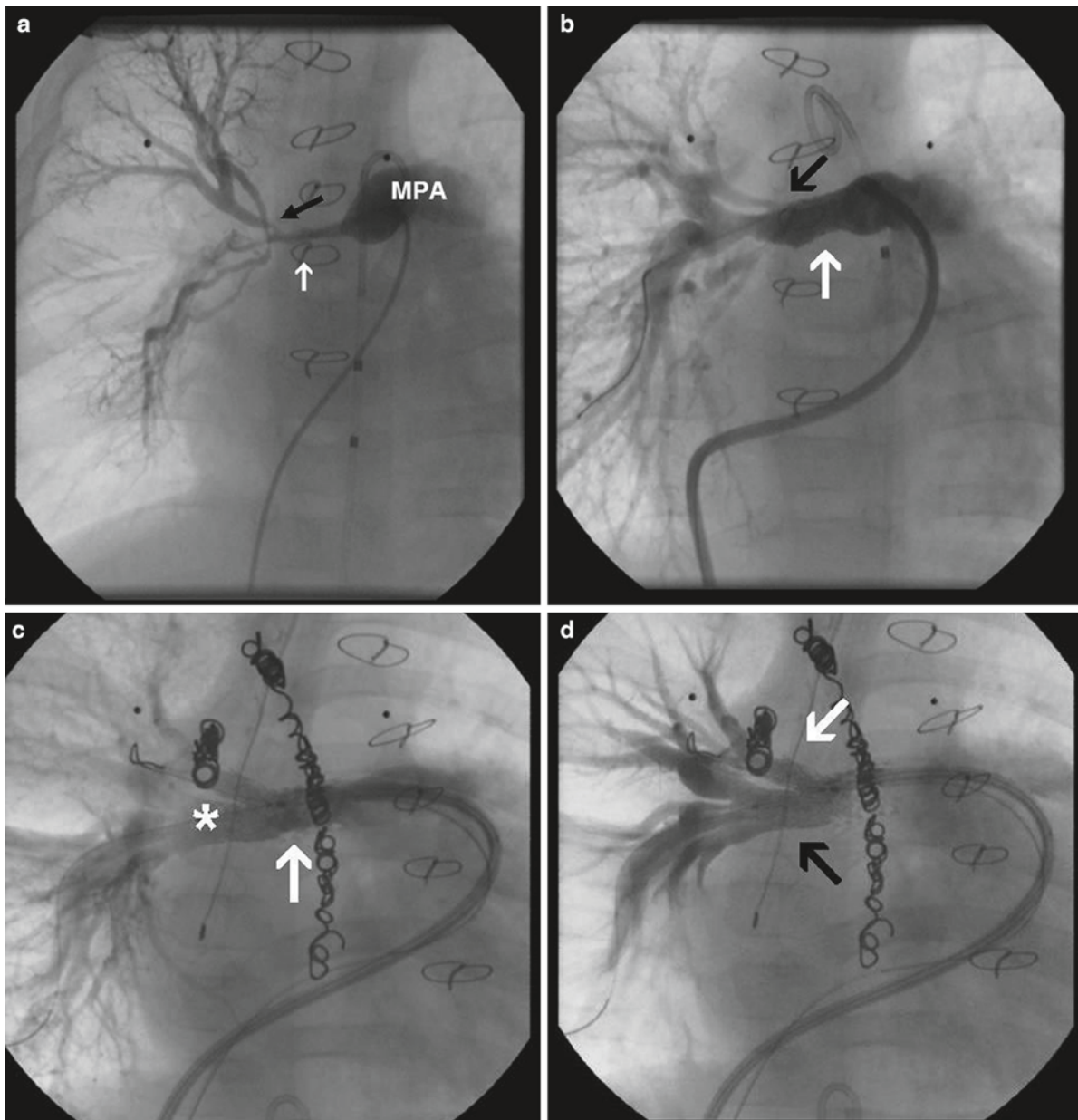


Fig. 21.6 Series of angiograms performed on a patient with absent central pulmonary arteries, multiple collaterals, status post-staged unifocalization with a right ventricle to pulmonary artery homograft, and fenestrated patch closure of the ventricular septal defect. (a) Note severe distal hypoplasia, long-segment proximal RPA stenosis (*white arrow*), and segmental right upper lobe stenosis (*black arrow*) after unifocalization of right pulmonary artery collaterals (this is on the same patient as shown in Fig. 21.3), (b) Following multiple transcatheter interventions including high

pressure pulmonary angioplasty and proximal RPA stenting (*white arrow*), there is significant improvement in the distal and proximal vessel diameters of the right upper lobe (*black arrow*) and remaining segments, (c, d) after additional transcatheter intervention in the right pulmonary artery (*asterisk*), including balloon angioplasty and stenting plus coiling of remaining aortopulmonary collateral flow, the vessel has been rehabilitated, with significant improvement in diameter of the right upper lobe, distal right lower and middle lobes, as well proximal RPA (*arrows*)

21.7 Long-term Outlook

The prognosis of TOF-PA is uncertain and depends on the specific anatomy and number and type of interventions. Long-term follow up data are not widely available. The results of published surgical series are not necessarily applicable to other patient groups, as there is significant heterogeneity in the anatomy, in addition to variable institutional expertise in surgery and interventional cardiology. Evolving and improving surgical techniques in combination with sophisticated cardiac catheter interventions will undoubtedly lead to on-going improvement in survival and decreased morbidity [4].

These patients are followed closely with regular electrocardiographic and full echocardiographic evaluations for the potential development of right ventricle to pulmonary artery conduit obstruction and stenosis of reconstructed pulmonary arteries, progressive right ventricular dysfunction, and evidence of arrhythmia.

Most patients with TOF-PA and small or absent central pulmonary arteries will require multiple cardiac catheterizations as a nonsurgical complement of the staged repair [Fig. 21.5] [4]. They are usually evaluated for pulmonary artery obstruction and persistent undesired collateral supply of pulmonary blood flow. Interventions include balloon angioplasty with or without stent placement and coil embolizations of residual aorto-pulmonary collaterals. The window of opportunity to achieve the most growth in the vascular bed is during the first 2 years of life, and thus, catheter and surgical intervention should be undertaken early in life.

Patients who undergo placement of a right ventricle to pulmonary conduit will require multiple conduit replacements during their lifetime, secondary to progressive conduit stenosis and/or insufficiency. Stent implantation of the stenotic homograft may delay the need for surgery, however, if the homograft was originally very small, surgical replacement is needed. The development of transcatheter valve technology will likely offer an alternative to surgical conduit replacement for older children with stenotic or dysfunctional homograft conduits.

A few patients may never reach the stage of complete repair because of very hypoplastic pulmonary arteries.

In such cases there is on going right to left shunting at ventricular level, associated with significantly reduced exercise tolerance and variable degrees of cyanosis. This is a debilitating condition with poorly associated quality of life.

There are few patients with absent central pulmonary arteries and multiple collaterals who have a balanced degree of pulmonary blood flow and who do relatively well without intervention until the second or third decade of life. Still, the risk of chronic cyanosis and polycythemia and stroke is significant in the long term. In addition, these patients are at risk of irreversible pulmonary hypertension (affecting the pulmonary segments without stenosis) as well as progressive loss of pulmonary vascular bed from stenosis and occlusion of lung segments (those supplied by vessels with severe stenosis). Late failure in this setting can only be managed with heart–lung transplantation. Thus, a management approach aimed at intervention during early childhood is preferred whenever feasible. It is physiologically advantageous to have a connection between the right ventricle and the pulmonary artery as the source of pulmonary blood flow when compared to an aorto-pulmonary shunt, in which a higher Q_p/Q_s is required to achieve the same degree of arterial saturation.

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Chapter 22

Pulmonary Atresia with Intact Interventricular Septum

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22.1 Anatomy

Pulmonary atresia with intact ventricular septum (PAIVS) is a cyanotic congenital cardiac lesion with an incidence quoted by various sources between 0.71 and 3.1% of all congenital heart disease. It is characterized by an imperforate pulmonary valve with completely fused commissures, variable degrees of dysplasia and narrowing of the pulmonic valve, variable hypoplasia of the right ventricle and tricuspid valve and a frequent association of coronary artery fistulae and sinusoids (Fig. 22.1). The pulmonary arteries are usually normal in size and the pulmonary blood flow is supplied by a patent ductus arteriosus (PDA). The right ventricular hypoplasia can be extensive and involve all three components, inlet, trabecular and infundibular parts or be confined to one area. The left sided heart is usually normal, but in severe cases the ventricular septum is displaced into the left ventricle and its cavity may be somewhat restricted. Occasionally, infants with PAIVS have shown signs of both right and left ventricular ischemia, likely related to the coronary artery fistulae. Association with atretic, hypoplastic, or obstructed central coronary arteries, called right ventricular-dependent coronary circulation (RVDCC) [1], carries a higher risk of morbidity and mortality.

A study by Hanley et al. showed that among 171 neonates with PAIVS, the Z-value of the diameter of the tricuspid valve was less than -2 in 52% of patients and less than -4 in 26%; The tricuspid valve diameter was highly correlated with right ventricular cavity size (which was small in 90% of patients and was severely

reduced in 54%). Coronary artery-right ventricular fistulas were present in 45% of patients, and RVDCC was seen in 9%; Z-value of the diameter of the tricuspid valve was negatively correlated ($P < 0.0001$) with the prevalence of both [2].

Another recent study, found an even higher incident of coronary abnormalities. Among 116 cases reviewed, fistulas were found in 87 patients (75%), interruptions of major coronary arteries in 40 patients (34%), lack of connections between the coronary arteries and the aorta in 18 patients (16%), and a single coronary artery, with the right coronary artery arising from the left, in 6 patients (5%). Though the presence of fistulas in itself was not associated with higher mortality, presence of RVDCC was associated with a 40% incidence of mortality [3].

22.2 Pathophysiology

Preoperative physiology is for the most part similar to any other form of single ventricle with PDA dependent pulmonary blood flow. Systemic venous blood returning to the heart enters the right atrium and then the right ventricle but because of pulmonary valve atresia the right ventricular blood returns back into the right atrium through an insufficient tricuspid valve. Eventually, the systemic venous return enters the left atrium through a patent foramen ovale where it mixes with pulmonary venous return. If right ventricular coronary sinusoids are present, blood is ejected into them during systole and then it enters the coronary arteries. Subsequent pulmonary blood flow is determined by the size of PDA.

Prognosis and further management depends on the degree of tricuspid valve insufficiency, coronary anatomy and the presence of ventriculo-coronary connections [1].

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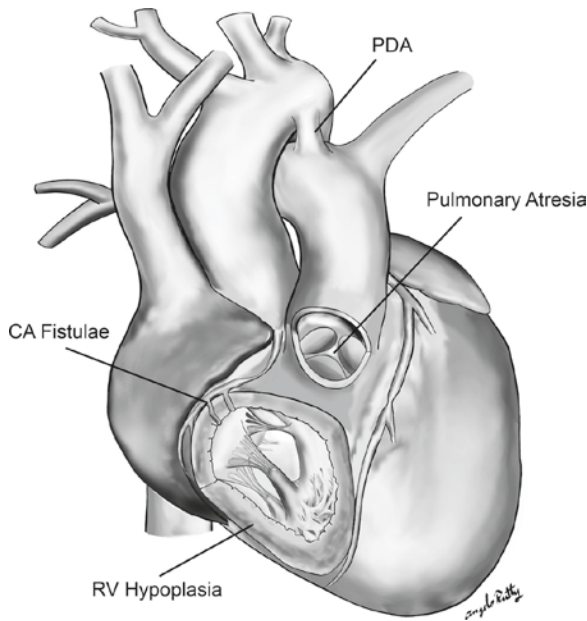


Fig. 22.1 Pulmonary atresia with intact ventricular septum. Note the presence of right ventricular (RV) hypoplasia and pulmonary valve atresia. The patent ductus arteriosus (PDA) is the only source of pulmonary blood flow. Coronary artery (CA) fistulae are frequently associated with this lesion

Intramyocardial sinusoid-coronary artery fistulae can be well established in PAIVS. Angiographically, blood can be demonstrated flowing from the right ventricular cavity through channels, into the coronary arteries. Fistulous connections of the sinusoids to the coronary circulation could lead to the retrograde perfusion of the myocardium with desaturated blood from the right ventricle. Furthermore, there might be complete coronary artery obliteration proximal to the fistulous connection due to intimal proliferation, thrombosis or kinking. In situations where right ventricular pressure decreases (such as surgical or transcatheter pulmonary valvotomy for right ventricular decompression), and proximal coronary blood flow is not adequate, a coronary artery steal into the right ventricular cavity could compromise myocardial perfusion distal to the fistula and cause ischemic changes. The presence of stenosis or interruption in major coronary artery branches, so that the distal perfusion is supplied either solely or in the most part by the right ventricle is recognized as a right ventricular dependent coronary artery circulation. The gold standard for diagnosis of this condition continues to be angiography.

22.3 Clinical Presentation

Infants with PAIVS usually are normal and well developed at birth. Cyanosis may be mild because pulmonary blood flow is provided by the PDA. Over the following 5–10 days cyanosis worsens and may suddenly become severe if PDA closes. Apart from cyanosis and mild, comfortable tachypnea, neonates are usually asymptomatic, unless hypoxemia is severe with PO_2 level below 25 mmHg and arterial saturation below 50%. These patients then develop metabolic acidosis with tissue organ dysfunction, pallor and mottled skin.

The physical exam can reveal a hyperactive precordium if tricuspid insufficiency is significant. The second heart sound is single, and there is often a blowing 2–3/6 systolic murmur due to the tricuspid insufficiency. In these situations, in addition to hypoxemia there may also be hepatomegaly due to volume overload.

22.4 Preoperative Assessment and Management

The following should usually be obtained in all patients:

- 1) *Chest X-ray*: In infants with significant tricuspid valve insufficiency, the cardiac shadow is enlarged. In those however with significant hypoplasia of the right ventricle the heart appears small. Small main pulmonary segments and pulmonary vascular markings that are determined by the patency of ductus arteriosus are observed.
- 2) *ECG*: Demonstrates right axis deviation, right ventricular hypertrophy and right atrial enlargement. In cases however of significantly hypoplastic right ventricle the electrical axis is often 0° – 30° . Rarely left forces predominate. There must be careful attention paid to the ST-T wave changes and serial ECGs may be warranted. Myocardial ischemia from coronary sinusoids occlusion has been reported and can present with ischemic electrocardiographic changes.
- 3) *Echocardiography*: Usually sufficient to establish the diagnosis. The following details need to be identified:
 - a) Patency and size of the ductus arteriosus.
 - b) Degree of right ventricular hypertrophy and hypertension, morphology (tripartite, bipartite or monopartite).

- c) Morphology and size of the tricuspid valve and degree of insufficiency.
- d) Morphology of the pulmonic valve (membranous and domes or thickened, dysplastic and immobile), and pulmonary artery anatomy.
- e) Ventricular-coronary artery communications with right ventricle need to be excluded. This can be difficult and in nearly all cases routine angiography is recommended in patients with PAIVS. Even when coronary sinusoids are seen with echocardiography, it is still very difficult to assess whether there is obstruction of distal coronary arteries and, thus, whether there is RVDCC.
- f) Size of the foramen ovale

4) Chromosome and Fish probe studies

5) *Catheterization and Angiography*: Diagnostic cardiac catheterization is almost always performed in newborns with PAIVS to rule out RVDCC. A right ventriculography is performed transvenously using an end-hole or angiographic catheter (often a hand injection if the ventricle is very hypoplastic) in AP/

Lat projection and angled angiography (right anterior oblique and long axial oblique projections) (Figs. 22.2a, 2b).

Therefore, the right ventriculogram can be diagnostic and determine the absence of sinusoids and coronary artery fistula. If no filling of the coronary arteries is seen, one can conclude that there are no right ventricular to coronary artery connections. Since the right ventricular pressure is supra-systemic any such connections fill very well during right ventriculography, whenever present. If coronary artery fistulas are seen, there may be evidence of retrograde filling of the aorta indicating the absence of coronary ostia atresia (Fig. 22.3a). The whole coronary tree can be sometimes delineated in detail from the right ventriculogram. It is essential to document the complete anatomy of the coronary arteries to determine the presence of stenosis or interruption in important coronary vessels, as with right ventricular decompression, segments of the myocardium fed by branches distal to the stenosis or interruption may experience ischemia.

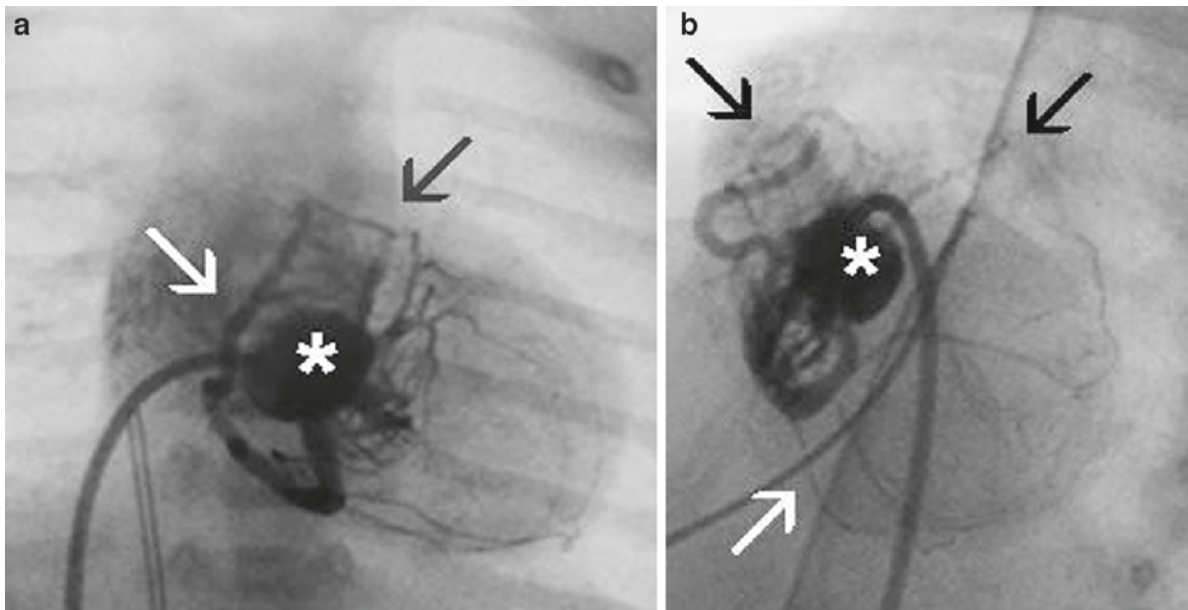


Fig. 22.2 (a) Right ventriculogram performed in straight antero-posterior projection in a patient with right ventricular dependent coronary circulation. There is a monopartite hypoplastic right ventricle (*white asterix*) and multiple right ventricular to coronary artery fistula filling the right coronary artery (*white arrow*) and the left coronary artery (*black arrow*). The distal left anterior descending is right ventricular dependant, as there is an interruption of the LAD immediately

following the black arrow, such that the distal branches of the LAD are supplied directly and solely by the right ventricle, (b) in left anterior oblique projection the right ventriculogram demonstrates extensive ventriculo-coronary connections filling both the right and left coronary artery systems (black arrows). The distal left system is supplied solely by the right ventricle (*white arrow*), indicating right ventricular dependant coronary artery circulation

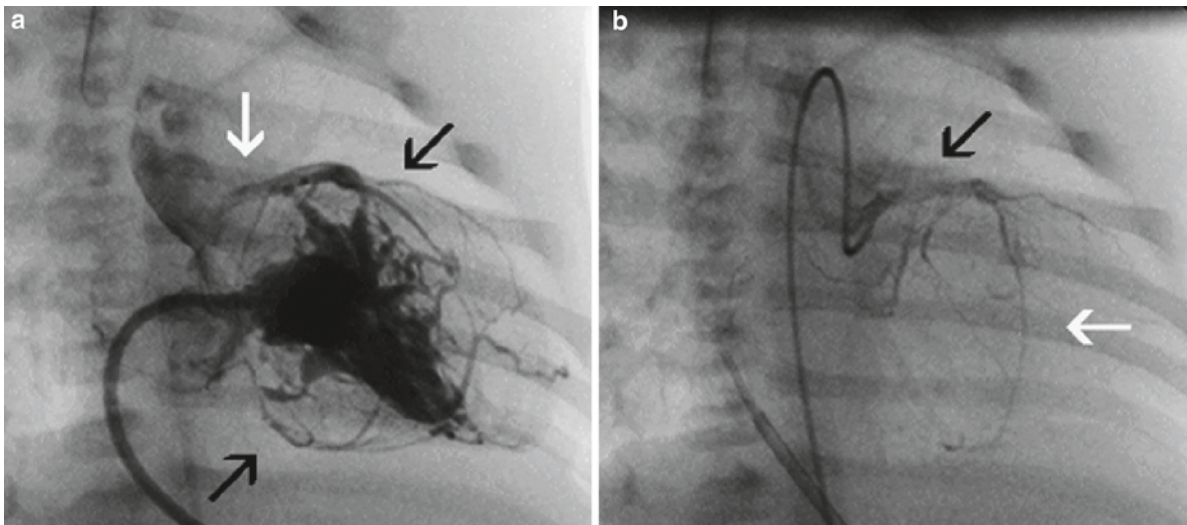


Fig. 22.3 (a) Right ventriculogram in RAO projection demonstrates extensive ventriculo-coronary artery connections filling both the right coronary and left coronary artery trees (black arrows). Note retrograde filling of the aorta from the left coronary artery (white arrow) showing no coronary ostia obstruction, (b) using a 3F coronary catheter selective left coronary angiography (black

arrow) demonstrates no evidence of stenosis or interruptions in the left coronary artery system with a thin left anterior descending coronary artery (white arrow) which fills without localized obstructions from the aorta. Thus, in this case, although extensive right ventricular to coronary artery fistulas are present, there is no evidence for RVDCC

Selective coronary angiography may be necessary to document normal origin of the coronary tree from the aorta and rule out significant stenosis (Fig. 22.3b). In newborns, 3F coronary catheters can be used for this purpose. Aortic root angiography may be enough to document coronary anatomy, and sometimes the right ventriculography will retrogradely fill the aorta documenting open coronary ostia as well as the coronary artery tree well enough, that RVDCC can be ruled out without the need for arterial angiography.

22.5 Management

Preoperative management is focused on correction of hypoxemia and acidosis by maintenance of ductal patency with a PGE₁ infusion. Ventilation and paralysis might be employed in a patient who is particularly acidotic and has poor left ventricular function. In patients with coronary artery sinusoids and confirmed or suspected RVDCC, afterload reduction is a relative contraindication. However, if necessary, afterload reduction should be used carefully as reduction in central aortic blood pressure could lead to impaired

coronary blood flow and myocardial ischemia and infarction.

In moderate to severe cases the following measures are recommended:

1. Secure intravascular access (central venous and arterial lines).
2. Prostaglandin E₁ infusion (0.01–0.05 µg/kg/min, unless ductus arteriosus is closed, then use a higher initial dose).
3. Mechanical ventilation, sedation and muscle paralysis may be necessary in cases of impending or existing significant organ dysfunction (including myocardial).
4. Volume resuscitation: the right ventricle is usually hypertrophic and restrictive and in cases of existing coronary artery sinusoids a higher filling pressure may be warranted. Use caution if left ventricular function is impaired.
5. Pure systemic vasoconstriction (phenylephrine, vasopressin) may be necessary in cases of impending myocardial infarction from occluded coronary sinusoids. Elevating systemic (aortic) blood pressure may prevent myocardial ischemia by promoting anterograde blood flow through narrow or kinked coronary sinusoids (in the absence of

coronary ostial atresia). Epinephrine, although maybe necessary when left ventricular function has deteriorated, may increase myocardial oxygen demand and should be used with caution.

6. Sodium bicarbonate for significant metabolic acidosis.
7. Keep hemoglobin above 13.5–15 g/dl.
8. Consider anticoagulation or anti-platelet therapy.
9. If the patient is in refractory cardiogenic shock, consider ECMO support as a bridge to heart transplantation.

22.6 Transcatheter Interventional Management:

Patients with membranous pulmonary atresia and good-sized tripartite right ventricles can undergo wire, laser or radio-frequency-assisted valve perforation followed by balloon valvotomy [4–6]. The technique of radiofrequency perforation has been perfected and expanded world wide with the use of the Baylis-Nykanen catheter system (Figs.22.4a–4d)

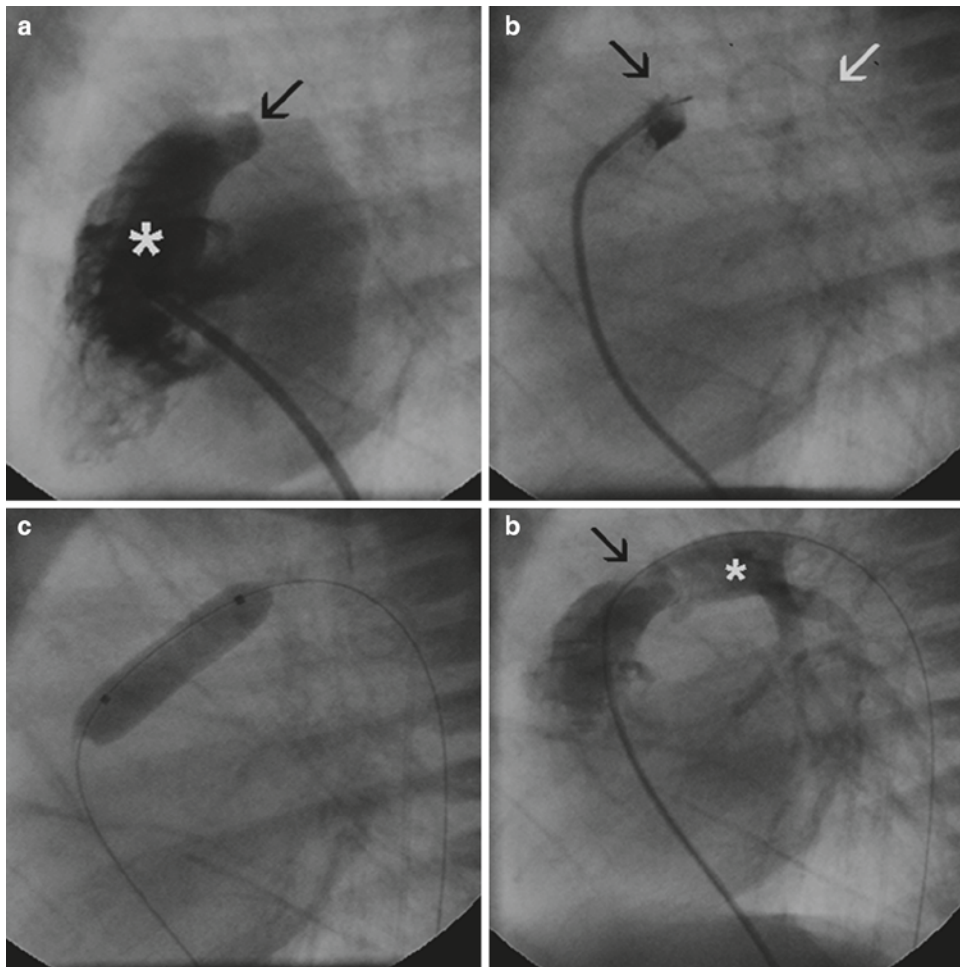


Fig. 22.4 (a) In lateral projections a right ventriculogram demonstrates a membranous pulmonary valve atresia (*black arrow*), with a reasonable size right ventricle (*white asterix*) and no evidence of any right ventricular to coronary artery connections. As commonly seen there is tricuspid valve regurgitation, so that contrast fills backwards the right atrium, (b) Using a 4F right coronary artery JR2 catheter, the radiofrequency wire is activated aimed at the membranous valve. The aortic pigtail catheter (*white arrow*) is positioned across the PDA or in the descending aorta for angiography, to document anatomy

of the main pulmonary artery. Following radiofrequency burn through the membranous valve, the tip of the wire is seen across the valve plate (*black arrow*), (c) following radiofrequency perforation, a guidewire is advanced across the valve down to the descending aorta through the PDA, and a balloon catheter is used then for the valvotomy, (d) angiography of the right ventricular outflow tract following radiofrequency perforation of the pulmonary valve demonstrates wide open pulmonary valve (*black arrow*), with unobstructed filling of the main pulmonary artery (*white asterix*)

Although successful perforation mostly using this technique has been reported in up 75–90% of selected patients, the procedure is definitive for only 35% of cases [4, 5, 7], as they commonly require additional intervention either transcatheter or surgical (placement of Blalock-Taussig shunt, or PDA stenting) [8]. Given that most patients with pulmonary atresia have hypoplastic right ventricular outflow tract and pulmonary annulus, many believe that in order to achieve adequate right ventricular decompression and to maximize right ventricular growth, a surgical right ventricular outflow tract patch is necessary. Thus, in the presence of marked pulmonary annular and right ventricular outflow tract hypoplasia, surgical management is preferred rather than transcatheter therapy as the best method to achieve maximal right ventricular outflow tract decompression.

Following initial right ventricular outflow tract decompression, some patients will be able to wean from prostaglandins. Those who do not after 2 weeks will require an additional source of pulmonary blood flow, either as a BT shunt or a PDA stenting.

During follow-up, additional transcatheter interventions may be indicated, such as transcatheter closure of atrial septal defect with device and coil embolization of a BT shunt.

22.6.1 Surgical Management

The surgical management is based on the degree of right ventricular hypoplasia and on the coronary anatomy, mainly the presence or absence of right RVDCC [2, 3, 9]. There are a number of surgical strategies available, including the following:

1. Two Ventricle Repair

This strategy is used in patients with mild RV hypoplasia, with a tricuspid valve Z-score >-2 , in the absence of RVDCC. Initially, these patients undergo placement of a right ventricular outflow tract patch with or without the addition of a systemic to pulmonary artery shunt (Fig. 22.5). The interatrial communication is left open. Subsequently, they undergo ASD closure and shunt occlusion in order to achieve a biventricular repair.

2. Single Ventricle repair

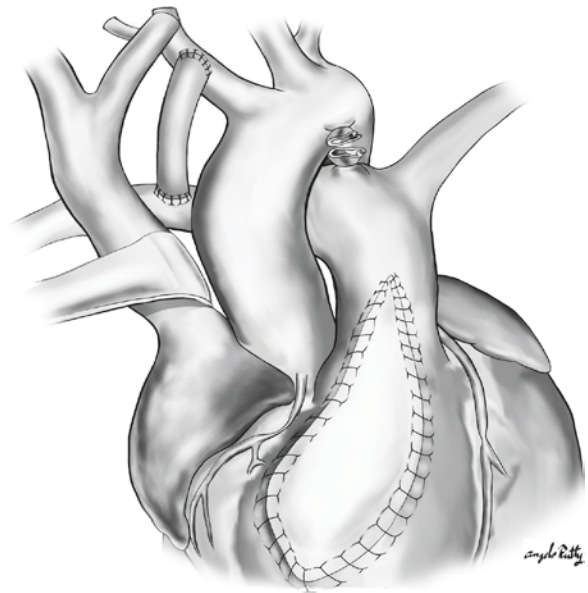


Fig. 22.5 Right ventricular outflow tract patch and a right systemic to pulmonary artery shunt. The PDA has been ligated and divided

This strategy is used in the presence of severe RV hypoplasia, with a tricuspid valve Z-score <-5 , and/or RVDCC. Initially, a systemic to pulmonary artery shunt is placed followed by a bidirectional Glenn. Eventually, the patient will undergo a Fontan procedure.

3. One and One-Half Ventricle Repair

This strategy is used in the presence of moderate RV hypoplasia, with a tricuspid valve Z-score >-2 but <-5 , in the absence of RVDCC. Initially, the patient undergoes placement of a RVOT patch and a systemic to pulmonary artery shunt. Subsequently a bi-directional Glenn is performed with closure of the ASD and shunt occlusion.

4. Cardiac Transplantation

This strategy is used in the presence of RVDCC with aorto-coronary atresia. Patients with this coronary anatomy have a very high incidence of sudden death [9].

22.7 Postoperative Management

The different aspects of postoperative management depend on the surgical or interventional procedure

performed; right ventricular decompression with transannular right ventricular outflow tract (RVOT) patch and placement of a modified Blalock-Taussig (BT) shunt versus radiofrequency balloon valvuloplasty or surgical pulmonary valvotomy and resection of infundibular muscle bundles, versus BT shunt without right ventricular decompression.

Following the former case, RVOT obstruction relief and placement of BT shunt, neonates return to the cardiac ICU intubated and likely with open chest. The medical management follows the common path of any other postoperative single ventricle physiology (see specific chapter in this book). However, some additional important differences include the following:

Low cardiac output syndrome due to:

1. *Unidentified RVDCC resulting in left ventricular ischemia and infarction.* This usually occurs immediately after surgery with decompression of the right ventricle and carries a poor prognosis. Depending on the degree and extension of ischemia patients may need ECMO support as a bridge to transplantation. Though effective medical management may not be possible, caregivers may consider the following:
 - a) Administration of alpha-1 agonists, e.g., phenylephrine, 0.1–3 µg/kg/min, to increase central aortic and coronary pressure (it will not be effective in cases of complete coronary ostial atresia).
 - b) Increase PEEP (or mean airway pressure via high frequency oscillation) as an effort to increase right ventricular pressure and thus promote retrograde coronary artery flow, through the coronary fistulas.
 - c) Volume administration to increase right ventricular volume.
 - d) Nitroglycerin 0.5–5 µg/kg/min.
 - e) Anticoagulation: Coronary fistulas due to their tortuosity and intimal proliferation they are prone to thrombosis. Currently however, there is no evidence whether anticoagulation is beneficial or not.
2. *“Circular shunt”:* This situation is due to the significant pulmonic insufficiency that results from the transannular patch. The blood from the BT shunt then flows retrogradly through the RVOT into the right ventricle in diastole. In patients with considerable tricuspid valve insufficiency, this blood flows further, retrogradly into the right atrium in systole. This “circular shunt” results in oxygenated

blood ejected from the left ventricle and aorta to return into the right atrium without adequate delivery of systemic cardiac output. Low cardiac output due to “circular shunt” can develop anywhere from day one to several days after surgery. Again this particular physiology is difficult to manage medically but caregivers may consider maneuvers to elevate pulmonary vascular resistance and lower systemic vascular resistance.

22.7.1 Monitoring and Laboratory Work Up

In severe cases, patients have an arterial line, central venous line (internal jugular or subclavian vein), pleural and mediastinal chest tubes, peritoneal drainage tube, foley catheter, and temporary pacing wires. Chest is likely open for 24–72 h, and mechanical ventilation is usually continued for 12–48 h after chest closure.

The following are obtained routinely:

- a. *Complete blood count, electrolytes, BUN, Creatinine,* immediately after surgery and every 24 h.
- b. *Arterial blood gases* every 1–4 h, *lactate* and *central venous saturation* every 4–6 h × 24 h, and then as needed.
- c. *Cerebral near infrared spectroscopy (NIRS, INVOS 5100 Cerebral Oximeter Somanetics Corporation, Troy, MI, USA).*
- d. *Electrocardiogram* daily for 48–96 h.
- e. *Echocardiogram* is not performed routinely. However an echography machine should always be readily available so a quick study can be obtained by one of the cardiac intensivists at any time without delay. This is especially important if there is suspicion of RVDCC or with any ischemic changes seen on routine electrocardiogram.
- f. Postoperative *head ultrasound*, especially with prolonged cardiopulmonary bypass (CPB) times.

22.7.2 Management of Specific Problems

- a) Mechanical Ventilation

Time-cycled pressure limited mode is most frequently used, aiming for approximately 8–10 ml/kg tidal volumes

with ideal plateau pressures of <25–28. FiO_2 is minimized to the 0.4–0.6 range to avoid potential oxygen toxicity. Target pO_2 levels range between 30 and 40. With prolonged CPB and impaired pulmonary compliance, consider administration of surfactant

b) Low Cardiac Output Syndrome (LCOS)

Beyond the reasons mentioned above, patients may develop LCOS as any other postoperative patient with a functional single ventricle. Unless there is suspicion of RVDCC, all patients are administered milrinone for 24–72 h at a range of 0.5–1.25 $\mu\text{g}/\text{kg}/\text{min}$. Ionized calcium levels are maintained between 1.1 and 1.3 mmol/L. If further inotropic support is needed, low dose dopamine 3–8 $\mu\text{g}/\text{kg}/\text{min}$ or low dose epinephrine 0.05–0.1 $\mu\text{g}/\text{kg}/\text{min}$ is utilized. It is important to consider that both dopamine and epinephrine may initiate or exacerbate arrhythmias, particularly JET.

c) Arrhythmias.

For management of JET see under Tetralogy of Fallot and Arrhythmias chapter. For other types of arrhythmias, please refer to the associated chapter.

d) Other

Sedation and analgesia are managed with fentanyl and/or dexmedetomidine, and for muscle paralysis cisatracurium is recommended.

Parenteral nutrition is started early after surgery and enteral feeds are started slowly after hemodynamic stability has been achieved and maintained for 72–96 h.

Management of patients with univentricular or one and a half ventricle physiology is further discussed in a specific chapter in this book.

22.8 Long-term Outlook

PAIVS is uniformly a fatal disease if not treated in early infancy. This disease is characterized by great morphologic heterogeneity and frequently poor outcome. Centers with aggressive approach towards biventricular repair report higher mortality. Careful stratification of patients and selection of the most appropriate surgical pathway and its impact on outcome was addressed in a study by Jahangiri et al. [10]

of 47 patients who underwent surgery between January 1991 and September 1998. A systemic-pulmonary artery shunt only was performed in all 16 patients with RVDCC, with 1 death. Fourteen of 16 patients with RVDCC underwent a bidirectional Glenn shunt at a median of 9 months after their first operation, 9 of whom have had a Fontan procedure (no deaths). In the 31 (66%) patients without RVDCC, 6 patients underwent only a systemic-pulmonary artery shunt, 23 had a shunt and right ventricular decompression, and 2 had only a transannular patch. In this group, 10 patients received a 2-ventricle repair, 6 had a one-and-a-half ventricle repair, and 8 patients had a Fontan procedure. There was 1 early death and the overall survival was 98% at 1, 5, and 7 years. Authors concluded that if the patients are stratified well, excellent survival can be achieved in the treatment of PAIVS [10].

Ascertainment of risk factors for poor outcome was a goal set forth by the UK and Ireland Collaborative study of Pulmonary Atresia with Intact Ventricular Septum, an ongoing population-based study of 183 patients born with this disease from 1991 through 1995 [11]. Low birth weight ($P=0.024$), unipartite right ventricular morphology ($P=0.001$), and the presence of a dilated right ventricle ($P<0.001$) were independent risk factors for death, whereas the presence of coronary artery fistulae, right ventricular dependence, or the tricuspid valvar Z score were not. After 9 years of follow-up, 29% have achieved a biventricular repair, 3% a so-called one-and-a-half ventricular repair, and 10% a univentricular repair, with 16% still having a mixed circulation (41% died). Patients with PAIVS and RVDCC are at the most severe end of the spectrum. In a study by Guleserian et al. of long-term outcome in 32 patients with PAIVS with RVDCC, aorto-coronary atresia was associated with 100% mortality. Median follow-up was 5.1 years (9 months–14.8 years). Overall mortality was 18.8% (6 of 32), with all deaths occurring within 3 months of BT shunt. No late mortality occurred among those surviving beyond 3 months of age. Authors concluded that single-ventricle palliation yields excellent long-term survival and should be the preferred management strategy for these patients. Those with aorto-coronary atresia have a particularly poor prognosis and should undergo cardiac transplantation [11].

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Chapter 23

Pulmonary Stenosis

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23.1 Anatomy

Pulmonic stenosis refers to an obstruction at or distal to the right ventricular outflow. Owing to various possible levels of obstruction, this disease is not a homogeneous entity. Obstruction can be found at the valvar level, the right ventricular (RV) infundibulum, and/or the supra-valvular level within the main pulmonary artery or distal to it at multiple levels. It is also found in association with ventricular septal defect and overriding aorta as in Tetralogy of Fallot (TOF) (see associated chapter). In patients suffering from congenital heart disease, 25–30% suffer from some form of pulmonary stenosis [1].

23.1.1 Pulmonary Valve Stenosis (PS)

Valvular PS with intact ventricular septum typically is an isolated anomaly and accounts for 5–10% of all congenital heart defects [1]. The valve leaflets are usually thin with fused commissures. A 1–2 mm central opening is seen, and the valve presents as a doming structure projecting into the main pulmonary artery. The right ventricle is typically hypertrophied and there is post-stenotic dilation of the main pulmonary artery. Valvular dysplasia is found in 10–20% of patients with all forms of PS. Dysplastic valves are trileaflet with markedly thickened cusps comprised of myxomatous tissue and little, if any, commissural fusion. Reduced mobility is exhibited, and the valve annulus is usually

hypoplastic. This entity is frequently found in patients with Noonan's syndrome [1].

23.1.2 Subvalvular Pulmonary Stenosis

Subvalvular PS is a rare condition in its isolated form. There are two distinct lesions described within this diagnostic entity. The first occurs when an obstructive fibrous or muscular band divides right ventricle into two chambers (main body and infundibulum) and is called a “double-chambered right ventricle.” The second is a diffuse fibromuscular narrowing of the infundibular portion of the right ventricle. Clinically, the disease is usually progressive with patients closely resembling those with isolated valvular PS. Cardiac catheterization with RV angiography is diagnostic; although currently, echocardiography is the only requirement preoperatively. The treatment is surgical. The approach is through a right atriotomy for the excision of the obstructive muscle bundle or through a right ventriculotomy for infundibular muscle resection.

23.1.3 Pulmonary Artery Stenosis

Lesions of pulmonary artery stenosis can present at the level of the main pulmonary artery, in right and left branch pulmonary arteries, at bifurcation sites, or at the distal branches. *Peripheral pulmonary artery stenosis* (PPS) occasionally occurs at a single level and refers to a narrowing in a branch pulmonary artery; however, multiple sites of obstruction are more characteristic. PPS is frequently a benign condition which presents

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most commonly with a systolic ejection murmur auscultated in infancy (physiologic PPS). It is seen in neonates due to relative discrepancy in size of the main pulmonary artery and the left and right branch PAs, since they carry only a small portion of the RV output to the lungs. This is usually a mild condition with no significant ill consequences. The murmur usually disappears within a few months.

PPS can also be pathologic and associated with genetic syndromes and congenital infections. In *Rubella syndrome* there is peripheral stenosis of the pulmonary arteries associated with patent ductus arteriosus (PDA) [2]. Intervention for this PPS is rarely needed. In *Noonan's syndrome*, peripheral pulmonary stenosis may be seen and branch pulmonary arteries could also be diffusely hypoplastic. This syndrome is associated with lymphedema, webbed neck, dysmorphic features, and hypotonia [3]. Patients with *Williams syndrome* develop PPS in association with supravalvular pulmonary and aortic stenosis with or without coarctation of the aorta or peripheral systemic arteriopathy; pulmonary valvar stenosis occurs less frequently [4, 5]. Diffuse pulmonary stenosis is seen with *Alagille syndrome*, which presents with pulmonary valve stenosis as well as diffuse main and branch pulmonary artery stenosis.

23.2 Pathophysiology

23.2.1 Pulmonary Valve Stenosis (PS)

In PS, right ventricular (RV) pressure increases to overcome the stenosis of the pulmonary valve. In the case of critical PS (ductal dependent), there is not enough antegrade flow across the pulmonary valve to allow a normal cardiac output. Thus, the PDA needs to remain open to allow adequate forward pulmonary blood flow via a left-to-right shunt. In addition, decreased compliance of the RV may occur and lead to the necessity of right-to-left shunting across the patent foramen ovale (PFO) to ensure adequate systemic blood flow. The neonatal myocardium undergoing hyperplasia and hypertrophy is capable of generating increased intraventricular pressure necessary to overcome fixed obstruction. However, the compliance of the RV decreases shortly after birth, signs of RV failure manifest as the complete right cardiac output is expected

to go through the stenotic valve. The noncritical PS is rarely seen in the intensive care unit, except in rare cases associated with complications during the postintervention recovery period (see below).

Untreated pediatric or adult PS usually becomes a progressive condition with the gradient across pulmonary valve, and hypertrophied infundibulum increasing over time. Continued elevation of RV end-diastolic pressure as a result of RV hypertrophy ultimately compromises diastolic RV myocardial perfusion. Ventricular arrhythmias and sudden death can occur. Evidence of RV subendocardial ischemia/infarction and fibrosis can be seen in postmortem cases with severe PS.

23.2.2 Branch Pulmonary Artery Stenosis

In the presence of branch pulmonary artery stenosis, there is an increase in the afterload to the right ventricle with subsequent RV hypertension and dysfunction. The impact of increased afterload is more deleterious in patients with associated pulmonary regurgitation (for example, patients who have had TOF repair) as the RV suffers from additional pressure and volume overload. The RV of patients with dysfunctional contractility patterns (poor coordination between the sinus and the infundibular portion of the RV) becomes dilated and it may lead to an increased risk of ventricular arrhythmias and sudden death. The degree of RV hypertension is dependent upon the severity of the arteriopathy (multiple versus single and unilateral versus bilateral stenosis). In the presence of any intracardiac septal defect, patients may exhibit significant arterial oxygen desaturation due to right-to-left shunting. Occasionally, desaturation may also be seen due to severe V/Q mismatch in the absence of a septal defect. The effect of branch pulmonary artery stenosis on blood flow distribution leads to increased flow to the unaffected branches with the potential development of segmental pulmonary artery hypertension in those branches without stenosis.

23.3 Clinical Findings

The clinical presentation of pulmonary stenosis is diverse due to variable severity of the obstruction. For valvular pulmonary stenosis presenting in the neonate

as critical PS cyanosis is usually apparent at birth due to suprasystemic RV pressure and right-to-left atrial shunting through a PFO. Infants may also become hypoxicemic and acidotic due to inadequate pulmonary flow and decreased cardiac output as the PDA begins to close. Initially, patients with mild to moderate degree of stenosis are usually asymptomatic, but as the gradient increases, they may present with fatigue and dyspnea precipitated by exertion. As the disease progresses and the obstruction become more severe with increasing age, untreated patients may become symptomatic at rest with manifestations of right heart failure: tachycardia, hepatomegaly, peripheral edema, dyspnea, angina, syncope, arrhythmia, and sudden death.

On physical examination, a careful palpation of the chest demonstrates a prominent RV impulse. In the case of valvular stenosis, auscultation elicits a normal first heart sound (S1) followed by an ejection click, best heard at the upper sternal border. The pulmonary stenosis is typically more severe, if the distance is shorter from S1 to the click. An early systolic click is noted in all cases of pulmonary stenosis except those with dysplasia of the pulmonary valve (more commonly seen in patients with Noonan's syndrome). A diamond-shaped ejection murmur is best heard at the left upper sternal border with radiation into the lung fields and the back. It is typically harsh and usually IV/VI or more. As the severity of the stenosis increases, the peak of intensity of the murmur occurs later. If bilateral obstruction is present, the murmur will be heard throughout the chest. A soft P2 secondary to decreased PA pressure due to severe stenosis may be noted. In mild cases of PS, the second heart sound (S2) can be normally split, and as the severity increases, it can become more widely split. In critical PS, S2 becomes single.

23.4 ECG

ECG reveals right axis deviation and several degrees of RVH, according to the severity of the stenosis. An RsR' pattern may be seen in V1. Right atrial enlargement may be noted in severe cases. In the case of severe valvular pulmonary stenosis associated with RV hypoplasia (a condition similar to that of pulmonary atresia with an intact ventricular septum), the RV forces will be decreased and left axis deviation may be seen in the newborn.

23.4.1 Chest Radiography

Chest radiography usually demonstrates normal heart size. Mild to moderate pulmonary stenosis is associated with dilatation of the main pulmonary artery and left pulmonary artery. Severe or critical pulmonary stenosis will result in oligemic lungs and an increased cardio-thoracic ratio. In branch pulmonary artery stenosis, if unilateral, differential or asymmetric flow distribution may be observed in the chest radiograph.

23.4.2 Echocardiography

In echocardiogram, the pulmonary valve is typically best assessed from the parasternal short-axis view. The right ventricular outflow tract (RVOT) is best interrogated from the parasternal short axis view and subcostal position [6]. The gradient across the pulmonary valve will determine the severity of the RVOT obstruction and/or PS. The maximum instantaneous pressure pulsed wave Doppler gradient is often at least 10% higher than the instantaneous peak-to-peak gradient measured in the cardiac catheterization laboratory. This discrepancy is due to a phase delay between peak velocities and pulmonary artery systolic pressure. In the presence of proximal branch pulmonary artery stenosis, gradients and anatomic narrowing can be documented in the branch pulmonary arteries. If the stenosis is distal, the lesion cannot be assessed by echocardiography.

23.5 Management

23.5.1 Pre-intervention

In severe pulmonary valve stenosis with profound hypoxemia and cyanosis due to right-to-left shunting at the atrial level, PGE₁ is necessary to preserve ductal patency. Mechanical ventilation may be utilized in the setting of coexistent lung disease, cardiogenic shock, and profound cyanosis.

Balloon pulmonary valvuloplasty is the treatment of choice for relief of valvular PS. When planning for balloon dilatation of pulmonary valve, the nature of the

valve leaflets has to be studied by 2D echocardiography and the pulmonary valve annulus must be measured to determine the size of the balloon needed.

In patients with branch pulmonary artery stenosis, a lung perfusion scan can assess the blood flow distribution and assist in the management approach. This test should be performed before and after the intervention to evaluate the success of the procedure.

23.5.2 Intervention

23.5.2.1 Valvular PS: Balloon Pulmonary Valvuloplasty

Mild pulmonary valve stenosis does not require therapeutic intervention. However, as stated above, balloon pulmonary valvuloplasty is the treatment of choice for children with moderate to severe stenosis. Cardiac catheterization should be performed to balloon-dilate the stenotic pulmonary valve and it is generally recommended that the procedure be performed for peak-to-peak gradients in excess of 40 mmHg. The decision to intervene, based upon the gradient value across the stenotic valve, is less useful in the setting of RV dysfunction or critical stenosis, in which case intervention may be indicated regardless of the gradient.

The procedure is performed under general anesthesia or intravenous sedation. In newborns and young infants general anesthesia is preferred. The femoral

artery and femoral vein are catheterized for hemodynamic measurements and right side angiography (Fig. 23.1a). The technique involves crossing the stenotic valve with a floppy guide-wire, exchange of the catheter for a balloon catheter, and inflation of the balloons with diluted contrast material for a few seconds (Fig. 23.1b). The currently recommended balloon/annulus ratio is 1.2–1.25 with a maximum of 1.4. The pressure gradient is determined post valvotomy. If significant, it is important to identify if the gradient is due to residual valvar PS or dynamic subpulmonary stenosis post valvotomy. Ventricular angiography can help with this diagnosis (Fig. 23.1c).

Immediate reduction of gradient, increase in jet width, and free motion of the pulmonary valve leaflets with less doming have been observed following balloon dilatation. Improvement of RV function, tricuspid insufficiency, and right-to-left shunt is also observed. Restenosis, defined as a gradient of ≥ 50 mmHg, has been observed in nearly 10% of children. Predictors of restenosis include balloon/annulus ratio < 1.2 and immediate post-valvuloplasty gradient of ≥ 30 mmHg, small pulmonary valve annulus, and postsurgical complex pulmonary stenosis. Redilatation with balloons that are larger than those used at the time of initial balloon valvuloplasty, produces excellent results and is the procedure of choice. Balloon pulmonary valvuloplasty is equally successful in neonates as well as in adult subjects. However, the chances of repeat intervention in the newborn with critical PS are higher than those for the infant, child, or adult presenting electively

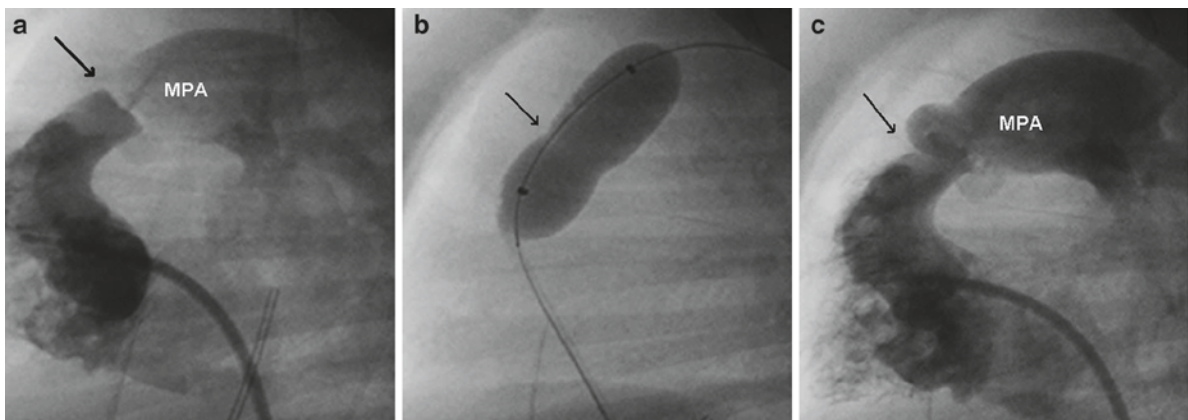


Fig. 23.1 (a) Right ventriculogram performed in lateral projection demonstrates a severe degree of pulmonary valve stenosis, with a tiny jet of contrast crossing the valve (*arrow*). The main pulmonary artery (MPA) is large with some poststenotic dilation. There is no

supravalvar obstruction, (b) balloon valvotomy of pulmonary valve, (c) right ventriculogram following balloon procedure demonstrates significant increase in valve orifice (*arrow*), with no evidence of residual obstruction. MPA main pulmonary artery

with moderate to severe PS. Life-long followup to identify the significance of residual pulmonary insufficiency is indicated [7, 8].

Complications during and immediately after balloon valvuloplasty have been typically rare (0.35% major complication rate by the VACA registry) [9]. However, the complication rate is higher in the newborn with critical PS. Reported complications include balloon rupture, blood loss requiring transfusion (especially in newborns), bleeding/hematoma at the catheter site, arrhythmias (including complete heart block), cardiac arrest, perforation of the RVOT with tamponade, and death. In the case of extensive wire perforation of the RVOT, emergency surgical intervention would be warranted. If a small guide-wire perforation occurs, pericardioscentesis and transfusion may be all that is needed [10]. “Suicidal” right ventricle (severe RV contractility failure associated to a severe RVOT obstruction) could be seen in patients post balloon dilatation of the pulmonary valve in the presence of severe RV hypertrophy. Immediately after the balloon procedure, there is an acute drop in cardiac output related to a lack of ejection of the right ventricle due to postdilatation dynamic subpulmonary muscular obstruction. This can also be seen post surgical relief and is more likely in patients with an initial RV pressure of over 100 mmHg with severe infundibular hypertrophy.

Previous surgery and pulmonary valve dysplasia are not contraindications for balloon valvuloplasty. Indeed, the use of high-pressure balloons for resistant pulmonary valves can increase success rate greatly.

23.5.2.2 Supravalvular and Peripheral Pulmonary Artery Stenosis

Supravalvular and peripheral lesions can be a challenge for effective management. Surgery can be performed for each lesion; however, the recurrence rate for branch lesions can be high, especially if there is a diffuse arteriopathy. The distal lesions are impossible to access surgically, and thus, transcatheter interventional strategies have become the standard of care. Patients with diffusely hypoplastic pulmonary arteries and/or discrete or multiple areas of branch stenosis may benefit from one or serial interventional catheterizations (single and multiple balloon dilations during the same or multiple procedures).

The *management options* for patients with PPS include:

- 1) Balloon pulmonary arterioplasty (BPA).
- 2) Stent implantation.
- 3) Surgical pulmonary artery plasty.

Indications for intervention include:

- 1) RV hypertension.
- 2) Abnormal differential blood flow distribution on lung perfusion scan (less than 30% of flow to the affected lung).
- 3) Segmental pulmonary artery hypertension in the unaffected vessels (mean distal pulmonary pressure of >25 mmHg).
- 4) Inadequate pulmonary blood flow distribution precluding corrective surgery (such as PPS associated to unrepaired TOF variants) or associated with cyanosis.
- 5) Presence of pulmonary artery distortion associated with single ventricle physiology in the form of cavopulmonary shunt or Fontan procedure.

23.5.3 Balloon Pulmonary Arterioplasty (BPA)

Since the results of surgical pulmonary artery plasty have been quite unsatisfactory in patients with PPS, transcatheter intervention remains the first line therapy (Fig. 23.2). However, surgical plasty continues to be the procedure of choice for specific conditions (such as stenosis associated with shunt anastomosis in patients undergoing further surgery) as well as for patients who have failed transcatheter management attempts for surgically reachable lesions.

In current practice, high-pressure balloons are almost always used to address both discrete and long diffuse lesions of pulmonary artery stenosis (Fig. 23.2a). Reported results indicate a success rate of 50–75%. Following the advent and availability of the cutting balloon (a bladed balloon sized up to 8 mm in diameter), the success rate has increased to over 90%. Restenosis postballoon dilation has been reported in up to 15–35% of cases, but the degree of restenosis is unpredictable as the underlying disease processes are variable. For example, the peripheral pulmonary arteriopathy of Williams syndrome is quite different from isolated discrete “coarctation” of the left pulmonary artery. In the

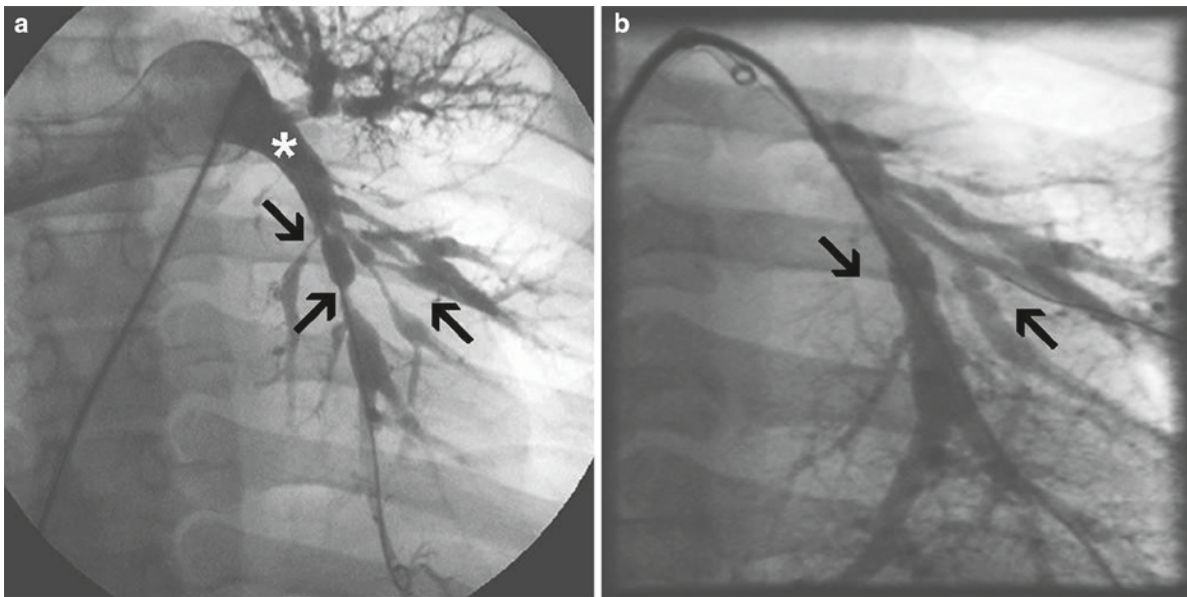


Fig. 23.2 (a) Left pulmonary artery angiogram performed in a patient with severe peripheral pulmonary artery stenoses. The arrows point to some of the areas of stenosis. The proximal left pulmonary artery (*) is mildly hypoplastic, but the worse stenosis

is at the lobar, segmental and subsegmental level, (b) following multiple pulmonary artery balloon dilation procedures in the left lower lobe, angiogram demonstrates significant angiographic improvement in vessel diameter post intervention (arrows)

latter, the results of BPA±stenting are excellent, while the former may be associated with less promising consequences. In addition, the definition of restenosis may highly vary in different studies. This can be demonstrated in pediatric literature where lack of vessel growth may be considered as restenosis when, in fact it may have been the natural course of the disease.

The incidence of complications reported varies from 6 to 10% and includes: nonfatal pulmonary artery tears, segmental pulmonary edema, distal vessel aneurysm formation, and deep vein thrombosis. The procedure-related mortality is considered to be 1%. Death occurs from vessel rupture (tears) or cardiac arrest in patients with suprasystemic RV pressure and poor RV function. Immediate transcatheter management of unconfined tears (coil embolization of bleeding vessel or tear itself) is used as an approach to reduce mortality. Reperfusion pulmonary edema occurs in about 4 % of cases and aneurysm can be seen in <5% [11].

High risk factors for BPA include:

1. Suprasystemic RV pressure
2. Associated RV dysfunction
3. History of vessel trauma/hyperperfusion edema at prior transcatheter procedures

4. Williams syndrome
5. Low cardiac output
6. Multiple peripheral distal lesions

Measures which can be used to avoid or lessen the potential fatal complications include the use of general anesthesia for the procedure, inotropic support if needed, and blood transfusion to treat any anemia. For those patients with RV dysfunction and suprasystemic RV pressure, the creation of an interatrial communication prior to the balloon procedures may be advantageous as it will lead to right-to-left shunting, and thus, preserve the blood pressure during balloon inflations. For high risk patients recovery in the intensive care unit should be planned.

23.5.3.1 Intravascular Stent Implantation

Balloon expandable intravascular stents implanted into the sites of pulmonary artery stenoses have been found to significantly improve the effectiveness of balloon angioplasty (Fig. 23.3).

Multiple reports in the literature have confirmed a high success rates for pulmonary artery stenting

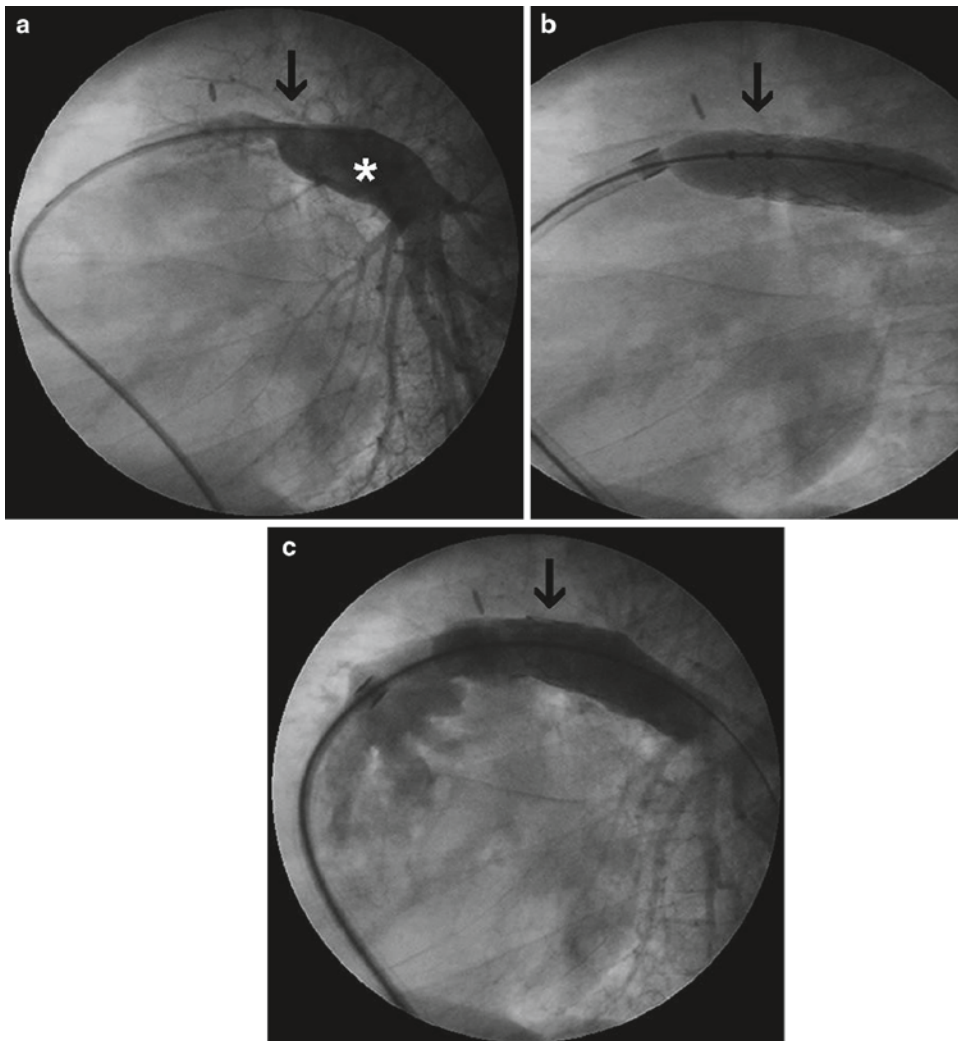


Fig. 23.3 (a) In the lateral projection selective left pulmonary (*) angiogram demonstrates severe proximal stenosis (arrow) (b) implantation of a stainless steel stent over a BIB

balloon across the area of stenosis (arrow), (c) following stent implantation there is significant angiographic improvement

(above 90%) and promising long-term results [12]. Stents are especially indicated and preferred when the stenosis is due to external compression (Fig. 23.4). Fractures, thrombosis, aneurysm formation, or stent migration are extremely rare. Stent redilation can be performed with success up to 10 years. However, stent implantation has theoretical disadvantages over BPA. These include: a need for larger introducer sheaths and subsequent dilations to keep up with somatic growth, the possible occlusion of branching vessels, and surgical implications. Significant restenosis is quite rare, except for that related to a lack of growth.

23.5.4 Post-Intervention

23.5.4.1 Valvuloplasty

Most patients after the newborn period who undergo balloon pulmonary valvuloplasty do not need intensive care monitoring. Typically, only overnight observation is required and patients are discharged the following day. In rare cases, patients develop “suicidal” right ventricle and need ICU monitoring with intravenous infusion of volume and beta-blockers followed by transition to oral propranolol to be weaned during the few weeks thereafter.

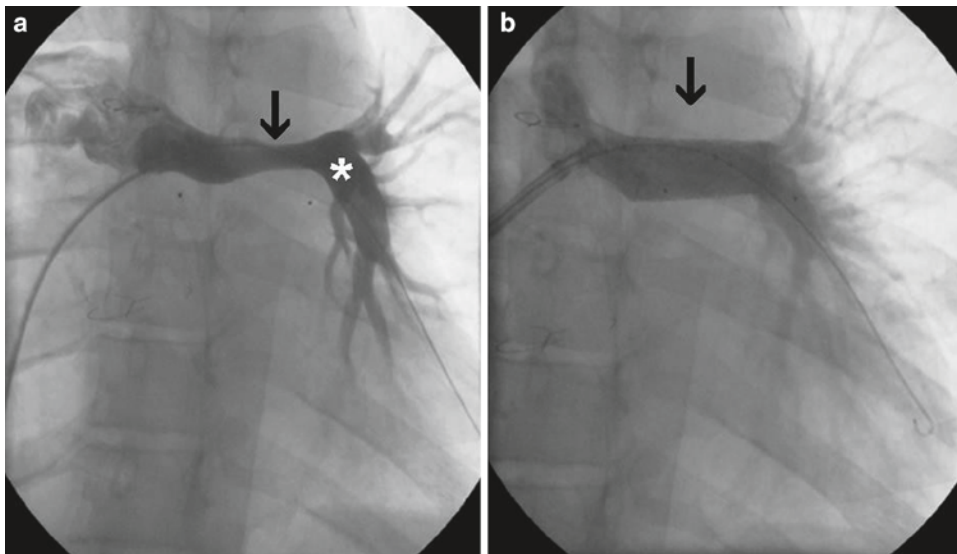


Fig. 23.4 (a) Selective left pulmonary artery (*) angiogram performed in a patient following Fontan after neonatal Norwood procedure. Note there is stenosis at the proximal left pulmonary

artery (*arrow*) which is related to inferior compression by the augmented neo-aortic arch (b) following stent implantation the stenosis is resolved (*arrow*).

In newborns with critical pulmonary valve stenosis, cyanosis commonly persists for at least two weeks following RV decompression and often patients need to be kept on prostaglandins for that period of time. Some patients require a surgical Blalock-Taussig shunt, or ductal stent placement, given their inability to wean from PGE₁. As the RV hypertrophy regresses, the RV compliance improves and more antegrade flow is seen across the pulmonary valve with less right-to-left shunting at the atrial level.

23.5.5 Pulmonary Artery Angioplasty

As mentioned above, some patients undergoing extensive pulmonary artery interventions are admitted to the cardiac intensive care unit due to the high risk of developing segmental pulmonary edema and bronchial bleeding (re-perfusion injury). Most of these patients must remain at least 24 h on mechanical ventilation. Diuresis and positive end expiratory pressure (PEEP) are particularly beneficial in this subset of patients. An admission chest X ray must be obtained to assess endotracheal tube placement, magnitude of pulmonary edema, and stent placement. Successful extubation is usually accomplished 24–48 h after admission. In

patients who have undergone stent placement, aspirin should be started after 24 h and once the bleeding has subsided. A few doses of first generation cephalosporin may be indicated after intervention. Aspirin is continued for 6 months in patients with pulsatile pulmonary arterial blood flow. Follow up lung perfusion scans can help assess the success of the intervention in patients with unilateral lesions [13].

23.5.6 Surgical Management

Surgical management is reserved for those patients in whom a balloon valvuloplasty and/or arterioplasty was not successful. Anatomically, these patients tend to present with a hypoplastic pulmonary valve annulus and a very dysplastic valve. Also, there could be a significant component of subvalvar and/or supralvalvar stenosis. Balloon pulmonary valvotomy could also be unsuccessful due to technical difficulties and inability to catheterize the hypoplastic RVOT [14]. The repair requires cardiopulmonary bypass and is usually performed under mild hypothermia. An open surgical valvotomy via a main pulmonary artery incision is routinely performed. In the presence of a very small pulmonary annulus with

or without subpulmonary stenosis, a transannular patch is required [15]. Supravalvar pulmonary stenosis is managed with a patch arterioplasty.

In a report based on a prospective 27-institution study of 101 neonates with severe to critical pulmonary stenosis, percutaneous balloon valvotomy and certain types of surgical valvotomy were identified as optimal initial procedures. The outcomes were similar and there was no difference in freedom from reintervention after the first procedure at 4 years of follow up care [15].

23.5.7 Post-operative Management

23.5.7.1 Pulmonary Valvotomy

Postoperative management is usually uncomplicated due to the relatively benign postoperative course. Patients are routinely admitted to the cardiac intensive care unit postoperatively for monitoring and care and usually arrive with an arterial line, central venous line (typically right internal jugular line), and occasionally with temporary pacing wires (in cases of right ventriculotomy and extensive infundibular muscle resection). The smallest or severely preoperatively ill patients will arrive intubated with a goal of extubation within the next 24 h. Excessive bleeding and cardiac arrhythmias are infrequent.

A small group of patients continue to have different degrees of cyanosis after a successful balloon dilation of the stenotic pulmonary valve. If oxygen saturations remain consistently below 70%, prostaglandins should be restarted and beta-blockers may be required for several weeks. Occasionally patients persist with refractory cyanosis despite the therapies and they may need a BT shunt. The origin of cyanosis is secondary to poor RV compliance and right-to-left atrial level shunting. Residual pulmonary regurgitation is initially well tolerated.

23.6 Long-Term Outlook

Patients with a pressure gradient across the pulmonary valve of less than 25 mmHg, rarely suffer from poor outcomes. Patients with a pressure gradient of 26–49 mmHg have a 21% chance of developing a progressive increase in this gradient. Patients with a pressure gradient of 50–79 mmHg across the valve

have a 79% chance of becoming worse and patients with 80 mmHg or higher pressure have a 97% chance of developing severe consequences [16]. Long-term survival and quality of life for 90 consecutive patients who underwent surgery for pulmonary stenosis between 1968 and 1980 was examined and was found to be good (25 years 93% survival, 67% of the patients was in NYHA Class I and maximal exercise capacity was 90% of normal). Pulmonary regurgitation was found in one third of the patients 22–33 years after surgical repair for isolated pulmonary stenosis, and reoperation for pulmonary regurgitation was necessary in 9%, especially after the transannular patch technique [17]. Patients treated with pulmonary balloon dilation also enjoy similarly excellent outcomes. In another study, 150 subjects were found to have a mean follow-up of 11.9 ± 3.1 (range 3.7–19.3 years). Freedom from reintervention at 1, 10, and 15 years was seen at 90, 83, and 77% respectively. Pulmonary regurgitation (PR) increased during follow up such that 57% of children had moderate or severe PR at the last follow up recorded. Tricuspid and pulmonary annuli grew with the child's growth and the PV demonstrated catch-up growth. It has been concluded that life-long follow up is essential, and excellent outcome can be anticipated [18]. Life expectancy in mild, moderate, or severe pulmonary stenosis after repair is within normal limits.

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Chapter 24

Left Ventricular Outflow Tract Obstruction

Michael Tsifansky, Ricardo Muñoz, and Victor O. Morell

24.1 Introduction

Left ventricular outflow tract obstruction (LVOTO) accounts for 5–10% of all congenital heart defects. LVOTO occurs at the valvar (70%), subvalvar (14%), and supra-valvar (8%) level, and several levels of obstruction often coexist (8%) [1]. Another type of muscular subaortic stenosis, present with hypertrophic cardiomyopathy, is known as hypertrophic obstructive cardiomyopathy. LVOTO may be further compounded by other left-sided anomalies (small left atrium, abnormal mitral valve, small left ventricle, aortic coarctation, or interrupted aortic arch) [1–4]. An often-seen complex of LVOTOs is the Shone's complex, a combination of a parachute mitral valve, supra-annular mitral ring, subaortic stenosis, and coarctation of the aorta [5]. Ventricular septal defects, abnormal attachments of the mitral or tricuspid valve apparatus, and pulmonary venous anomalies may also coexist with LVOTO. Critical LVOTO presents as shock in the early neonatal period. Less severe defects may become clinically significant later in childhood or remain silent into adulthood [6].

24.2 Valvar Aortic Stenosis

24.2.1 Anatomy

The normal aortic valve has an area of about 2 cm²/m² of body surface area (BSA) [7] and is tricuspid (right, left, and noncoronary cusps), and tri-commissural.

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The stenotic aortic valve can be monocuspid or more frequently bicuspid due to the fusion of the right and the left cusps (Fig. 24.1). Bicuspid valves are commonly associated with left heart abnormalities and with coarctation of the aorta.

The severity of the aortic stenosis (AS) can be described as trivial, mild, moderate, or critical, depending on the orifice size and on the echocardiography-measured peak systolic ejection gradient (PSEG) or on the catheter-obtained peak-to-peak transvalvular gradient (Table 24.1). In neonates with aortic valve stenosis, the valve is usually gelatinous with thickened and poorly formed leaflets. In severe disease, left-ventricular (LV) filling is restricted, and the atrial level right-to-left shunt decreases, thereby decreasing the LV contribution to systemic cardiac output. This may lead to the underdevelopment of the left-sided structures and increase the risk for aortic coarctation.

24.2.2 Pathophysiology

Obstruction to left ventricular outflow results in LV pressure overload and concentric LV hypertrophy. LV wall stress is directly proportional to LV systolic pressure and LV diameter, and inversely proportional to LV wall thickness, so LV hypertrophy is a means of maintaining contractility and the cardiac output. The increase in wall thickness initially leads to normalization of the wall stress; therefore, the LV contractility is preserved. Nevertheless, the progressive increase in myocardial mass may cause interstitial fibrosis and left ventricular diastolic dysfunction, and finally systolic dysfunction. The stiff ventricle is dependent on the atrial contractility to maintain an effective cardiac output. Atrial arrhythmias may lead to significant hemodynamic

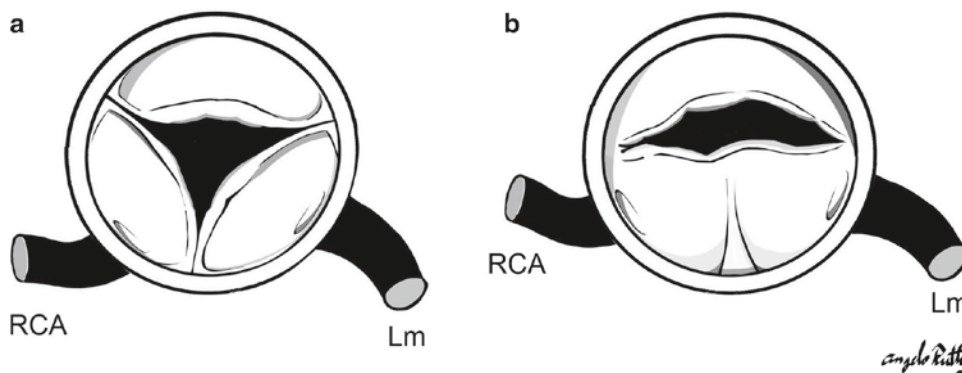


Fig. 24.1 (a) Normal trileaflet aortic valve. (b) Bicuspid aortic valve

Table 24.1 Classification of valvular aortic stenosis

Classification	Echo PSEG, mmHg ^a	Catheter gradient, mmHg ^a	Valve area, cm ² /m ² BSA
Trivial	<25	<10	>0.7
Mild	25–50	11–40	>0.7
Moderate	50–80	41–80	0.5–0.7
Severe	>80	>75	<0.5
Critical	30–80		

^aAll gradients disclosed assuming normal cardiac output; in the setting of ventricular dysfunction transvalvar gradients may be underestimated. Echocardiographic gradients are usually estimated in patients without sedation and catheter gradients are estimated in sedated patients. The latter measurement is the most precise indicator of obstruction.

instability in patients with AS. A number of factors predispose the hypertrophied left ventricle to subendocardial ischemia, including increased myocardial oxygen consumption, elevated LV end-diastolic pressure, low aortic diastolic pressure (thus, low coronary perfusion pressure), compression of subendocardial blood vessels by the hypertrophied muscle (thus, compromised subendocardial blood flow), and limited systolic myocardial perfusion [6, 8, 9]. Patients with ischemia are predisposed to ventricular arrhythmias, syncope, and sudden death.

In neonates with critical aortic valve stenosis, myocardial hypertrophy and subendocardial ischemia start in utero, leading to endocardial fibroelastosis (EFE). EFE impairs both systolic and diastolic functions of the left ventricle, which further compromises forward flow across the aortic valve and contributes to LV failure [10]. Closure of the ductus arteriosus in such patients results in cardiogenic shock. Infants with severe stenosis may develop congestive heart failure (CHF) over the first few weeks of life.

Their pathophysiology is similar to that outlined above; however, since for them ductal flow is not essential for systemic perfusion, frank cardiogenic shock is uncommon with its closure. Those with milder aortic valve stenosis are less likely to develop CHF. However, left ventricular hypertrophy, ischemia, and limited increase of cardiac output with exercise may lead to angina or syncope on exertion.

24.2.3 Clinical Presentation

Neonates with critical stenosis present in cardiogenic shock and respiratory distress after the ductus arteriosus closes, and are often misdiagnosed with septic shock [9]. They are tachypneic and poorly perfused; their pulses are often faint, and there may be no murmur on physical examination. They are severely acidotic.

Older infants with severe stenosis present in CHF with feeding difficulties and failure to gain weight. They display decreased peripheral perfusion, tachypnea, a gallop with a harsh systolic murmur, and hepatomegaly.

Children with milder obstruction usually present with an asymptomatic murmur or, much less frequently, with anginal chest pain and exertional syncope.

The typical adult presentation is the triad of angina pectoris, syncope, and heart failure. Physical examination shows pulsus parvus et tardus (a delayed and slow-rising pulse), narrow pulse pressure, and a harsh crescendo-decrescendo murmur at the second right intercostal space, radiating to the sternal notch [11]. An early systolic click and a single or reversely split S₂ typically accompany the murmur. The finding of a reversely split second heart sound may

indicate severe AS associated with a bundle-branch block and/or left ventricular dysfunction. In the setting of severe LV dysfunction, the stroke volume falls and the systolic ejection murmur becomes softer. Some patients may have aortic insufficiency associated with AS. AI is diagnosed by a decrescendo murmur that begins immediately after the second heart sound.

24.2.4 Chest Radiography

In neonates and infants, the chest X-ray typically shows cardiomegaly and pulmonary edema. Pulmonary edema is secondary to LV dysfunction, high end-diastolic pressure with the subsequent left atrial hypertension and pulmonary venous congestion. Pulmonary hypertension may be evident in this subset of patients. In older children and adults, mild cardiomegaly and a prominent aortic arch are present (post-stenotic dilation).

24.2.5 ECG

In infants, electrocardiography may be normal in mild AS. In older children and adults, left ventricular hypertrophy and ST-T changes are present.

24.2.6 Echocardiography

Echocardiography is usually diagnostic and sufficient to plan a catheter-based or surgical intervention [12]. Cardiac and aortic anatomy, including the size and function of the aortic and mitral valves, size of the atrial communication, presence of other intracardiac defects, especially those contributing to the LVOT obstruction, and the size of the aorta should be evaluated, since neonates with significantly underdeveloped left-sided structures may require a univentricular type repair. Presence of antegrade systolic flow into the ascending aorta and the transverse arch by pulsed and color Doppler is *sine qua non* to allow biventricular repair. Conversely, presence of retrograde flow from the ductus arteriosus into the aortic root signifies that the left-sided structures are inadequate for biventricu-

lar repair. In an M-mode image of a bicuspid valve, the coaptation line is eccentric, while in a parasternal short 2D image, a bicuspid valve looks football-shaped. A stenotic valve appears as a Y in diastole and as a small O with three thickened commissures in systole. Unicommissural valve appears as an eccentric circular orifice without distinct cusps. In infants, the left ventricle is often dilated, while in the older children and adults it tends to be hypertrophied. Gradients in neonates with aortic stenosis may underestimate the severity of the obstruction due to the presence of patent ductus arteriosus and severe ventricular dysfunction.

Neonates admitted with cardiogenic shock due to inadequate atrial communication may need an emergent balloon atrial septostomy performed in the intensive care unit. A small group of these patients may need extracorporeal membrane oxygenation (ECMO) prior to the balloon atrial septostomy. The decision to proceed with a transcatheter or surgical intervention is based on the size of left-sided structures, the trans-valvar gradient, and the severity of ventricular dysfunction.

24.2.7 Cardiac Catheterization

Diagnostic catheterization is done if significant questions about cardiac or vascular anatomy remain after echocardiographic assessment (this is infrequent), or if percutaneous balloon dilation of the stenotic aortic valve is planned. The technique typically involves retrograde approach via the femoral (or, in infants, umbilical) artery. Approach through carotid artery cutdown and through jugular, femoral, or umbilical vein (transseptal) has also been described, but is not commonly used. In addition to the transvalvular gradient, narrowed pulse pressure in the ascending aorta and elevated LV end-diastolic pressure are found. The aortography is remarkable for a thickened, fused, and domed valve that restricts the contrast. Other patients with aortic stenosis, who may benefit from catheter-based studies, include those with angina with ST-T wave changes (to evaluate LV pressure and the coronary arteries) and those with syncope (to evaluate LVOT), although these indications are not universally accepted. Balloon valvuloplasty of the aortic valve is described separately.

24.2.8 Preoperative Management and Indications for Intervention

24.2.8.1 Neonates

Neonates with critical aortic valve stenosis who present in shock and heart failure require emergent infusion of Prostaglandin E₁ (PGE₁, alprostadil) to reestablish ductal flow and, therefore, the systemic cardiac output, and to alleviate pulmonary hypertension caused by severe LV failure. The dose of PGE₁ should be kept low (0.01–0.025 µg/kg/min), so as to avoid apnea, fever, and hypotension.

Gas exchange and acid–base status should be followed closely and corrected as needed, as these infants are not likely to tolerate acidosis. Bicarbonate infusion may be required to correct acidosis; however, ongoing acidosis most likely signifies inadequate cardiac output, and reasons for this should be sought.

Mechanical ventilation with tidal volume of 8–12 ml/kg and with adequate positive end-expiratory pressure (PEEP) of 6–8 cm H₂O is frequently required to treat pulmonary edema secondary to left-atrial and pulmonary-venous hypertension and hypoxia.

Inotropic support (dopamine or epinephrine) may be required to improve the infant's cardiac performance. If the LV or the mitral valve is too small, an atrial-level left-to-right shunt as well as a patent ductus arteriosus may be required to maintain cardiac output.

It is prudent to abstain from enteral feedings in unstable infants with ductus-dependent systemic circulation, and parenteral nutrition may be started if feasible. Many centers administer H₂-blockers or proton-pump inhibitors to the fasting infants, although their utility has not been shown. Electrolytes and fluid balance should be closely followed and optimized.

There is no role for prophylactic antibiotics in such infants, but antibiotics are often started before the diagnosis is established because of concerns for septic shock. In such case it is reasonable to finish 48–72 h of broad coverage while awaiting cultures.

Sedation with low-dose fentanyl and midazolam infusions may be used as needed to decrease the metabolic needs and improve infants' comfort. The α₂-agonist dexmedetomidine is becoming a popular sedation option in some centers because of

ease of use and predictability of hemodynamic effects [13].

Head and renal ultrasonography are performed, and karyotype is checked before the repair of the aortic stenosis, if time allows.

24.2.8.2 Older Infants and Children

In these patients the left-sided cardiac structures are adequate for the maintenance of cardiac output, and they usually do not require intensive preoperative management. Surgical or catheter-based intervention is indicated in the presence of any of the following:

- a. Catheterization-derived peak-to-peak gradient >50 mmHg [14] or mean echocardiographic Doppler gradient >30–40 mmHg across the aortic valve.
- b. Syncope
- c. Chest pain
- d. Signs of myocardial damage
- e. ECG S-T changes at rest or with exercise [6, 14].

24.2.9 Surgical Management

24.2.9.1 Surgical Versus Catheter-Based Intervention

In neonates appropriate for a biventricular repair, percutaneous balloon valvotomy has been preferred over the surgical valvotomy [15]. Most recent studies demonstrate that with adequate preoperative stabilization the results of the two approaches are comparable [16], although balloon valvuloplasty is less effective if the aortic valve is very dysplastic or if the aortic annulus is very small. The choice between the two is often based on institutional preferences and expertise. Aortic balloon valvuloplasty may be particularly appealing in neonates with very poor LV function.

24.2.9.2 Aortic Valvotomy

Once on cardiopulmonary bypass, the patent ductus arteriosus, if present, is ligated to prevent retrograde flow into the pulmonary arteries. After aortic cross-clamping and the administration of cardioplegia, the

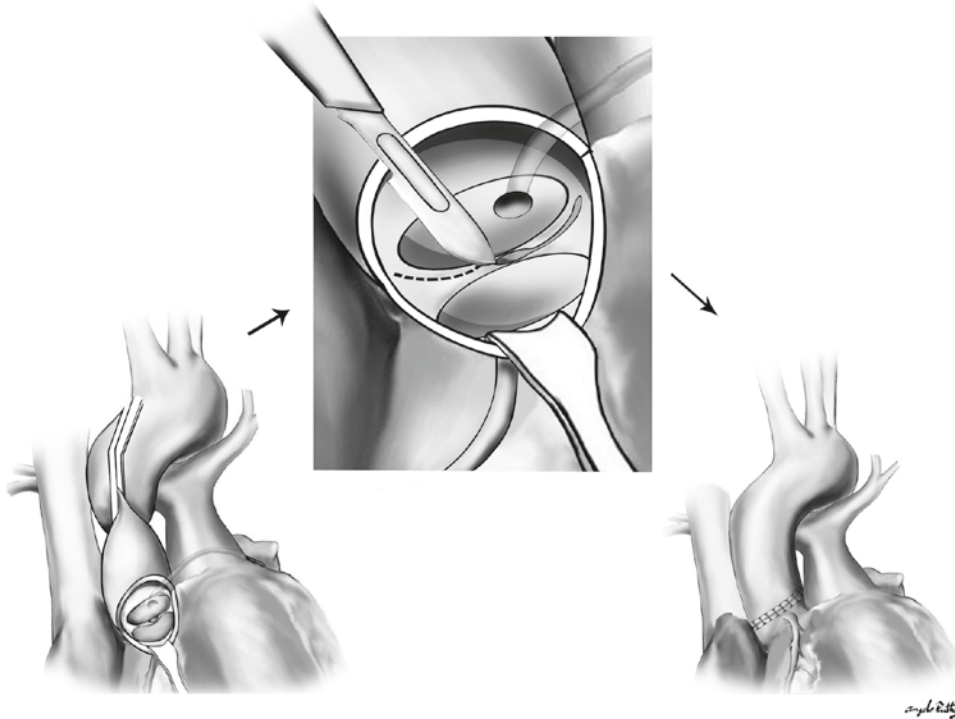


Fig. 24.2 Open surgical valvotomy. Via a transverse aortotomy the aortic valve is inspected and the valvotomy is performed

Table 24.2 Comparison of aortic valve replacement options

Valve replacement option	Need for anticoagulation	Growth potential	Option for neonates and infants	Freedom from reoperation for valve related problems at 10 years
Mechanical valves	Yes	No	No ^a	40–90% [21–23]
Homograft	No	No	Yes	50–80% [21, 22, 24]
Pulmonary autograft	No	Yes	Yes	85–95% [21, 24, 25]

^aThe smallest commercially available mechanical valve is 16 mm in diameter

proximal ascending aorta is opened approximately 1 cm above the right coronary artery. Then, the valvotomy is performed by opening the intercommissural raphe almost to the aortic annulus [10] (Fig. 24.2).

24.2.9.3 Aortic Valve Replacement

In general, all patients born with a stenotic aortic valve will eventually require a valve replacement. There are several options for aortic valve replacement in pediatric

patients (Table 24.2; please see Chapter on Prosthetic Valves in this book).

24.2.9.4 Mechanical Valves

On cardiopulmonary bypass and under cardioplegic arrest, a proximal aortotomy is performed. The native aortic valve leaflets are excised, and the mechanical prosthesis is implanted. In the presence of annular hypoplasia an aortic root enlargement

procedure is used in order to place an adequate size valve [10].

24.2.9.5 Aortic Allografts

On cardiopulmonary bypass and under cardioplegic arrest the coronary buttons are harvested, and the proximal aortic wall and the aortic valve are excised. The allograft is then sutured to the aortic annulus

proximally and to the ascending aorta distally. The coronary arteries are reimplanted [10].

24.2.9.6 Pulmonary Autograft (Ross Procedure)

The Ross procedure involves harvesting the pulmonary root (pulmonary valve and proximal main pulmonary artery), which is then used to replace the aortic root (Fig. 24.3). The RV-to-pulmonary artery continuity

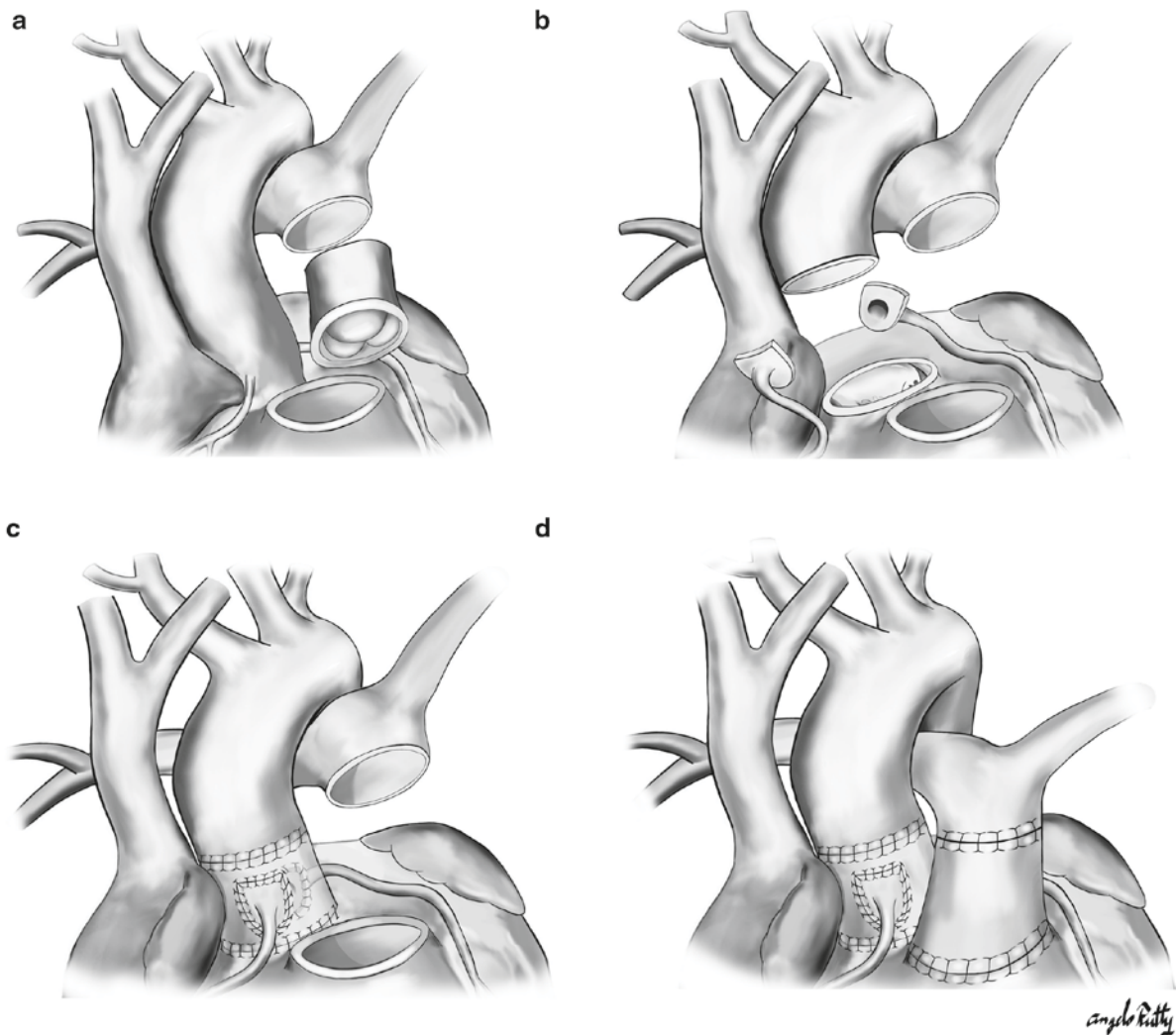


Fig. 24.3 Ross procedure. (a) The pulmonary autograft is harvested. (b) After harvesting the coronary buttons the proximal aortic wall and the abnormal aortic valve are excised. (c) Aortic

continuity is reestablished using the pulmonary autograft; note that the coronary buttons have been reimplanted. (d) A pulmonary homograft is placed in the pulmonary position

is reestablished with a conduit, most frequently a pulmonary homograft. This procedure also requires coronary artery reimplantation [10, 17].

24.2.9.7 Aortic Annular Enlargement Procedures

In some patients, a component of aortic annular hypoplasia contributes to their aortic stenosis. Several surgical techniques (Fig. 24.4) have been described for the management of this specific anatomic problem, including:

- *Manouguian*: The posterior longitudinal aortotomy is made and extended through the commissure between the left and the non-coronary aortic cusps into the anterior leaflet of the mitral valve. The annulus is then enlarged with a prosthetic patch.
- *Nicks*: The aortotomy is extended into the non-coronary sinus and the aortic annulus, but not into the mitral valve. A prosthetic patch is then used to enlarge the annulus.
- *Konno*: A vertical aortotomy is extended through the aortic root into the interventricular septum, to the left of the right coronary artery. The incision is closed with a prosthetic patch. This is a very useful technique when managing patients with multi-level obstruction (valvar and subvalvar stenosis).

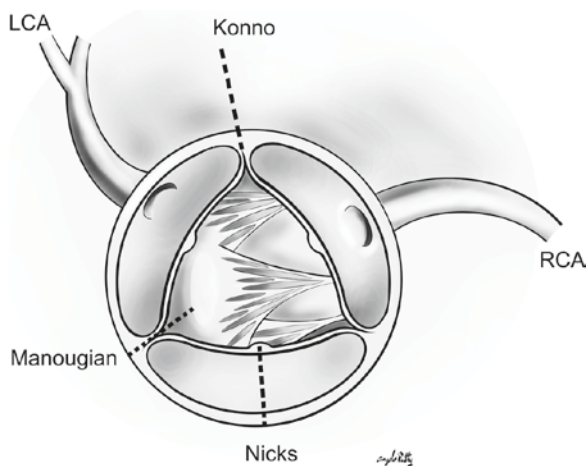


Fig. 24.4 Annular enlargement procedures

24.2.9.8 Balloon Valvuloplasty of the Aortic Valve

The approach for the procedure is as described for diagnostic catheterization. A 3-4F sheath is used in infants and a 4-8F sheath in older children and adults. Long, low-pressure balloon of roughly equal diameter to that of the aortic annulus is used to minimize injury to the valve and residual aortic regurgitation. Some interventional cardiologists use adenosine during the procedure to achieve a short-lived and reversible cardiac standstill. If the patient has more than mild AI, a catheter intervention is not the procedure of choice [14].

24.2.10 Postoperative Management

24.2.10.1 Neonates

Neonates recovering from surgical or interventional repair of critical aortic stenosis often have pulmonary hypertension and myocardial dysfunction, and may need significant support. They may require mechanical ventilation, inotropic support, and diuretics. Nitric oxide (NO) therapy may be considered in selected patients with critical hypoxic pulmonary vasoconstriction; however, NO may increase pulmonary venous return and potentially overload the failing LV.

24.2.10.2 Monitoring

After the surgical or interventional repair of the aortic stenosis, the hemodynamic management in the ICU is largely guided by echocardiographic findings, including right- and left-ventricular function, volume status, residual lesions (aortic stenosis or regurgitation), and the presence of procedure-specific complications. An echocardiogram should be done in the operating room or catheterization suite and then repeated frequently, because as the left-ventricular function improves, the trans-valvular gradient may change. Intra-operative placement of a left-atrial line

should be considered, especially if the size of the left-sided structures is small.

24.2.10.3 Cardiovascular Management

Low-dose (3–5 $\mu\text{g}/\text{kg}/\text{min}$) dopamine infusion is typically started in the operating room and continued for several days in the ICU. Less frequently, low-dose epinephrine may be required. Milrinone infusion is also routinely used for its inotropic, lusitropic, and afterload-reducing effects. The inotropes are usually weaned off after the extubation, and the infant is transitioned to an angiotensin-converting enzyme (ACE) inhibitor for long-term treatment, especially in the presence of aortic regurgitation. However, aggressive afterload reduction is contraindicated in the presence of significant residual aortic stenosis.

In some centers the ductus arteriosus may be left open if the adequacy of the left-sided structures is in question. If ductal patency is required for more than 3–5 days or left-atrial/pulmonary-venous hypertension persists for more than several days, the adequacy of left-sided structures for systemic cardiac output should be questioned, and the cardiac anatomy should be reevaluated [8]. Previously unappreciated aortic coarctation and/or arch hypoplasia should be specifically sought and excluded by echocardiography or MRI.

Patients with significant pulmonary hypertension, failing myocardium, and/or cardiogenic shock may be supported by extracorporeal membrane oxygenation (ECMO) if improvement is expected. Otherwise, alternative treatments should be considered, including univentricular repair and cardiac transplantation.

24.2.10.4 Respiratory Management

Mechanical ventilation may be needed for several days after the procedure. Goals of the ventilatory support are the same as during the preoperative period. The infant is weaned to extubation when hemodynamically stable. Inotropes are usually continued through extubation. Failure to wean from the ventilator should alert the intensivist to the possibility of persistent left-atrial/pulmonary venous hypertension as a result of poorly compliant small LV and/or residual aortic stenosis or insufficiency.

24.2.10.5 Fluids and Nutritional Management

Fluids are restricted to 1/2–2/3 maintenance, and the sodium load is minimized after surgical repair. Both the fluids and the sodium load are gradually liberalized over the next few days, as the infant's hemodynamics and renal function normalize. Fluid and sodium restriction is usually unnecessary after a catheter-based intervention.

Diuretics are started within 6 h of the surgical or interventional procedure in many centers, while others prefer to postpone them for 12–18 h. Feedings are started slowly when the hemodynamics are stable, the infant has bowel sounds, and the abdominal exam is benign. When the infant is no longer significantly fluid-overloaded, diuretics are decreased and administered enterally.

24.2.10.6 Older Infants and Children

These patients are usually much easier to care for than neonates, and their recovery is rapid. With uncomplicated repair cardiopulmonary bypass and aortic-cross clamping is usually brief, and the patients may not require significant inotropic support. Typically they leave the operating room on a combination of a phosphodiesterase inhibitor and a vasodilator. When the procedure involves coronary artery reimplantation, nitroglycerin may be initiated and continued for the next 24–48 h after surgery. These patients may be extubated soon after the procedure.

Early extubation also facilitates pain control and sedation. Because LV systolic function is typically preserved in these patients, relief of aortic stenosis is typically followed by systemic hypertension. If surgical correction was undertaken, aggressive control of hypertension is desirable in the first 1–2 days so as to protect the aortic sutures. Vasodilators and beta-blockers are usually effective. Pulmonary hypertension and myocardial dysfunction are infrequent beyond the immediate neonatal period, but, if present, they are treated similarly to those in neonates.

If epidural catheters are used after valve replacement, and anticoagulation is planned, the epidural catheter should be removed at least 3 h before commencing anticoagulation.

24.2.10.7 Complications

Procedure-specific complications should be looked for and identified prior to discharge from the ICU.

Complications of balloon valvotomy include residual aortic stenosis, aortic regurgitation, ventricular dysfunction, mitral regurgitation, and arrhythmias. Trivial stenosis is expected and preferred to insufficiency, because it is better tolerated and still leaves re-valvotomy as a future option, whereas aortic insufficiency requires a valve replacement, which is challenging in small infants. Ventricular arrhythmias may occur transiently during the procedure, and rarely complete heart block may follow it. Anemia from blood loss during access is not uncommon in small infants.

Complications of surgical valvotomy and valve replacement are mentioned elsewhere in this volume.

24.3 Subaortic Stenosis

24.3.1 Anatomy

Subaortic stenosis refers to the obstruction of the LVOT below the aortic valve annulus; it may coexist with valvar and supra-valvar obstruction. Subaortic stenosis comprises several anatomic types: [1, 6]

- *Discrete anterior subvalvar membrane* (most frequent): This occurs in children and adolescents because of subtle distortion of the LVOT and resulting turbulent blood flow which causes endocardial damage and fibrosis.
- *Diffuse tunnel-like obstruction involving the muscular septum*: This occurs mostly following a resection of a simple subaortic membrane and is due to post-surgical scarring and progressive fibromuscular proliferation in the context of a distorted LVOT.
- *Discrete projection of the conal septum into the LVOT*.
- *Hypertrophic obstructive cardiomyopathy* (described separately).
- *Other unusual space-occupying lesions* (Duplication of the anterior mitral leaflet, accessory endocardial cushion tissue, anomalous chordal or papillary-muscle insertion into the septum): Most of these occur in the setting of another congenital heart defect, such as

partial atrioventricular canal or L-transposition of the great arteries. Coarctation of the aorta, interrupted aortic arch, and ventricular septal defects could also be associated with this anomaly.

24.3.2 Pathophysiology

Pathophysiology of subaortic stenosis is very similar to that of aortic stenosis. Subaortic stenosis results in pressure overload of the LV and concentric LV hypertrophy. The subaortic obstruction causes blood flow acceleration across the subaortic area which generates a jet that causes damages the aortic valve with resulting aortic insufficiency.

24.3.3 Clinical Presentation

Symptomatic isolated subaortic stenosis is rare, but with severe obstruction, fatigue, and dyspnea may be present. Its first presentation may be syncope and anginal pain, or sudden death. Physical exam is similar to that of aortic stenosis; in fact, clinical differentiation between valvar and subvalvar aortic stenosis is usually impossible. Aortic regurgitation often coexists with subaortic stenosis and usually produces a soft early-diastolic component to the murmur. When present, aortic regurgitation in the context of subaortic stenosis carries a high risk of endocarditis.

24.3.4 Chest Radiography and ECG

Chest X-ray and electrocardiography findings are indistinguishable from those of aortic stenosis.

24.3.4.1 Echocardiography

Echocardiography is diagnostic and sufficient to plan the surgery [12]. Parasternal long-axis, apical long-axis, and apical five-chamber views best display the subaortic membrane. Parasternal long-axis and parasternal short-axis views best display the tunnel-like obstruction. Particular attention should be paid to the competence

of the aortic valve, since new-onset significant aortic regurgitation is an indication for surgery. Diagnostic catheterization is rarely done for subaortic stenosis alone, and interventional therapies are not effective at present. If a catheterization is done, access is as for aortic stenosis. A typical aortography of subaortic stenosis shows a jet of contrast without doming of the aortic valve.

24.3.5 Preoperative Management and Indications for Intervention

Unless these patients present with sudden death, they are rarely severely ill or unstable. They undergo elective repair and do not require preoperative management. Aside from finding new-onset aortic regurgitation, [14] indications for repairing an isolated subaortic membrane are unclear. In general, surgical treatment is

indicated in the presence of a mean echocardiographic gradient of 40–50 mmHg.

24.3.6 Surgical Aspects

The surgical approach involves a median sternotomy incision, cardiopulmonary bypass, and cardioplegic arrest. Via a proximal aortotomy the membrane is visualized and sharply excised (Fig. 24.5). We routinely perform a myomectomy (resection of a segment of left ventricular outflow tract muscle underneath the right coronary cusp) in order to enlarge the outflow tract and reduce the incidence of recurrence. In cases where the obstruction is more diffuse a modified Konno procedure is used. Through a right ventriculotomy, an incision is made in the interventricular septum, underneath the aortic valve. The obstructing left ventricular outflow tract muscle is resected, and the incision in the interventricular septum

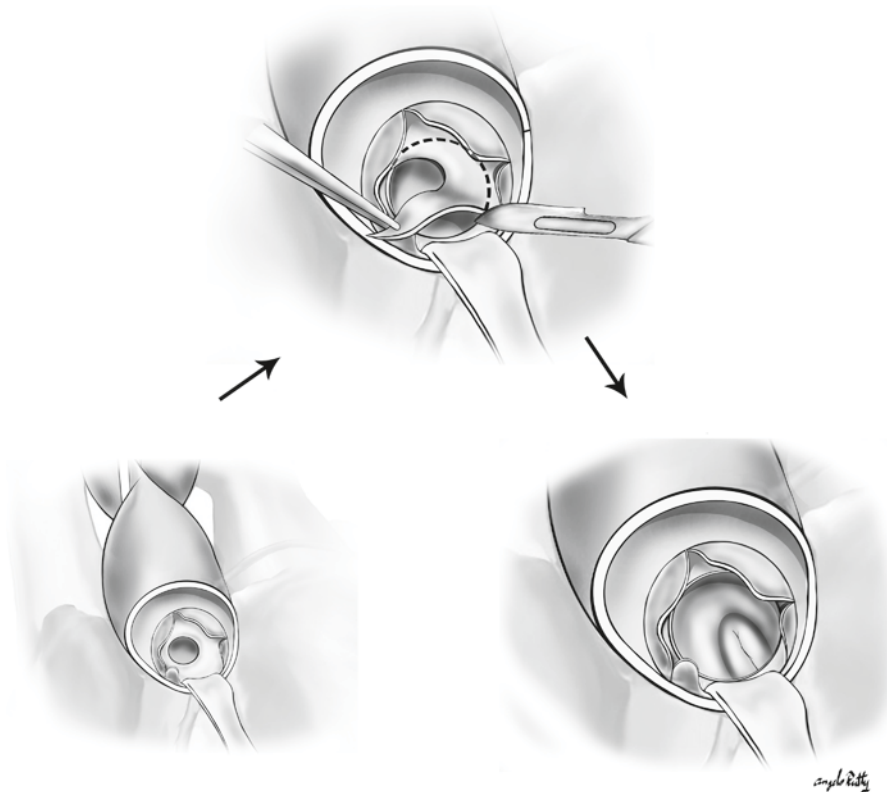


Fig. 24.5 Repair of subaortic stenosis. The fibromuscular membrane is sharply excised from the distal left ventricular outflow tract. Note that the membrane is very close to the aortic valve

is closed with a patch, enlarging the left ventricular outflow tract [10]. The mortality rate associated with simple subaortic resection is less than 2%.

24.3.7 Postoperative Management and Complications

Typically these patients are extubated in the operating room and have an uncomplicated recovery in the ICU.

Meticulous attention should be paid to the electrocardiogram, especially to new onset of left bundle-branch block, third degree A-V block, and ventricular arrhythmias. If the repair included reimplantation of the coronary arteries, a careful comparison with the preoperative ECG should be made to detect S-T segment and T wave abnormalities. If coronary ischemia is suspected, serial troponin levels should be followed, and an echocardiogram done to rule out ventricular dysfunction and/or regional wall motion abnormalities. Nitroglycerin should be initiated, and the patient should be emergently transferred to the cardiac catheterization laboratory to define the nature of the myocardial compromise. The hypertrophic left ventricle is particularly sensitive to ischemia and infarction, and both hypertension and hypotension should be avoided in this setting. All patients should have a transesophageal echocardiogram (TEE) in the operating room, and information on ventricular function, residual mitral insufficiency, residual aortic stenosis, and/or insufficiency should be readily available on admission to the ICU. Careful control of systemic hypertension is achieved with beta-blockers and vasodilators.

An occasional neonate with a Ross-Konno and postoperative ventricular dysfunction or an older patient with postoperative ventricular dysfunction due to significant subaortic resection should be managed as described earlier for the postoperative management of aortic valvotomy patients.

24.4 Supraaortic Stenosis

24.4.1 Anatomy

Supraaortic stenosis, an obstruction of LVOT at the level of the sino-tubular junction or proximal ascending aorta, is the least common type of LVOTO. Supraaortic

stenosis may be part of Williams syndrome (elastin gene disorder, see Clinical Presentation); it may occur sporadically, or display an autosomal-dominant familial inheritance. It may coexist with valvar and subvalvar obstruction, and associated valvar disease correlates strongly with the need for reoperation. The sino-tubular junction is usually quite thick, creating a wedge-like projection at the junction of the sinuses of Valsalva with the ascending aorta and giving the region an “hour-glass” appearance. Occasionally, aortic valve leaflets adhere to the sino-tubular junction, although normally they are unaffected. The coronary ostia are usually thick and may be stenotic. The coronary arteries are dilated, tortuous, and aneurismal, even in young children. In cases of Williams syndrome, the entire ascending aorta, including the aortic arch branches, may be thick and narrow; pulmonic stenosis is frequently present, and the main pulmonary artery may also be narrow. In children with Williams syndrome, coarctation of the abdominal aorta, and subclavian and renal artery stenosis may also be seen [9].

24.4.2 Pathophysiology

Pathophysiology of supraaortic stenosis is similar to that of aortic stenosis and subaortic stenosis. Supraaortic stenosis results in pressure overload of the LV and concentric LV hypertrophy. Additionally, because the coronaries originate proximal to the supraaortic obstruction, they are exposed to high pressure (which accounts for their morphology) and perfused during systole rather than diastole. However, coronary flow may also be compromised by obstruction at the sinuses of Valsalva and the coronary ostia. Distorted coronary morphology coupled with myocardial oxygen supply/demand mismatch (for reasons described under aortic stenosis) may put these patients at significant risk for sudden death [9].

24.4.3 Clinical Presentation

Patients with the familiar form of supraaortic stenosis present in infancy with signs of mild CHF; severe CHF is rare. Patients with Williams syndrome (hemizygous deletion of part of chromosome band 7q11.23, elastin

gene deletion) present with stigmata of the syndrome: elfin faces, prominent forehead, long philtrum, enamel hypoplasia, friendly personality, hyperacusis, and unusual affinity for music. Hypercalcemia, peripheral pulmonic stenosis, coarctation of the aorta, subclavian artery stenosis and renal artery stenosis are frequent [18]. These patients may be asymptomatic from the cardiovascular standpoint, or the cardiovascular abnormalities may be evident from a variety of clinical findings, such as systolic ejection murmur, syncope, systemic hypertension, cerebral vascular accidents, myocardial infarction, syncope, and sudden death. Physical exam findings are similar to those of aortic stenosis; however, the systolic murmur is best heard along the right upper sternal border, and the click is absent. Systolic hypertension is frequent and may be more pronounced in the right arm. This finding may be related to the Coanda effect, or it may result from stenosis of the origin of the contralateral subclavian artery.

24.4.4 Chest Radiography

Chest X-ray findings are similar to those of aortic stenosis; however the ascending aorta is usually not dilated.

24.4.5 ECG

Electrocardiographic findings are also similar to those of aortic stenosis. Right ventricular hypertrophy may also be present if RVOTO or branch pulmonary artery stenosis is present.

24.4.6 Echocardiography

Echocardiography is diagnostic and sufficient to plan the surgery. Parasternal long-axis and apical long-axis views best display the supra-aortic narrowing, while the suprasternal view best shows the diffuse hypoplasia of the ascending aorta and the aortic arch. The morphology of the aortic valve and the gradient across the obstruction should be investigated. Similarly, the morphology of the RVOT should be investigated and RV pressure

assessed. Particular attention should be paid to the morphology of the coronary arteries, although magnetic resonance (where available) may provide higher quality images than echocardiography [9, 12]. Diagnostic catheterization is rarely necessary, but MRI may be advisable to further define the aortic arch and the other vessels.

24.4.7 Preoperative Management and Indications for Intervention

Preoperatively, these patients are rarely severely ill or unstable, so they undergo an elective repair and do not require preoperative management. The goal is to treat the supra-aortic stenosis before the development of severe left-ventricular hypertrophy and progressive coronary stenosis. Generally, Doppler gradients of 30–50 mmHg and evidence of sino-tubular junction narrowing necessitate surgical repair [10, 14]. A child with a smaller gradient and without evidence of significant left-ventricular hypertrophy may be closely followed.

24.4.8 Surgical Aspects

In patients with supra-valvar aortic stenosis, the area of narrowing tends to be circumferential (“napkin ring”) and appears as a fibrous ridge at the level of the sino-tubular junction. The fibrous process that affects the aortic wall can involve the origin of one or both coronary arteries, at times causing coronary ischemia. Therefore, it is important to visualize the origin of both coronary arteries at surgery.

The surgical approach involves a median sternotomy incision, cardiopulmonary bypass, and cardioplegic arrest. First, the ascending aorta is opened longitudinally across the area of narrowing. Then the fibrous ridge is excised and the aorta augmented with a patch that extends across the area of narrowing and into the aortic sinuses (Fig. 24.6). An inverted Y-shaped patch is commonly used, extending into the two anterior sinuses (Fig. 24.7). Occasionally, all three aortic sinuses may need enlargement (Fig. 24.8). In patients with diffuse ascending aortic narrowing, a long-segment patch

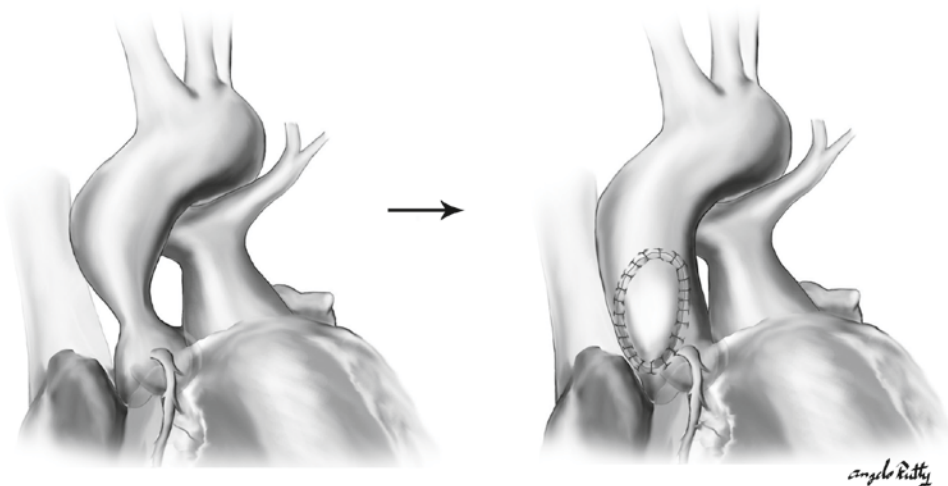


Fig. 24.6 Single-patch technique

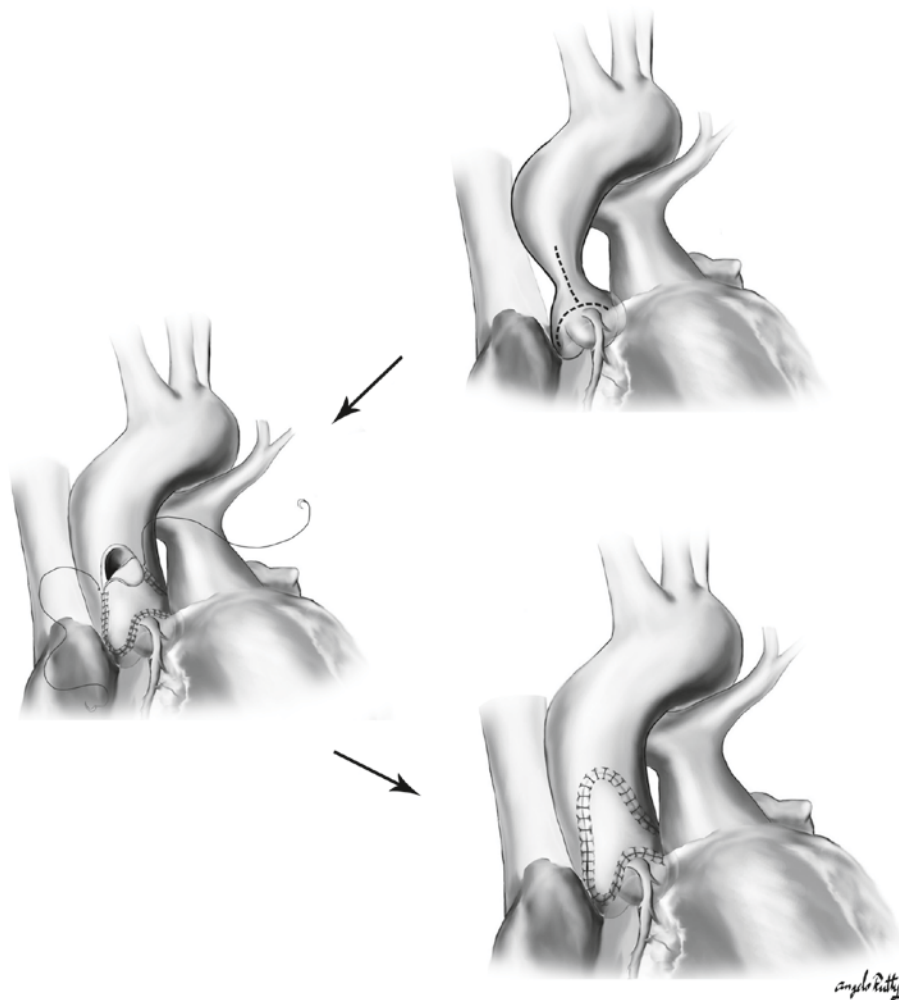


Fig. 24.7 Repair of supralvar AS with an inverted Y-shaped patch. The aortotomy is extended into the two anterior aortic sinuses. After resection of the fibrous ridge, the aorta is repaired with an inverted Y-shaped patch.

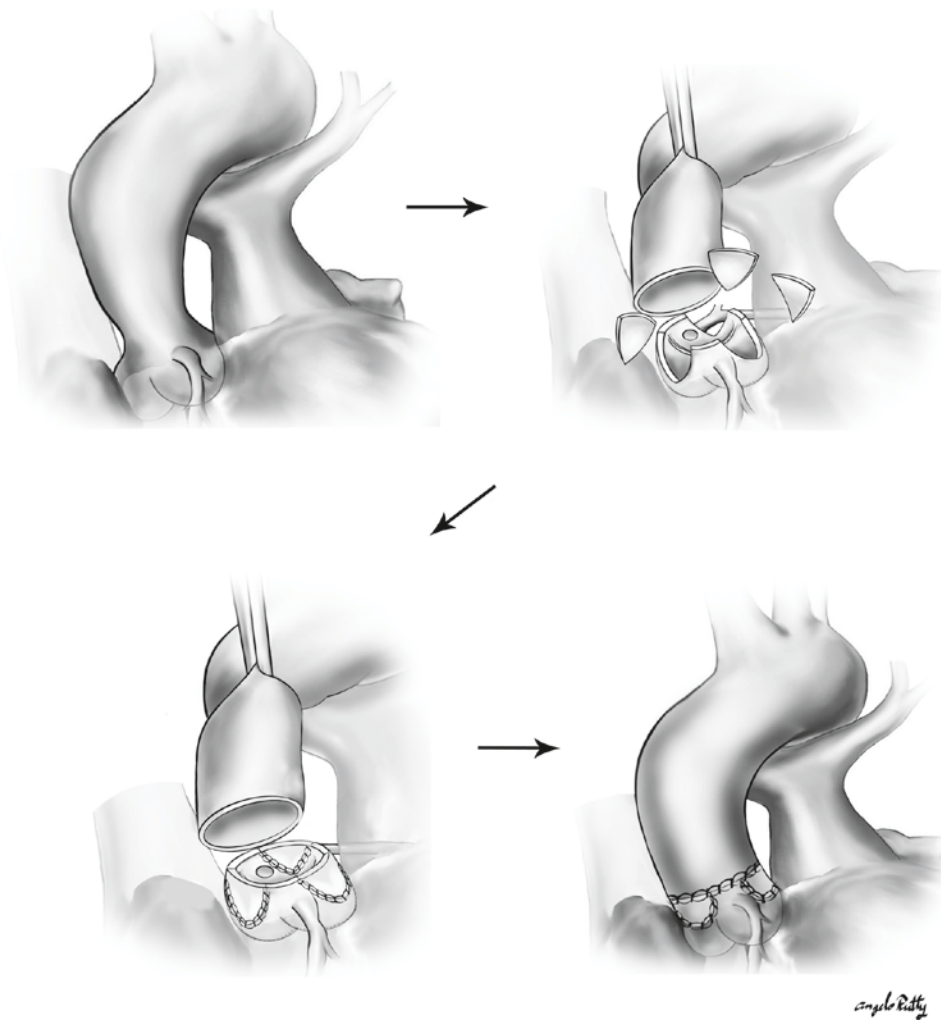


Fig. 24.8 Three-patch technique. After transecting the aorta just above the area of narrowing all three aortic sinuses are augmented with patches.

aortoplasty will be required [10]. The mortality rate associated with the surgical management of supraaortic stenosis is less than 5%.

24.4.9 Postoperative Management and Complications

Patients with discrete supraaortic stenosis are typically extubated in the operating room or soon after arriving in the ICU, and their postoperative course is uncomplicated. Patients with more diffuse forms of supra-aortic obstruction can have a more

complex postoperative course and are managed similarly to the patients with repaired valvar aortic stenosis. As with the other types of LVOTO, careful attention should be paid to adequate sedation and control of hypertension to protect the aortic sutures for the first 1–2 days. In addition, several issues specific to the repair of supraaortic stenosis should be kept in mind. After the relief of the supraaortic obstruction, the coronary perfusion pressure (and thus, the coronary flow) may actually decrease creating coronary insufficiency, and afterload-increasing agents (e.g., α 1-agonists) may be needed to correct that. On the other hand, if the aortic arch narrowing is inadequately addressed, the supra-aortic gradient will in effect be

transferred more distally, and this possibility should be investigated if the patient is exhibiting low cardiac output.

Finally, patients with Williams syndrome may show RV hypertension due to main or branch pulmonary artery stenosis [8]. Therefore, it may be advisable to dilate and/or stent the pulmonary arteries prior to surgical intervention. Sedation of patients with Williams syndrome may be challenging because their hyperacusis and unique personality [19, 20]. We found that dexmedetomidine in addition to small doses of benzodiazepines is very useful in this setting.

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Chapter 25

Coarctation of the Aorta

Michael Tsifansky, Ricardo Muñoz, Jacqueline Kreutzer, and Victor O. Morell

25.1 Introduction

Coarctation of the aorta (CoA) and interrupted aortic arch (IAA) may be seen as the two ends of the spectrum of extracardiac obstruction to the left ventricular (LV) output. The term “aortic coarctation” describes a discrete narrowing of the descending aortic lumen at the level of ductus arteriosus by a single posterior shelf of tissue; “aortic hypoplasia” refers to a narrowed aortic segment of some length in the absence of such discrete shelf; “atretic arch” defines an interruption to the patency of the aortic arch lumen with the two blind ends of the arch connected only by a fibrous strand; finally, IAA describes the complete discontinuity between the proximal and the distal ends of the aortic arch. As with other causes of obstruction to LV output, these lesions may coexist with each other and be further compounded by intra- and extracardiac defects [1]. Congenital CoA is a frequent pediatric cardiovascular lesion, especially among Caucasian boys. It is less common among African American boys and even less among African American girls. CoA is not commonly associated with genetic anomalies, except for girls with Turner syndrome, in whom it is frequent. Notably, CoA can be acquired, e.g., after Takayasu arteritis or as a result of cardiac surgery. IAA, unlike CoA, is a rare lesion. However, it is often associated with DiGeorge Syndrome ($\Delta 22q11$).

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25.2 Coarctation of the Aorta

25.2.1 Anatomy

CoA is usually found in the thoracic descending aorta at the level of the ductus arteriosus (“juxtaductal”), just distal to the origin of the left subclavian artery (Fig. 25.1). The actual narrowing is due to a ridge-like infolding of the tunica media along the posterior aortic wall, creating the posterior shelf. Evidence exists that in patients with CoA fibrodectal tissue is present in the aorta beyond the ductus arteriosus, and that the closure of the ductus is accompanied by further narrowing in the aorta itself, as the ectopic ductal tissue contracts [2]. The left subclavian and intercostal arteries are often dilated, whereas the right subclavian artery sometimes originates below the coarctation. Other vascular anomalies often found in patients with CoA include berry aneurysms of the circle of Willis [3], as well as coronary [4–9] and renal artery [10] anomalies.

CoA presenting in neonates may be a “complex CoA,” i.e., one complicated by intracardiac anomalies. Many infants presenting with severe CoA may also have a ventricular septal defect, and CoA may be part of the Shone complex [11], which includes a parachute-type mitral stenosis, a supra-mitral ring, and a subaortic stenosis. Less frequently, double-outlet right ventricle, truncus arteriosus, aorto-pulmonary window, and single ventricle may be present. However, right-ventricular outflow tract obstruction is rare in such patients.

On the other hand, CoA presenting beyond infancy is usually a “simple CoA,” i.e., an isolated lesion. However, such patients develop a rich network of engorged collateral vessels as a means to supply

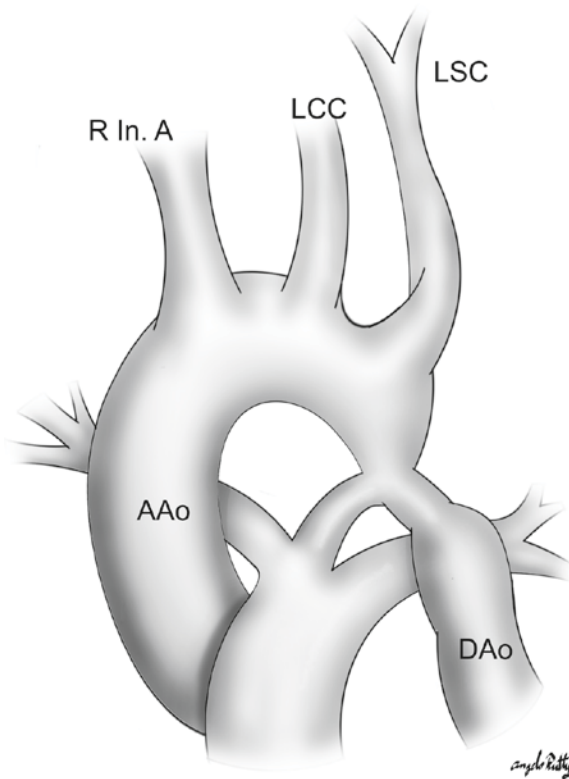


Fig. 25.1 Aortic coarctation. Note the area of narrowing in the proximal descending aorta, just distal to the left subclavian artery (LSC). *AAo* ascending aorta; *RIn.A* right innominate artery; *LCC* left common carotid artery; *DAo* descending aorta

organs distal to the coarctation. These vessels erode the lower edges of the ribs, producing the appearance of rib-notching on chest X-rays and may result in increased bleeding after the repair of CoA via lateral thoracotomy.

25.3 Pathophysiology

In neonates with critical CoA, closure of the ductus arteriosus results in cardiogenic shock from severe obstruction to left ventricular output with resultant LV failure, elevated left-atrial (LA) pressure, left-to-right shunting across the foramen ovale, and pulmonary edema. In the presence of an associated VSD, the pulmonary edema is more pronounced. The systemic

sequelae of LV failure in these patients include renal failure and necrotizing enterocolitis.

Infants and children with milder CoA do not develop acute heart failure. In these patients, the heart compensates by several mechanisms, including (1) concentric myocardial hypertrophy (to maintain normal wall stress), (2) increase in LV end-diastolic volume, mobilizing preload-recruitable cardiac output (Frank–Starling Law), (3) increase in sympathetic outflow, resulting in increased inotropy, and (4) development of the collateral circulation, which decreases the LV afterload. If the CoA is not addressed, however, many patients will ultimately develop congestive heart failure during the first 6 months of life. CoA compounds the hemodynamic effects of coexisting left ventricular outflow tract obstruction and left-sided regurgitant lesions. While complex cases of CoA typically result in worse outcomes, a coexisting ventricular septal defect may actually protect the LV from failure by providing an alternative outflow as the ductus arteriosus closes.

The pathophysiology of the older child and adult with CoA is similar to that of infants with noncritical CoA. In them, LV pressure overload also results in concentric hypertrophy, increased sympathetic tone, multiple collaterals, and, congestive heart failure (CHF). However, the progression to CHF is much slower.

25.4 Preoperative Management and Indications for Intervention

25.4.1 Neonates

Neonates with CoA presenting in shock require aggressive medical management, including an infusion of Prostaglandin E₁ (PGE₁) to reestablish ductal flow and the ductal-dependent systemic cardiac output, and to alleviate the pulmonary hypertension seen in severe LV failure. Opening of the ductus arteriosus may be sufficient to reestablish some antegrade flow across the coarctation. Perfusion of the post-ductal vasculature will come from two sources – the pulmonary artery (oxygen saturation 75–80%) and the left ventricle (oxygen saturation 90–95%). The post-ductal saturation will depend on the relative contribution of each

source, which should be remembered in the differential diagnosis of the desaturating infant with the CoA/PDA physiology. Interpretation of post-ductal oxygen saturations is more complex in patients with intracardiac communications.

To reverse established cardiogenic shock in a neonate with CoA, PGE₁ should begin at a relatively high dose (0.1 µg/kg/min) and then lowered to about 0.01–0.03 µg/kg/min as the cardiogenic shock resolves. Conversely, in a stable neonate with a prenatal diagnosis of critical CoA, the dose of PGE₁ should be kept low (0.01–0.03 µg/kg/min) to decrease side-effects (apnea, fever, hypotension, and decreased pulmonary vascular resistance).

The ratio of systemic-to-pulmonary blood flow (Qp:Qs) should be optimized. The use of room air or sub-ambient inspired oxygen concentrations may be required, and blood pCO₂ of 40–45 is desirable. Gas exchange and acid–base status should be corrected, because these infants may not tolerate hypoxia or acidosis. Fluid restriction to 75% of maintenance is beneficial during the acute phase, although an occasional small fluid bolus may be needed. As these infants stabilize, judicious use of diuretics may be required. Severe ventricular failure, frequent apneas due to PGE₁, or inability to balance the systemic and the pulmonary circulations may necessitate mechanical ventilation. Tidal volume of 8–12 ml/kg and positive end-expiratory pressure (PEEP) of 6–8 cm H₂O are frequently required to treat pulmonary edema secondary to left-atrial and pulmonary-venous hypertension and hypoxia. Bicarbonate infusion to correct acidosis and inotropic support of the myocardium may be needed until cardiogenic shock resolves. However, ongoing acidosis and cardiogenic shock need to be investigated, including careful reanalysis of the cardiac and vascular anatomy and function. Cardiogenic shock unresponsive to full medical therapy is rare, but it necessitates an emergent repair. On the other hand, those infants who respond to medical treatment should be physiologically stable prior to the surgical repair.

Due to the risk of necrotizing enterocolitis (NEC), unstable infants with critical CoA should not be fed enterally; they need parenteral nutrition. These patients should be monitored for abdominal distension and bloody stools, which would signify the development of NEC. Many centers administer

H₂-blockers or proton-pump inhibitors to fasting infants, although their benefit has not been clearly shown. Enteral feeds can be carefully started in hemodynamically stable infants with appropriately balanced Qp:Qs. Electrolytes and fluid balance should be optimized. While there is no role for prophylactic antibiotics, they are often started before the diagnosis is established because of concerns for septic shock. In such cases, it is reasonable to complete 48–72 h of therapy while awaiting cultures. Sedation with low-dose fentanyl and midazolam or dexmedetomidine infusions may be useful to decrease the infants' metabolic needs and improve comfort. Head and renal ultrasonography need to be performed, and karyotype should be checked before the repair.

25.4.2 Older Infants, Children, and Adults

These patients present much less acutely and can often undergo an elective surgical repair without the need for preoperative hospitalization. Common sequelae of longstanding unrepaired CoA include stroke, systemic arterial hypertension, and heart failure.

25.4.3 Surgical and Interventional Aspects

25.4.3.1 Timing of Surgery

In general, all patients with severe CoA should undergo elective surgical repair within a week or two of their diagnosis, but patients with signs of left ventricular failure may need a more urgent intervention. It is appropriate to allow sick neonates to recover before proceeding with surgical repair, but the occasional patient who does not respond to the prostaglandin infusion will require an emergent operation. Finally, whether associated anomalies are addressed at the time of the CoA repair or at a separate time is dictated by the nature of the anomalies as well as the clinical status of the infant. For example, it is not infrequent to perform the repair of a VSD associated with a CoA as a follow-up surgery [12].

25.4.3.2 Surgical Technique

Several surgical techniques are used in the management of isolated aortic coarctation. These procedures are performed via a left posterolateral thoracotomy and require a period of aortic clamping. A median sternotomy approach is commonly used in the presence of associated intracardiac anomalies.

25.4.3.3 Resection and End-to-End Anastomosis

After mobilization of the aorta, the ductus arteriosus is ligated and divided. The aorta is clamped proximally and distally and the area of coarctation excised. The two ends of the aorta are then approximated with a running suture (Fig. 25.2).

25.4.3.4 Resection and Extended End-to-End Anastomosis

With this technique, the undersurface of the proximal aortic end is open longitudinally up to the takeoff of the left common carotid artery. A counter-incision is made along the greater curvature of the descending aorta, and the two ends are then sutured together (Fig. 25.3). This repair is especially useful in patients with distal aortic arch hypoplasia.

25.4.3.5 Prosthetic Patch Aortoplasty

In this technique, a longitudinal incision is made through the area of coarctation and extended proximally and distally. The aortotomy is then repaired with a synthetic patch (Fig. 25.4). This repair is appropriate for the management of patients with poor aortic mobility and in the redo setting.

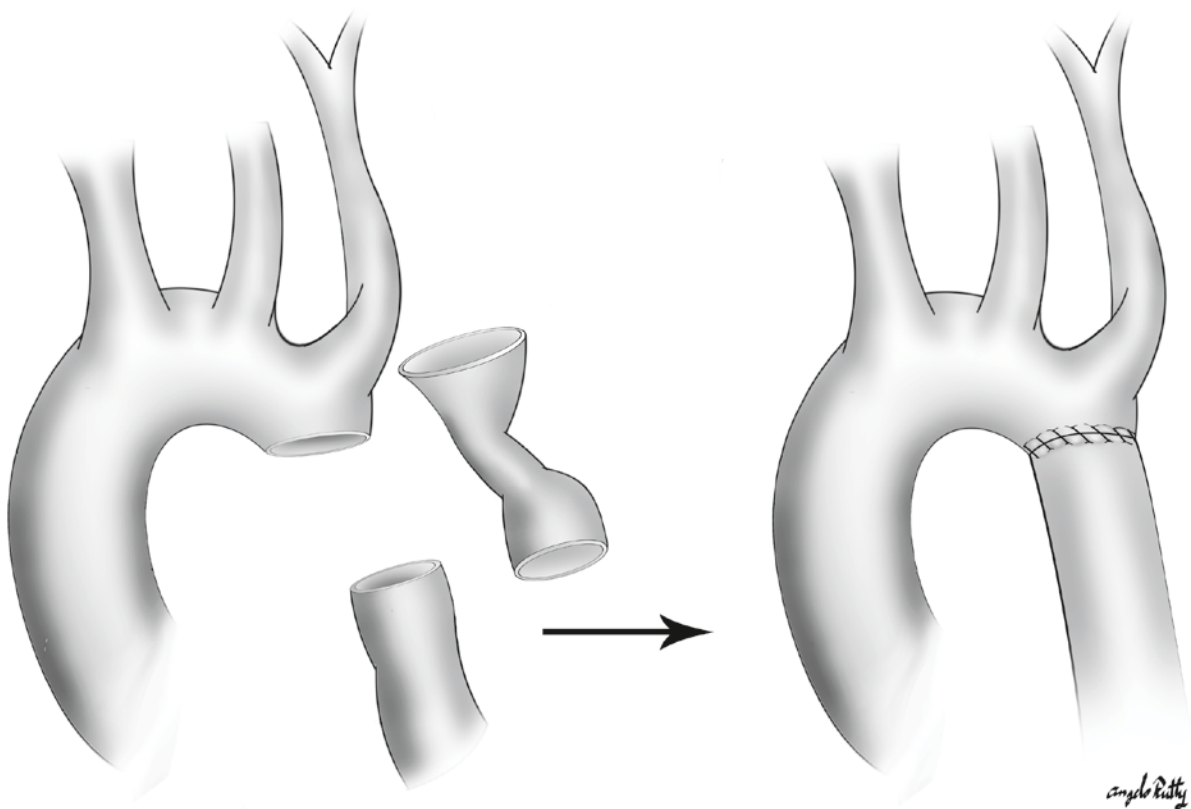


Fig. 25.2 End-to-end repair. The area of coarctation is resected and the two aortic ends are sutured together

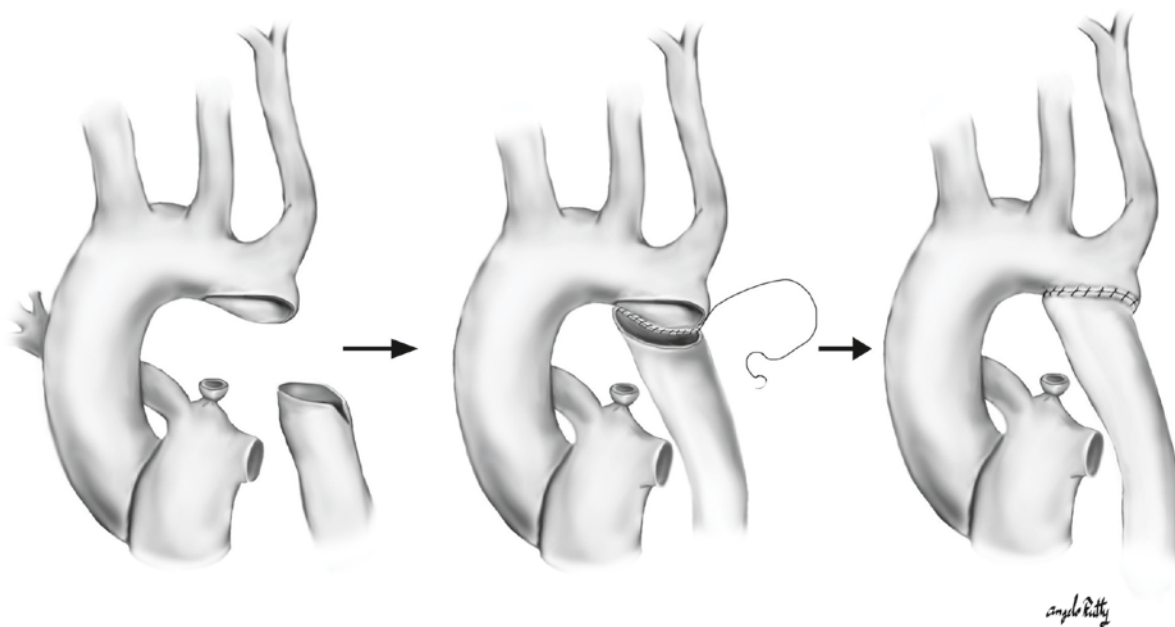


Fig. 25.3 Extended end-to-end repair. Note the placement of the distal aortic segment to the undersurface of the distal aortic arch

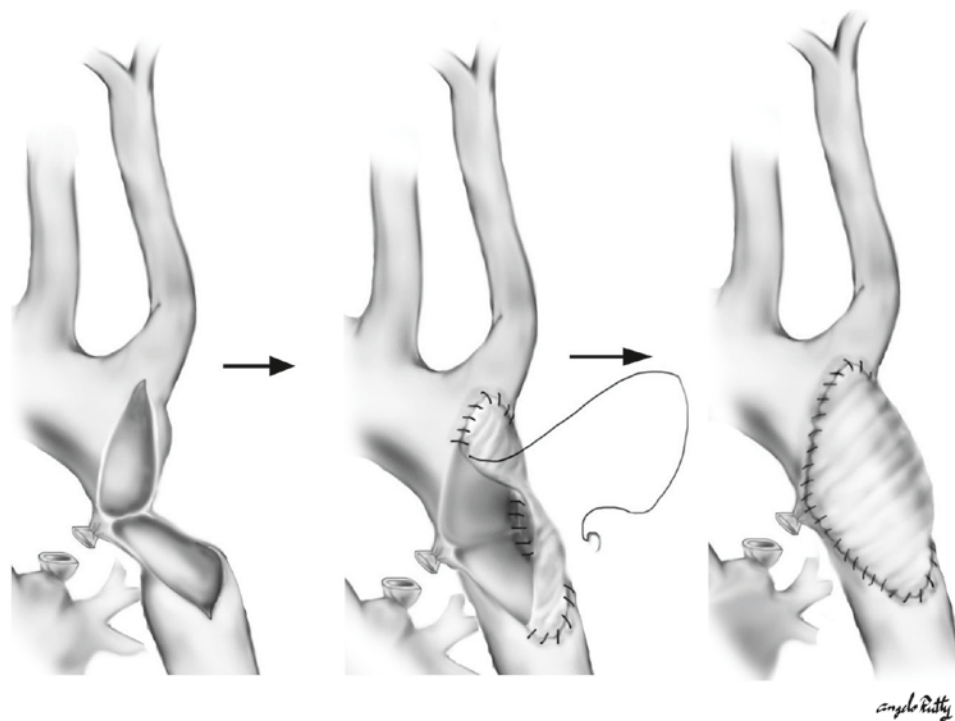


Fig. 25.4 Patch aortoplasty

25.4.3.6 Subclavian Flap Aortoplasty

In this repair, the left subclavian artery is ligated and divided distally. A longitudinal arteriotomy is then made along the length of the artery and extended across the aortic isthmus and the area of coarctation. The opened left subclavian artery is folded down and sutured to the edges of the aortotomy, thus serving as a patch (Fig. 25.5). The major disadvantage of this technique is the possibility of left arm ischemia and/or growth disturbance.

25.4.3.7 Transcatheter Interventions

Although balloon dilation has been used as a treatment for CoA since the 1980s, its role for native coarctation continues to be controversial [13]. However, in the case of postoperative re-coarctation, balloon angioplasty is the treatment of choice. If used to treat native coarctation, it is applied to patients over 2 years of age with a simple coarctation, and never to neonates, except the very rare cases who are not surgical candidates, in whom it is a palliative intervention.

From a technical standpoint, the coarctation is usually crossed retrograde using the femoral-artery approach. In patients with postoperative coarctation after single-ventricle palliation, the coarctation is typically addressed transvenously, to minimize the risk of femoral–arterial damage. Simultaneous pre- and post-coarctation pressures are recorded, and the coarctation area is imaged by biplane angiography. The angioplasty balloon with a diameter no larger than 1.2 times that of the healthy vessel before and after the area of stenosis is positioned over a wire across the coarctation and inflated for a few seconds. The pressures across the coarctation are then re-measured, and the area is re-imaged angiographically. The interventional approach is appealing because it avoids surgery and aortic cross-clamping. It is particularly attractive for the patients with a history of previous surgery and for those with native coarctation, but minimal collateral arterial formation. Yet, it carries a risk of acute aortic dissection and, when done for a native coarctation, results in a higher rate of re-coarctation, especially in infants. In addition, in native coarctation there is a worrisome incidence of post-angioplasty aortic aneurysm formation.

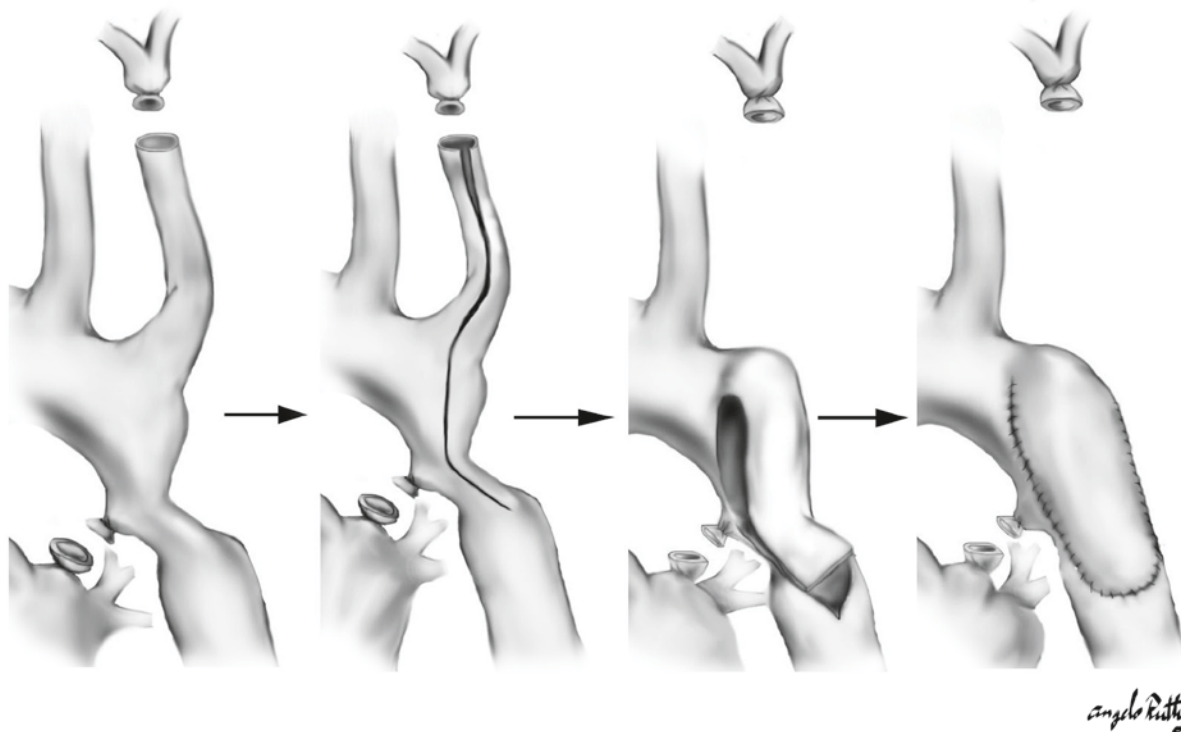


Fig. 25.5 Subclavian flap aortoplasty

In postoperative coarctations (Fig. 25.6) balloon angioplasty is the treatment of choice regardless of the surgical technique used for the repair, as it offers a high success rate, low complication rate, and low incidence of reintervention [14].

Over the last decade, primary coarctation stenting has become an alternative to surgery for the older child, adolescent and young adult with CoA (Fig. 25.7). This technique limits the incidence of aneurysm formation post-angioplasty and greatly increases the success rate of the procedure. Complication rates have decreased to

approximately 6% most recently. The complications of primary coarctation stenting include aortic dissection, stent malposition, femoral arterial damage, cerebrovascular accidents, and death (0.3%) [15, 16]

25.4.4 Surgical Complications

The most dreaded complication associated with aortic coarctation repair is spinal cord ischemia leading to

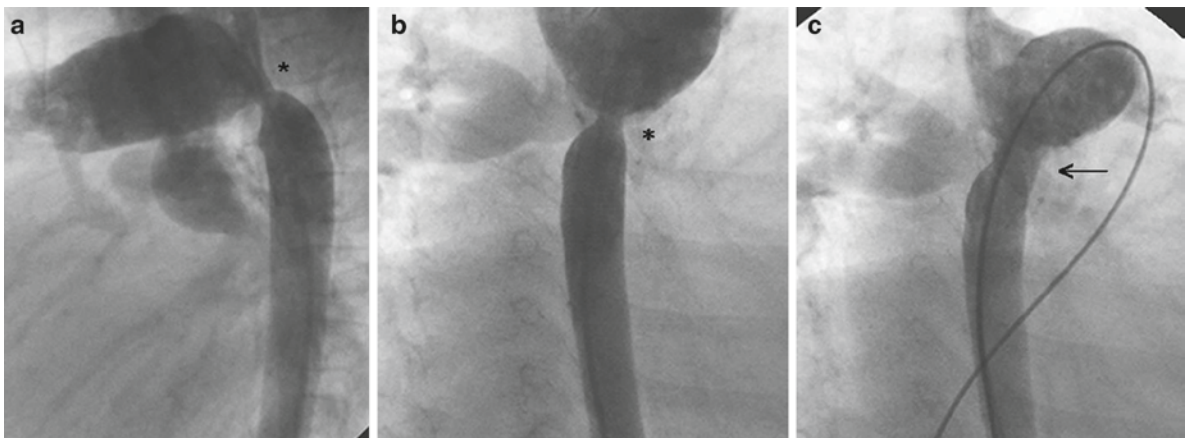


Fig. 25.6 Postoperative coarctation of the aorta. Aortogram in the lateral projection (a) and the anterior-posterior projection with caudal angulation, (b) demonstrate a severe postoperative coarcta-

tion of aorta (*) following Norwood procedure for hypoplastic left heart syndrome. Immediately after antegrade balloon angioplasty there is significant angiographic improvement (arrow)

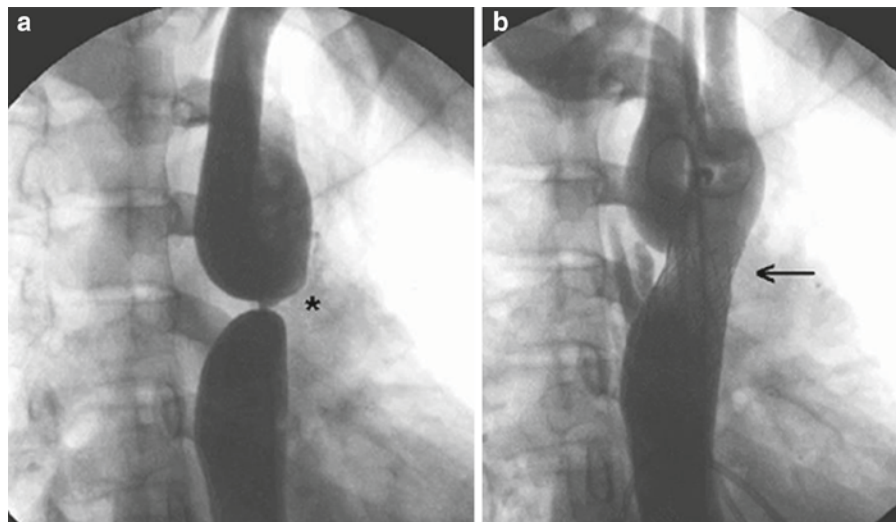


Fig. 25.7 Coarctation stenting. (a) Aortogram performed in AP projection demonstrates a severe discrete native coarctation of aorta (*). Aortogram following stent implantation demonstrates marked angiographic improvement (arrow)

paraplegia. The reported incidence of paraplegia in neonates and infants is approximately 0.4%; [17, 18] for older children and adults it has been reported to be higher (2.6%) [19]. More frequently observed complications include chylothorax, recurrent laryngeal nerve injury, phrenic nerve injury, and recurrent coarctation (15%). The operative mortality is less than 2%.

25.4.5 Postoperative Management

25.4.5.1 Monitoring

Patients should be monitored with an indwelling arterial and central line and assessed for cardiac and respiratory rate, continuous ECG and oxygen saturation. Near-infrared spectroscopy (NIRS) is a useful tool to assess regional perfusion, particularly in the splanchnic vascular bed. Noninvasive blood pressure measurements in the upper and lower limbs will help identify any residual or recurrent aortic coarctation.

25.4.5.2 Respiratory Management

Neonates recovering from uncomplicated surgical repair of critical CoA are usually extubated in the operating room or upon admission to the intensive care unit (ICU). Patients who had a complicated preoperative course may require mechanical ventilation for 12–24 h after CoA repair because of reactive pulmonary vascular bed and a risk of pulmonary hypertension. If clinically significant pulmonary hypertension is present, it should be treated in the standard fashion, including sedation and nitric oxide.

Complex arch repairs that require circulatory arrest and median sternotomy may also require longer mechanical ventilation. Once hemodynamically stable, these infants are weaned to extubation

25.4.5.3 Cardiovascular Management

The hemodynamic management in the ICU is guided by the presence of any residual cardiac lesions (intracardiac or extracardiac), the postoperative ventricular function, and the volume status. Dopamine (3–7 µg/

kg/min) and/or milrinone (0.5–1 µg/kg/min) infusion may be started in the operating room and continued for several days in the ICU. Inotropes are usually weaned after the extubation.

Tachycardia and systemic hypertension may occur after the repair (see below). Therapy is ensured with beta-blockers and vasodilators. A continuous Esmolol infusion offers the advantage of titration and may later be replaced by oral beta-blockers. Vasodilation may be titrated with sodium nitroprusside or with intravenous calcium inhibitors.

25.4.5.4 Fluid Management and Nutrition

Fluid restriction is unnecessary after CoA repair unless cardiopulmonary bypass was used to repair associated intracardiac lesions. Infants are fed very slowly when they are hemodynamically stable, have bowel sounds, and only if the abdominal exam is benign. A peculiar morbidity following CoA repair is the post-coarctectomy syndrome, which manifests as abdominal pain and tenderness as well as hypertension, fever, and leukocytosis 2–3 days after the CoA repair. The etiology of the post-coarctectomy syndrome seems to involve a sudden increase in mesenteric perfusion after the coarctectomy, resulting in mesenteric necrotizing arteritis [20].

25.4.6 Complications

In older patients, persistent postoperative systemic hypertension is common after CoA repair. Its etiology is likely multifactorial, involving baroreceptor dysfunction, increase in circulating catecholamines and renin, and the presence of mesenteric arteritis [21]. It is crucial to control the systemic hypertension diligently in the first 24–48 h postoperatively in order to prevent anastomotic leaks, the post-coarctectomy syndrome and to minimize bleeding. Esmolol, labetalol, nifedipine, or nitroprusside may be used to keep systolic blood pressure below 80–90 mmHg. However, aggressive afterload reduction is contraindicated in the presence of significant residual aortic stenosis. Once extubated and fed, the infants are transitioned to an angiotensin-converting enzyme (ACE) inhibitor or beta-blocker for long-term treatment, especially in the presence of aortic regurgitation.

A chylothorax (due to thoracic duct injury) may complicate the postoperative course, and, if not adequately drained, it may affect the respiratory effort of the patient. It may be addressed by changing the infant's diet to Portagen, whose entire fat content is in the form of medium-chain fatty acids, which do not enter the thoracic duct. Octreotide infusion may also be attempted. However, often more drastic measures are required, such as cessation of all enteral feeding for at least 2 weeks (and institution of parenteral nutrition), followed by Portagen. If the chylothorax still persists, thoracic duct ligation should be considered. Lymphocytes, immunoglobulins, and antithrombin III are lost into the chylous effusion and should be closely followed for as long as the chylothorax persists.

25.4.6.1 Other Acute Complications

Injury to the recurrent laryngeal nerve may also occur after CoA repair. It leads to paralysis of the left vocal cord, which manifests as stridor and respiratory distress upon extubation. Its net effect is a partial airway obstruction, which potentiates the negative intrathoracic pressure (and thus LV afterload) on inspiration. Small infants may not tolerate this well and may require continuous positive airway pressure (CPAP), heliox or reintubation (especially if their cardiac function is marginal). If the recurrent laryngeal nerve has not been severed, its function usually recovers in about 7 days, at which time CPAP wean or extubation may be attempted. If the infant again develops stridor and respiratory distress, complete transection of the nerve is likely. Such infants need to undergo an airway endoscopy, and, unless another reason for stridor is found, they should be considered for a tracheostomy.

Injury to the phrenic nerve manifests as hemidiaphragmatic paralysis and is often initially seen on the chest X-ray as an elevated hemidiaphragm. The diagnosis (paradoxical movement of the paralyzed hemidiaphragm – up on inspiration and down on expiration) can be made with fluoroscopy or ultrasound. During the diagnostic study it is important to avoid positive pressure ventilation because it can interfere with the paradoxical movement of the diaphragm. The respiratory status of young infants is especially compromised by hemidiaphragmatic paralysis, and in them prompt surgical intervention is required.

25.4.6.2 Older Infants and Children

While the principles of care (blood-pressure control, attention to abdominal exam and careful feeding, and search for signs of spinal ischemia) remain the same as for neonates, older patients are much easier to care for, and their recovery is rapid. They are usually extubated in the operating room. However, due to more extensive collaterals, they may experience more significant bleeding. In those patients who undergo interventional balloon-dilation and stenting of CoA, signs of bleeding should also be vigilantly sought. Bleeding can occur either at the sight of the aortic intervention or from the point of entry in the groin. Therefore, several serial hemoglobin values are often obtained, and close attention is paid to the groin. In addition, serial neurological exams should be performed in patients recovering from interventional balloon-dilation and stenting of the CoA site because strokes can occur in this subset of patients.

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Chapter 26

Interrupted Aortic Arch

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26.1 Anatomy

The anomaly of interrupted aortic arch (IAA) involves a complete interruption or atresia of a segment of the aortic arch. It can be associated with a single ventricle, malalignment ventricular septal defect (VSD), left ventricular outflow tract obstruction (LVOTO), anomalous right subclavian artery, aortopulmonary window, truncus arteriosus, and/or transposition of the great arteries [1].

The Celoria and Patton classification is used to describe the anatomic location of the atretic segment (Fig. 26.1):

Type A: Distal to the left subclavian artery (1/3 of cases).

Type B: Between the left subclavian artery and the left common carotid artery (most common; nearly 2/3 of cases).

Type C: Between the left carotid artery the innominate artery (least common; around 1% of cases).

The type B IAA is commonly associated with an aberrant right subclavian artery and a conoventricular VSD with posterior malalignment causing left ventricular outflow tract obstruction. In addition, this interruption is associated with absence of the thymus and DiGeorge syndrome.

In addition, classification of IAA can be based on the anatomy of the subclavian arteries and is divided into normal subclavian arteries or an aberrant right subclavian artery situated retroesophageal (present in 50% of type B interruption, but also may be seen in type A) [2, 3].

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26.2 Pathophysiology

IAA is a ductal dependent anomaly, as adequate blood supply to the distal arch is dependent on a patent ductus arteriosus (PDA). Without medical intervention, the infant develops cardiogenic shock, metabolic acidosis, and multiorgan dysfunction. The precipitant factor for the onset of shock is a closing ductus with resultant systemic hypoperfusion. In the setting of an intact atrial and ventricular septum, the lower half of the body will be supplied by the PDA with desaturated blood, and differential cyanosis will be present [4].

The pathophysiology of IAA with VSD and/or ASD is different. A left-to-right shunt across ASD or VSD level is present, and the blood that is ejected from the right ventricle and shunted through the PDA to the distal arch is less desaturated than the blood in patients without intracardiac communications. Thus, differential cyanosis may not be clinically appreciated. Nevertheless, assuming normal lung gas exchange and absence of an aberrant right subclavian artery, the brain and right arm oxygen saturation will be higher than that in the lower extremities [5].

Patients with transposition of the great arteries and IAA type B exhibit a distinct physiology that is dependent upon the following factors: (1) intracardiac communications (2) pulmonary hypertension, and (3) lung pathology. In the absence of intracardiac and extracardiac communications, the neonate has parallel circulation with no effective pulmonary and systemic blood flow [6]. Refractory cardiogenic shock will appear soon after birth, and the only chance of survival is a rapid atrial septostomy coupled with the initiation of prostaglandin E_1 . If only an insufficient atrial communication exists, a cascade

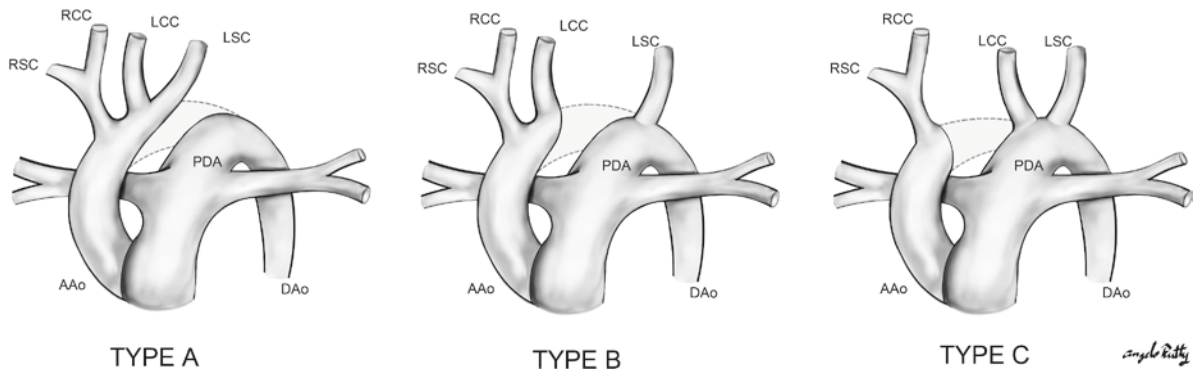


Fig. 26.1 Classification of interrupted aortic arch (Celoria and Patton). The interrupted lines represent the atretic aortic segment. AAo ascending aorta; RSC right subclavian artery; RCC

right common carotid artery; LCC left common carotid artery; LSC left subclavian artery; PDA patent ductus arteriosus; DAo descending aorta

of hypertension from the left atrium through the pulmonary circulation is initiated. At this point, a pulmonary artery to distal arch shunt will occur across the PDA. Because the pulmonary artery carries the more oxygenated blood (as the PA is connected to the left ventricle), the lower half of the body will have higher oxygen saturation compared to the upper part of the body in a condition known as “reversed differential cyanosis. The same physiology applies in any patient with pulmonary hypertension. In neonates with significant lung disease and pulmonary hypertension, pulmonary venous desaturation will exist and reversed differential cyanosis may not be apparent. In the presence of an aberrant right subclavian artery arising after the interruption, the oxygen saturation measured on the right arm may not be different from those measured in the lower extremities [7].

26.3 Clinical Presentation

The clinical presentation of IAA is similar to that in patients with coarctation of the aorta. These infants usually remain clinically stable as long as the PDA remains open. Once the PDA becomes smaller, there is not a reliable source of blood supply to the lower body, and cardiogenic shock and multiorgan dysfunction appears. Physical examination at this point reveals tachypnea and weak femoral pulses. Weak right brachial pulses may be present in patients with an

aberrant right subclavian artery arising post-interruption. Carotid pulses may allow the physician to differentiate the anatomy and pathophysiology of this disorder, especially in IAA type B. If all pulses are weak, severe LVOTO, ventricular dysfunction and/or aortic stenosis must be suspected. This finding is accompanied by poor systemic perfusion, loud systolic murmur (VSD and LVOTO), tachypnea, and increase work of breathing.

26.3.1 Electrocardiogram

The ECG reveals prominent right ventricular forces, but is otherwise nonspecific.

26.3.2 Chest Radiography

The chest X-ray demonstrates cardiomegaly, pulmonary edema secondary to overcirculation, and/or ventricular enlargement.

26.3.3 Echocardiography and MRI

At present, echocardiography and MRI are the gold standard for the diagnosis of IAA. Catheterization is rarely indicated.

26.4 Preoperative Management

The preoperative management of IAA is similar to that of critical coarctation of the aorta.

PGE₁ must be initiated, and inotropic support should be started and planned according to the echocardiographic findings regarding the ventricular function.

If the infant is in cardiogenic shock and/or has significant work of breathing, endotracheal intubation should be performed, and hyperoxia, hypocarbia and alkalosis must be avoided to promote right to left shunt across the PDA and to increase systemic blood flow.

In selected cases, it may be necessary to decrease the systemic vascular resistance with milrinone and/or increase the pulmonary vascular resistance with a hypoxic mixture to avoid pulmonary overcirculation. The goal of therapy is to maintain optimal distal arch perfusion with right to left shunting across the PDA. This goal can be monitored by physical examination (peripheral pulses, perfusion, and urine output). A pre-ductal saturation above 90% and a post ductal saturation of approximately 70% signify good gas exchange and appropriate distribution of the cardiac output.

Recently, near-infrared spectroscopy (NIRS), featuring input from brain, renal, superior mesenteric artery, and foot electrodes, has been used to assess regional tissue perfusion. However the clinical value of this approach remains investigational [8].

Biochemical indicators such as lactate levels, arterial and/or venous blood gases, and liver and renal function tests must be closely monitored. Chromosome studies are routinely requested to rule out a DiGeorge (22q11 deletion) or a CHARGE (CHD7 mutation on chromosome 8q12.1) syndrome and other congenital anomalies, and

irradiated blood must be administered until DiGeorge syndrome is eliminated from the differential.

In addition, renal and head ultrasounds are routinely obtained to rule out anomalies.

If possible, once the patient has reached hemodynamic stability, enteral trophic feeds at approximately 20 ml/kg/day should be initiated and slowly advanced if tolerated. If enterocolitis is suspected, the cardiac repair is deferred until it improves, and the infant is treated with broad spectrum antibiotics, maintained nil per os (NPO) for 10–14 days, and given parenteral nutrition. Serial abdominal radiograms should be closely followed in these infants.

In the author practice, if sepsis is suspected, ampicillin and cefotaxime are initiated. They are discontinued if cultures remain negative after 72 h of therapy.

26.4.1 Surgical Management

The surgical repair of an interrupted aortic arch requires cardiopulmonary bypass, moderate-to-deep hypothermia and cardioplegic arrest. A period of circulatory arrest and/or low flow is required for the arch repair. A unique aspect of the arterial cannulation is the fact that two canulas are needed, one for each end of the aorta, in order to perfuse both the upper and lower body [9, 10].

The repair consists of uniting the two ends of the aorta and closing the VSD. The aortic reconstruction requires extensive mobilization of the distal aortic segment in order to allow for a stress-free aortic anastomosis (Fig. 26.2). We routinely augment the undersurface of the aorta across the area of anastomosis; this technique

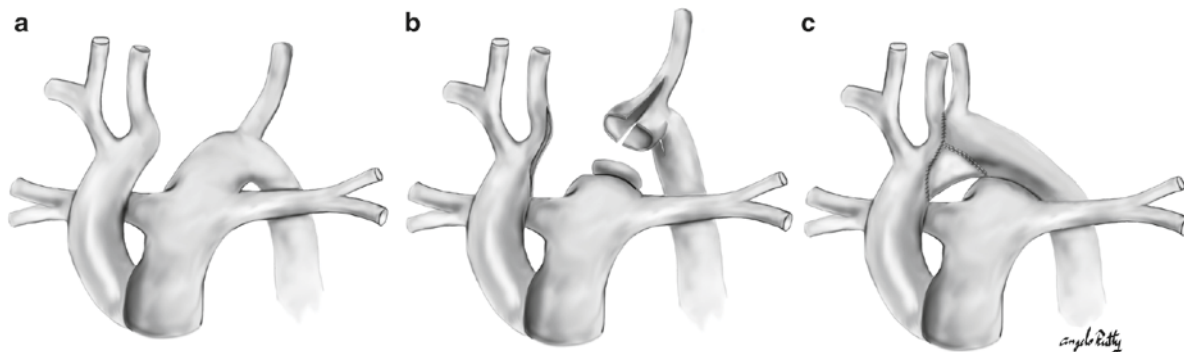


Fig. 26.2 Repair of type B interruption. (a) Discontinuity of the aorta between the left common carotid artery and the left subclavian artery, (b) the ductus arteriosus is divided and the distal aortic segment is opened superiorly into the proximal left subclavian

artery and inferiorly into the descending aorta, past the area of ductal tissue. The proximal aortic segment is opened into the origin of the left common carotid, (c) the two aortic ends are sutured together and the anastomosis is augmented with a prosthetic patch

has been reported to decrease the incidence of recurrent arch obstruction [6, 11, 12]. When present, the ventricular septal defect is closed via a right atriotomy. The mortality rate associated with the repair of an IAA is approximately 8% [13].

26.5 Postoperative Management

The postoperative management will depend upon the associated congenital heart disease [14]. There are four main paradigms:

1. Isolated IAA
2. IAA with ventricular septal defect (VSD) and left ventricular outflow tract obstruction (LVOTO)
3. IAA with VSD and transposition of the great arteries (TGA)
4. IAA with VSD and truncus arteriosus (TA)

26.5.1 Isolated IAA

Postoperative care of isolated IAA is similar to that after the repair of coarctation of the aorta. Attention should be paid to possible residual arch gradient, and evaluation of the femoral pulses and the blood pressure of the four extremities is mandatory [15].

26.5.1.1 Cardiovascular Management

The inotropic support of choice is milrinone and low-dose epinephrine (if needed). Some infants may benefit from the use of an arterio-venodilator such as sodium nitroprusside. In cases without circulatory arrest, milrinone alone is sufficient. Diuretic therapy is initiated within 6–8 hr after surgery.

26.5.1.2 Respiratory Management

Extubation should be planned within 48 h of chest closure in complicated cases or within 24 h in uncomplicated. Similar to coarctation of the aorta, the caregiver should be aware of the complications related to injury of the structures near the aortic arch such as left lung

atelectasis (left bronchial compression by a reconstructed arch), or damage to the recurrent laryngeal nerve, thoracic duct, phrenic nerve, and sympathetic ganglia.

26.5.1.3 Metabolic Management

If patients have DiGeorge syndrome, they may require frequent calcium supplementation. A full endocrine and immunologic evaluation should be completed as a wide spectrum of this syndrome exists with mild to severe endocrine and immune deficiencies.

26.5.2 IAA with Ventricular Septal Defect (VSD) and Left Ventricular Outflow Tract Obstruction (LVOTO)

Currently in patients with these anomalies all defects are repaired in one surgical stage [16, 17]. Therefore, the postoperative care is very challenging. In addition to the aforementioned management of the arch repair, one needs to be aware of the potential complications of VSD and LVOTO repair [15, 18].

As a general rule, the caregiver must always find evidence of an adequate surgical repair [19]. Residual defects may have devastating consequences, especially in infants after cardiopulmonary bypass, cardioplegic arrest, and circulatory arrest.

In an infant with a combination of residual arch obstruction and residual VSD, significant LV dysfunction and low cardiac output syndrome will develop due to LV volume (left to right shunt across the VSD) and pressure overload (residual arch obstruction). Left ventricular dysfunction will lead to left atrial hypertension, pulmonary venous hypertension, pulmonary edema, pulmonary hypertension, and eventually RV dysfunction. The clinical signs of these residual defects are a VSD murmur, weak pulses in lower extremities, pulmonary edema, and signs of congestive heart failure with potential cardiogenic shock. An echocardiogram and perhaps cardiac catheterization (for the evaluation of Qp:Qs must be done promptly to decide on surgical reintervention [20].

VSD closure also implies a possibility of a conduction system injury and/or inflammation giving rise to arrhythmias and atrioventricular block. Depending

upon the surgical approach (via right atrium-tricuspid valve, pulmonary valve or ventriculotomy), the intensivist may see various degrees of tricuspid or pulmonary valve incompetence in addition to ventricular dysfunction.

More specific details regarding the postoperative care of VSD and LVOTO are discussed elsewhere in this volume.

26.5.3 IAA with VSD and Transposition of the Great Arteries (TGA)

In patients with these abnormalities, the presence of residual arch obstruction, injury to the extracardiac structures (phrenic nerve, thoracic duct, etc), conduction abnormalities, and a residual VSD must be evaluated. Details of postoperative care of arterial switch will be discussed in the chapter regarding transposition of the great arteries. Some of the potential morbidities of this repair include ventricular dysfunction, mitral regurgitation, arrhythmias secondary to coronary insufficiency, bleeding due to multiple suture lines, supra-valvular pulmonic stenosis, and supra-valvular aortic stenosis [21]. These patients may need ECMO shortly after surgery until ventricular function improves [22].

26.5.4 IAA with VSD and Truncus Arteriosus (TA)

In patients with these conditions immediate postoperative complications of truncus arteriosus must be avoided. These include pulmonary hypertension, branch pulmonary artery stenosis, right ventricular dysfunction, conduit stenosis, conduction system abnormalities, arrhythmias, coronary ostium injury, and truncal valve insufficiency and/or stenosis [11].

26.6 Long Term Outcome

Surgical results for repair of IAA are improving and short and long term outcomes are influenced by the initial surgical approach (single-stage complete

repair versus staged palliative repair), coexistence of other associated anomalies, low birth weight, and experience of the cardiovascular team [23–28]. A recent study which compiled 20 years of surgical experience in patients with IAA and associated anomalies revealed that regardless of operative technique, there is still a long-term probability of reoperation and/or reintervention [13]. The actuarial survival including early mortality was 92% at 1 year, 81 % at 5 years, and 75% at 10–15 years. Another study of 472 neonates reported that reintervention was more likely for those who had a diagnosis of truncus arteriosus, IAA repair by a method other than direct anastomosis with patch augmentation, and/or the use of polytetrafluoroethylene as either an interposition graft or a patch [6]. Patients with low birth weight, immediate presentation, type B IAA, and major associated cardiac anomalies remain at a high risk for death [29].

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Chapter 27

Mitral Valve Anomalies and Related Disorders

Cécile Tissot, Eduardo M. da Cruz, Afksendyios Kalangos, and Shannon Buckvold

This chapter will discuss mitral disorders with the exception of mitral stenosis to which a specific chapter has been dedicated in this book. It will also provide information about some associated entities such as Marfan syndrome (MFS) and rheumatic disease.

27.1 Mitral Valve Anatomy and Physiology

The normal mitral valve apparatus consists of four components: the annulus, leaflets, tendinous cords, and papillary muscles [1]. The normal mitral valve consists of two leaflets, the anterior leaflet and the posterior leaflet, suspended from the fibrous mitral valve annulus at the level of the atrioventricular junction. The anterior leaflet guards approximately two-thirds of the left atrioventricular orifice, but occupies only one-third of its circumference. The posterior leaflet is subdivided into three sections, or scallops (P1, P2, P3); it guards approximately one-third of the left atrioventricular orifice, but occupies two-thirds of its circumference. The two leaflets coapt at the anterolateral and posteromedial commissures; each scalloped section of the posterior leaflet (P1, P2, P3) coapts with the anterior leaflet in areas designated A1, A2, A3 [2] (Figs. 27.1 and 27.2). Thus, for proper mitral valve function, the mitral valve leaflets require proper functioning of all eight areas of coaptation (two commissures and six leaflet sections). The valve leaflets are

normally prevented from prolapsing into the left atrium by the tendinous cords attached to the underside of the valve that insert into the papillary muscles. The papillary muscles are normally symmetric, occupying the anterolateral and posteromedial aspects of the left ventricle, below the anterolateral and posteromedial commissures, and each of them typically has tendinous insertions that support both valve leaflets [2].

27.2 Etiology and Presentation of Mitral Diseases

27.2.1 Marfan Syndrome

Marfan syndrome (MFS) is a heritable connective tissue disorder which may affect the eyes, cardiovascular system, skeletal system, lungs, spinal cord, skin, kidney, and other systems [3]. The diagnosis is clinical, made predominantly by applying the Ghent criteria (Table 27.1). Cardiovascular complications in MFS have accounted for more than 90% of premature deaths in the era prior to open-heart surgery [4]. While nearly all Marfan patients continue to exhibit cardiovascular involvement [5], current anticipatory guidance and effective management have allowed patients with MFS to achieve near-normal life expectancies [6]. However, neonatal MFS, with severe mitral and/or tricuspid insufficiency and infantile pulmonary emphysema, continues to carry a very poor prognosis, with a life expectancy of 2 years [7].

The estimated incidence of MFS is 2–3 per 10,000 individuals [8], and the estimated prevalence is 1 in 5,000 individuals [9]. MFS exhibits autosomal dominant inheritance with complete penetrance but variable

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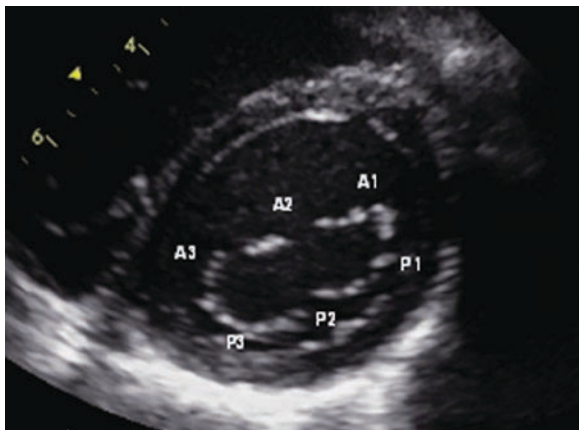


Fig. 27.1 Echocardiography short axis view of the mitral valve, with the scallops of the anterior (A) and posterior (P) leaflets identified: A1 anterolateral; A2 middle; A3 posteromedial; P1 anterolateral; P2 middle; P3 posteromedial

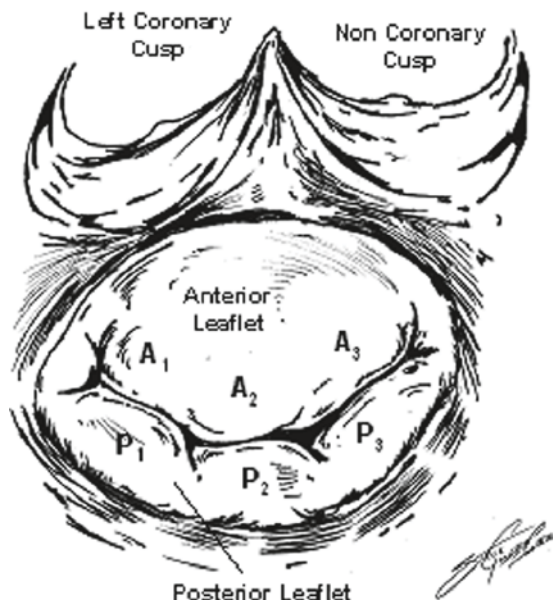


Fig. 27.2 Mitral valve anatomy (drawing from Steven P. Goldberg, MD)

expression in 75% of patients, while sporadic occurrence accounts for the remaining 25% [6]. Preimplantation and prenatal genetic diagnosis is available; however, because variable expression of the syndrome exists even within families, molecular diagnosis of MFS cannot predict disease severity [10]. The birth prevalence of neonatal MFS, the most severe phenotypic expression of MFS, is quite rare; one study reports a prevalence of 1 per 27,000 live births [11].

Table 27.1 Ghent diagnostic criteria. An index case must meet two major criteria in two organ systems and a minor criterion in a third system (Adapted from [20])

System	Major criteria	Minor criteria
Family history	MFS in parent, child or sibling	
Genetics	Mutation of FBN1	
Cardiovascular	Aortic root dilation Dissection of ascending aorta	Mitral valve prolapse Calcification of the mitral valve (<40 years) Dilatation of the pulmonary artery Dilatation/dissection of descending aorta
Ocular	Ectopia lentis	Flat cornea elongated Globe myopia
Skeletal	Pectus excavatum needing surgery Pectus carinatum Pes planus Positive wrist or thumb sign Scoliosis >20° or spondylolisthesis Armspan-height ratio >1.05 Protrusio acetabulae Diminished extension elbows <170°	Moderate pectus excavatum High arched palate Typical facial features Joint hypermobility
Pulmonary		Spontaneous pneumothorax Apical bulla
Skin		Striae Recurrent or incisional herniae
Central nervous system	Lumbosacral dural ectasia	

The most common cardiovascular abnormalities in pediatric MFS are dilation of the aorta (Figs. 27.3 and 27.4) and mitral valve prolapse [12], the morphology of which can be characterized both by histology and gross pathology. This chapter will concentrate on the description of the mitral anomalies.

27.2.2 Mitral Valve in Marfan Syndrome

In MFS, the mitral valve leaflets are most frequently abnormal. The mitral valve in patients with MFS demonstrates progressive histologic and morphologic

abnormalities. Fibrillin density is reduced and accompanied by partial fragmentation of the longer fibrillin-coated elastic fibers, with abnormal globular change in the fibrillin coating of remaining portions of elastic fibers [13]. Both the anterior and posterior leaflets tend to become elongated and redundant, with some degree of thickening. Chordal elongation and rupture can occur. Progressive annular dilation and calcification can be demonstrated in 30% of MFS patients [14]. Massive calcification of the mitral valve annulus has been reported in adolescence [15].

All phases of mitral regurgitation – acute, chronic compensated, and chronic decompensated – have been described in neonates and children with MFS [16].

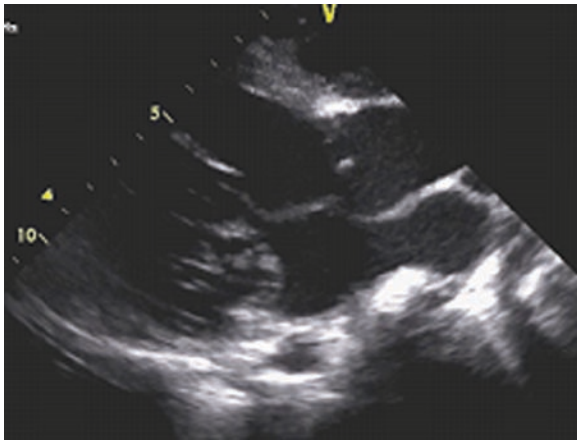
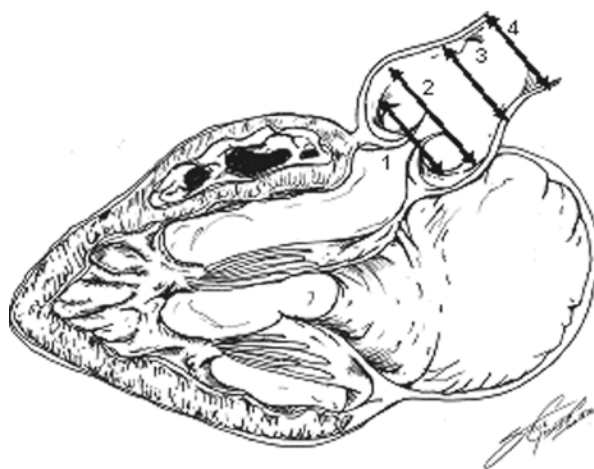


Fig. 27.3 2D echocardiography of a patient with Marfan syndrome demonstrating dilation of the sinuses of Valsalva and abnormal mitral valve

As the anterior and posterior leaflets of the mitral valve become elongated, redundant, and somewhat thickened [14], it results in the prolapse of the anterior leaflet or the posterior leaflet or both [17]. Mitral valve prolapse can be demonstrated in 17% of children at age 5 [12]; in 75% of adolescents at age 15 [12]; and in 80% of young adults at 30 years of age [14]. It has been suggested that 100% of children with evolving phenotypic expression of MFS will develop mitral valve dysfunction by 18 years of age, and one half of children with mitral valve dysfunction will develop mitral regurgitation (MR) before 25 years of age [12]. By 30 years of age, 13% would have developed moderate-to-severe MR [14]. In fact, in the pediatric MFS population, mitral valve dysfunction and regurgitation contribute most to morbidity and mortality, and have been suggested to be of prognostic significance [14, 18]. Severe MR in very young children is a feature of the infantile and neonatal expression of MFS [19–21].

27.2.3 Arrhythmias

Patients with MFS have a greater prevalence of cardiac dysrhythmias when compared to healthy patients without MFS [22]. In children and adults with MFS, ventricular dysrhythmia can occur and progress with or without significant valve disease [23]. Young patients with MFS with stable cardiovascular involvement on medical therapy are more likely to die from dysrhythmia than from aortic dissection [24]. Ventricular tachycardia



Aorta (End-Diastole)

	N	Mean ± SD	Range
1 Aortic Annulus	68	1.9 ± 0.2	1.4-2.6
2 Sinus of Valsalva	68	2.8 ± 0.3	2.1-3.5
3 Sinotubular Junction	64	2.4 ± 0.4	1.7-3.4
4 Ascending Aorta	44	2.8 ± 0.3	2.1-3.4

Fig. 27.4 Echocardiographic measurements in Marfan syndrome (drawing from Steven P. Goldberg, MD)

can occur as a consequence of mitral valve prolapse [25]. Atrial tachyarrhythmia can take place secondary to atrial dilation in the setting of valvar regurgitation.

27.2.4 Myocardial Dysfunction

Symptomatic myocardial dysfunction in MFS rarely occurs in the absence of significant valvar regurgitation. Chronic left ventricular volume overload from aortic or MR causes ventricular dilation and increased end-diastolic pressure. To maintain cardiac output in accordance with the Frank–Starling mechanism, increased end-diastolic pressure results in increased ventricular performance until the point beyond which compensation cannot be maintained and circulatory failure results. In the setting of valvar regurgitation, the left ventricle is hyperdynamic. A “normal” appearing left ventricle in the setting of significant valvar regurgitation may be a harbinger of progressive left ventricular failure. The clinical features of cardiac failure in MFS can be described by the general features of cardiac failure described elsewhere in this Chapter 49.

27.2.5 Diagnosis

27.2.5.1 Clinical Presentation of Marfan Syndrome

Classic MFS

MFS is most often suspected on the basis of skeletal and ophthalmic features that suggest the diagnosis. Due to its variability and tendency towards an evolving phenotype, the diagnosis of MFS is primarily clinical, made by applying the Ghent criteria (Table 27.1). However, when the clinical diagnosis is less clear, a full range of diagnostic studies can be performed, and the objective findings can be assembled to make the diagnosis [3].

Atypically Severe MFS

Though MFS exhibits a significant degree of clinical variability, both within and among families with MFS, no generally accepted clinical grading system exists

for MFS. Tiecke et al have proposed that a reasonable preliminary definition of “atypically severe” MFS be considered for MFS patients who manifest severe cardiovascular disease and require operative intervention for aortic root dilation or severe aortic or mitral valvular dysfunction before 17 years of age [26].

Neonatal Marfan

As a genetic diagnosis, MFS is always present from birth and therefore symptoms of MFS in the neonatal period are insufficient to support a diagnosis of neonatal MFS [21]. Rather, the diagnosis of neonatal MFS is reserved for neonates with the most severe phenotypic expression of MFS: severe cardiac valvular insufficiency and cardiac failure, and congenital pulmonary emphysema [18, 27]. Mortality in infants with neonatal MFS can be as high as 95% in the first year of life from relentlessly progressive, severe mitral, tricuspid, and/or aortic insufficiency [21, 28] that is often complicated by scoliosis, congenital pulmonary emphysema, and pulmonary hypertension [20]. In addition to the cardiac and pulmonary manifestations, neonatal MFS exhibits a distinctive neonatal phenotype [18, 20, 21, 27, 29]:

- Very loose skin, as if “two sizes too big,” lending an aged appearance to the face
- Dolichocephaly
- Dislocated lenses, iridodonesis, megalocornea
- Down-slanting palpebral fissures
- Crumpled, low-set ears
- High arched palate
- Micrognathia
- Anterior chest deformity
- Flexion contractures
- Hyperextensible joints
- Dislocated hips
- Arachnodactyly

27.2.6 Presentation of Mitral Complications of Marfan Syndrome

Many of the cardiovascular complications of MFS sufficient to require admission to the intensive care unit are likely to be characterized by general signs and symptoms

of cardiac failure. Infants may exhibit symptoms like failure to thrive, tachypnea, coughing, wheezing, diaphoresis, irritability or listlessness, tachycardia, and poor perfusion. Children and adolescents may show dyspnea, orthopnea, reduced exercise tolerance, syncope or presyncope, chest pain, or palpitations. Tachypnea, increased breathing, or hyperpnea may result from pulmonary edema, bronchial compression from cardiac enlargement, or the metabolic acidemia and hypoxemia may result from the poor peripheral balance of oxygen demand-delivery. Pulmonary hypertension frequently complicates the course of these patients in the intensive care unit. Additionally, if the ventricular function is compromised, the patient may be at risk for thromboembolism.

MFS patients with severe mitral valve regurgitation enter the ICU with decompensated MR. Contractile and ejection functions are impaired; the hemodynamic consequences are reduced forward output and increased pulmonary vascular congestion. The clinical presentation is variable, depending on the degree of hemodynamic compromise, and can be dominated by the typical features of cardiac failure, circulatory shock, and respiratory failure from pulmonary edema.

In all MFS patients with mitral complications, caregivers must be cautious in identifying other compromised potential cardiovascular functions related to the aortic valve, the aorta and the myocardial function. As a matter of fact, clinical presentation of an aortic aneurysm in children with MFS is typically asymptomatic; it is detected by serial echocardiographic evaluation. Complications of aortic root aneurysms from rupture, dissection, and tamponade can occur in children with MFS [30–32]; however, early aortic dissection is more characteristic of the recently described Loeys–Dietz syndrome.

Lastly, endocarditis should be considered in any patient with MFS who shows acutely progressive valvular disease, recurrent fevers, or persistent constitutional symptoms of anorexia, weight loss, malaise, or personality changes. Perivalvular abscess can be associated with conduction abnormalities, including complete heart block [33].

Other clinical features on physical examination often include:

- An S3, heard immediately after S2, from the rapid, large volume flow into the LV
- An S4, heard immediately before S1, from flow into noncompliant or stiff ventricle during atrial contraction
- A holodiastolic decrescendo murmur at the left sternal border; also at the right sternal border if associated with aortic root dilation
- Austin Flint murmur, a soft mid-diastolic rumble heard at the apex, when severe regurgitant jet renders partial anterior mitral leaflet closure
- Widened pulse pressure with bounding palpable pulses.

27.2.7 ECG

The resting electrocardiogram in MFS may include findings of [22]:

- Atrial fibrillation
- Premature atrial beats
- Long QT interval and decreased QT dispersion
- ST segment depression
- Premature ventricular beats, with occasional R on T configuration
- Prolonged atrioventricular conduction time

Ventricular arrhythmias are associated with increased left ventricular size, mitral valve prolapse, and abnormalities of repolarization; they are an important cause of sudden death in Marfan patients [34]. Complete heart block may be indicative of endocarditis complicated by perivalvular abscess [33].

27.2.8 Imaging

Echocardiography is the cornerstone method to diagnose mitral anomalies in patients with MFS. In grown-up patients transthoracic echocardiography may be limited and transesophageal approach may be required.

However, other techniques like angio CT scan and MRI are essential to complement the assessment of the mitral valve and function and to identify aortic compromising, particularly in the context of suspected aortic dissection.

- A displaced LV apical impulse from chronic aortic insufficiency
- Soft or absent S2 from incomplete aortic valve closure

27.2.9 Rheumatic Fever

Rheumatic fever is a delayed nonsuppurative sequela of group A beta-hemolytic streptococcal (GABHS) pharyngitis in children. The disease has a delayed onset after the initial infection and presents with various other manifestations including arthritis, carditis, chorea, subcutaneous nodules or erythema marginatum.

The incidence of rheumatic heart disease has decreased dramatically in industrialized countries over the past several years related to the introduction of penicillin and a change in the virulence of the Streptococci. A dramatic decline in both the severity and mortality from acute rheumatic fever has occurred in the past 30 years in these countries. The prevalence of rheumatic heart disease in the US is now less than 0.05 per 1,000, with rare regional outbreaks [35–38].

In contrast, rheumatic fever and rheumatic heart disease have not decreased in developing countries. Around 5–30 million children and young adults are estimated to have chronic rheumatic heart disease worldwide [39, 40].

Race and sex does not influence the disease incidence. However, aboriginal populations in Australia and natives from Hawaii, Maori and New Zealand have a higher incidence of rheumatic fever even with antibiotic prophylaxis of streptococcal pharyngitis [41, 42]. Rheumatic disease in females is usually worse with a higher incidence of chorea and a worse prognosis of carditis.

Rheumatic fever is principally a disease of childhood, occurring between 5 and 15 years, with a median age of 10 years at diagnosis.

Rheumatic heart disease is still the major cause of acquired valve disease in the World [43, 44].

Though the exact pathogenesis of rheumatic fever remains unclear, it is believed to result from an autoimmune response. It develops following GABHS pharyngitis and almost only infections of the pharynx initiate or reactivate rheumatic fever [45]. Rheumatic fever has also been described in aboriginal populations from Australia following GABHS skin infection [41, 46, 47].

The initial infection consists of sore throat, fever, malaise and headache in a small percent of patients for several weeks before leading to rheumatic fever.

Penicillin treatment shortens the clinical course of streptococcal pharyngitis and more importantly prevents the major sequelae [48].

Acute rheumatic heart disease produces a pancarditis involving the pericardium, epicardium, myocardium and endocardium. Endocarditis is manifested as mitral and aortic valve insufficiency [49]. The most commonly affected valve is the mitral valve (65–70% of patients), followed by the aortic (25%) and the tricuspid (10%) valves. The pulmonary valve is rarely affected. Whether myocardial dysfunction during acute rheumatic fever is related primarily to myocarditis or is secondary to severe valve insufficiency is not known [50, 51]. When pericarditis is present, it is usually self-limiting and rarely results in constrictive pericarditis.

Congestive heart failure secondary to severe valve insufficiency is a complication of acute and chronic rheumatic fever. Recurrent episodes of rheumatic fever may cause progressive damage to the valves. Severe scarring of the valves develops months to years after the initial episode of rheumatic fever and is responsible for most cases of mitral valve stenosis in adults.

Patients with a history of rheumatic fever are at a high risk of recurrence. The risk of recurrence is high within 5 years of the initial episode and if the patient is of younger age at the time of the initial episode. The risk of carditis and severity of valve damage increases with each attack.

27.2.10 Clinical Presentation

Acute rheumatic disease is a systemic disease with a large variety of symptoms.

Antecedent of a sore throat 2–5 weeks prior to onset of symptoms is present in 70% of patients. Systemic complaints are frequent including fever, fatigue, weight loss, headache, malaise and pallor. Abdominal pain is common.

Major clinical manifestations are as follows:

- Fever: is usually greater than 39°C at the onset of symptoms. The fever decreases spontaneously in 1 week, but low-grade fever can persist for 2–3 weeks.
- Arthritis: Polyarthritis is the most common symptom and frequently is the earliest manifestation (70–75%). The arthritis involves usually in the large joints, beginning in the lower extremities (knees, ankles) and migrating to other large joints in the upper extremities (elbows, wrists). Affected joints are painful, erythematous, swollen and warm. The

pain is out of proportion to clinical findings. The arthritis persists for about 1 week, is migratory and responds dramatically to aspirin [52]. Polyarthrititis is more common and more severe in teenagers and young adults than in younger children.

- Carditis: Pancarditis is the second most common complication of rheumatic fever (50%). The classical clinical presentation is a new or changing murmur and tachycardia that is out of proportion to the fever. The murmurs of acute rheumatic fever are from valve regurgitation (most commonly mitral or aortic) and the murmurs of chronic rheumatic fever from stenosis, most commonly mitral. Dyspnea, edema, cough, orthopnea and oedema are signs of congestive heart failure. Chest discomfort, chest pain and a pericardial friction rub are signs of pericarditis. All degree of heart block can be seen, including atrioventricular dissociation [53].
- Sydenham chorea: is a late manifestation of acute rheumatic fever, occurring 1–6 months after the initial sore throat [54, 55]. Patients with chorea often do not demonstrate other Jones criteria, and this criteria alone is sufficient for the diagnosis. Complete resolution of the symptoms typically occurs in 3 months, but some patients can have wax and wane symptoms for several years.
- Pediatric autoimmune neuropsychiatric disorder (PANDAS): is characterized by obsessive–compulsive personality disorder [56]. Patients tend to show aggressive and compulsive comportment. They may also show emotional lability, separation anxiety and oppositional behaviors.
- Erythema marginatum: begins as pink nonpruritic macules or papules located on the trunk and proximal limbs but never on the face [57]. The lesions form a serpiginous ring with erythematous raised margins and central clearing. The rash is classically exacerbated by heat. The rash occurs early in the course of the disease and remains for long after the resolution of other symptoms.
- Subcutaneous nodules: are firm, non-tender, mobile and are located over the extensor surfaces of the elbows, knees, ankles, knuckles, scalp, and spinous processes of the lumbar and thoracic vertebrae. They are rare but strongly associated with severe rheumatic carditis [58].
- Arthralgias: may be reported upon presentation. Arthralgia cannot be considered a minor criteria if arthritis is present.

27.2.11 Diagnosis: Jones Criteria

The modified Jones criteria [59, 60], revised by the American Heart Association in 1992 [61] and reviewed in 2002 [62], provide guidelines for the diagnosis of rheumatic fever. The diagnosis of rheumatic fever requires evidence of a previous GABHS pharyngitis as well as the presence of two major or one major and two minor criteria (Table 27.2). These criteria are not absolute, and the diagnosis can be made in patients with only confirmed streptococcal pharyngitis and chorea.

Three settings may be identified without strict adherence to the Jones criteria:

- Chorea: may occur late and be the only manifestation of the disease.
- Indolent carditis as the only manifestation in patients who have received medical attention months after the onset of rheumatic fever.
- Recurrent rheumatic fever: a patient with a history of rheumatic fever, especially rheumatic heart disease, with evidence of a recent GABHS infection with either a single major or two minor criteria.

The AHA guideline 2002 update [62] concluded that the role of echocardiography in the diagnosis of rheumatic fever was controversial in patients without cardiac findings on clinical exam. It was concluded that echocardiographic Doppler evidence of mitral or aortic regurgitation alone should not be either a major or a minor criterion in the diagnosis of rheumatic fever.

Table 27.2 Jones criteria

Jones criteria:	
Preceding streptococcal infection	Positive throat culture Rapid streptococcal antigen test Elevated or rising streptococcal antibody titer
Major diagnostic criteria	Carditis Polyarthrititis Chorea Subcutaneous nodules Erythema marginatum (erythema annulare)
Minor diagnostic criteria	Fever Arthralgia Prolonged PR interval Elevated acute-phase reactants (ESR, CRP)

27.2.12 Laboratory in Rheumatic Fever

- Throat culture for GABHS: Usually are negative in about 75% of patients by the time rheumatic fever appears [41]. Isolation of the organism prior to the initiation of antibiotic therapy is important to help confirm the diagnosis of streptococcal pharyngitis and to allow typing of the organism.
- Rapid antigen detection test: Allows rapid detection of GABHS antigen with specificity >95% but a sensitivity of only 60–90%. Thus, a throat culture should be obtained [63].
- Antistreptococcal antibodies: Are at their peak at initial presentation and are useful for confirming previous GABHS infection [64]. Antibody titers should be performed 2 weeks apart to detect a rising titer. Most patients with acute rheumatic fever have elevated antibodies titers to at least one of the anti-streptococcal antibodies [65, 66]. The most common antibodies tested include:
 - Antistreptolysin O (ASLO)
 - Anti-DNase B
 - Antihyaluronidase
 - Antistreptokinase
 - Antistreptococcal esterase
 - Anti-nicotinamide adenine dinucleotide (anti-NAD)
 - Antistreptococcal polysaccharide
 - Anti-teichoic acid
 - Anti-M protein
- Acute-phase reactants: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are elevated and have high sensitivity but low specificity [67, 68].
- Mild normochromic normocytic anemia: Anemia secondary to acute inflammation may be seen during acute rheumatic fever.
- Heart reactive antibodies: Rapid detection test for B-cell marker D8/17 by immunofluorescence is positive in 90% of patients with rheumatic fever, and may be useful for identifying patients who are at risk [69, 70].

27.2.13 Other Studies in Rheumatic Fever

- Chest Radiography
Cardiomegaly, pulmonary congestion, and other findings consistent with heart failure may be observed.

• ECG

Sinus tachycardia is a common finding. Alternatively, some children present sinus bradycardia from increased vagal tone. First-degree atrioventricular block (prolongation of PR interval), probably related to localized myocardial inflammation of the atrioventricular node, is a common finding and is one of the Jones criteria. Second and third-degree atrioventricular have been described. In patients with acute pericarditis, ST segment elevation may be present.

• Echocardiography

In individuals with acute rheumatic heart disease, echocardiography identifies and quantitates valve insufficiency and ventricular dysfunction. In patients with mild carditis, Doppler evidence of MR may be present during the acute phase of disease and usually resolves in some weeks or months. In contrast, patients with moderate-to-severe carditis have persistent mitral or aortic regurgitation [71]. According to the 1992 revised Jones criteria, evidence of new MR from Doppler echocardiography, in the absence of accompanying auscultatory findings, is not sufficient for making the diagnosis of carditis [72, 73].

Three mechanisms of mitral insufficiency have been described with rheumatic fever (Fig. 27.5): prolapse of the aortic leaflet, rupture of the tendinous chords and non-coapting retracted immobile mural leaflet [74, 75]. The aortic valve usually shows improper central coaptation of the leaflets. Echocardiographic features of MR from acute rheumatic valvulitis are annular dilatation, elongation of the chordae to the anterior leaflet, and a posterolaterally directed MR jet. A distinctive feature of acute rheumatic valvular disease is focal nodular thickening of the tips and bodies of the leaflets [76]. Left ventricular dilation is frequently seen and contributes to MR.

In individuals with chronic rheumatic heart disease, echocardiography assesses the progression of valve stenosis. The leaflets of affected valves become thickened diffusely, with fusion of the commissures and chordae tendineae (Fig. 27.6). Increased echodensity of the mitral valve is often seen.

27.2.14 Complications of Rheumatic Disease:

- Congestive heart failure from valve insufficiency (acute rheumatic fever) or stenosis (chronic rheumatic fever)

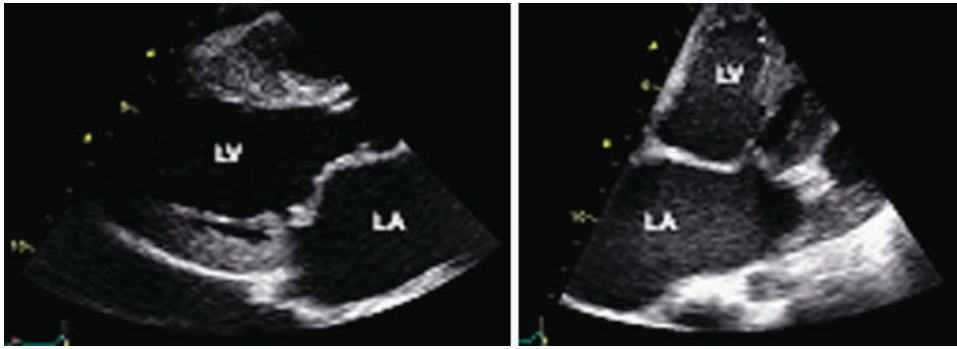


Fig. 27.5 Color Doppler echocardiography long axis and four chamber view demonstrating a rheumatic mitral valve with thickened leaflet, absence of central coaptation and marked left atrial dilation secondary to severe regurgitation

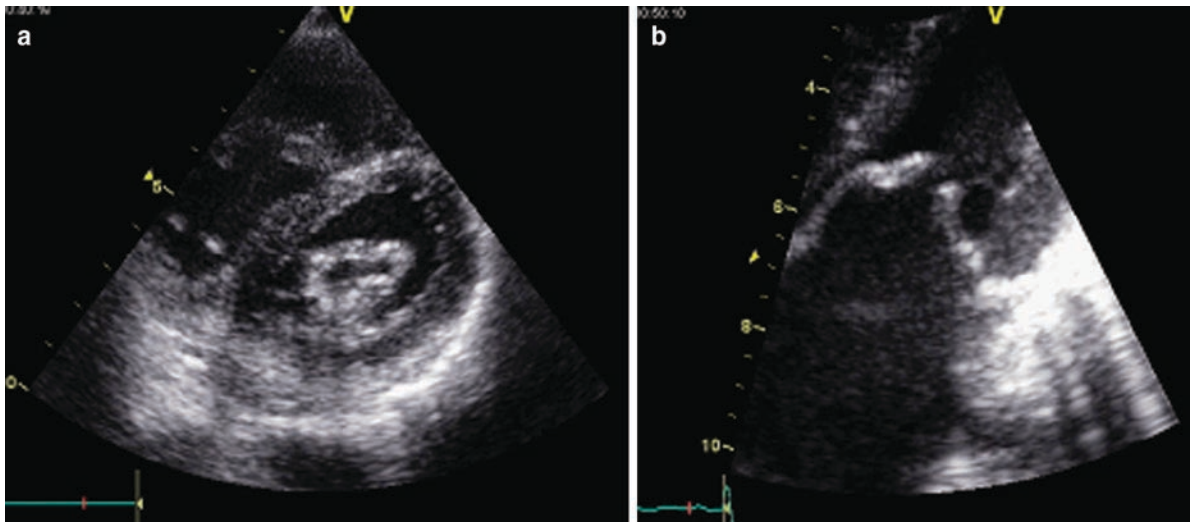


Fig. 27.6 (a) 2D echocardiography with severe rheumatic mitral stenosis: short axis view (left) demonstrating thickened leaflets and limited mitral orifice area, four chamber view (right)

demonstrating limited leaflet excursion. (b) 2D echocardiography in four chamber view showing a severe rheumatic mitral stenosis with limited leaflet excursion

- Thrombus formation, pulmonary emboli, and systemic emboli
- Infective endocarditis
- Atrial flutter, multifocal atrial tachycardia, or atrial fibrillation from chronic mitral valve disease and atrial dilation

anomalies are seen in association with other lesions in the context of hypoplastic left ventricle syndrome variant or Shone's complex. Shone's complex is characterized by a constellation of left heart obstructive lesions: supralvalvar stenosing mitral ring, parachute mitral valve, left ventricular subaortic obstruction, and coarctation of the aorta [77].

27.2.15 Congenital Mitral Valve Anomalies

Isolated congenital mitral valve diseases are uncommon in children, occurring in 0.5% of patients with congenital heart defects. More frequently, mitral valve

27.2.16 Annular or Mitral Valve Hypoplasia

In annular or mitral valve hypoplasia, all components of the valve apparatus are morphologically normal but

relatively small in relation to the size of the tricuspid valve. Some degree of hypoplasia of the left ventricle and left ventricular outflow tract obstruction are universally present, creating a variant of hypoplastic left ventricle syndrome [78]. Occasionally, annular hypoplasia may result from a dilated coronary sinus and left-sided vena cava. The dilated coronary sinus may cause left ventricular inflow obstruction, which can be demonstrated by abnormal Doppler inflow patterns and increased left atrial “a” waves during cardiac catheterization [79].

27.2.17 Congenital Mitral Valve Stenosis

Congenital mitral stenosis, including supralvalvar mitral ring, parachute mitral valve and anomalous arcade or hammock mitral valve, are extensively discussed in a chapter (?) in this book.

27.2.18 Congenital Mitral Valve Regurgitation

Congenital MR is uncommon; however, malformations of each of the major components of the mitral valve apparatus have been described in the etiology of MR:

- Annular dilation secondary to anterior or posterior leaflet prolapse
- Leaflet abnormalities, including leaflet dysplasia [2], abnormal leaflet morphology [80], posterior leaflet hypoplasia with chordal shortening [81], isolated cleft of the anterior or posterior leaflet [82] or of both mitral valve leaflets [83], and anterior leaflet fenestrations.
- Commissural abnormalities
- Chordal abnormalities, including chordal length, organization, and insertion
- Papillary muscle abnormalities, including alterations in papillary muscle number, positioning, and chordal attachments

27.2.19 Isolated Mitral Cleft

Isolated cleft of the anterior mitral leaflet is a rare cause of MR (Figs. 27.7 and 27.8). This defect is very different from the cleft atrioventricular valve found in

the patient with atrioventricular septal defect [84]. The anomaly is characterized by a cleft dividing the anterior leaflet of the mitral valve into two portions with a normally positioned mitral annulus and intact atrioventricular muscular and membranous septum.

27.2.20 Double Orifice Mitral Valve

This defect is characterized by two complete mitral orifices supported by their own tension apparatus [85]. Three types have been described:

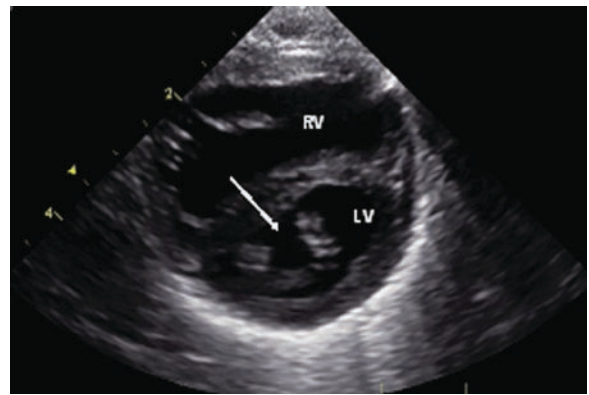


Fig. 27.7 Echocardiography short axis view demonstrating the cleft mitral valve (arrow)



Fig. 27.8 Mitral cleft (drawing from Steven P. Goldberg, MD)

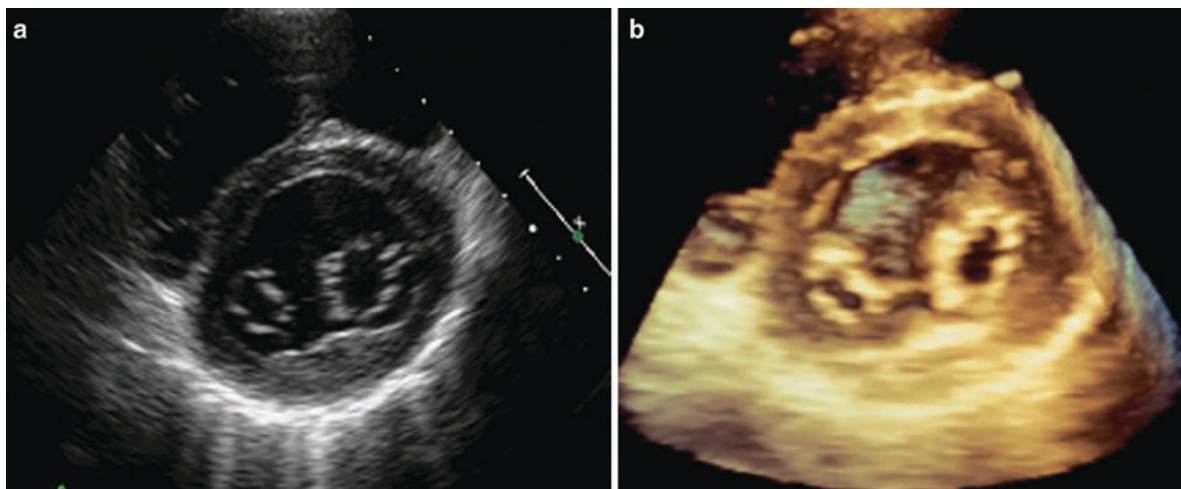


Fig. 27.9 (a) 2D echocardiography short axis view demonstrating a double orifice mitral valve (3D reconstruction by Shawn Popylisen). (b) 3D echocardiography in short axis view demonstrating a double orifice mitral valve (3D reconstruction by Shawn Popylisen)

1. Eccentric or hole type is the most common, and is characterized by a small accessory orifice at the anterolateral or posteromedial commissures.
2. Central type is the next most common, and is characterized by excessive leaflet tissue which bridges the central zones of the anterior and posterior leaflets, thereby dividing the mitral orifice into two. The resulting two orifices may be equal or unequal, and they are usually supported by separate tendinous chords that insert into separate papillary muscles.
3. Duplicate mitral valve is an exceptionally rare entity, and is characterized by two mitral valve annuli and valves, each with its own set of leaflets, commissures, chordae, and papillary muscles.

Double orifice mitral valve may occur in isolation or in association with atrioventricular septal defect, and though this condition can be associated with mitral stenosis or insufficiency, it can be asymptomatic, occurring only as an incidental echocardiographic finding (Figs. 27.9 and 27.10).

27.2.21 Mitral Valve Prolapse

The etiology of this common condition is not clear and is probably multifactorial. It can be seen in individuals with a wide range of congenital heart malformations including MFS, ischemic heart disease, hypertrophic



Fig. 27.10 Double orifice mitral valve (drawing from Steven P. Goldberg, MD)

cardiomyopathy, pectus excavatum, as well as in thin patients (Fig. 27.11). It is usually diagnosed on the clinical basis of a mid systolic click and a late systolic murmur of MR.

27.3 Pathophysiology of Mitral Regurgitation

Mitral regurgitation (MR) can be described in three phases: acute, chronic compensated, and chronic decompensated. In all phases of MR, blood is ejected into

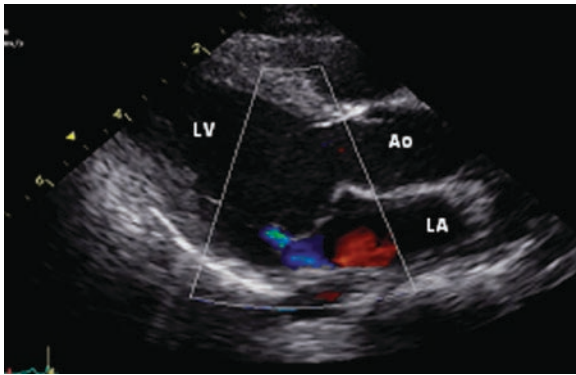


Fig. 27.11 Echocardiography long axis view of a patient with Marfan syndrome, demonstrating mitral valve prolapse and dilation of the sinuses of Valsalva

both the aorta and the low pressure left atrium. Left ventricular wall stress (afterload) is reduced secondary to the significantly decreased outflow resistance. However, increased left atrial volume leads to increased left atrial pressure, both of which are transmitted to the left ventricle, increasing both left ventricular end-diastolic volume and pressure. The stroke volume and left ventricular work increase, yet aortic flow decreases [86, 87]. Both acute and chronic dilation of the left atrium from MR lead to elevated left atrial pressure and reduced pulmonary venous return to the left atrium, with consequent increased pulmonary venous pressure and reflex pulmonary arteriolar vasoconstriction. This further results in right ventricular hypertension and right ventricular dysfunction. Annular dilation occurs as a consequence of left atrial and left ventricular dilation, which further exacerbates MR. Severe left atrial dilation increases the risk of atrial arrhythmias and of respiratory compromise from left mainstem bronchial compression, reduced lung capacity, and pulmonary edema from elevated pulmonary capillary hydrostatic pressure.

27.3.1 Acute Severe Mitral Regurgitation

In acute severe MR, the sudden volume overload imposed on the left atrium increases LV preload, which modifies the inotropic state and results in a modest increase in left ventricular stroke volume. As compensatory hypertrophy has not occurred, the ability of the left ventricle to continue to make adjustments in inotropic state is limited; forward stroke volume and cardiac output are soon reduced [86, 87].

27.3.2 Chronic Compensated Mitral Regurgitation

In chronic compensated MR, a series of new sarcomeres are added to existing myocytes, thereby increasing individual myocardial fiber length and adjusting the length–tension relationship to allow the left ventricle to bear the volume load, increase performance, and maintain forward cardiac output [86, 87].

27.3.3 Chronic Decompensated Mitral Regurgitation

In chronic decompensated MR, chronic left atrial volume and pressure overload are transmitted to the left ventricle, resulting in impaired contractile function and ejection such that ejection fraction decreases, end-systolic volume increases, and cardiac failure ensues. A normal ejection fraction can be a sign that heralds left ventricular dysfunction. Indeed, intervention for MR should be considered prior to the onset of left ventricular dysfunction, as left ventricular dysfunction may not be reversible even with mitral valve surgery [86, 87].

27.4 Physical Examination in Mitral Regurgitation

The physical exam of a patient with MR is characterized by a pansystolic murmur loudest at the apex and radiating to the left axilla and to the back. The first heart sound is usually diminished and the second heart sound is split.

Other clinical features on physical examination often include:

- A displaced LV apical impulse from chronic severe MR
- An apical thrill, though significantly impaired LV function may attenuate this finding
- A loud P2, in the setting of severe pulmonary hypertension
- An S3, heard immediately after S2, from the rapid, large volume flow into the LV

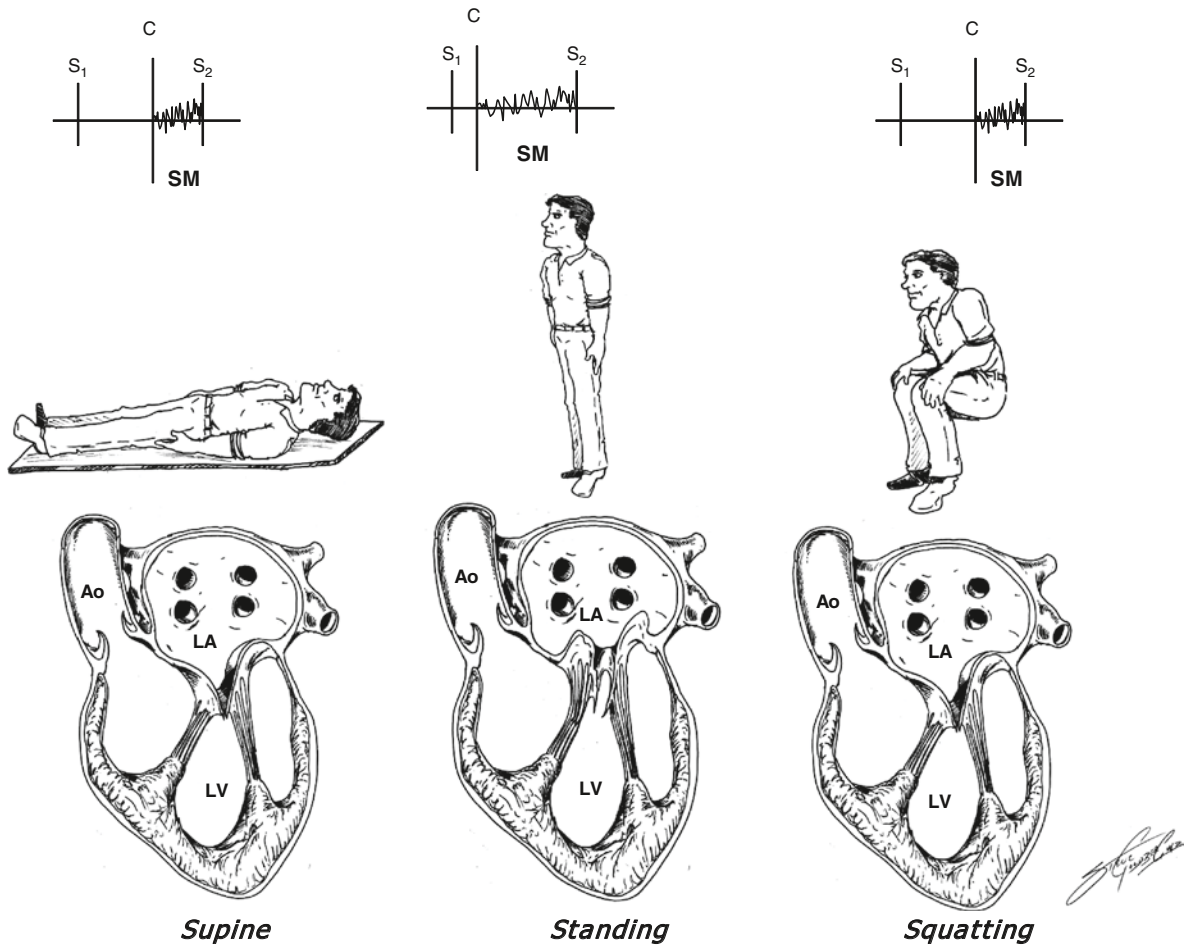


Fig. 27.12 Postural changes and auscultatory phenomena in patients with mitral valve prolapse, with alteration of systolic click (C) and systolic murmur (SM). As the LV volume decreases

- An S4, heard immediately before S1, from flow into noncompliant or stiff ventricle during atrial contraction
- Small volume peripheral pulses with sharp upstroke

27.4.1 Mitral Valve Prolapse

The physical exam is characterized by a systolic click that varies with postural change. The systolic click moves towards S1 with upright position and new click may appear. The systolic murmur of MR becomes louder and longer in duration (holosystolic). A MR murmur may be present only with the patient in the upright position. Rarely, a systolic precordial “honk” may be heard. Prompt squatting results in a movement of the systolic click away from S1 and

(upright position), the systolic click moves towards the first heart sound (S1) and the murmur becomes more holosystolic [87] (drawing from Steven P. Goldberg, MD)

the systolic murmur of MR moves back to late systole. These postural changes are related primarily to change in left ventricular volume, myocardial contractility and heart rate (Fig. 27.12). Left ventricular volume is decreased in the upright position compared to the supine position, and reflex tachycardia occurs in the supine position [88].

27.5 Preoperative Management

Several diagnostic studies are likely to be valuable in guiding clinical management of patients who come to the ICU with decompensated cardiac failure secondary to mitral valve disease, regardless of whether the etiology of mitral valve disease is MFS, rheumatic fever, or congenital malformation:

- Electrocardiogram: to establish heart rhythm, and to detect signs of ischemia, strain, and chamber enlargement.
 - Ventricular strain can often be demonstrated with ventricular failure from decompensated valvar insufficiency.
 - Signs of left ventricular strain
 - * ST depression with upward convexity in left precordial leads
 - * T-wave inversion in left precordial leads
 - * ST elevation in right precordial leads
 - * Tall T waves in right precordial leads
 - Signs of right ventricular strain
 - * ST segment depression in right precordial leads
 - * Wide QRS-T angle $>90^\circ$
 - Chamber enlargement and pulmonary hypertension associated with chronic mitral valve disease may be demonstrated.
 - Signs of left atrial enlargement:
 - * Left axis deviation
 - * First-degree atrioventricular block
 - * Broad notched P waves in leads I, II, aVF
 - * Biphasic P wave in lead V1 with deep portion of negative deflection
 - Signs of left ventricular enlargement:
 - * Tall R wave in V6
 - * Deep S wave in V1
 - * Deep Q waves in lead III (≥ 4 mm) or V6 (≥ 5 mm)
 - Signs of right ventricular hypertrophy suggestive of pulmonary hypertension:
 - * Tall R wave in V1
 - * Deep S wave in V6
 - * qR pattern in V1
- Chest X-ray: to establish heart size and evaluate pulmonary edema. Left atrial enlargement is seen as elevation of the left main stem bronchus with opening of the carina's angle on the antero-posterior projection.
- Echocardiography: to quantify severity of valvar regurgitation and LV dysfunction; to delineate the mechanism of valvar regurgitation, including assessment of:
 - Aortic root dimensions: annulus, sinus of Valsalva, sinotubular junction, ascending aorta (Fig. 27.4)
 - Pattern of aortic root dilation: loss of sinotubular junction contour associated with increased risk of dissection [89].
 - Mitral annulus size and shape
 - Valvular function
 - * Leaflet anatomy: number, size, location, and location of commissures to predict
 - * Location and spacing of papillary muscles
 - * Leaflet morphology: elongated, thickened, calcified, myxomatous, vegetations
 - * Leaflet motion: normal, flail, prolapsed, restricted
 - * Leaflet function: mechanism and adequacy of leaflet coaptation
 - Subvalvular apparatus
 - * Papillary muscle architecture, number, symmetry, and positioning, particularly relative to the commissures
 - * Presence of endocardiofibroelastosis as a marker of the adequacy of subendocardial perfusion
 - * Chordae structure and function
 - Left atrial size
 - Size and direction of regurgitant jets to ascertain mechanism of valvar pathology
 - Atrial septal geometry; septal bowing
 - Left ventricular size (end-systolic volume and dimension) and function, including wall motion abnormalities
 - Estimation of left atrial pressure
 - Estimation of regurgitant fraction (mitral or aortic regurgitation)
 - Estimation of mean mitral gradient (mitral stenosis)
 - Estimation of right ventricular and pulmonary artery pressures
- Transesophageal echocardiography can be a valuable tool for preoperative assessment, particularly if the transthoracic echocardiogram is compromised by poor acoustic windows.
- 3D echocardiography is an emerging tool that may provide useful imaging of abnormal valves.
- Cardiac catheterization: indications include assessment of pulmonary vascular reactivity in pulmonary hypertension, or investigation of mitral stenosis, in which case there is a pressure gradient between the "a" pressure wave of the left atrium and the left ventricular end-diastolic pressure. The left atrial pressure is elevated in either mitral stenosis or MR.
- Cardiac MRI: can be used to generate cardiac volumetric data; to delineate ventricular function;

and to demonstrate a panoramic view of the thoracic aorta.

- Laboratory data: such as BNP, CKMB, troponin I, lactate, BUN, creatinine, hepatic function tests, and blood gases are often useful to establish biochemical evidence of circulatory shock. Serologic markers for inflammation, such as CRP, ESR and procalcitonin [24] are useful when rheumatic fever or endocarditis is suspected.
- Blood culture (3 mL in infants; 10 mL adolescents): may be considered if bacterial endocarditis is suspected as the etiology for decompensation.

27.5.1 Clinical Monitoring

The clinical management of patients who are admitted to the ICU with cardiovascular embarrassment from mitral valve dysfunction secondary to MFS, RF, or congenital mitral valve malformations begins with airway, respiratory, cardiac, and circulatory stabilization.

27.5.2 Monitoring

Patients with hemodynamic compromise often require routine continuous cardiovascular monitoring, which includes:

- Continuous cardiorespiratory monitoring with telemetry
- Central venous pressure monitoring
- Continuous arterial pressure monitoring, with attention to the pulse wave contour
- Occasional pulmonary artery pressure monitoring
- Continuous or intermittent central venous saturation to monitor adequacy of global tissue oxygen delivery; progression of cardiac failure; response to therapeutic interventions
- NIRS (near infrared spectroscopy) may be a useful tool to monitor changes in regional oxyhemoglobin saturation, particularly of the frontal lobes of the brain, and also of the kidney and gut
- Continuous urine output monitoring via Foley catheter
- Serial echocardiographic assessment, especially in the setting of severely compromised left ventricular function, to monitor for clot and embolism risk,

progression of cardiac failure, response to therapeutic interventions

- Serial laboratory monitoring for biochemical evidence for adequacy of global oxygen delivery

27.6 Medical Management

27.6.1 Medical Management of Marfan Syndrome

The medical management of each cardiovascular lesion focuses on the hemodynamic consequence of the lesion, irrespective of its etiology.

Decompensated cardiac failure is treated with preload reduction through diuresis, afterload reduction through vasodilation, and ventricular performance augmentation with inotropes and inodilators. The recommended drug of choice for this purpose is milrinone.

Many patients with MFS are on chronic beta-blockade therapy to decrease inotropy, chronotropy, ectopy, and aortic wall stress [90]. Chronic beta-blockade therapy may complicate the treatment of acute decompensated heart failure by rendering the myocardium less responsive to catecholamine infusion. For this reason, phosphodiesterase inhibitors, such as milrinone, and calcium sensitizers, such as levosimendan, may be preferable, as they increase contractility through increasing cAMP and improving the calcium-troponin C interaction, respectively, without specifically requiring adrenergic receptor stimulation.

In MFS patients with acute decompensated heart failure complicated by ventricular dysrhythmias and fibrillation, catecholamine infusion may decrease the defibrillation threshold, possibly by increasing coronary artery perfusion [91].

27.6.2 Medical management of Rheumatic Fever

The goal of treatment for patients with rheumatic fever consists of:

- Symptomatic relief of acute inflammation
- Eradication of GABHS

- Prophylaxis against future infection to prevent recurrent cardiac disease
- Supportive treatment of heart failure

27.6.2.1 Anti-inflammatory Treatment

Treatment of the inflammatory manifestations of acute rheumatic fever uses salicylates and steroids. Aspirin in anti-inflammatory doses (80–100 mg/kg/day in children and 4–8 g/day in adults) effectively reduces all manifestations of the disease except chorea, and the response typically is dramatic [92]. Target salicylate blood level is 20–30 mg/dL. Aspirin should be maintained at anti-inflammatory doses until the signs and symptoms of acute rheumatic fever are resolved or resolving (6–8 weeks) and the acute phase reactants (CRP, ESR) have returned to normal. When discontinuing therapy, Aspirin should be withdrawn gradually over weeks while monitoring the CRP and ESR for rebound.

In patients with moderate-to-severe carditis, oral prednisone (2 mg/kg/day) is usually used for 2–4 weeks, but studies on the effect of corticosteroids in the treatment of rheumatic carditis have shown conflicting results [93–97]. Prednisone should then be tapered over 2 weeks, while maintaining salicylates for an additional 2–4 weeks.

Chorea is most frequently self-limited, but may be alleviated with phenobarbital or diazepam.

27.6.2.2 Eradication of GABHS (Primary Prophylaxis)

Antibiotic therapy with oral penicillin V (250 mg tid for children and 500 mg tid for adults) should be started and maintained for 10 days regardless of the presence or absence of pharyngitis at the time of diagnosis [98].

A single dose of intramuscular benzathine penicillin G (600,000 Units for children <27 kg and 1.2 million units in children >27 kg and adults) is an alternative if compliance is an issue (Table 27.3). For patients who are allergic to penicillin, erythromycin can be used. Other options include clarithromycin, azithromycin, or a first-generation cephalosporin.

For recurrent GABHS pharyngitis, a second 10-day course of the same antibiotic may be repeated. GABHS carriage is difficult to eradicate with conventional penicillin therapy. Thus, oral clindamycin (20 mg/kg/day for 10 days) is recommended.

27.6.2.3 Prophylaxis of Recurrence (Secondary Prophylaxis)

Prophylactic therapy is indicated after rheumatic fever to prevent recurrent streptococcal infection and further damage to the valves [99, 100]. Antibiotic prophylaxis should be started immediately after resolution of the acute episode [101, 102].

- An injection of benzathine penicillin G intramuscularly (600,000 Units for children <27 kg and 1.2 million units in children >27 kg and adults) every 4 weeks is the recommended regimen for most patients. In areas where rheumatic fever is endemic, in patients with residual carditis and in high risk patients, the administration should be made every 3 weeks [103].
- In patients with valve prosthesis under anticoagulation, oral penicillin V (250 mg twice daily for children and adults) prophylaxis should be used (Table 27.4). Data from the World Health Organization indicate that the recurrence risk of GABHS pharyngitis is lower when penicillin is administered parentally.

Table 27.3 Primary prophylaxis of rheumatic fever

Agent	Dose	Mode	Duration
Benzathine Penicilline	≤27 kg: 600,000 U	Intramuscular	Once
	>27 kg: 1,200,000 U	Intramuscular	Once
Penicillin V	Children: 250 mg 2–3 times daily	Oral	10 days
	Adolescents/Adults: 500 mg 2–3 times daily	Oral	10 days
Allergy to Penicillin: Erythromycin	20–40 mg/kg/day 2–4 times daily (maximum 1 g/day)	Oral	10 days

Table 27.4 Secondary prophylaxis of rheumatic fever

Agent	Dose	Mode
Benzathine Penicillin	1,200,000 U every 4 weeks (every 3 weeks for high risk patients)	Intramuscular
Penicillin V Allergy to Penicillin:	250 mg twice daily	Oral
Erythromycin	250 mg twice daily	Oral

Table 27.5 Duration of secondary prophylaxis of rheumatic fever

Category	Duration
RF with carditis and residual heart disease	10 years or greater since last episode and at least until age 40, sometimes life-long prophylaxis
RF with carditis but no residual heart disease	10 years or well into adulthood, whichever is longer
RF without carditis	5 years or until age 21, whichever is longer

The duration of antibiotic prophylaxis is controversial. The American Heart Association currently recommends [102, 104] that patients with rheumatic fever without carditis receive prophylactic antibiotics for 5 years or until aged 21 years, whichever is longer, and that patients with carditis but no valve disease receive prophylactic antibiotics for 10 years or until they are well into adulthood and that patients with carditis and valve disease receive antibiotics at least 10 years or until aged 40 years (Table 27.5) [105].

27.6.3 Medical Management of Congestive Heart Failure

Treatment of congestive heart failure includes inotropic support, diuretics, afterload reduction, supplemental oxygen, bed rest, and sodium and fluid restriction.

Patients with congestive heart failure from acute valve insufficiency will probably require continuous intravenous inotropic support. The beneficial role of digoxin in cardiac failure is controversial [106–108]. Digoxin should be started only after checking serum electrolytes due to the increased toxicity of digoxin with hypokalemia.

Diuretics frequently are used in conjunction with inotropic agents. Furosemide is usually the first choice. Spironolactone is often added in conjunction with furosemide as a potassium-sparing diuretic.

Afterload reduction with angiotensin converting enzyme inhibitors (ACE inhibitor) may be effective in improving cardiac output, particularly in the presence of mitral and aortic insufficiency [109]. Captopril is used in infant <6 months, while enalapril is usually preferred in older children related to its longer half-life. ACE inhibitors should be started carefully with a small, initial test dose because some patients have an abnormally large response to these agents with hypotension. ACE inhibitors should be administered only after correcting hypovolemia.

Potassium supplementation may be necessary because of the mineralocorticoid effect of corticosteroid and the salt wasting effect of the diuretics. Potassium level should be maintained in the normal range particularly in patients on digoxin.

When heart failure persists or worsens during the acute phase after aggressive medical therapy, surgery is indicated to decrease valve insufficiency.

27.6.3.1 Prophylaxis of Endocarditis

Patients with rheumatic heart disease and valve damage require a single dose of antibiotics 1 h before surgical and dental procedures to help prevent bacterial endocarditis [104, 110]. Patients who had rheumatic fever without valve damage do not need endocarditis prophylaxis. Penicillin, ampicillin, or amoxicillin should not be used for endocarditis prophylaxis in patients already receiving penicillin for secondary prophylaxis due to an increased relative resistance of oral streptococci to penicillin and aminopenicillins. Alternate drugs recommended by the American Heart Association for these patients include oral clindamycin (children: 20 mg/kg; adults: 600 mg), azithromycin or clarithromycin (children: 15 mg/kg; adults: 500 mg).

27.7 Interventional Catheterization

27.7.1 Percutaneous Balloon Mitral Valvuloplasty

Approximately 40% of patients with acute rheumatic fever subsequently develop mitral stenosis later in life. For patients with mitral stenosis who require relief of obstruction, percutaneous balloon mitral valvuloplasty is

the preferred treatment and gives results comparable to surgical commissurotomy [111]. 2D-echocardiographic assessment of mitral valve morphology is the most important predictor of outcome. An echocardiographic score can be determined according to the valvar and subvalvar mitral anatomy, with a score <8 predicting good immediate and long-term results [112, 113]. More details are discussed on the chapter dedicated to mitral stenosis.

27.7.2 Percutaneous Mitral Valve Repair

Percutaneous MR repair is an emerging area of interventional cardiology. Direct percutaneous repair of the mitral valve is undergoing trials using the Evalve mitral clip and Edwards mitral suture devices [114–116]. Additional data is needed to evaluate the long-term outcome of these techniques.

27.8 Surgical Management of Mitral Valve Diseases

27.8.1 Surgical Considerations

Optimal surgical management for MR remains controversial (Table 27.6). Surgical options consist of mitral annuloplasty, commissuroplasty, valvuloplasty, splitting of papillary muscles with resection of subvalvular apparatus, chordal substitution, chordal shortening or mitral valve replacement [117].

In MFS, the underlying connective tissue disorder is a risk factor for compromise of repair durability. In the majority of cases, MR is caused by leaflet prolapse, and in the remaining minority, by annulus dilatation. Marfan patients have more bileaflet and anterior mitral leaflet prolapse and present earlier for surgery when compared to patients with mitral myxomatous disease.

Table 27.6 Indication for surgery for chronic mitral regurgitation (MR) (From [126])

Symptoms	LV EF	LVESD
NYHA II – IV	>60%	<45 mm
Asymptomatic or symptomatic	50–60%	≥45 mm
Asymptomatic or symptomatic	<50%	or ≥45 mm
Pulmonary artery systolic pressure ≥50 mmHg		

Mitral valve repair feasibility is lower in MFS than in myxomatous valve disease. Nonetheless, despite the important elastic fiber alterations in leaflet tissue and the multisystem involvement, mitral valve repair in MFS gives satisfactory long-term results in terms of freedom from reoperation in children and even in adults presenting with advanced valve pathology.

In rheumatic fever, surgery to decrease valve insufficiency may be lifesaving when heart failure persists or worsens after aggressive medical therapy. Valve replacement appears to be the preferred surgical option for patients with high rates of recurrent symptoms after annuloplasty or other repair procedures. In children, mitral valvuloplasty is preferred [118].

27.8.2 Mitral Valve Repair

Many techniques for mitral valve repair have been described. Mitral valve repair without the use of prosthetic materials is feasible for the majority of patients and carries an appropriate growth pattern of the mitral valve annulus after surgery [119].

For repair of MR, valvuloplasty techniques are available to repair all four major components of the mitral valve apparatus: annulus, leaflets, chordae, and papillary muscles.

The annulus can be remodeled via commissuroplasty or annuloplasty using a Carpentier ring (metallic ring) or using a Kalangos or biodegradable ring [120]. The leaflets can be repaired, patched or extended with autologous pericardium, detached and reconstructed, or resected; the chordae can be shortened, transferred, fenestrated, or artificially implanted; the papillary muscles can be elongated, shortened or split.

For repair of mitral stenosis, fused mitral valve commissures can be directly incised; mitral valve excrescences can be excised or shaved; fused tendinous chords can be split; and supra-annular mitral rings can be directly excised. For repair of parachute mitral valve, splitting of a solitary papillary muscle and fenestration of the interchordal spaces can be performed.

Intraoperative assessment of the valve competency and motion is made by “floating” the mitral valve, or injecting and filling the left ventricle with iced saline solution to lift the valve leaflets and expose the valve function. A Hegar dilator is used to measure the mitral valve diameter to ensure normal orifice size for body

weight. Transesophageal echocardiography following separation from cardiopulmonary bypass is imperative for the assessment of mitral valve function. Results for operative interventions in MR are generally more favorable than those for mitral stenosis.

27.8.3 Mitral Valve Replacement

Mechanical valves are indicated when reconstructive procedures have failed in young children. Tissue valves are available but are disadvantageous, as they calcify and degenerate at an accelerated rate in small children [121]. The respective sizes of the patient and the prosthetic valve are the greatest considerations in selecting an artificial mitral valve.

Limited mechanical prosthetic valves are available for use in children, particularly in small children [122]. The bileaflet mechanical valve is the most commonly used in children. It can be sutured in the supra-annular position. A special design with a supra-annular sewing cuff is available for small children, which allows an effective valvar orifice situated at the annular level. Anticoagulation is compulsory; coumadin is used most commonly, with a target INR between 2.5–3.5. Unfortunately, complications are not uncommon. Indeed, mitral valve replacement in young children is associated with substantially increased risk of morbidity and mortality [123].

Complications following mitral valve replacement include:

- Complete atrioventricular block
- Atrial fibrillation
- Bleeding
- Thromboembolism
- Severe intravascular hemolysis
- Prosthetic valve dysfunction
- Prosthetic valve endocarditis

27.8.4 Minimally Invasive Surgery

Minimally invasive approaches have been increasingly described in adults and involve various modifications of the surgical approach, as in a small parasternal incision from the inferior border of the right second costal margin or a minithoracotomy. Cardiopulmonary

bypass is provided via the femoral vessels, and the aorta is internally cross-clamped with a balloon occlusion cannula. Advantages are diminished pain and discomfort and earlier hospital discharge.

27.9 Postoperative Management

27.9.1 Postoperative Monitoring

The postoperative monitoring of patients following mitral valve surgery is an extension of the monitoring and vigilance required in the preoperative period, including anticipation of common postoperative complications following mitral valve surgery. As with preoperative monitoring, postoperative monitoring should include:

- Continuous cardiorespiratory monitoring with telemetry that includes data recording and storage, which allows waveform review and analysis, as risk of atrial dysrhythmias is great in the patient with a dilated left atrium, and risk of ventricular dysrhythmias is increased in the patient with a dilated, poorly functioning left ventricle
- Central venous pressure monitoring
- Continuous arterial pressure monitoring, with attention to the pulse wave contour
- Pulmonary artery pressure monitoring, particularly in patients at risk for pulmonary vascular reactivity as in those with mitral valve stenosis
- Continuous or intermittent central venous saturation to monitor adequacy of global tissue oxygen delivery; progression of cardiac failure; response to therapeutic interventions
- NIRS may be a useful tool to monitor changes in regional oxyhemoglobin saturation, particularly of the frontal lobes of the brain, but also of the kidney and gut
- Continuous urine output monitoring via indwelling catheter
- Serial echocardiographic assessment, especially in the setting of severely compromised left ventricular function, to monitor for clot and embolism risk, progression of cardiac failure, response to therapeutic interventions
- Serial laboratory monitoring for biochemical evidence for adequacy of global oxygen delivery

Additionally, postoperative monitoring following mitral valve surgery should also include:

- Left atrial pressure monitoring, utilizing equipment with enough fidelity to appreciate differences and alterations in the “a” and “v” pressure waveforms
- Epicardial atrial and ventricular pacing wires, which allow epicardial electrocardiogram recordings that can be useful in the analysis of postoperative dysrhythmias

27.9.2 Postoperative Complications

Regardless of the etiology of mitral valve disease, whether by MFS, RF, or congenital malformation, mitral valve surgery requires excellent technical surgical results if significant postoperative complications are to be averted. Transesophageal echocardiography should be performed in the operating room following separation from cardiopulmonary bypass so that the surgical result can be assessed and immediately addressed with reoperation, if persistent regurgitation or stenosis is identified, particularly with associated left atrial hypertension. Consideration of the intravascular volume at the time of echocardiographic study is important, as hypovolemia leads to underestimation of the severity and hemodynamic consequence of residual lesions.

27.9.2.1 Left Atrial Hypertension

Causes of elevated left atrial pressure after mitral valve surgery are:

- Residual mitral valve regurgitation, which may be suggested by giant “v” waves on the left atrial pressure tracing
- Residual mitral valve stenosis, which may be suggested by large “a” waves on the left atrial pressure tracing
- Prosthetic mitral valve leaflet immobility, dysfunction, or thrombosis, which may also be suggested by large “a” waves on the left atrial pressure tracing
- Loss of atrioventricular synchrony, which may be suggested by canon “a” waves on the left atrial pressure tracing

- Left ventricular dysfunction
- Pericardial effusion
- Tension pneumothorax with cardiac tamponade

27.9.2.2 Pulmonary Hypertension

In patients with long-standing mitral valve stenosis or regurgitation, the pulmonary vascular changes of medial thickening and intimal fibrosis associated with progressive pulmonary vascular disease may complicate the postoperative course. Standard therapy for pulmonary hypertension should be administered as pulmonary hypertensive crises are common. In small children with valve replacement in supra-annular position, the relatively large prosthesis can impede pulmonary venous inflow or left ventricular inflow, thereby promoting pulmonary hypertensive crises. In patients with pulmonary hypertension and postoperative left ventricular dysfunction, or residual mitral valve dysfunction, cautious use of nitric oxide therapy is indicated, as the increased pulmonary venous return may worsen pulmonary hypertension or left ventricular dysfunction.

27.9.2.3 Low Cardiac Output

Low cardiac output syndrome can complicate any bypass surgery. Post mitral stenosis repair, decreased left ventricular compliance can lead to low cardiac output in the initial postoperative period. Post MR repair, adaptation of the left ventricular volume overload can lead to low cardiac output. Additionally, left ventricular function may be compromised by the significantly increased afterload associated with a newly competent valve. Therapy consists of maintenance of optimal heart rate either with atrial pacing or isoproterenol as the cardiac output is highly rate-dependent. Adequate preload should be maintained, but volume should be replaced slowly as excessive fluid infusion can lead to rapid left atrial pressure elevation and subsequent pulmonary hypertension crisis.

Adequate left ventricular filling pressure should be maintained to accommodate for diastolic dysfunction. Afterload reduction with milrinone infusion is beneficial to increase cardiac output, especially in patients with left ventricular dysfunction. Afterload reduction

may also be useful for reducing the hemodynamic consequences of residual MR. When poor cardiac output does not respond to conventional medical therapy, mechanical assistance may be necessary.

27.9.2.4 Arrhythmia

Atrial flutter, atrial fibrillation, multifocal atrial tachycardia secondary to chronic mitral valve disease and atrial dilation can complicate the postoperative period. Atrial arrhythmias are not well tolerated especially when left ventricular compliance is impaired. Management of such arrhythmia is essential in the early postoperative period in order to restore atrioventricular synchrony and optimize cardiac output.

27.9.2.5 Anticoagulation

Heparin infusion should be started when bleeding through the chest tubes have ceased and when the coagulation profile has normalized. A heparin bolus is initially administered followed by an infusion rate targeting a PTT of 50–70 s or a anti-Xa inhibition test for which units are 0.5–0.7 U/mL. When the intracardiac lines, the chest tubes and the pacing wires have been removed, transition to coumadin can be initiated.

27.9.2.6 Prosthetic Valve Malfunction

Proper function of the prosthetic valve should be carefully monitored, especially in small children with the prosthesis in a supra-annular position. Leaflet malfunction may be suspected on the basis of serial chest X-rays in which leaflet position is fixed (Fig. 27.13). When thrombosis is suspected, as in acute prosthetic valve dysfunction, streptokinase or tissue plasminogen activator therapy may be attempted. Chronic valve malfunction may be secondary to tissue entrapment of the valve leaflets. The surgical appearance is that of a pannus of tissue, which encroaches upon the valve leaflets. The usual presentation is intermittent left atrial hypertension and absence of a valve click.

27.9.3 Special Considerations of the Marfan Patient in the ICU

27.9.3.1 Respiratory

Patients with MFS and associated severe pectus deformity with kyphoscoliosis often have reduced lung volumes and can be anticipated to demonstrate varying degrees of respiratory insufficiency, pulmonary hypertension, and right heart dysfunction when hospitalized

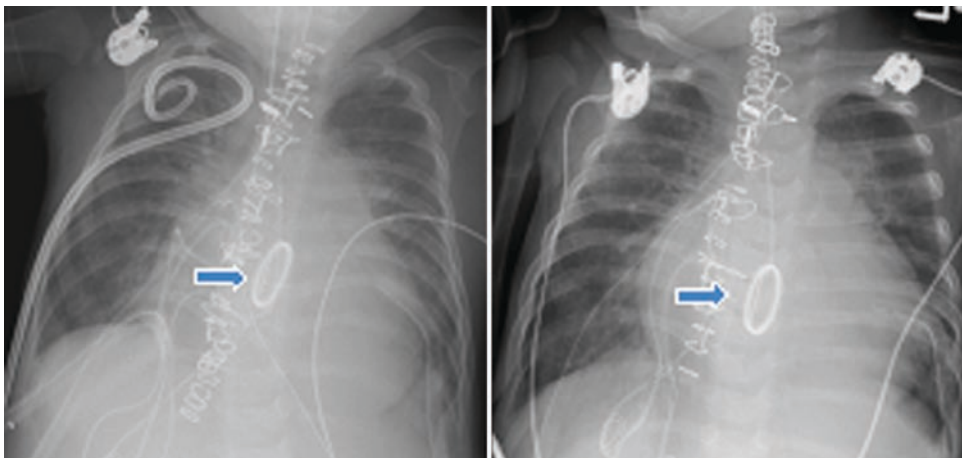


Fig. 27.13 Serial chest X-rays on a patient with a #16 ATS prosthesis turned upside down in the mitral position. A malfunctioning posterior leaflet (arrows) is fixed in position, contributing to the patient's failure to progress from continuous positive airway pressure

in the intensive care unit for management of either decompensated cardiac failure or postoperative intervention. Additionally, patients with MFS are at increased risk for spontaneous pneumothoraces and should be considered in the differential diagnosis in the MFS patient with sudden decompensation.

27.9.3.2 Abdominal

Patients with MFS and associated aortic dilation are at risk for dissection of the abdominal aorta, which can cause mesenteric ischemia and bowel perforation. Heightened awareness of this complication should accompany assessment of abdominal pain in the patient with MFS.

27.9.3.3 Orthopedic

Consideration of cardiac position should be made in the MFS patient with kyphoscoliosis and significant pectus deformities with or without repair, as standard cardiac compression techniques may be ineffective in this population. Nuss bar surgical correction of severe pectus deformities may also complicate resuscitative procedures in the intensive care unit.

27.9.3.4 Sudden Death

MFS patients are at increased risk of ventricular arrhythmia and sudden death.

27.9.4 Long Term Outcome

27.9.4.1 Prognosis of Marfan Syndrome

Long term outcome in MFS patients is determined by the severity of cardiovascular manifestations. Neonates with phenotypic expression of MFS and cardiovascular involvement are most severely affected, and often do not survive past 2 years of age without multiple valve replacements or heart transplantation. Children with MFS and mitral valve involvement can also have significantly limited lifespans, particularly if valve

dysfunction is rapidly progressive and accompanied by compromised ventricular function. Perisurgical complications related to mitral valve replacement denote the greatest risk of mortality in young patients with MFS. Alternatively, mitral valve disease can often be slowly progressive, with increased risk to female patients in the second and third decades of life.

Aortic root dilation and dissection often occurs in the third and fourth decades, such that by age 40, the risk of fatal aortic dissection is considerable without surgical intervention. Since the association between aortic aneurysm diameter and risk for dissection and rupture is clearly established, echocardiographic aortic root surveillance is the gold standard (Fig. 27.2). Aortic root replacement surgery is recommended for aortic diameter greater than or equal to 5.0 cm; rapid growth of aortic diameter (>1 cm/year); a family history of premature aortic dissection at <5 cm; and the presence of greater than mild aortic regurgitation. Compared with urgent and emergency replacement of the aortic root, prophylactic aortic root replacement is associated with excellent results in the modern surgical era: 93.5% survival at 5 years; 91% survival at 10 years; 59% survival at 20 years [124, 125].

27.9.4.2 Prognosis of Rheumatic Fever

The manifestations of acute rheumatic fever resolve during a period of 3–4 months in the majority of patients. Rheumatic heart disease is the major cause of morbidity after rheumatic fever and it is the major cause of mitral insufficiency and stenosis in the world. Variables that correlate with severity of valve disease are the number of previous attacks, the length of time between the onset of disease and beginning of treatment, and the sex, the prognosis being worse for females. Without recurrent attacks, valve insufficiency resolves in 70–80% of patients. In patients with carditis and valve insufficiency, numerous factors (severity of initial carditis, presence of recurrences, time elapsed since rheumatic fever) affect the likelihood that valve abnormalities and the murmur will disappear.

Following the development of antibiotics, the mortality rate in developed countries has decreased to nearly 0%, but has remained 1–10% in developing countries. Prior to penicillin, 60–70% of patients developed valve disease after acute rheumatic fever as opposed to 9–39% nowadays.

27.9.4.3 Prognosis After Mitral Valve Repair

Prognosis after mitral valve repair is good with an event-free rate at 15 years of about 73% [126]. The current risk of mitral valve reoperation in the pediatric age group is low, and the long-term results are satisfactory, irrespective of severe deformation of the mitral valve apparatus and associated complex cardiac anomalies [117]. Patients with significant associated congenital cardiac abnormalities are at a higher risk of early death after mitral reconstructive surgery. Mitral repair with a technique that allows annular growth is possible in most children with good long-term functional results [127].

27.9.4.4 Prognosis After Mitral Valve Replacement

Mitral valve replacement is an accepted alternative when the valve cannot be repaired, with a reported freedom from reoperation of 66–86% [126, 128]. A multi-institutional study reported a 1 year survival of 79%, a 5 years survival of 75% and a 10 years survival of 74% for children <5 years of age [128]. The majority of deaths occur early after initial replacement, with little late attrition despite repeat MVR and chronic anticoagulation. Adverse outcome is common, particularly in the young child undergoing palliative surgery or requiring additional surgical procedures [129]. Complications include heart block requiring pacemaker, endocarditis, thrombosis, and stroke [128]. Complete atrioventricular canal, Shone's syndrome and increased ratio of prosthetic valve size to patient weight increase the risk of adverse outcome. Reasons for second mitral valve replacement are prosthetic valve stenosis in the majority of cases, thrombosis or endocarditis [129]. Younger patients (<2 years), low weight, smaller prostheses (<20 mm) and greater ratio of prosthesis size to body size were risk factors for second mitral valve replacement [129].

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Chapter 28

Mitral Stenosis

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28.1 Introduction

When considered separately from mitral valve anomalies associated with atrioventricular septal defects and with hypoplastic left heart syndrome, congenital mitral valve malformations resulting in mitral stenosis are rare. Reported prevalence is 0.4–0.5% of congenital heart defects [1–3]. Acquired mitral stenosis is primarily related to rheumatic heart disease and, though uncommon in the United States, remains a considerable problem for children worldwide.

28.2 Anatomy

In a normally formed mitral valve apparatus, the anterior leaflet attaches to the anteromedial one-third of the annulus and inserts into the anterolateral papillary muscle. The posterior leaflet attaches to the posterolateral two-thirds of the annulus and inserts into the posteromedial papillary muscle [3]. The chordae tendineae attach the undersurface of the mitral valve leaflets to the papillary muscles. These divide into primary, secondary, and tertiary chordae starting from the papillary muscles with progressive branching to insertion into the leaflets [2].

Congenital mitral stenosis results from anatomic deformity of one or multiple portions of the mitral valve apparatus (Fig. 28.1). Isolated or combined abnormalities of the annulus, leaflets, chordae tendineae, and papillary muscles can result in stenosis at the valvar,

subvalvar, and supravalar levels. Malformations resulting in reduction of the effective mitral valve orifice include hypoplasia of the valve annulus, fusion of the commissures, and thickened valve leaflets with rolled, dysplastic edges. Shortened, fused, thickened chordae tendinae may limit mitral valve mobility and reduce the secondary orifice area, normally created by the interchordal spaces [4]. The papillary muscles may be normal, underdeveloped, fused, or abnormally positioned resulting in a decreased intrapapillary distance and affecting mobility of the mitral valve [2]. The lesions responsible for congenital mitral stenosis include typical (symmetric) mitral stenosis, parachute mitral valve, parachute-like asymmetric mitral valve, mitral arcade, double orifice mitral valve, and supravalar mitral ring. Cor triatriatum is similar in terms of clinical presentation and pathophysiology to mitral stenosis, but results from formation of an accessory membrane related to abnormal pulmonary venous incorporation into the wall of the left atrium during embryologic development.

Congenital mitral stenosis can be classified in the following anatomic groups:

- a. Typical symmetric mitral stenosis
- b. Parachute mitral valve
- c. Mitral arcade
- d. Double orifice mitral valve
- e. Supravalar mitral ring

Sometimes a combination of lesions is present.

Typical (symmetric) congenital mitral valve stenosis involves abnormalities of several portions of the apparatus including hypoplasia of the valve annulus, dysplastic valve leaflets, short and thick chordae tendinae, and small symmetric closely spaced papillary muscles [3, 5].

Parachute mitral valve refers to an abnormality resulting from shortened thickened chordae tendinae

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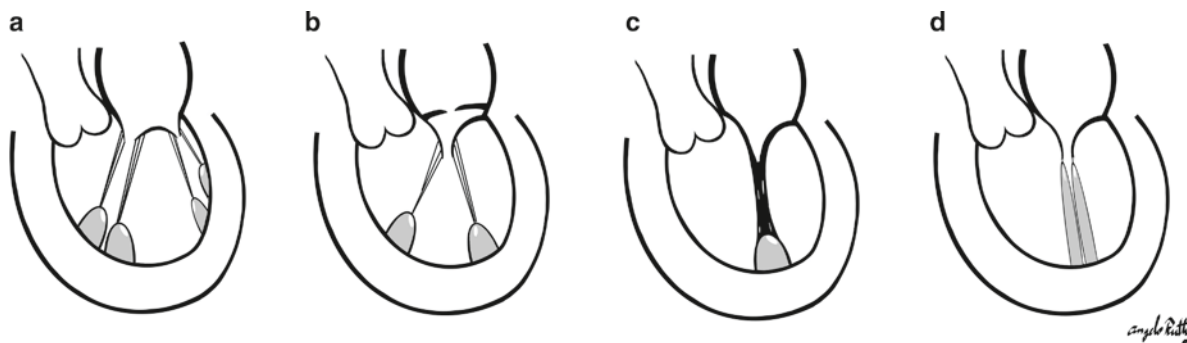


Fig. 28.1 Types of congenital mitral stenosis. (a) double orifice mitral valve, (b) supravalvar mitral ring, (c) “parachute” mitral valve, (d) “hammock” mitral valve

from both mitral valve leaflets inserting into a single papillary muscle limiting leaflet mobility [4, 6]. Most patients with parachute mitral valve have additional cardiac lesions. Commonly associated defects include coarctation of the aorta, bicuspid aortic valve, subvalvar aortic stenosis, left ventricular hypoplasia, valvar aortic stenosis, and supravalvar mitral stenosis as well as atrial septal defect, ventricular septal defect, patent ductus arteriosus, and other more complex cardiac lesions [6]. Patients with parachute mitral valve and atrial septal defect often have more severe left heart lesions and are more likely to be selected for non-biventricular repair than patients without an atrial septal defect. This is likely reflective of the fetal physiology associated with the underdevelopment of the left sided structures.

Parachute-like asymmetric mitral valve involves a lesion with two asymmetric papillary muscles. The dominant papillary muscle is elongated, displaced toward the mitral valve annulus, positioned higher in the left ventricle, and attached along its base and lateral side to the left ventricular wall. The chordae tendinae attach predominantly to one papillary muscle, limiting mitral valve mobility and reducing the effective mitral valve orifice [6, 7].

Mitral arcade or hammock mitral valve occurs when the papillary muscles continue as a muscular structure to the free edge of the leaflets, with absence or near absence of the chordae tendinae, resulting in obstruction to left ventricular inflow [2, 4].

Double orifice mitral valve can be complete or incomplete, symmetric or asymmetric. The two openings can be created by an adhesion between the two leaflets [8], by a hole-type lesion creating a secondary orifice in the lateral commissure [9], or by the presence

of redundant leaflet tissue forming a bridge between the anterior and posterior leaflets [10]. Double orifice mitral valve can manifest with mitral regurgitation, mitral stenosis, or a combination thereof. It is associated with both partial and complete atrio-ventricular septal defects and obstructive left-sided lesions, as well as with more complex congenital heart disease [11].

A *supravalvar mitral ring* is created by a circumferential shelf-like ridge of connective tissue attached to the atrial surface of the mitral valves [2, 4]. It can be partial or complete, and becomes obstructive if it interferes with the primary mitral valve orifice [4, 8]. Although a supravalvar mitral ring can rarely occur as an isolated lesion, the majority are associated with other mitral valve defects [2]. Therefore, close evaluation of the entire mitral valve apparatus is required when a supravalvar mitral ring is identified. Likewise, careful echocardiographic evaluation for the presence of a supravalvar mitral ring should be undertaken when other mitral valve anomalies are present. The supravalvar mitral ring can be differentiated from cor triatriatum by its position below the left atrial appendage [8].

Shone’s complex, described in 1963 by Shone, Sellers, and Anderson [12], refers to the combination of four lesions including supravalvar mitral ring, parachute mitral valve, sub aortic stenosis, and coarctation of the aorta. The term is generally used whenever there is mitral valve disease associated with left ventricular outflow tract obstruction and aortic arch obstruction.

Acquired mitral stenosis is most frequently secondary to rheumatic carditis, and results from thickening, calcification, fibrosis, and eventual fusion of the mitral valve leaflets, commissures, and chordae tendinae, forming a funnel-shaped valve [13–15]. In the pediatric

population in the United States, acquired mitral stenosis from rheumatic carditis is uncommon. A specific chapter in this book further discusses this disease.

Other conditions can also cause abnormalities in the mitral valve and should be considered in the differential diagnosis for mitral stenosis. These include systemic lupus erythematosus, malignant carcinoid, rheumatoid arthritis, polyvalvar mucoid congenital disease, and mucopolysaccharidosis of the Hunter–Hurler phenotype, Fabry disease, and Whipple disease [13, 16]. Lutembacher syndrome refers to the combination of mitral stenosis with an atrial septal defect [13, 15].

28.2.1 Pathophysiology

Abnormalities of the mitral valve apparatus result in a reduced effective valve orifice area and obstruction to left ventricular filling. A diastolic gradient is generated between the left atrium and left ventricle due to the reduced size of the effective mitral valve orifice. The mitral valve gradient is determined by the size of the opening and by the amount of diastolic inflow, and therefore, depends on cardiac output and the length of time for diastole filling [15]. As the area of the valve decreases, a higher transmitral gradient and an increased left atrial pressure are required to maintain cardiac output [13]. Elevated left atrial pressure is then transmitted to the pulmonary venous system, raising the pulmonary venous and pulmonary capillary pressures. Pulmonary edema develops when the hydrostatic pressure of the pulmonary vascular bed exceeds the plasma oncotic pressure [3, 16]. Long-standing pulmonary venous hypertension and pulmonary congestion result in elevated pulmonary arterial pressure, pulmonary alveolar fibrosis, and thickening of the pulmonary arteriole bed with reduced pulmonary compliance [13, 14, 17]. Changes and congestion in the pulmonary vascular bed affect ventilation by compressing small bronchiolar airways and alter the mechanics of gas exchange [3]. Respiratory symptoms are therefore often the first manifestation of disease in patients with significant mitral valve stenosis. The relationship between mitral valve area, diastolic filling time, heart rate, and cardiac output is explained by the Gorlin formula, as follows [18].

$$\text{Mitral valve area} = \frac{\text{diastolic flow (mL/s)}}{(31.5) \times (\text{square root of mean diastolic gradient})}$$

$$\text{where diastolic flow} = \frac{(\text{C. O.}) \times (\text{RR interval})}{(60) \times (\text{diastolic filling time})}$$

Patients develop symptoms with exercise or in other situations with tachycardia and demand for increased cardiac output. Because the area of the mitral valve orifice is fixed, and there is less diastolic filling time with increasing heart rate, a higher transvalvar gradient, and higher left atrial pressure are required to maintain or increase cardiac output [13]. This is also manifest when previously asymptomatic women with mitral stenosis develop symptoms during pregnancy due to the requisite increase in cardiac output. Likewise, patients with atrial arrhythmias who have a rapid ventricular response develop exacerbation of symptoms due to tachycardia and to a decrease in the degree of ventricular filling that normally occurs with atrial systole [13].

With prolonged pulmonary venous hypertension and pulmonary edema, changes occur in the pulmonary arteriole bed and eventually result in pulmonary hypertension. With the development of pulmonary hypertension, there is pulmonary insufficiency, right ventricular dilation, dilation of the tricuspid valve annulus, and functional tricuspid valve regurgitation, which ultimately manifest as right heart failure. Mitral stenosis can also be exacerbated by coexistent mitral regurgitation, decreased left ventricular systolic or diastolic function, elevation of the left ventricular end diastolic pressure, and by other left sided obstructive lesions. The degree of mitral valve stenosis may be underestimated when there is a significant atrial septal defect as part of the cardiac output is diverted through the atrial septum, and these patients can have symptoms related to low cardiac output.

28.3 Clinical Presentation

Manifest symptoms with mitral stenosis are related to the degree of stenosis and are a reflection of elevated left atrial pressure, pulmonary venous congestion, and low cardiac output, development of pulmonary hypertension and right heart failure, or development of an arrhythmia.

Patients with mild mitral stenosis are usually asymptomatic. Those with moderate stenosis develop symptoms with exertion and those with severe stenosis often

have symptoms at rest. In adults, moderate mitral stenosis correlates with a mitral valve area of 1–2.5 cm², and severe mitral stenosis correlates to a mitral valve area of less than 1 cm². Initial presentation is most commonly due to symptoms with exertion described as decreased exercise tolerance in older children, and feeding difficulty in infants. Infants may present with increased work of breathing, fatigue or diaphoresis with feeds, recurrent respiratory infections, tachypnea, and failure to thrive [16, 19]. Older patients may complain of dyspnea with exertion, orthopnea, nocturnal dyspnea, chronic cough or wheezing, hemoptysis, and palpitations. Hemoptysis occurs due to rupture of dilated thin-walled bronchial vessels in the setting of long-standing pulmonary venous hypertension [13, 14], and atrial flutter and fibrillation are not uncommon in long-standing mitral stenosis. Patients with mitral stenosis should also be assessed for symptoms of hoarseness, which can occur if an enlarged left atrium causes compression of the recurrent laryngeal nerve [13, 16]. Patients who have pulmonary hypertension secondary to mitral stenosis will have fewer symptoms of lung congestion, and more complaints reflective of low cardiac output.

Physical findings are related to the degree of mitral stenosis, and to the presence or absence of pulmonary hypertension and right heart failure. The murmur of mitral stenosis is a low pitched diastolic rumble with presystolic accentuation, heard best at the apex and in the left lateral decubitus position [14–16]. The length of the diastolic murmur is directly related to the degree of mitral stenosis [15]. In patients with congenital mitral stenosis, S1 is either normal or of decreased intensity, and P2 is accentuated if pulmonary hypertension is present. With the development of pulmonary hypertension a right ventricular lift is present, and there may be a Graham Steell murmur of pulmonary insufficiency [15]. Signs of right heart failure include hepatomegaly, ascites, peripheral edema, and jugular venous distension. With rheumatic mitral stenosis, there is a loud opening snap after the second heart sound that is not present with congenital mitral stenosis [3, 16].

28.3.1 Chest X-ray

Chest film may demonstrate pulmonary congestion with redistribution of pulmonary blood flow to the upper lobes [14, 17], left atrial enlargement with

elevation of the left mainstem bronchus [2, 16], prominent pulmonary arteries, and right ventricular enlargement [14, 19].

28.3.2 ECG

Electrocardiogram shows a broad notched P wave in lead II due to left atrial enlargement, and right ventricular hypertrophy with right atrial enlargement once pulmonary hypertension develops. Atrial flutter and fibrillation are not uncommon in association with mitral stenosis.

28.3.3 Echocardiography

Transthoracic echocardiography is imperative for definition of mitral valve anatomy with careful attention to the morphology of the annulus, leaflets, chordae tendinae, papillary muscles, and supra-valvar area. Evaluation of left atrial size, mitral regurgitation, and for presence of an atrial septal defect and other associated cardiac anomalies is also performed. Any patient with abnormalities of the mitral valve apparatus must carefully be evaluated for the presence of an associated supra-valvar mitral ring that may contribute to stenosis and affect the management plan [20]. The mitral valve in congenital mitral stenosis is often dysplastic with thickened leaflets, rolled edges, and shortened tethered chordae tendinae [20]. The number, position, and relationship of the papillary muscles should be assessed. Right and left ventricular function are evaluated as are signs of pulmonary hypertension, and degree of tricuspid regurgitation. Doppler measurements are made of the peak and mean mitral valve gradient. The mean transmitral valve pressure gradient has fair correlation with the transmitral gradient measured by cardiac catheterization. Left atrial pressure can be estimated if an atrial level defect is present, and if the patient has an accurate central venous pressure available. Measurement of pressure half-time of mitral valve inflow reflects the time needed for the peak diastolic inflow velocity to decrease by 50% and is inversely proportional to the mitral valve area [15, 20]. As the severity of mitral stenosis increases, the pressure half-time lengthens. In children the mitral valve area can be

calculated at the time of cardiac catheterization by the Gorlin and Gorlin equation. In adults the mitral valve area can be estimated by echocardiography using an empirically derived constant (220) divided by the pressure half-time, with fair correlation to the area obtained with the Gorlin and Gorlin formula. The accuracy of this method has not been reliable in children when compared with mitral valve area obtained by calculation by the Gorlin formula, and is usually not used for pediatric patients [20, 21]. There are several other echocardiographic formulas for estimating mitral valve area in children including the continuity equation and the PISA (proximal isovelocity surface area) technique. Both are well described in standard echocardiography textbooks [20]. In the presence of an atrial septal defect, the severity of mitral valve stenosis may be underestimated; this should be considered during interpretation of the study. In adults mitral stenosis is categorized as mild if the mean gradient is less than 5 mmHg, moderate when the mean gradient is 5–10 mmHg, and severe when the mean gradient is greater than 10 mmHg [22]. In children, mild mitral stenosis has been defined as a mean gradient of less than 5 mmHg, moderate stenosis falls between 6 and 12 mmHg, and severe stenosis is described when the mean gradient is greater than 13 mmHg [19].

Transesophageal echocardiography may be indicated when transthoracic images are inadequate, or for evaluation for thrombus in patients with atrial flutter or fibrillation.

Exercise testing can be helpful for objective evaluation of functional capacity and to monitor for deterioration or improvement with time or intervention [17].

Cardiac catheterization is performed when additional diagnostic data is necessary or when interventional balloon mitral valvuloplasty is indicated. Data obtained at cardiac catheterization include standard right heart hemodynamic measurements, thermodilution cardiac output, and simultaneous left atrial and left ventricular pressure for direct assessment of the transmitral gradient (Fig. 28.2). The transmitral gradient is the diastolic gradient from the left atrial a wave to the left ventricular end diastolic pressure [16]. If no intervention is planned, and no atrial level defect is present for access to the left atrium, the transmitral gradient can be estimated by recording simultaneous pulmonary capillary wedge and left ventricular end diastolic pressures.

Patients with mild to moderate stenosis may have normal or mildly elevated pulmonary artery pressure. Those with severe mitral stenosis often have elevated pulmonary artery pressure, and elevated pulmonary

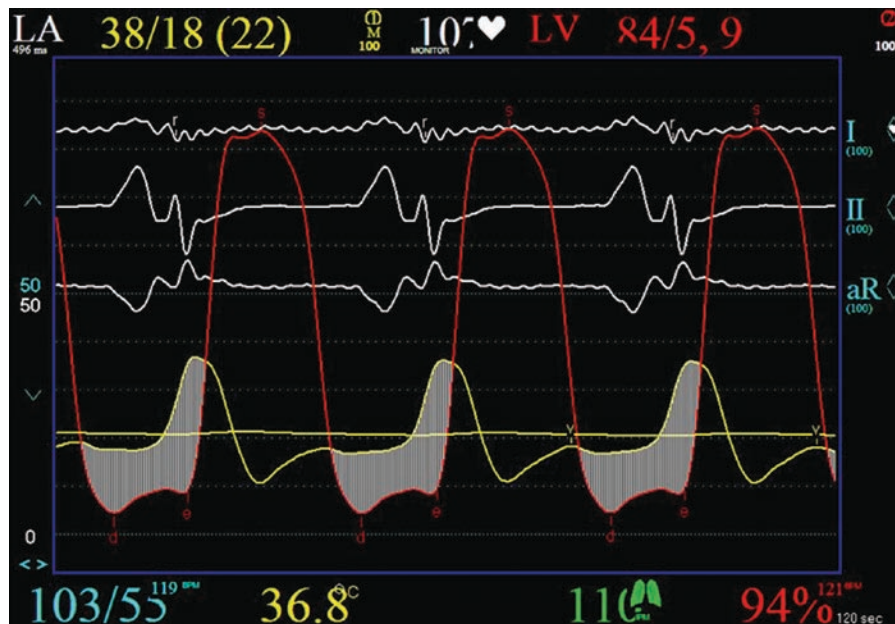


Fig. 28.2 Hemodynamic trace of simultaneous left atrial and left ventricular pressure measurements with the mean mitral valve gradient represented by the shaded area between the left atrial and left ventricular waveforms

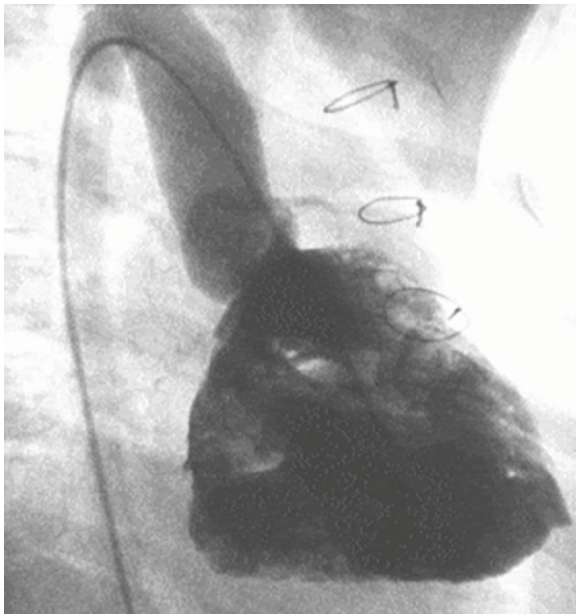


Fig. 28.3 Left ventricular angiography showing double orifice mitral valve

vascular resistance [13]. Angiography is performed of the left ventricle, left atrium, and other locations as indicated by severity of disease and presence of associated lesions (Fig. 28.3).

Hemodynamic assessment with supplemental oxygen and nitric oxide is performed as indicated related to the severity of pulmonary hypertension. Balloon dilation of the mitral valve should be considered in patients with severe congenital mitral stenosis in the absence of a supralvalvar mitral ring, and in those with significant rheumatic mitral valve stenosis. Surgical resection is the preferred intervention for stenosis related to a supralvalvar mitral ring. Balloon mitral valvuloplasty in children is performed with a standard low pressure angiography balloon (Fig. 28.4), or the specialized Inoue balloon. Double balloon technique may be necessary due to the relatively large mitral valve annulus size. Access to the mitral valve may require transeptal puncture with or without balloon dilation of the atrial septum [23]. Successful results from balloon valvuloplasty in adults and children with rheumatic mitral stenosis are comparable to surgical intervention [23], with an average reduction in the mitral valve gradient from 17 to 5.2 mmHg and improvement in mitral valve area from 0.84 to 2 cm² [24]. Mitral balloon valvuloplasty in children with rheumatic mitral stenosis has a 14.3% incidence of

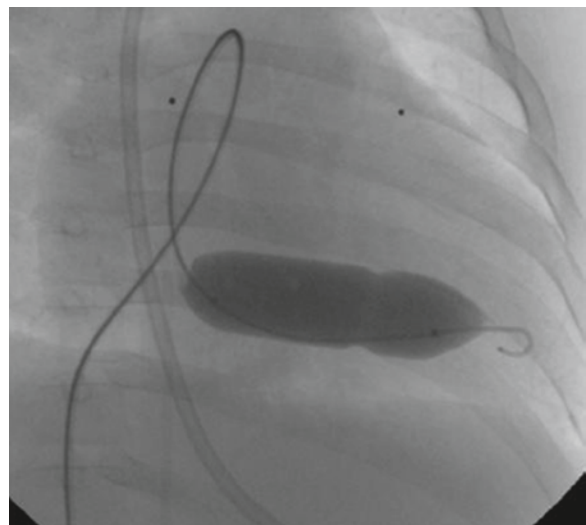


Fig. 28.4 Spot cine of inflation of a standard low pressure angioplasty balloon across the mitral valve

restenosis, and a 93% event free survival at 5 years and a 79% event free survival at 10 years [24]. Complication rates for balloon mitral valvuloplasty in children with rheumatic disease are similar to those in adults. Dilation of congenital mitral stenosis carries a higher risk of morbidity and mortality [23], and is often complicated by associated cardiac lesions. Despite the complexity of balloon valvuloplasty for congenital mitral valve stenosis, with increasing experience, results are improving. Lock reports 90% five-year survival in patients with typical congenital mitral stenosis who require balloon mitral valvuloplasty, with less than 2% of procedural mortality and an average delay of 4 years to surgical intervention [25].

28.3.4 Preoperative Management

Observation is often all that is required in asymptomatic patients with mild mitral stenosis as it is not usually progressive. In patients with more significant disease, medical management is used to reduce symptoms and delay the need for intervention.

Patients with mitral stenosis may be admitted to the intensive care unit with respiratory failure, low cardiac output syndrome, atrial arrhythmias, infectious endocarditis, or a combination thereof. In addition, these patients can be admitted after balloon valvuloplasty

for observation or treatment of complications related to the procedure.

Respiratory failure can be secondary to multiple factors including left atrial hypertension, pulmonary edema, pulmonary hypertension, and pneumonia, especially viral pneumonia secondary to respiratory syncytial virus.

Patients have limited ability to augment cardiac output to compensate for any increase in metabolic demand as inflow of blood across the mitral valve is obstructed. Prompt intervention with positive pressure ventilation will improve the ventilation perfusion mismatch. With mechanical ventilation, moderately high ventilatory settings are usually required including peak inspiratory and end expiratory pressures with pressure mode ventilation and tidal volume with volume mode ventilation. In the subset of patients with true elevation of pulmonary vascular resistance, inhaled nitric oxide is useful as a selective pulmonary vasodilator, though it can lead to an increase in left atrial pressure and pulmonary edema.

When the mitral valve area is small, the left atrial pressure should be kept appropriately high to maintain a sufficient transmitral gradient to sustain adequate cardiac output.

The relationship between the diastolic filling time, cardiac output, and the transvalvar gradient is also important to consider. The gradient across the mitral valve increases markedly with increased heart rate and cardiac output. It is always preferable to avoid tachycardia to allow appropriate time for left ventricular filling. Medical management should target slowing the heart rate. Immediate goals in an intensive care setting include: (1) normalization of temperature, (2) when necessary, use of inotropic agents and doses that cause the least tachycardia, (3) use of beta-blockers and calcium channel blockers for rate control in older children, though these agents are contraindicated in neonates and infants. Diuretics are added judiciously to decrease symptoms attributed to pulmonary venous congestion with attention to prevention of hypovolemia [2].

Right ventricular dysfunction may be present secondary to pulmonary artery hypertension. Diuretics, inotropic support, and optimization of the ventilation perfusion mismatch with decrease of pulmonary vascular resistance are the key elements of therapy.

In infants and children it is important to ensure adequate nutrition and higher calorie formula, or tube feeds may be indicated. In patients with chronic atrial arrhythmias, selective treatment of the specific arrhythmia

and appropriate anticoagulation is required. Patients with rheumatic heart disease should receive antibiotic prophylaxis to prevent recurrence of rheumatic fever. Patients who remain symptomatic despite maximal medical management should be considered for percutaneous intervention if the anatomy of their lesion is amenable to balloon valvuloplasty. This is true particularly in patients with rheumatic mitral stenosis and symmetric congenital mitral valve stenosis. Patients with supra-valvar mitral ring should not routinely be referred to for balloon valvuloplasty as their outcome is better with surgical intervention. Patients with parachute mitral valve tend to have less successful results with balloon valvotomy due to the asymmetric anatomy of the valve [6]. Balloon mitral valvuloplasty is generally not considered if there is more than mild mitral regurgitation at baseline. Balloon mitral valvuloplasty may delay or obviate the need for surgical intervention, which is particularly crucial in infants and small children [25]. Patients who have failed medical management and/or balloon mitral valvuloplasty, those with anatomy unfavorable to percutaneous intervention, and those with significant regurgitation should be referred to for surgical repair [19].

28.3.5 Surgical Management

The main indication for surgical intervention is the presence of symptoms or severe pulmonary hypertension. The operative management is intended to relieve the obstruction across the mitral valve but, not infrequently patients are left with residual gradients. Therefore, a detailed preoperative echocardiographic assessment of the valve is vital in determining the anatomy of the valve lesion and the chances of a successful repair.

The surgical approach requires cardiopulmonary bypass with bicaval cannulation, mild to moderate hypothermia, and cardioplegic arrest. The valve is usually exposed via a left atriotomy, along Waterston's groove. Left atrial enlargement is usually present facilitating the surgical exposure. Repair of a supra-valvar ring requires complete excision of the fibrous membrane (Fig. 28.5); commissurotomies are utilized to enlarge the effective valve orifice (Fig. 28.6). Surgical techniques utilized for the management of an abnormal sub-valvar apparatus (i.e., single papillary muscle) include

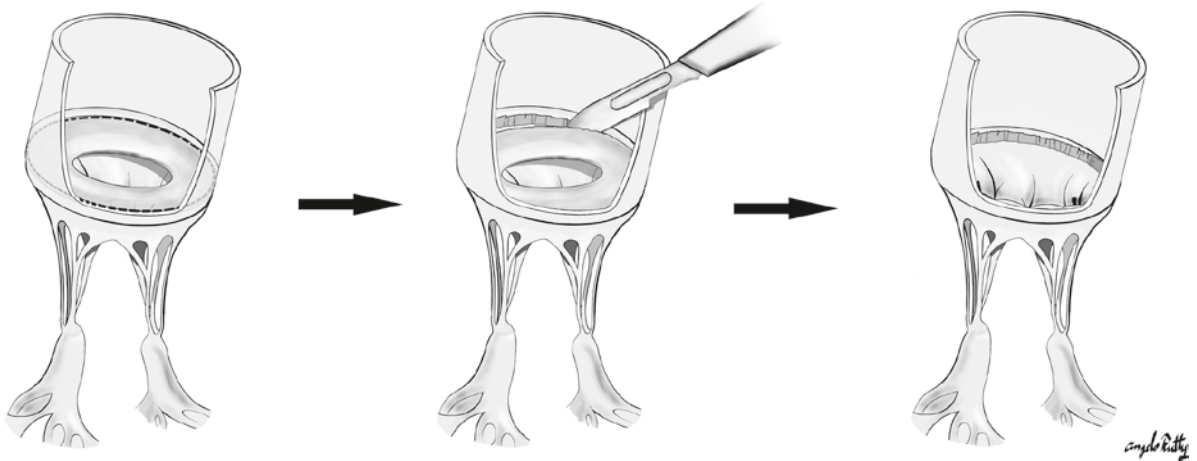


Fig. 28.5 *Repair of supra-valvar mitral ring.* The valve is exposed via a left atriotomy and the fibrous ridge sharply excised. Care is taken not to injure the underlying mitral valve leaflets

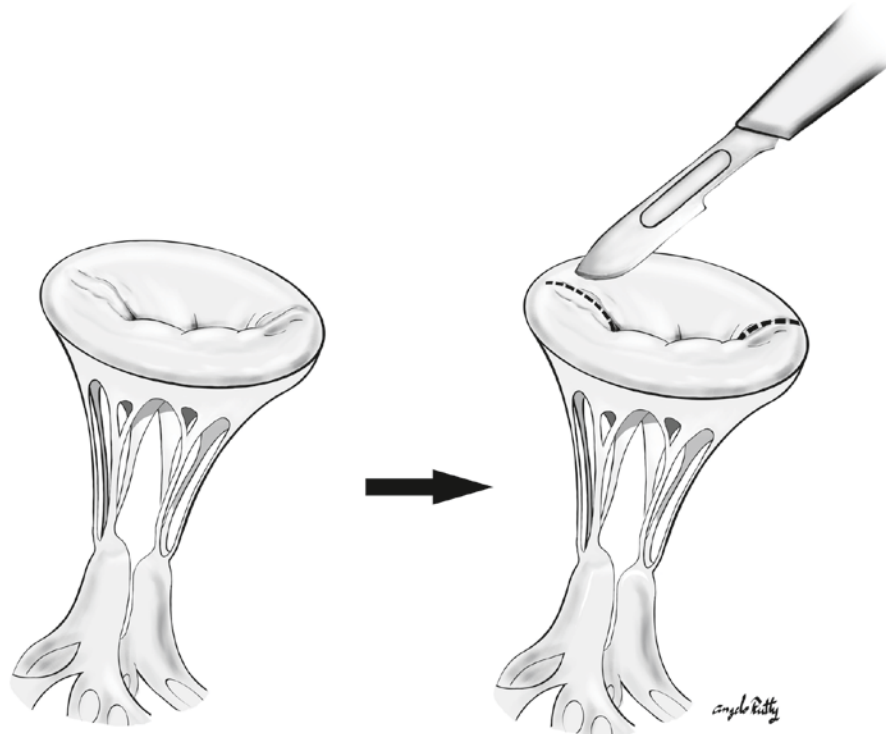


Fig. 28.6 *Mitral valve commissurotomy.* The effective valve orifice is enlarged by sharply opening areas of commissural fusion

fenestration of the interchordal spaces and splitting of the papillary muscles (Figs. 28.7 and 28.8).

If the repair is unsuccessful or if the valve is deemed as not repairable then mitral valve replacement is required. In infants and small children with a small

mitral valve annulus the prosthetic valve might need placement in a supra-annular position (Fig. 28.9). The operative morbidity and mortality associated with the surgical management of mitral stenosis is not insignificant, as high as 20% [19, 26, 27].

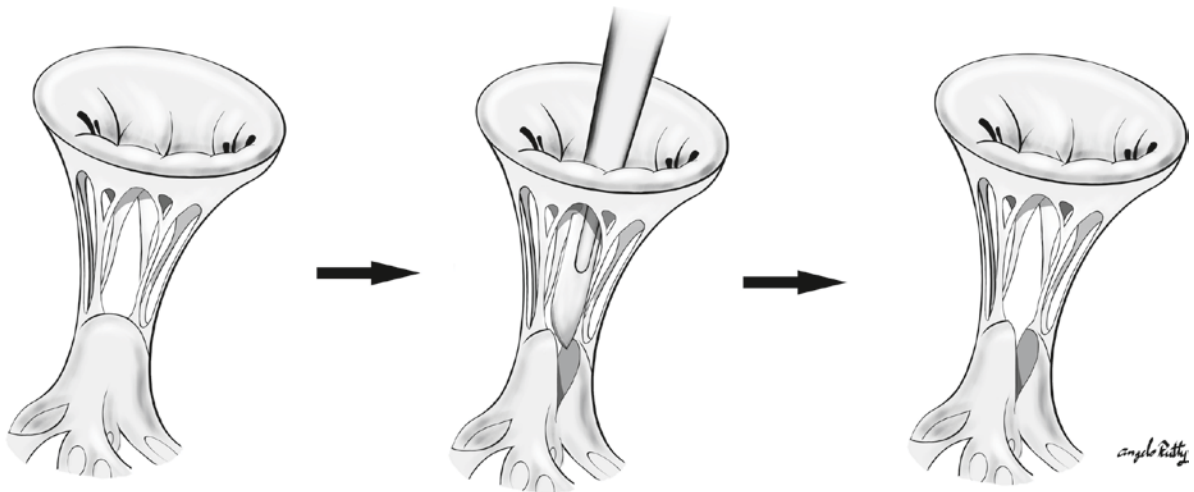


Fig. 28.7 Splitting of single papillary muscle

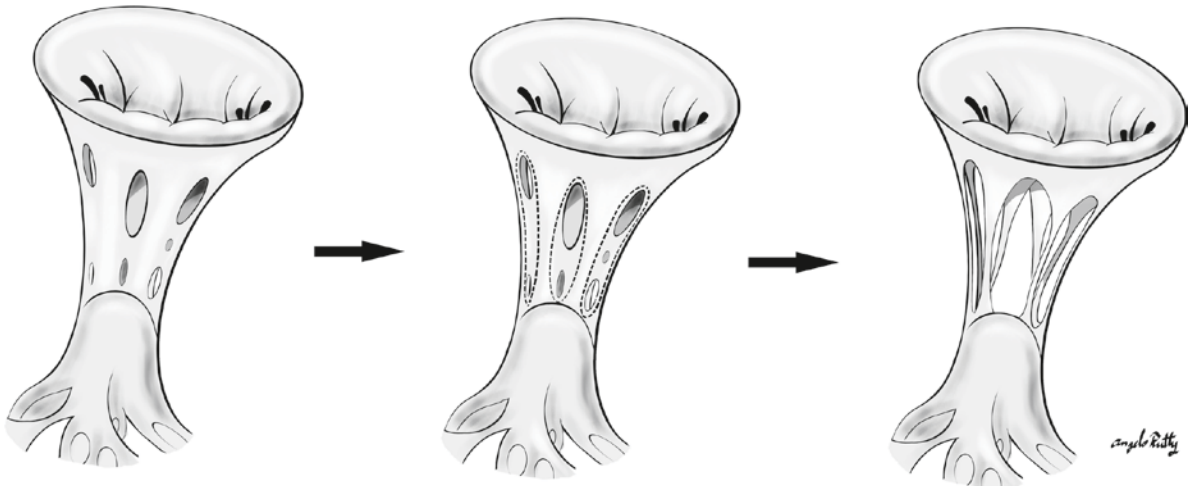


Fig. 28.8 Fenestration of the interchordal spaces

28.3.6 Postoperative Management

The principles of postoperative care are similar to those of preoperative management. Specific therapy is tailored to the results of surgical repair. Morbidity is related to residual mitral stenosis, pulmonary hypertension, low cardiac output syndrome, right ventricular failure, arrhythmias, atrioventricular block as a complication of prosthetic valve replacement, and presence of coexistent lesions such as left ventricular hypoplasia, sub-aortic stenosis, aortic stenosis, and arch hypoplasia. Maintenance of sinus rhythm is of critical importance

in this subset of patients to maintain adequate cardiac output.

In general primary valvuloplasty is the procedure of choice, and mitral valve replacement is avoided when possible. Prosthetic valves in young children are problematic due to the need for chronic anticoagulation and because the prosthetic valve often needs to be placed in supra-annular position due to small annular size. Left atrial, pulmonary venous, and pulmonary arterial hypertension may result from the relatively large size of the prosthetic valve in comparison with the left atrial size. This is a more significant issue for small infants [26].



Fig. 28.9 *Mitral valve replacement in the supra-annular position.* The prosthetic valve is sewn circumferentially to the left atrial tissue between the pulmonary veins and the mitral valve annulus

Transesophageal or transthoracic echocardiogram must be routinely obtained to assess right ventricular function, left ventricular function and filling, and the gradient across the prosthetic valve. Furthermore, it is important to evaluate for evidence of perivalvar leak.

The approach and therapy of the aforementioned postoperative complications are described in the section on preoperative management. If inotropic support is needed after surgery, the agent that causes the least tachycardia while augmenting contractility is the drug of choice. Normal temperature must be maintained at all times during the immediate postoperative period. Afterload reducing agents can be used cautiously. Patients with intravascular depletion who develop tachycardia and hypotension may have decreased coronary perfusion. Systolic systemic hypertension ought to be avoided in order to reduce the strain on the mitral valve after a surgical plasty.

After surgical repair, patients require 24–48 h of mechanical ventilation, especially if the chest is left open. An open chest improves ventricular compliance and minimizes the effect of positive pressure ventilation on pulmonary vascular resistance. While the chest

is opened, sedation, analgesia, and neuromuscular blockade are required. The chest is normally closed 24–48 h after surgical intervention. In addition, sedation, neuromuscular blockade, and inhaled nitric oxide are required in patients with pulmonary hypertension [28]. A pulmonary artery catheter and left atrial line may be helpful in guiding the medical management for discerning the etiology of postoperative pulmonary hypertension.

28.4 Long-term Outlook

Outcome related to mitral valve stenosis is variable dependent upon age at presentation, severity of stenosis, presence of associated cardiac defects, and valve morphology. Children with mild stenosis often remain asymptomatic and have no progression in the degree of stenosis with somatic growth. Infants with symptomatic congenital mitral stenosis, and associated left sided obstructive heart lesions continue to have a higher incidence of morbidity and mortality. Despite improved results with percutaneous balloon mitral valvuloplasty and with primary surgical valvuloplasty, children with congenital mitral valve stenosis remain at risk for development of restenosis, need for reoperation, placement of a prosthetic valve, and life-long anticoagulant therapy. Fortunately, many patients with valvar mitral stenosis who have developed pulmonary hypertension and right ventricular failure show reversal of pulmonary hypertension over time after an intervention is performed to increase the effective mitral valve area.

In a retrospective review reported by Moore et al in 1994, in a population of 85 infants with congenital mitral stenosis, 36% required intervention; 18 underwent balloon dilation of the mitral valve, and 13 underwent surgery. Freedom from mortality at 2 years was 70% in the group of patients who had balloon valvuloplasty and 60% in those who had surgical intervention. In the group of infants who underwent balloon dilation symptomatic improvement persisted in only 40% of patients. Procedural mortality was related to the need for repeat balloon dilation and degree of left ventricular hypoplasia [5].

In patients with parachute mitral valve and parachute-like asymmetric mitral valve, in 2004 Schaverien et al report 82% survival at 1 year and 77% survival at 10 years in a study population of 84 patients.

Presence of an atrial septal defect and left ventricular hypoplasia were identified as independent risk factors for death [6].

McElhinney et al report a retrospective review of outcomes for 108 patients with severe congenital mitral stenosis who underwent balloon mitral valvuloplasty or surgical mitral valve intervention from 1985–2003 at Children’s Hospital, Boston. In those patients who underwent balloon mitral valvuloplasty, there was a decrease in peak and mean mitral valve gradients by a median of 33% and 38%, respectively. Balloon valvuloplasty was complicated by development of significant mitral regurgitation in 28% of patients. Overall survival was 84% at 1 year and 77% at 5 years with an overall trend toward improved survival during the second decade of the study. Younger age and need for initial mitral valve replacement were associated with worse survival [27].

Rheumatic mitral stenosis is not commonly encountered in the pediatric population in the United States, but results for percutaneous intervention with balloon mitral valvuloplasty are encouraging [24].

Due to the variety of mitral valve pathology, the rarity of disease and the frequent presence of associated defects, congenital mitral stenosis remains a challenging defect to study and in which to predict a long-term outcome. Patient and family counseling related to outcome should be individualized dependent upon the severity of disease and presence of associated cardiac defects.

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Chapter 29

Prosthetic Valves

Peter D. Wearden

Many challenges are faced by pediatric patients and their surgeons in finding acceptable replacement heart valves for diseased, diminutive, or absent native valves. First of the challenges is valve size. Many prosthetic valves available in the market today are applicable only to the largest of pediatric patients. Even the smallest of commercially available valves can have unacceptable gradients. This can, at times, be circumvented by various surgical techniques, annular enlargement, or valve positioning. Other obstacles faced in this patient population include the issues of somatic growth, valve calcification, structural deterioration, thromboembolism, and the need for anticoagulation and its associated monitoring requirements. This chapter reviews the currently available prosthetic valves, valve choice for various locations and indications in the pediatric patient, and lastly, management and complications of prosthetic valve placement in children. (Figs. 29.1 and 29.2 demonstrate currently available prosthetic and tissue valves.)

29.1 Currently Available Prosthetic Valves

The currently available choices of prosthetic valves can be broadly divided into *mechanical* or *biologic* valves. Each of these categories can be further divided by valve design, construction, and tissue of origin or

processing of biologic materials. There are certain nuances of valve design of mechanical valves, or preservation of bioprosthetic valves, which are generally proprietary and are not the subject of this chapter.

29.1.1 Mechanical Valves

The design types of mechanical prosthesis include the *caged ball design* (Starr–Edwards Silastic Ball Valve, Edwards Lifesciences, Inc., Irvine, CA) and the *tilting disk* prosthesis.

Tilting disk prostheses includes both *single disk* and *bileaflet* prostheses. The single disk prostheses are the Medtronic–Hall (Medtronic Inc, Minneapolis, MN), the Omicarbon valve prosthesis (Medical CV, Inc., Inver Grove Heights, MN), and the Monostrut cardiac valve prosthesis (Alliane Medical Technologies, Inc., Irvine, CA). Bileaflet prostheses include the most commonly used valves today, the St. Jude Medical (SJM) valve (St. Jude Medical, Inc., Minneapolis, MN), the On-X prosthetic valve (Medical Carbon Research Institute, Austin, TX), the ATS Medical Open Pivot mechanical heart valves (ATS Medical, Inc., Minneapolis, MN), and also the Carbomedics prosthetic heart valves (Sulzer CarboMedics, Inc., Austin, TX).

The caged ball design was the first mechanical heart valve widely available. However, it is generally no longer used. Its usefulness in the pediatric population was somewhat limited by its high profile design.

Differences in the other valve designs include not only whether there are one or two leaflets but also the material which they are manufactured from, including titanium alloys, tungsten graphite, cobalt-based alloys, and pyrolytic carbons.

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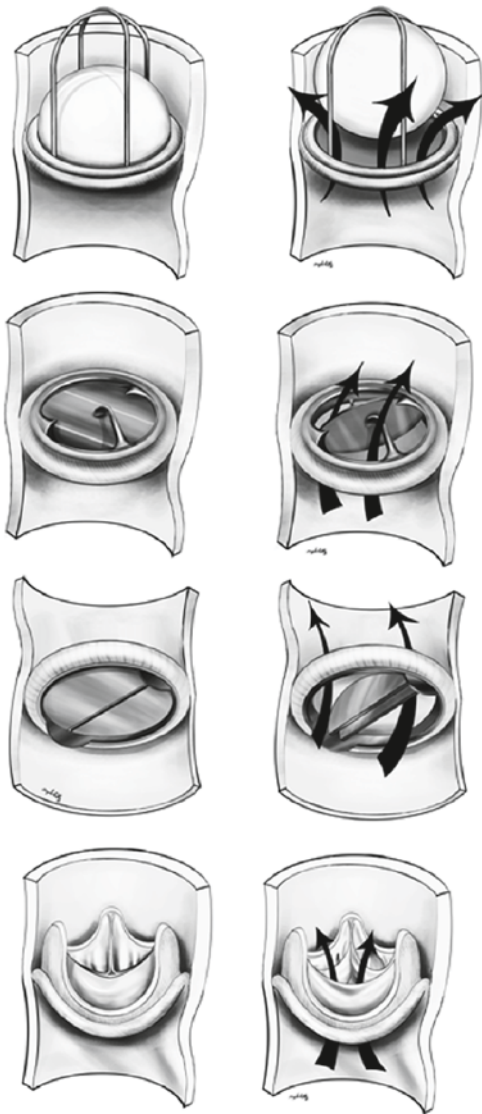


Fig. 29.1 This figure illustrates the most commonly used prosthetic valves. From top to bottom: Caged ball valve design which is no longer commonly used, a single tilting disk valve, a bileaflet tilting disk valve, and a stented porcine prosthesis

Opening and valve washing patterns vary from valve to valve and may affect, among other things, appropriate valve orientation, the ability of retained valvular tissue or sutures to obstruct the valve, and the washing of the valve by blood. Some diastolic regurgitation has been noted to improve continuous washing of the valve with blood and to decrease the incidence of thromboembolism [1, 2]. The type of valve can often be determined from its radiographic appearance. Also each valve has distinctive flow patterns during

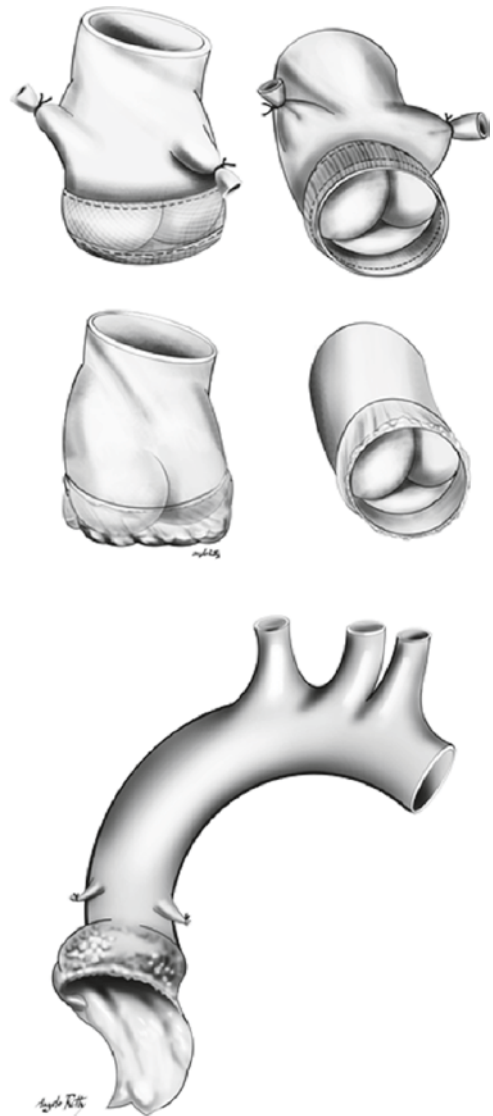


Fig. 29.2 Common biologic valves. From top to bottom: stentless porcine aortic prosthesis, pulmonary homograft (note the attached right ventricular muscle), and an aortic homograft with arch vessels (note the attached anterior leaflet of the mitral valve and ligated coronary arteries)

both systole and diastole, and they are referred to as “signature jets” on echocardiography.

Depending upon the manufacturer, valves are generally available in odd sizes from 19 to 31 mm for the aortic (semilunar) position and from 19 to 33 mm for the mitral (atrioventricular) position. Several valve manufacturers have designed valves for “supra-annular” positioning. These valves sit above the annulus, or sewing ring which is still secured to the annulus, without

obstructing the coronary arteries. This allows for a valve with a larger effective orifice area (EOA) to be placed thereby decreasing the gradient. The most common of these valves are the SJM high performance (HP) and Regent valves, the CarboMedics Top Hat valve and the ATS Open Pivot AP series of valves. Valves smaller than 19 mm, as would often be required in the smallest of children, include the 17 mm Monostrut Valve, 17 mm SJM HP and Regent valves, and 16 mm ATS Medical Open Pivot AP valves.

29.1.2 Bioprosthetic Valves

Bioprosthetic valves have the distinct advantage of not needing lifelong anticoagulation. The trade-off, however, is durability. Xenograft valves calcify when placed into the human circulation ultimately leading to their failure. This calcification process appears to occur more rapidly in younger patients. Various treatments including, glutaraldehyde, amino-oleic acid, and polysorbate 80 have been employed to fix the tissue and decrease mineralization. There has also been a trend to move from high pressure fixation to low pressure fixation in an attempt to preserve normal tissue architecture. The bioprosthetic valves include both stented (or supported) and stentless prostheses. The tissue of origin is generally porcine with the exception of a bovine pericardial valve manufactured from fixed bovine pericardium.

The stented valves include the Hancock and Mosaic valves (Medtronic, Inc.). The mosaic valve is the latest generation valve and differs from the Hancock series in having a different antimineralization treatment, zero pressure fixation, and predilation to increase EOA. The mosaic valve also has a semiflexible stent. These valves are generally available in sizes from 21 to 35 mm. The other currently available stented porcine prosthesis is the Carpentier Edwards Standard Valve (Edwards Life Sciences, Inc.). The Carpentier-Edwards PERIMOUNT valve (Edwards Life Sciences, Inc.) is a stented prosthesis made from bovine pericardium. This valve is manufactured from pericardium, as opposed to the porcine valves which are simply stented. The leaflets are manufactured with low pressure fixation and mounted in a support frame. This valve is available in sizes from 19 to 29 mm. A PERIMOUNT Plus valve is also available for the mitral position and is available in sizes from 27 to 33 mm.

Non allograft stentless bioprosthesis lack a rigid metal stent and therefore should have little inherent gradient across the valve. When implanted, these valves may be supported by the aortic root of the patient using, what is known as, the subcoronary or inclusion cylinder technique. They may also be implanted by fully replacing the aortic root in a manner similar to root replacement with an aortic homograft. Because of the diminished gradient, these valves are felt to be less likely to result in patient-prosthesis mismatch, a condition in which the EOA of an inserted prosthetic valve is too small in relation to the body size of the patient and cardiac output. This results in higher gradients than would be expected from a normally functioning prosthesis. This lack of inherent gradient in stentless valves is thought to result in better ventricular remodeling, or regression of ventricular hypertrophy. The technique of insertion is, however, significantly more complicated than that of stented valves. The currently available stentless valves are all porcine and include the Toronto SPV valve (St. Jude Medical, Inc.), the Medtronic Freestyle stentless aortic bioprosthesis (Medtronic, Inc.), and the Edwards Prima Plus stentless bioprosthesis (Edwards Life Sciences, Inc.). These valves are available in sizes from 19 to 29 mm depending upon the manufacturer.

29.1.3 Bioprosthetic Conduits

29.1.3.1 Xenograft Conduits

The Contegra bioprosthesis (Medtronic, Inc.) consists of bovine jugular vein with an integral, natural, trileaflet venous valve and a natural sinus slightly larger than its lumen. It is preserved in buffered glutaraldehyde solution and has surgical handling characteristics similar to allograft material. It is available for implantation in the right ventricular outflow tract (RVOT) in patients less than 18 years of age and is available in diameters from 12 to 22 mm. Shelhigh Pulmonic (Shelhigh, Inc., Union, NJ) valved conduits are also available in the United States with a Humanitarian Device Exemption (HDE) from the Food and Drug Administration. Both bovine and porcine tissue is available for use in the RVOT and have been treated with a proprietary anti-calcification treatment.

29.1.4 Allograft Valves

Allograft valves have now been used for over 40 years and are frequently the only valves appropriate for the smallest of patients. Both cadaveric aortic and pulmonary valves are currently widely used. Sufficient supply of donors may, at times, affect valve availability. Liquid nitrogen cryo-preservation has replaced antibiotic storage techniques. Depending upon donor size, all sizes of allografts are available.

29.2 Valve Choice and Outcomes by Location

29.2.1 Tricuspid Valve Replacement (TVR)

Compared with other valves, the tricuspid valve is the least commonly replaced in both adults and children with the most common indications being irreparable Ebstein's type valves or valves destroyed by endocarditis. In general, bioprosthetic valves are preferred for TVR, with most surgeons avoiding mechanical valves in this location because of the very low velocity of flow across the valve. Kiziltan examined the Mayo Clinic's experience with TVR for Ebstein's anomaly and in 149 patients with a mean follow-up of 4.5 years (17.8 years longest) found the survival to be 92.5% at both 10 and 15 years. Freedom from replacement was 97.5% and 60.6% at 10 and 15 years. Interestingly, the authors found that the reoperation rate for bioprostheses in this location was significantly less than for all other cardiac positions [3]. Husain and Brown in their review of the topic make several recommendations with regard to surgical technique including: (1) placing the valve cephalad to the coronary sinus, atrioventricular node, and right coronary artery to avoid compression of these structures; (2) ensuring that the struts of the bioprosthesis straddle the area of the membranous septum and conduction tissue; (3) seating the valve with the heart beating to observe for conduction disturbances; (4) performance of a right atrial maze at the time of TVR if indicated [4].

29.2.2 Mitral Valve Replacement (MVR)

With the evolution of mitral valve repair techniques, MVR in children is generally only undertaken with the failure of medical management and/or mitral valve repair. The most common indications for MVR in a child are: rheumatic disease, endocarditis, mitral stenosis (i.e., Shone's complex), and after failed AV canal repair. Replacement of the mitral valve in children less than 1 year of age should be delayed as long as possible because of the significant morbidity and mortality associated with replacement [5, 6]. MVR carries the highest mortality of any pediatric valve procedure and has a much worse long term prognosis. The reported operative mortality has ranged from 10 to 30% with 5 and 10 year survival between 50 and 80% [7, 8]. Alexiou observed 14% mortality but further observed that the operative mortality at their institution had decreased to 3.6% in the past decade [9]. It has also been fairly well demonstrated that older children generally do better with MVR [9, 10], whereas, others have observed only a 33% survival in 5 and 10 year children, undergoing MVR at an age less than two [11]. Many of the issues regarding poor outcomes in younger children are related to considerable risk associated with an increased ratio of prosthetic valve size relative to body weight [12]. Much of the short and long term mortality in small annulus sizes is associated with implantation in the supra-annular position. Other risks when attempting to oversize the prosthesis include: *subaortic obstruction, prosthetic leaflet entrapment, and conduction block*. Low profile bileaflet valves have become the valve of choice for this location. Bioprosthetic xenografts have been found to have limited durability at the mitral position in children and are currently rarely used. Lower profile or supra-annular aortic valves can be particularly useful for smaller patients. When these valves are used in this location they are removed from their holder and are "reversed" for implantation. Caldaroni's paper developed from the pediatric care consortium examined 139 patients less than age five with a median follow-up of 6.2 years. The median longevity they observed for a mitral valve implanted in a child less than age five was 12.7 years. They found survival to be 79%, 75%, and 74% at 1, 5, and 10 years respectively. This suggests that most of the mortality occurs in the early period

following valve placement [12]. This is confirmed by Alexiou's findings of a 5 and 10 year survival for hospital survivors of 90.3%, again point to most of the mortality being incurred in the early post operative period [9]. Another group reviewed their experience in patients less than 5 years of age, requiring MVR. In 35 children they observed an actuarial survival of 51% at 20 years, a surgical mortality of 17% and a freedom from reoperation of 50% at 10 years [5]. When examining the linearized rate of reoperation following mechanical MVR in children, the incidence has been found to be 3.8% per patient year with a freedom for reoperation of 85.7% at 10 years, which is similar to that observed by others [9, 13].

Brief mention should be made of the Ross II technique. This technique uses a pulmonary autograft placed in the mitral position. The technique was originally introduced by Donald Ross in 1967. The pulmonary autograft is generally placed within a dacron graft. Kabbani recently reported on 88 patients aged 4–64 years utilizing this technique. At an average follow-up of 5 years, he reported a freedom from degeneration of 93.4%, freedom from reoperation of 94.2%, and freedom from all death of 86.0% [14].

29.2.3 Pulmonary Valve Replacement (PVR)

Valve replacement, or conduit placement, between the right ventricle and pulmonary arteries is one of the more common operations required for congenital heart disease. The list of indicated operations includes: Tetralogy of Fallot, pulmonary atresia, D- or L-transposition of the great arteries with pulmonary stenosis, Truncus Arteriosus, and the Ross procedure. Valved conduits constructed of many of the previously mentioned mechanical or bioprosthetic valves can be obtained commercially or manufactured. More recently, the Contegra bovine jugular vein has seen greater usage in smaller children. This valved vein is also the basis for the “percutaneous” pulmonary valves to be placed endovascularly currently in development. Most commonly used, however, is the pulmonary valve allograft. Implantation of a bioprosthetic valve in the older (adult) patient with Tetralogy of Fallot previously

treated with a transannular patch has become one of the most common adult congenital heart procedures.

Historically, allografts are the most commonly utilized valves in this location because of size and space limitations, as well as the ease in implantation. With regard to these homografts, the reported results of longevity vary from study to study depending upon age and indication. Some of the more favorable results demonstrate an actuarial freedom from reoperation of 89% at 10 years and 80% at 20 years [15]. Others have reported a substantially lower freedom from reoperation of 81% at 5 years and 70% at 7 years [16]. Allograft freedom from reoperation, has, however been reported to be as high as 85% and 69% at 5 and 10 years post implantation in pediatric patients [17]. The reasons for potential valve failure include valvular calcification resulting in stenosis and insufficiency as well as patient somatic growth. Endovascular stents can prolong the period of time required for valve reoperation in both the instances by reducing the valve gradient, but always render the valve incompetent. Pulmonary vascular resistance has been found to effect pulmonary homograft longevity in patients with congenital heart disease, and may reflect much of the variability seen in homograft longevity. When examining the Ross Registry, or implantation of pulmonary homografts in patients with an otherwise normal pulmonary vasculature, homograft survival to 80% at 25 years has been observed [18]. Obviously, smaller and younger patients are risk factors for RV to PA conduit failure. Patient growth is accompanied by an attendant need for increased pulmonary blood flow resulting in functional stenosis. The freedom for reoperation in neonates implanted with a pulmonary homograft is only 22% at 5 years [19]. Oversizing of the homograft is, however, not a panacea and can result in kinking or compression of the conduit by the sternum. It remains questionable whether allograft longevity is affected by the immune response of the patient to the antigenicity of the allograft.

While there is limited data available for the implantation of mechanical heart valves in the pulmonary position, xenografts have been used extensively. One large series demonstrated a greater freedom from reoperation for porcine valved conduits than either irradiated or cryopreserved homografts. In this series, the Hancock valve in the RV to PA position had a freedom from reoperation of 87% at 5 years, 60.7% at 10

years, and 45.1% at 15 years compared with allograft survival of 65% at 5 years, 37% at 10 years, and 18% at 15 years [20]. In another study xenograft survival in the pulmonary position has been reported to be comparable with that of homografts with a 10 year survival of 85% [21]. With regard to the Contegra xenograft, short and midterm results demonstrate a freedom from reoperation that matches or exceeds that for pulmonary homografts [22].

More recently, several studies have been published relative to the use of mechanical valves in the pulmonary position. Historically, there has been little interest in this utilization because of what was thought to be an unacceptably high incidence of valve thrombosis in this location. This notion was based upon several small series, in mostly adult patients, albeit studies related to congenital heart disease have not found this to be the case [23, 24]. Another group proposed the hypothesis that the monostrut tilting disk valve was less susceptible to panus ingrowth and obstruction than the bileaflet mechanical valve [25]. Others have not found bileaflet valves to have any greater risk of thrombosis, the greater risk in the earlier studies being due to inadequate anticoagulation. These studies, although relatively small in number and for shorter periods of follow-up, have shown excellent valve function. Based on other published data, one group estimated the risk of reoperation at 15–20% at 10 years for allografts or xenografts versus a risk of reoperation of 4% at 14 years in their study and a postulated lifetime risk of reoperation at 8% [24]. If these devices were to be used, that would seem to be most applicable to younger patients, though not so young they could “outgrow” their prosthesis. Also appropriate would be those patients who are taking coumadin for other indications, particularly atrial fibrillation or other cardiac prostheses, and those with no contraindication to anticoagulation, which would exclude young women in child bearing age. The largest group of patients in which the greater implementation of these devices may be helpful are adult patients with Tetralogy of Fallot. It is felt that the need for anticoagulation of mechanical valves in the aortic position is greater because the velocity of flow across the valve is less, however, the result of emboli to the lung is perhaps less morbid than systemic embolization. Clearly in counseling patients with regard to valve choice, consideration the incidence of anticoagulation related hemorrhage and the lifestyle changes has to be considered.

29.2.4 Aortic Valve Replacement (AVR)

In most small and growing children, the Ross procedure has become the standard operation for conditions requiring AVR. This operation which involves the transfer of the pulmonary valve to the aortic position (autograft) and replacement of the pulmonary valve (discussed at length elsewhere in this text) has supplanted much of the debate regarding types of AVR in children. For mechanical valve replacement, a mortality of 6–13% has been reported [26]. Turrentine compared pediatric AVR with pulmonary autografts, mechanical valves, xenografts, and aortic homografts. The survival rate at 10 years in these patients was 95.2% for pulmonary autografts and 87.8% for mechanical valves [27]. Much controversy, however, remains, when discussing AVR in children who are not candidates for the pulmonary autograft, (connective tissue disorder, diseased pulmonary valve) or in those teens who have reached their full growth potential.

29.2.5 Mechanical AVR

In a review of 55 pediatric patients undergoing mechanical AVR the event free survival at 1, 5, and 20 years was 96, 92, and 88% respectively. Freedom from reintervention at the same time periods was 98, 96, and 92% respectively [28]. Another group reported the linearized rate of reoperation for mechanical AVR in children to be 4.2% per patient year [13]. Lupinetti examined 100 consecutive AVRs at a single institution comparing mechanical to “human” (allograft or autograft) valve replacement with mean ages of 12.1 and 10.4 years respectively. The 4 year actuarial survival was 83% in the mechanical group and 98% in the human group. When examining freedom from all valve related complications the same authors found it to be 61% for mechanical valves and 88% for human valves [29]. Alexiou reported on 56 children with a mean age of 11.2 (range 1–16 years) undergoing mechanical AVR. Mean follow-up was 7.3 years. He reported a 5.3% operative mortality and actuarial freedom from reoperation at 10 and 20 years of 86.4% which is a linearized rate of 1.3% per patient year. The authors do report using aggressive root enlargement techniques to optimize the size valve which they placed. The actuarial survival for the hospital

survivors was 96.1% and 89.6% at 10 and 20 years respectively [30].

29.2.6 Bioprosthetic AVR

29.2.6.1 Xenograft

Currently, there is little enthusiasm for xenograft bioprostheses in the pediatric patient population. They have been associated with high rates of early degeneration, calcification, and structural failure with reoperation rates as high as 50% at 4 years [31, 32]. Ruzmetov examined 174 AVRs over 31 years. This population included xenografts, allografts, mechanical valves, and autografts. The authors found that 60% of all xenografts placed in children had to be replaced at 5 years [33]. Few would argue that this type of valve is a viable option for the pediatric population except in the most limited of circumstances.

29.2.6.2 Homograft

Gerosa, McKay, and Ross compared 143 children undergoing pulmonary autograft or allograft ($n=106$) AVR. This group found a 15.6% early mortality, a 16.7% late mortality, and a 54% 15 year actuarial freedom from reoperation in the homograft group [34]. In 336 adult patients undergoing aortic root replacement with 346 allografts, one group found the incidence of reoperation for structural deterioration to be 1.5% per patient year. The rate of deterioration decreased with increasing age at implant. Those implanted with a homograft at age 35 had a 70% freedom from structural valve deterioration at 10 years compared with an 80% freedom when implanted at 45 years, 88% at 55 years, and better than 90% freedom from reoperation if implanted at 65 years [35]. This type of longevity is not seen in children due to somatic growth and a much greater rate of calcium turnover and mineralization in the growing child. Ruzmetov, however, found that only 14% of homografts required replacement at 11 years in a small sample of patients with a mean age of 11 years [33].

While at this point in time allograft replacement of the aortic valve is the preferred operation in most pediatric centers, homograft and mechanical AVR are still commonly utilized with excellent outcomes. Much of

the decision making will be related to the tolerance of both the surgeon and the family to the risks of reoperation but also to the risks of anticoagulation and alterations in lifestyle required by the various choices.

29.3 Complications of Valve Replacement

In deciding which prosthesis should be placed into a given child, as has been discussed, the factors most commonly considered are the expected longevity of the valve, the complication rate, and the impact upon lifestyle. As has been demonstrated above, the longevity of the valve in children is primarily affected by two factors: somatic growth and valve degeneration. The effect of somatic growth is essentially the same for mechanical and bioprosthetic valves when compared to valves which have the potential for growth (autografts). Valve degeneration is particularly affected by the age of the patient, with an increasing rate of calcification in younger patients who have greater rates of calcium metabolism and turn over. The incidence of complications particularly thrombosis, thromboembolism, and bleeding complications or anticoagulant-related hemorrhage (ARH) does vary by valve type as well as valve location and can be considerable. For instance, in Beirlein's paper on the long term follow-up of mechanical MVR in children, it was found that the freedom from all adverse events, including death, redo MVR, bleeding, thromboembolism, and endocarditis was 45% and 17% at 5 and 10 years respectively [11]. This means that, based on the rates observed in this study, nearly all children will have some complication, or require replacement, of their MVR in the 10 years following valve replacement. These risks have been best calculated in adult patients in large studies, while much smaller series of children provide the currently available information for this age group. Extrapolation from adult data is reasonable, but certainly is not an exact surrogate for the rates of pediatric complications. This is related to age, comorbidities, and other risks faced by the adult population as well as differing flow characteristics in different sized patients.

The following examines the most common risks of prosthetic valve placement, their incidence in the adult population and the available data for the pediatric population.

29.3.1 *Thrombosis*

In adults, thrombosis of the valve is an unlikely complication of mechanical or bioprosthetic valve replacement. In a large series of patients with the SJM bileaflet valve, the incidence of valve thrombosis was reported as 0.2% for AVR and 0.5% for MVR. In this series, the calculated incidence was 0.06% per patient year for AVR and 0.18% per patient year for MVR [36]. If one considers within the population of patients with thrombosis, non structural dysfunction of the valve, the incidence of valve failure in pediatric patients is probably much higher. This is related to panus ingrowth particularly with regard to the mitral valve. Location plays a role in the incidence of mechanical valve thrombosis. Thrombosis of mechanical tricuspid valves has been reported to be 20 times more frequent than left-sided valves, and mechanical mitral valves develop thrombosis at a rate 2–3 times greater than aortic valves. In one series, the failure rate for MVR in children because of this ingrowth was as high as 31% [13]. Valve thrombosis is generally manifested by pulmonary congestion, evidence of decreased cardiac output, or systemic embolization. Patients generally have an acute deterioration but at times there can be a slower onset of deterioration. Once the diagnosis is made, intravenous heparin therapy should be initiated. Depending upon the size of the thrombus further therapy with fibrinolysis or surgery should be considered. Thrombolytic therapy, in adults, has been reported to have a success rate of 70% and a mortality of 9–10%, but also carries a high risk of embolization and is reserved for critically ill patients with a highest risk of operative mortality [37]. Generally, pediatric patients should undergo valve replacement when presenting with this condition.

29.3.2 *Thromboembolism*

The incidence of thromboembolism of the SJM valve in adult patients has been reported as 1.9% per patient year for AVR and 2.8% per patient year for MVR. Shanmugam in a series of 55 pediatric patients with AVR and a mean follow-up of 12 years found no incidence of thromboembolism [28]. In examining 32 pediatric patients with both AVR and MVR Sachweh found the incidence of thromboembolism to be 1.2% per year for both AVR and MVR [13]. Cannegieter in

examining a large adult series including multiple types of mechanical valves found the incidence in adults of major embolization to be approximately 4% per patient year with no anticoagulant therapy, 2% per year with only antiplatelet therapy, and 1% per year with coumadin therapy [38]. Others have reported the rates of thromboembolism from 0.7 to 6% per patient year. Alexiou in examining the rate of thromboembolism in children with mechanical AVR, found a linearized rate of 0.3% per patient year [30]. The same author observed an incidence of 0.9% per patient year in children following MVR [9]. Mazitelli reported a 20 year freedom from thromboembolism of 91.2% and Iyer reported the same variable to be 98.8% at 8 years [39, 40]. Champsaur and Milano reported linearized rates of thromboembolism to be 0.3% and 0.7% per patient year respectively in children [26, 41]. Based on this information, it would appear that the rates of thromboembolism in children undergoing mechanical AVR are less than in adults. This could be attributable to the lack of comorbidities which affect the rates of thromboembolism, such as atrial fibrillation which is less common in children. Additionally, children do not generally have other risk factors for stroke, not related to mechanical valve replacement, such as atherosclerotic disease, diabetes, and smoking. Poor ventricular function also increases the incidence of thromboembolism and may be present in children or adults.

29.3.3 *Bleeding*

Bleeding complications for prosthetic valves is related to long term anticoagulation, generally with coumadin. Obviously this risk is obviated by the lack of an anticoagulation requirement in those patients with bioprosthetic valves. Many authors will therefore refer to this complication as ARH. In Emery's review of over 4,000 patients receiving the SJM valve in adults this incidence was reported to be 2.7% per patient year for AVR and the same for MVR [36]. When examining 41 pediatric patients implanted with mechanical valves in either the aortic or mitral position, Larsen observed no episodes of thrombosis or thromboembolism but an 11% incidence of ARH which is translated to an occurrence of 1.4% per patient year [42]. In another series of 55 pediatric patients with AVR, the linearized rate of bleeding was found to be only 0.15% per patient year [28].

This low incidence of ARH in children has been described by others and linearized to 0.65% per year for MVR and 0% per year for AVR [13]. Generally, the incidence of ARH is felt to be higher for MVR than AVR because of the necessity for higher INRs in these patients. Alexiou found the incidence of all bleeding complications in children to be 0.3% per patient year following AVR, with no life threatening bleeding episode [30] which has been confirmed by several others. In examining long term follow-up for children following MVR, Beierlein found the freedom from important bleeding events to be 76% and 71% at 10 and 15 years respectively [11]. For MVR in children, as in adults, the incidence of ARH is higher due to higher INRs (0.9% per patient year) [9]. While popular medical consensus would be that, anticoagulation of children is more difficult than adults, with regard to bleeding complications the data above suggest that children have equal to slightly lower incidences of ARH when being anticoagulated for mechanical valves.

29.3.4 Mechanical Failure

As discussed above, structural deterioration of bioprosthetic valves is an inevitable consequence of their utilization in the human. This incidence is nonlinear with deterioration, and subsequent “failure” increasing a much greater rate after a certain period of time. In children this time frame is often very short. Mechanical valves on the other hand should have no incidence of intrinsic valve failure. While there have been notable exceptions in the past of valve failure, all of the currently marketed valves have been used for extended periods of time and demonstrated excellent durability [43].

29.4 Management

29.4.1 Anticoagulation

The same anticoagulation guidelines that have been developed for adults in regard to INR have been recommended for children. The Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic therapy: evidence-based guidelines

confirmed this finding based on published reports. They further recommended the addition of aspirin in those children with a lack of response to vitamin K antagonists or with a contraindication to the administration of the full dose of vitamin K antagonists [44]. The same conference, in an evidence-based review of the literature, recommended a target INR of 2.5 (range 2.0–3.0) for mechanical aortic valves and a target INR of 3.0 range (2.5–3.5) for mechanical mitral valves in the absence of additional risk factors [45, 46]. Because of the smaller numbers of patients, there are not currently guidelines with regard to anticoagulation of mechanical pulmonary valves, but most would treat for a higher INR as in the case of the mechanical mitral valve. Systematic follow-up of INR as part of an anticoagulation program is beneficial to both the patient and clinician.

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Chapter 30

Hypoplastic Left Heart Syndrome

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Hypoplastic left heart syndrome (HLHS) is the most common severe congenital heart defect which constitutes 1–2% of all congenital heart anomalies and 7–9% of total anatomic abnormalities diagnosed within the 1 year of life. It is also the most common congenital cardiac malformation involving a single ventricle. It is more frequent in males, with a 67% male predominance. Without surgical intervention HLHS is a uniformly fatal condition with a 95% mortality rate within the 1 month of life. A multifactorial mode of inheritance is likely present for most cases [1].

30.1 Anatomy

HLHS (Fig. 30.1) defines a spectrum of cardiac abnormalities with the hallmarks of hypoplasia of the left ventricle and ascending aorta. The aortic and mitral valves are usually abnormal, with the defects ranging from stenosis and hypoplasia to complete atresia. A large patent ductus arteriosus (PDA) is usually present, and a patent foramen ovale (PFO) or atrial septal defect (ASD) may be observed, while the ventricular septum is usually intact.

The exact cause of HLHS is unknown. Most likely, the primary abnormality occurs during aortic and mitral valve development secondary to an inflammatory or ischemic event in utero, and the valves fail to develop normally. Minimal or absent blood flow due to the aortic and mitral valve atresia prevents the left

ventricle and the ascending aorta from growing. The ascending aorta is frequently so diminutive that its function is reduced to that of a common coronary artery receiving blood supply in retrograde manner from the PDA.

Associated congenital heart defects:

- Coarctation of the aorta
- Interrupted aortic arch
- Total or partial anomalous pulmonary venous return
- Coronary artery abnormalities
- Complete atrioventricular canal
- Endocardial fibroelastosis (especially in diminutive left ventricle with aortic atresia and mitral stenosis)

30.2 Pathophysiology

The newborn infant with HLHS displays complex cardiovascular physiology with ductal-dependent systemic and coronary blood flow. Pulmonary venous return entering the left atrium cannot cross the stenotic, hypoplastic, or atretic mitral valve into the LV and is instead shunted across the PFO or an ASD to the RA where it mixes with the systemic venous blood. If the atrial septum is intact the pulmonary venous connection may be totally anomalous. The RV functions as the pumping chamber for both the pulmonary and the systemic circulations, which are connected in parallel by the PDA. Of special note, coronary and cerebral perfusion is also dependent on the blood flow through the PDA (unless the proximal coronary arteries arise from the pulmonary trunk). The proportion of flow to the pulmonary (Q_p) and systemic circulations (Q_s) depends on the ratio of the pulmonary vascular resistance to the

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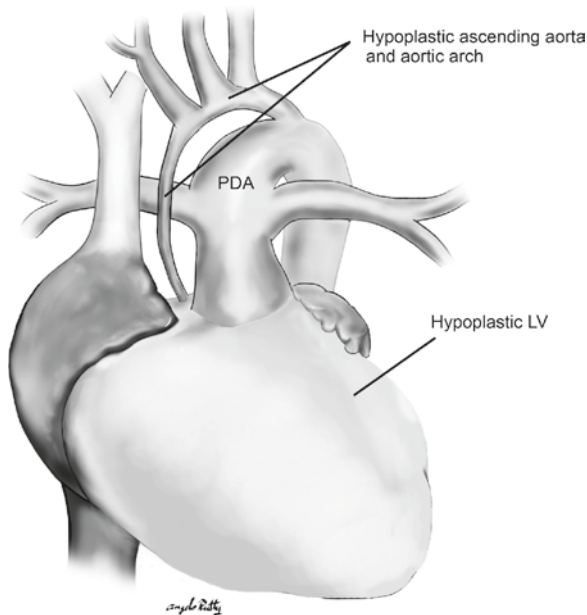


Fig. 30.1 Hypoplastic left heart syndrome

systemic vascular resistances. In order for a neonate to survive the preoperative period, the two circulations have to be delicately balanced to achieve a Q_p/Q_s ratio of 1. In the postnatal period, pulmonary vascular resistance falls, and the Q_p/Q_s ratio increases. Thus the RV output is preferentially directed away from the systemic circulation, resulting in profound underperfusion of the coronary arteries and the vital organs, metabolic acidosis, and oliguria. Therefore, increased pulmonary blood flow and oxygen saturation come at the expense of an increased risk of myocardial and cerebral ischemia.

A Q_p/Q_s ratio close to 1 is maintained when the systemic saturation is 70–80% and the P_aO_2 is 30–40 mmHg. It is of paramount importance to remember that these arterial saturations and P_aO_2 suggest a good balance between the pulmonary and systemic blood flow only if the mixed venous saturation and pulmonary venous saturation are normal. If either mixed venous or pulmonary desaturation is present, an arterial saturation of 80% may indicate pulmonary overcirculation. Equation 1 illustrates this point.

$$Q_p/Q_s = (S(ao) - S(v))/(S(pv) - S(pa)), \quad (1)$$

where $S(ao)$ is the saturation of aortic blood, $S(v)$ is the mixed venous saturation, $S(pv)$ is the pulmonary venous saturation, and $S(pa)$ is the pulmonary arterial saturation. Note that if the lungs are normal, $S(pv)$ is approximately 100%, but if they are not normal it will be lower.

Note also that because of the single ventricle physiology, $S(ao)$ equals $S(pa)$.

The closure of the PDA in patients with HLHS leads to severe systemic and coronary underperfusion, with profound metabolic acidosis, cardiogenic shock, and death. Thus, maintenance of a patent ductus with PGE_1 administration is essential.

30.3 Clinical Presentation

It has been suggested that prenatal recognition and delivery at or in close proximity to a center skilled in the care of critical congenital heart disease increases the infant's chances for survival [2].

Infants with HLHS typically presents within the first 24–48 h of life. Most neonates are full-term and initially appear normal. Infants present as PDA closure begins with symptoms of decreasing systemic blood flow quickly progressing to shock (hypothermia, poor feeding, lethargy, tachycardia, tachypnea, grayish skin color, hepatomegaly, and weak pulses). Without prompt recognition and intervention, death ensues rapidly.

Infants with pulmonary venous obstruction (absent or restrictive PFO or obstructed total pulmonary anomalous venous return) may present sooner with symptoms of low cardiac output, respiratory failure, and severe cyanosis.

Occasionally an infant with persistence of the PDA and high pulmonary vascular resistance may present later due to balanced pulmonary and systemic blood flow.

Once ductal patency is established and resolution of shock has begun, HLHS mostly manifests as tachycardia, tachypnea, and variable degree of cyanosis.

Auscultatory findings are usually nonspecific. Single second heart sound, soft systolic ejection murmur of increased flow auscultated over pulmonary artery, occasional apical mid-diastolic murmur of increased flow across the tricuspid valve, and third heart sound gallop are usually heard.

30.3.1 Chest Radiography

Chest radiograph is not specific for HLHS; RA enlargement, cardiomegaly and pulmonary vascular markings ranging from lacy-reticular pattern to frank pulmonary edema in infants with obstructed pulmonary venous return could be seen.

30.3.2 ECG

The electrocardiogram typically shows sinus tachycardia, right-axis deviation, right atrial enlargement, and right ventricular hypertrophy with a qR configuration in the right precordial leads. A paucity of left ventricular forces is noted in the left precordial leads [1].

30.3.3 Echocardiography

Echocardiographic diagnosis is relatively simple and all views should be utilized. Once HLHS is suspected, the study should focus on the following aspects:

- a. RV dimensions, thickness, and systolic function
- b. Presence and severity of tricuspid regurgitation and pulmonary regurgitation
- c. Ductal patency
- d. Mitral valve, aortic valve, coronary arteries, aortic branching, and presence of coarctation
- e. Diameter of the innominate artery (as a site of possible shunt take-off) and diameter of the ascending aorta and transverse aortic arch
- f. Direction and magnitude of shunts (left-to-right at the PFO/ASD, right-to-left at the PDA)
- g. Systemic and pulmonary venous return [3].

30.4 Preoperative Management

Due to the complexity of the physiology of HLHS and the extent of monitoring, the preoperative management should always take place in the neonatal, pediatric, or, preferably, pediatric cardiac intensive care unit. The ultimate goal of preoperative management is to provide and maintain an adequate distribution of the cardiac output.

Appropriate venous access includes a central venous line, preferably an umbilical venous line (double or triple lumen) or a Peripherally-Inserted Central Catheter (PICC), for continuous PGE₁ infusion, inotropic support, and total parenteral nutrition. If the previous is not possible, a femoral, subclavian or internal jugular venous line is placed. However, in general, an attempt is made in this period to preserve the internal jugular or subclavian vein to avoid thrombosis of the

superior vena cava which prohibits the Glenn procedure in the future. It is safe and effective to administer PGE₁ through a good peripheral line while obtaining central venous access. Arterial access may be as a peripheral or a central umbilical arterial line.

Frequent serial blood gas monitoring is mandatory. ECG, arterial oxygen saturation, invasive blood pressure, and CVP should be monitored continuously.

Currently, near infrared spectroscopy (NIRS) is routinely used for continuous monitoring of regional cerebral and renal or splanchnic tissue oxygenation index (rSO₂) as an additional means of judging the adequacy of systemic perfusion.

30.4.1 Medical Care

- a. PGE₁ infusion
- b. Correction of metabolic acidosis with sodium bicarbonate (1–2 meq/kg/dose)
- c. Prevention of systemic underperfusion by limiting pulmonary overcirculation. Nitrogen or carbon dioxide is added to the inspired gas delivered by regular nasal cannula, high-flow nasal cannula, or hood. Hypoventilation to increase the pulmonary vascular resistance can be accomplished by intubation, sedation, and controlled mechanical ventilation; however, *it is preferable not to intubate these infants*. Diuretics are helpful in the management of pulmonary overcirculation and fluid retention.
- d. Inotropic support is used infrequently; it is indicated in severely ill neonates with concurrent sepsis or low cardiac output and severe acidosis. Dopamine at 3–5 µg/kg/min is usually sufficient.
- e. Systemic afterload reduction with milrinone at 0.125–1 µg/kg/min is currently used to avoid systemic underperfusion and to prevent or treat pulmonary overcirculation, while reducing the myocardial workload and improving inotropy and lusitropy. Sodium nitroprusside may also be used, but systemic hypotension must be avoided.
- f. Intravenous antibiotics are indicated, if the infant is at risk for a perinatally acquired infection, and when clinical suspicion of concurrent sepsis is high.
- g. A head and abdominal ultrasound should be routinely requested prior to surgery as patients with HLHS may have brain and renal abnormalities. If necessary, a head CT and/or MRI must also be completed.

30.4.2 Cardiac Catheterization

Cardiac catheterization is no longer indicated prior to Stage I surgical correction, unless the infant for various reasons is not a candidate for Norwood Stage I repair and the hybrid procedure (PDA stenting and pulmonary arteries banding) is necessary, or whenever necessary to elucidate the anatomy of complex pulmonary venous returns.

30.5 Surgical Management

30.5.1 Hybrid Procedure

Experimentation with the hybrid procedure began in the early 1990 [4]. Search for the new technique was prompted by high first-stage and inter-stage mortality, concern for multiple exposures to cardiopulmonary bypass during the traditional staged approach, and the need to develop a palliative technique for the infants awaiting cardiac transplantation. The procedure is a combination of surgical and interventional approaches (Fig. 30.2). Percutaneous stenting of the arterial duct and balloon atrial septostomy are done within the first

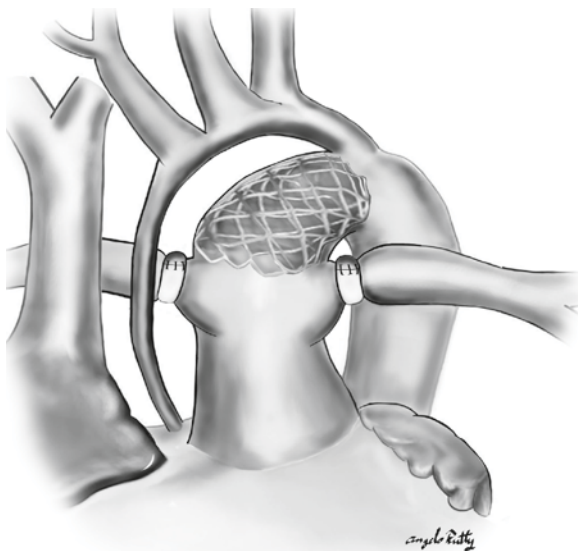


Fig. 30.2 Hybrid procedure. The constricting bands are placed in the proximal aspect of both branch pulmonary arteries and the ductus arteriosus is stented. The atrial septostomy is not shown

few days of life in the catheterization laboratory. Banding of the proximal branch pulmonary arteries is then performed through a median sternotomy. An open atrial septectomy may also be performed if balloon septostomy was not done. These patients then undergo a palliative one-stage procedure with reconstruction of the aortic arch and a bidirectional cavopulmonary connection at the age of 3.5–6 month [5]. The completion of a transcatheter Fontan procedure with only one exposure to cardiopulmonary bypass, aortic cross-clamping, and circulatory arrest have been reported as well using the hybrid approach. However, authors have reported a 27% mortality rate after the hybrid procedure, including hospital and inter-stage mortality, and a 41% overall mortality in a series of 29 patients [6].

30.6 Norwood Procedure (Stage I)

The Norwood procedure requires cardiopulmonary bypass and a period of deep hypothermic circulatory arrest and/or low flow perfusion. This repair has undergone several modifications over the years, but there are three main basic surgical principles:

1. The construction of a reliable source of pulmonary blood flow (either a modified Blalock–Taussig shunt or a Sano shunt) without causing distortion of the pulmonary arteries (Fig. 30.3).
2. The reconstruction of the transverse aortic arch with the incorporation of the proximal aortopulmonary anastomosis without compromising the coronary bloodflow and/or leaving residual arch obstruction (Fig. 30.4)
3. The creation of a large interatrial communication (atrial septectomy), allowing unobstructed pulmonary venous return into the RA (Fig. 30.5).

There has been a significant effort in trying to determine the best source of pulmonary blood flow for patients undergoing a Norwood procedure. Patients with an RV-to-PA conduit (Sano shunt) have a higher diastolic blood pressure when compared to patients with a BT shunt, which has theoretical advantages (minimizing coronary ischemia) in the management of these patients. However, it is still unclear whether the Sano shunt results in a survival advantage. The operative mortality for the Norwood procedure is 10–20%.

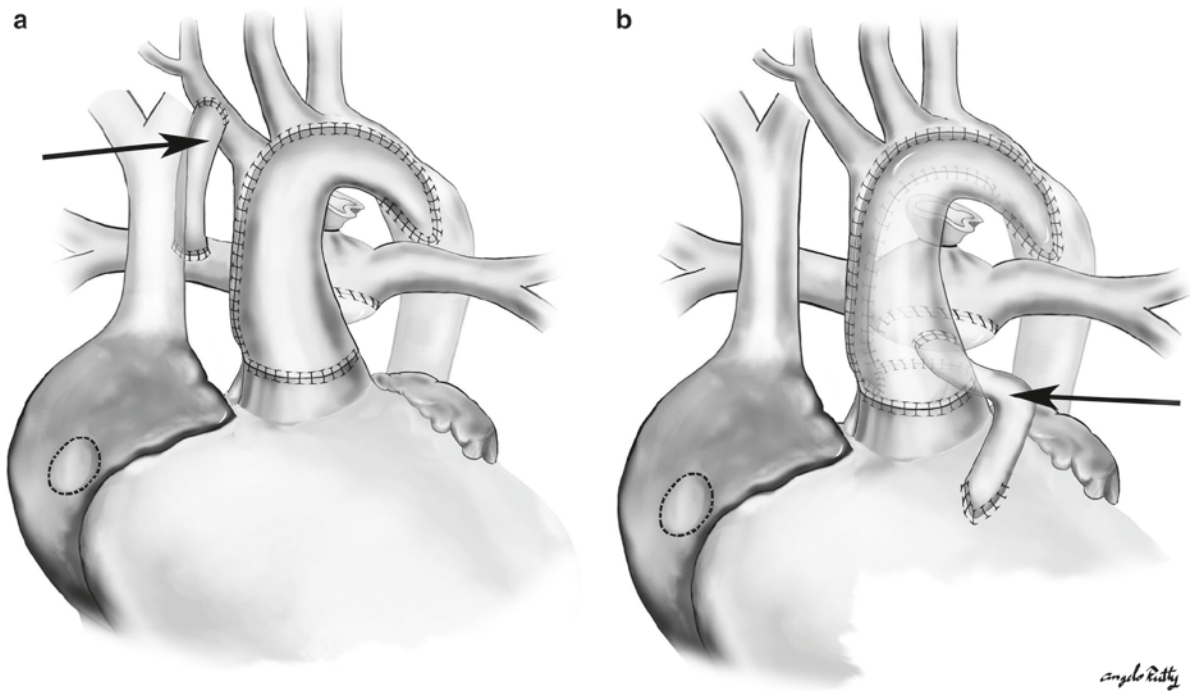


Fig. 30.3 (a) Right modified Blalock–Taussig shunt; (b) Sano shunt

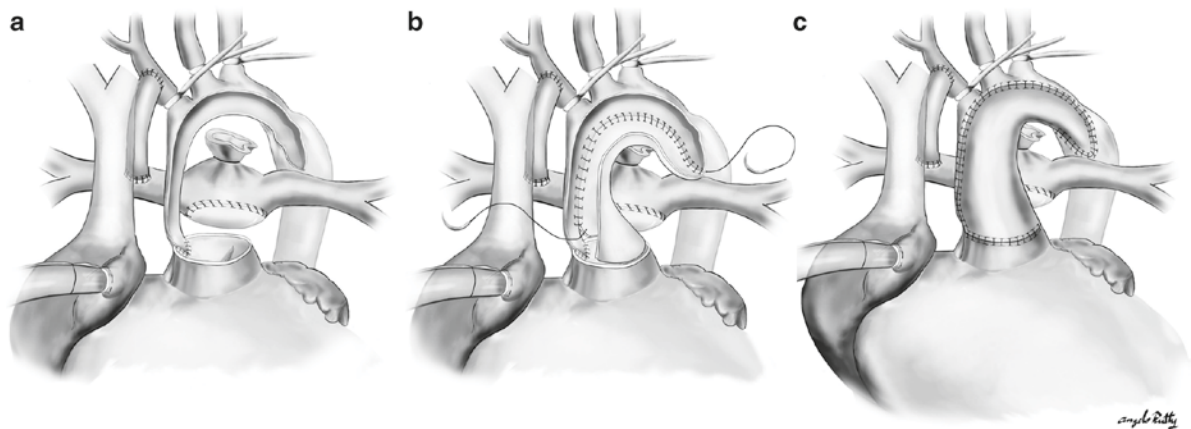


Fig. 30.4 (a) After construction of the “shunt” and division of the main pulmonary artery the pulmonary trunk is sutured to the proximal ascending aorta in a side to side fashion; (b–c) The aorta is enlarged with a prosthetic patch

30.7 Postoperative Management

Infants are critically ill and unstable immediately following the Stage I Norwood procedure. Patients may arrive from the operating room with an open or closed chest according to the surgical course and experience of the cardiovascular team. Extreme attention to the details of patient status, technical sophistica-

tion, and sufficient patient volume are all necessary prerequisites for a successful patient recovery.

30.7.1 Monitoring

Invasive monitoring of arterial pressure, CVP, pulse oximetry, and regional cerebral and renal perfusion is done continuously.

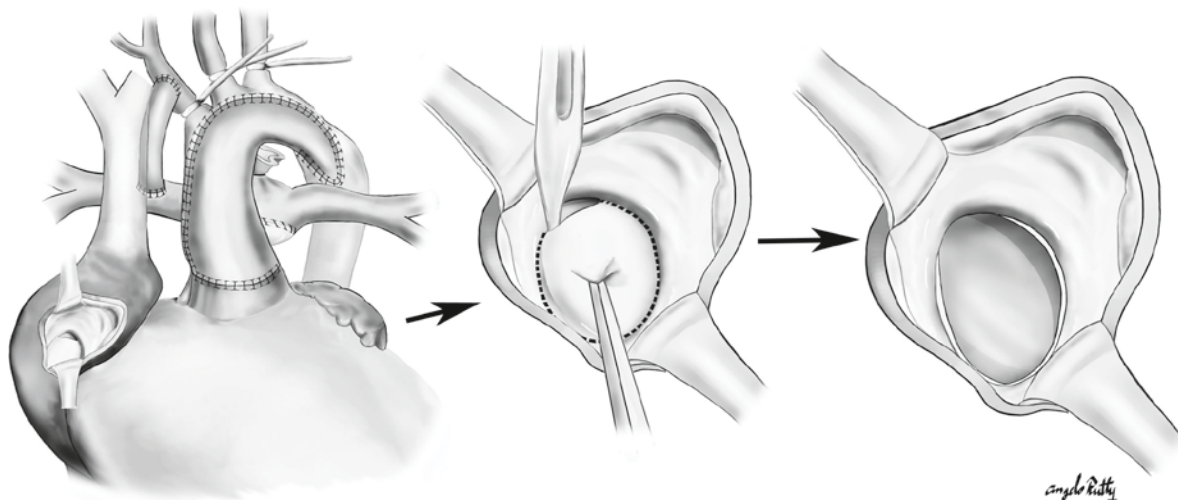


Fig. 30.5 The interatrial septum is visualized through the right atrial cannulation site and then excised

Arterial blood gases and electrolytes are monitored hourly, and the lactate level and mixed venous saturation (SvO_2) should be checked at least every 1–2 h during the first 4–6 h or until normal.

30.7.2 Respiratory Management

Mechanical ventilation with relatively deep sedation and paralysis is utilized routinely. Muscle relaxants may be discontinued once the chest is closed or 12 h after surgical repair if chest is closed upon arrival to the intensive care unit. The extubation is usually planned within 24 h after chest closure. Early extubation is encouraged in the absence of significant residual anatomic and/or hemodynamic lesions, with a normal chest X-ray, and normal neurological examination.

30.7.3 Cardiovascular Management

Low cardiac output state (LCOS) is a significant problem complicating patients' course post-Norwood operation. It usually manifests as hypotension, poor perfusion, metabolic acidosis, low mixed venous saturation, hyperlactatemia, oliguria, and hypoxemia.

Inotropic support with low-dose epinephrine (usually less than $0.1 \mu\text{g}/\text{kg}/\text{min}$) or low-dose dopamine (usually $3\text{--}5 \mu\text{g}/\text{kg}/\text{min}$) is routinely used. Therapy should be focused on significant afterload reduction

to avoid systemic under perfusion, which can be achieved with milrinone and/or, if tolerated without hypotension, with sodium nitroprusside. Alternatively, some institutions routinely use alpha-blocker agents such as phenoxybenzamine.

Early and preferably semi-elective mechanical support of circulation with venoarterial ECMO is indicated in the cases of borderline cardiac output refractory to medical management.

Technical surgical reasons for the LCOS should be sought and addressed promptly if found.

Balancing pulmonary and systemic flow remains the focus of postoperative management. Changing pulmonary vascular resistance in the immediate post bypass period could lead to significant desaturation or systemic steal with resultant volume overload of the right ventricle and systemic hypoperfusion. Manipulation of sedation, mechanical ventilation, and systemic vascular resistance is usually necessary. A saturation of approximately 75% with a PaO_2 of 30–35 mmHg is appropriate and reflects proper balance of pulmonary and systemic flow. Causes of pulmonary venous desaturation such as pneumothorax, atelectasis, high pulmonary vascular resistance, or effusion should be treated aggressively.

LCOS and unbalanced circulation are the most common causes of death in the immediate postoperative period. It is of critical importance to appropriately address the unfavorable trends in the laboratory and physiologic parameters to avoid catastrophic events.

Bleeding is common after Norwood repair due to multiple suture lines, and transfusions of various blood products are frequently required. It is beneficial

to achieve hemostasis as early as possible and vigilance is required to replace all coagulation factors, platelets if there is an ongoing hemorrhage, and red blood cells. Fresh frozen plasma (FFP) drip could be utilized during the first 24 h to replace drainage. Thromboelastogram (TEG) provides useful information facilitating the choice of products to be utilized in patients with persistent bleeding.

Feeding is usually started once the infant is stable from a hemodynamic standpoint. Oral feeding is preferred, but gavage feedings of high calorie formula (28–30 kcal/oz) is also used with the aim to provide at least 120–140 kcal/kg/day. At hospital discharge (approximately 3–4 weeks after surgery), most infants remain on afterload reduction with Captopril or Enalapril, diuretics for right ventricular volume overload, and aspirin to prevent thrombosis of the shunt.

30.8 Long-Term Outlook

Since the development of the staged approach for the repair of HLHS in the early 1980s, the improvement in long-term outlook for these patients is tightly linked to advances in surgical technique and care. Better understanding of complex physiology of HLHS and well-structured follow-up care have led to improvement in inter-stage mortality. The largest report to date on outcome analysis and risk factors for death associated with the Norwood procedure was done in 2003 by the Congenital Heart Surgeons Society [7] where 985 neonates were enrolled from 29 participating centers between 1994 and 2000. Of those, 710 patients underwent the Norwood procedure with overall survival after surgery reaching 72%, 60%, and 54% at 1 month, 1 year, and 5 years, respectively. The inter-stage mortality was 37%. Almost 60% of patients reached the cavopulmonary anastomosis stage by 18 months of age. Risk factors for death occurring before subsequent transition (cavopulmonary shunt, cardiac transplantation, or Fontan operation) were identified in three categories:

1. Patient-specific variables: lower birth weight, smaller ascending aorta, older age at Norwood operation
2. Institutional variables: institutions enrolling less than ten neonates and two institutions enrolling more than 40 neonates

3. Procedural variables: shunt originating from aorta, longer circulatory arrest time, and the technique of surgical management of the ascending aorta.

Of neonates undergoing cavopulmonary shunt, 91% had reached a subsequent transition state by 6 years after the procedure, consisting of Fontan operation (79%), death (9%), or cardiac transplantation (3%). Risk factors for death occurring before subsequent transition included younger age at cavopulmonary shunting and the need for right atrioventricular valve repair. From the late 1990s most large centers have been reporting significant improvement in early mortality after the Norwood operation with a few centers reporting stage I survival rates higher than 90% [8]. Accumulation of surgical experience with Norwood stage I repair and introduction of the Sano modification have changed the profile of factors affecting patients' survival. In a review of 333 patients with HLHS who underwent the Norwood procedure between 1992 and 2004, the following factors were listed that influenced early mortality after the Norwood procedure: pulmonary blood flow supplied by a right ventricle to pulmonary artery (RV-to-PA) conduit, arch reconstruction with pulmonary homograft patch, and increased operative weight improved early mortality while increased periods of cardiopulmonary bypass and deep hypothermic circulatory arrest increased early mortality [9]. Introduction of the Sano modification to the Norwood stage I repair (NW-RVPA) have been reported by some centers to reduce early mortality and inter-stage mortality related to a more stable and efficient hemodynamic profile with higher diastolic blood pressure and a lower Q_p/Q_s ratio [10–12]. However, centers with large surgical volume, significant experience with Norwood Blalock–Taussig shunt modification (NW-BTS), and low stage I palliation mortality for HLHS did not appreciate similar differences in early morbidity and mortality between the NW-RVPA and NW-BTS procedures [13]. Larger long-term randomized controlled studies are needed to ascertain the absence of adverse effects of ventriculotomy on performance of a single ventricle.

Some cardiac centers perform transplantation for the management of HLHS. Survival following transplantation has improved as advances in pre- and post-operative management continue along with new options for immunosuppression. The overall 5 years survival rate after cardiac transplantation is approximately 70% or close to the results for surgical approach

with staged reconstruction. Most studies report some degree of neurodevelopmental disabilities in patients with HLHS compared to general population or patients with other single ventricle physiology.

A multicenter study of neurodevelopmental outcomes of 48 school-age patients who had undergone primary heart transplantation or the Norwood procedure for palliation of HLHS showed mean neurocognitive test results that were significantly below population normative values regardless of the surgical approach [14]. As the mortality associated with HLHS decreases and survival approaches that of the other complex congenital heart defects, the neurodevelopmental outcome and long-term quality of life for patients with palliated HLHS is becoming a new focus of attention.

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Chapter 31

Single Ventricle. General Aspects

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31.1 Introduction, Anatomy and Physiology, Classification

This chapter concentrates on general aspects of the classification and physiology of the single ventricle. Specific chapters in this book are dedicated to anomalies with single ventricle physiology, like the hypoplastic left and right syndrome (i.e., chapters 22 and 30).

Single ventricle anatomy and physiology is common to a wide group of complex congenital cardiac defects, with an incidence of 5/100,000 alive newborns, and an equal gender distribution.

Three genetic anomalies have been documented in animal models in association with this disease: these anomalies involve the *Mef2c* null, the *dHAND/Hand2* null, and the *fog-2* null genes (1–3).

Single ventricles are often associated with complex cardiac malpositions, heterotaxia with levo- or dextro-isomerism.

This anomaly, complex by definition, may have atrioventricular concordance or discordance, different types of atrioventricular connections, concordant or discordant ventricular–arterial connections and may be associated with multiple other defects with or without aortic (less frequent) or pulmonary (more frequent) valvular or subvalvular obstruction or both (exceptional).

In the context of heterotaxia we may also identify anomalous systemic venous returns (i.e., interrupted inferior vena cava with azygos continuation) or pulmonary venous connections (partial or total anomalous pulmonary venous return with or without obstruction)

that significantly complicate the surgical and medical management of these patients.

The atrioventricular connection may be a single inlet (i.e., mitral or tricuspid atresia), a double inlet (two functional atrioventricular valves), or a common inlet (likewise the atrioventricular septal defect). Atrioventricular valves may be overriding or straddling across large interventricular communications.

The single ventricle may be morphologically left, right, or undefined.

Often, the normal ventricle communicates with a rudimentary hypoplastic undeveloped ventricle through the bulboventricular foramen which may play an important role in the pathophysiology of the single ventricle when restrictive. Such restriction may be the source of a subvascular aortic or pulmonary obstruction. The same principle applies to anatomic forms where we can document complex subvascular obstructions, often due to conal septal muscular or fibrous structures.

Ventriculo-arterial connections may be concordant or discordant and aortic or pulmonary stenosis or atresia may co-exist.

By definition, *a single ventricle physiology is applicable to any cardiac defect that would not allow a biventricular type repair*. Hence, cardiac defects with single ventricle physiology include various anatomic forms:

1. Complex congenital cardiopathies with a single functional ventricle, with right, left, or undetermined morphology:
 - Hypoplastic left heart syndrome (HLHS)
 - Right-sided heart malformations:

Pulmonary atresia with intact interventricular septum and severe right ventricular hypoplasia (nontripartite ventricle)

Tricuspid atresia

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- Severe forms of Ebstein's disease
- Heterotaxia syndromes with left or right isomerism (i.e., Ivemark syndrome)
 - “Criss-cross” type anomalies
2. Cardiac defects with significant ventricular unbalance:
 - Atrioventricular septal defect
 - Double outlet right ventricle
 3. Cardiac defects with multiple interventricular septal defects (“swiss-cheese” type VSD)

From the pathophysiological standpoint patients may have:

- a. Decreased systemic flow in case of aortic subvalvular and/or valvular and/or vascular obstruction
- b. Decreased pulmonary flow in case of pulmonary subvalvular and/or valvular and/or vascular obstruction
- c. High pulmonary flow with pulmonary hypertension if there is no pulmonary protection; this may co-exist with left-sided obstructions
- d. Restrictive intracardiac mixing at the atrial and/or the ventricular level

31.2 Clinical Aspects

Clinical expression of this anomaly depends on the anatomic and functional associations.

Most patients are diagnosed in the neonatal period, particularly those who have a ductal-dependent circulation because of pulmonary or aortic obstruction. These patients become cyanotic or progress toward cardiogenic shock once the ductus arteriosus becomes restrictive or closes.

Depending on the associated lesions, patients may have a cardiac murmur, usually ejective in nature if there is a vascular obstruction, regurgitant in case of incompetent atrioventricular valves, continuous if there is a largely patent ductus arteriosus or in presence of collateral circulation. The first heart sound is usually normal (may be split in case of severe Ebstein) and the second sound unique, and loud in case of pulmonary hypertension. When there is an obstructive systemic physiology, pulses will be weak, absent or asymmetrical and the patient will display signs of low cardiac output or shock or progressive lethargia, diaphoresis, difficulty to feed, tachypnea, and tachycardia. When an obstructed total anomalous pulmonary venous return is present, patients rapidly progress

to shock in the context of a “white lung” syndrome. The same applies to patients with HLHS in which the atrial septal defect is restrictive or even absent, requiring an emergent intervention at birth in order to enlarge the communication with an eventual stent insertion.

31.2.1 Chest X-ray

Radiological findings are very heterogeneous and depend of the anatomic and physiological characteristics of the malformation. Heterotaxic diseases or isomeric forms often show signs of situs inversus or ambiguous with left or right isomerism, levo or dextrocardia. Forms with pulmonary obstruction will present with oligemic lungs. When the pulmonary bed is unprotected the chest X-ray will display excessive blood flow with increased vascular markings. The presence of diffuse interstitial infiltrates or a “white-lung” aspect strongly suggests an obstructed pulmonary venous return. Likewise, there may be various degrees of cardiomegaly.

31.2.2 Electrocardiogram

The ECG, although unspecific, may provide information regarding axis deviation and predominance that may be useful in steering the diagnosis. It is also useful to rule-out any associated arrhythmias or conductive disorders.

31.2.3 Echocardiography

Transthoracic echocardiography remains the cornerstone of diagnosis (4), allowing the fine identification of the anatomy and of the physiological characteristics of the disease. Transesophageal echocardiography is often used in the operating room to further elucidate intracardiac anatomic details and postoperative results.

31.2.4 Cardiac Catheterization

In the modern setting, diagnostic cardiac catheterization of patients with single ventricle is seldom required

in the neonatal period, unless there is a complex venous return requiring elucidation or when there are doubts about the pulmonary resistances (5–7). Nevertheless, the cardiac catheterization remains an important diagnostic assessment of patients awaiting a cavo-pulmonary connection (see below).

Interventional procedures play an important role in the joint management of these anomalies with the surgical team or else for electrophysiological studies (please see chapters 5 and 53). Modern programs are currently developing hybrid approach for different scenarios and particularly for hypoplastic left heart syndrome.

31.2.5 Other Diagnostic Techniques

MRI (8) and angio CT scan are important diagnostic tools and will probably become the reference in the near future in the diagnosis of both the anatomy and the pathophysiology of the single ventricle.

31.3 The Specific Case of the Tricuspid Atresia

Tricuspid atresia (Fig. 31.1) follows the above described principles and management may vary depending on the anatomic form.

This is probably the only type of single ventricle physiology safely allowing a total cavo-pulmonary connection in a single step without the risks of an unfavorable ventricular remodeling.

Anatomical variations are classified as a combination of type I, II, or III with the subtypes a, b, or c (Figs. 31.2 and 31.3), as follows:

Type I: with normal ventriculo-arterial concordance

Type II: with d-transposition of the great arteries

Type III: with l-transposition of the great arteries, frequently associated with aortic coarctation or with subaortic obstruction by a double conal septum

Subtype a: with pulmonary atresia

Subtype b: with significant pulmonary valvular or subvalvular stenosis

Subtype c: without pulmonary protection



Fig. 31.1 2D echocardiography showing a tricuspid atresia with a hypoplastic right ventricle communicating with the left ventricle by a bulboventricular foramen (RA right atrium; LA left atrium; MV mitral valve; TA tricuspid atresia; LV left ventricle; RV rudimentary right ventricle; BVF bulboventricular foramen)

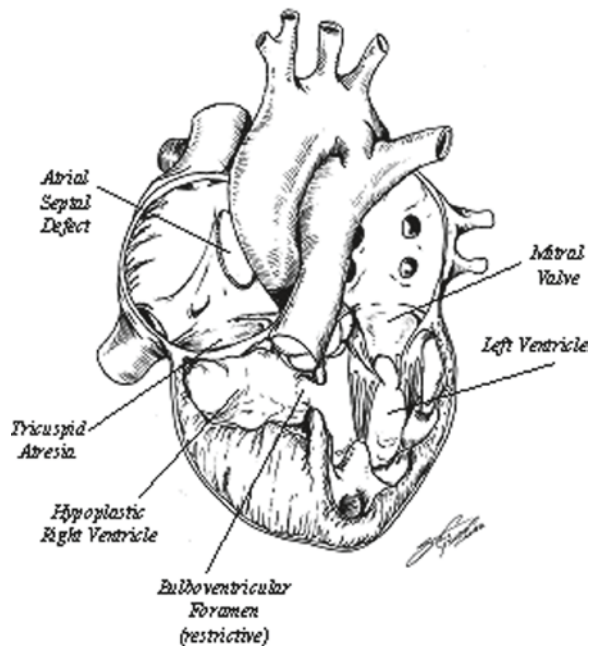


Fig. 31.2 Type 1c tricuspid atresia, with well positioned vessels, a large bulboventricular foramen and without pulmonary stenosis or atresia

31.4 Surgical Management of Single Ventricles: General Principles

The concept of univentricular type “repair” implies that patients will need a sequence of palliative interventions steering the therapy toward a common pathway achieving

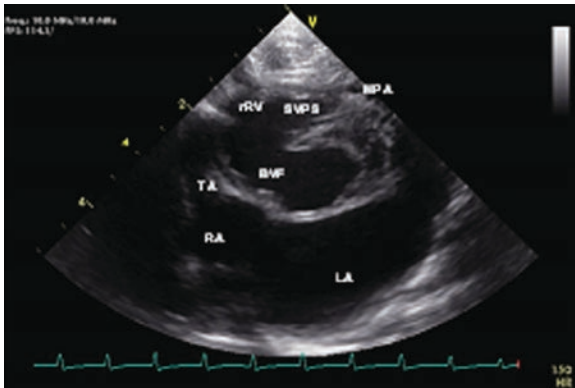


Fig. 31.3 2D echocardiography showing a type 1b tricuspid atresia (LA left atrium; RA: right atrium; TA: tricuspid atresia; rRV: rudimentary right ventricle; BVF: bulboventricular foramen; MPA: main pulmonary artery; SVPS: severe subvalvular pulmonary stenosis)

the ultimate goal of a total cavo-pulmonary connections or modified Fontan type physiology (9–11).

There are essentially three palliative phases:

1. Neonatal palliation
2. Cavo-pulmonary connection in two steps, exceptionally performed in a single step in the case of tricuspid atresia:
 - Modified Glenn connection (Fig. 31.4), bidirectional Glenn connection, Hemi-Fontan or partial cavo-bipulmonary connection (or bicavo-bipulmonary, in case of right and left superior vena cava)
 - Modified intra or extracardiac Fontan connection (Fig. 31.5) or total cavo-pulmonary connection

The most commonly followed algorithm is as follows:

- First Phase: Neonatal palliation
 - Modified Blalock–Taussig or a central shunt in case of a right obstruction. Alternatively, some teams may consider stenting the ductus arteriosus
 - Surgical repair of any left obstruction: i.e., aortic coarctectomy
 - Norwood, Sano or Damus–Kaye–Stensel type intervention, hybrid approach or orthotopic heart transplant in case of HLHS or unbalanced ventricles with severe and irrecoverable left obstruction
 - Pulmonary artery banding in case of high pulmonary flow with pulmonary arterial hypertension (unprotected pulmonary flow)

- Second Phase: 3–6 months of age:
 - Partial cavo-pulmonary connection (modified Glenn procedure or Hemi-Fontan procedure)
- Third Phase: 2–6 years of age:
 - Total cavo-pulmonary connection (modified Fontan procedure; intra or extracardiac ; with or without fenestration)

31.4.1 Variants with Aortic or with Pulmonary Obstruction

31.4.1.1 Patients with Subvalvular or Valvular Pulmonary Obstruction

These patients have a significant ductal-dependent and therefore PGE₁-dependent cyanosis requiring a neonatal palliation. The classic intervention is a modified Blalock–Taussig or a central shunt. In some cases, the alternative of interventional percutaneous balloon dilatation of the right outflow tract or ductal stenting may be considered.

31.4.1.2 Patients with Obstruction of the Aortic Arch

These forms are almost always associated with high pulmonary flow and pulmonary hypertension. Therefore, patients require a surgical palliation associating aortic arch repair (i.e., coarctectomy) with a pulmonary artery banding. Surgical techniques are decided upon the team's choice and the degree of aortic hypoplasia and may be performed through a thoracotomy, or else through a sternotomy with hypothermic circulatory arrest or using specific cannulation techniques to ensure an adequate cerebral perfusion.

31.4.1.3 Patients with HLHS or with Complex Left Ventricular Outflow Tract Obstructions

Details concerning therapy of HLHS is further discussed in a specific chapter (chapter 30). HLHS is a complex disease for which different alternatives might be considered:

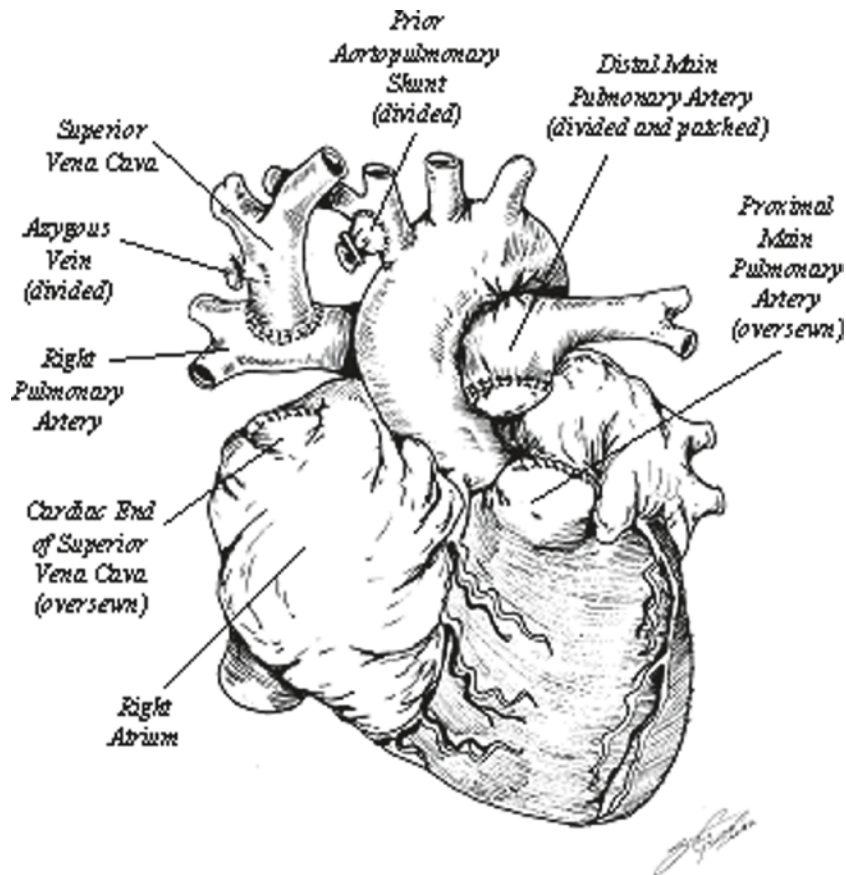


Fig. 31.4 The modified Glenn anastomosis or partial cavo-pulmonary connection

- Therapeutic abstention: may be an option in certain environments or by family choice
- Norwood type intervention (stage I) or Sano procedure
- The hybrid approach: following this approach, a stent is inserted in the ductus arteriosus to ensure its patency and pulmonary circulation is protected by selective surgical pulmonary branch bandings or by intravascular prosthesis inserted by catheterization. Patients may subsequently progress toward a combination of stage 1 and 2 Norwood procedure (associating the removal of the ductal stent, plasty of pulmonary arteries, the creation of a neo-aorta with repair of the isthmic aortic obstruction and a partial cavo-pulmonary connection) or towards an orthotopic heart transplant, in which case the need for neonatal pulmonary protection is controversial. Indications for this approach vary depending on the institutions but may include: prematurity, low birth-weight, significant ventricular dysfunction, significant tricuspid regurgitation, lung disease, or other associated malformations, and parental choice.
- In case of complex subaortic obstruction surgical approach may be a Damus-Kaye-Stensel intervention in which, like in the Norwood procedure, the main pulmonary artery is anastomosed to the ascending aorta (neo-aorta) with correction of any eventual aortic coarctation and creation of a modified Blalock–Taussig shunt.
- Other situations: in some anatomic forms like the type IIc tricuspid atresia with d-transposition of the great arteries, unprotected pulmonary flow and restrictive bulboventricular foramen at the origin of significant subaortic obstruction, the alternative of an arterial switch may be discussed, transforming the aortic obstruction into a protective subpulmonary obstruction.

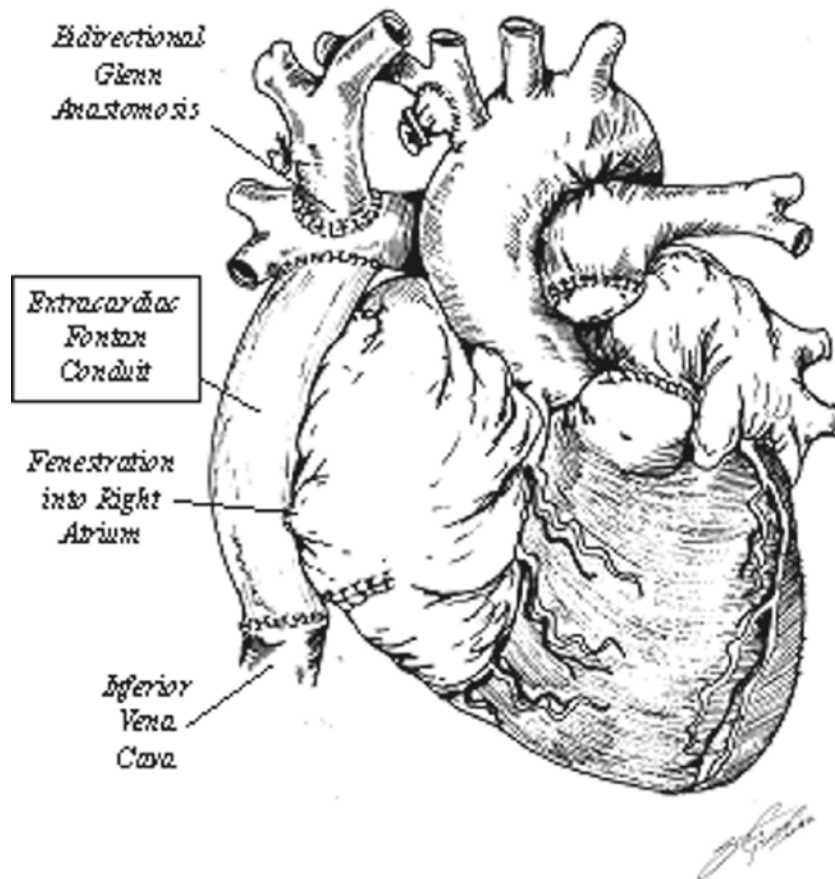


Fig. 31.5 Extracardiac fenestrated modified Fontan or total cavo-pulmonary connection

31.4.1.4 Patients with Hypoplastic Right Heart Syndrome

This group of cardiac malformations is initially approached as any severe right-sided obstruction, by creating a modified Blalock–Taussig or a central shunt.

31.4.2 Variants without Pulmonary Protection (May Be Associated with Left Obstructions)

Such patients need an intervention aiming to protect their pulmonary vascular bed from high flow and pulmonary hypertension. Hence, a pulmonary artery banding is the indication.

31.4.3 Complex Variants with Heterotaxia

In the context of heterotaxia, single ventricles are usually associated with cardiac malpositions and with complex anomalous systemic or pulmonary venous returns that require complex interventions at the time of the above-described palliations. Other associative defects have been described and are intimately linked to the type of isomerism, dextro or levo. These include anomalies of the atrioventricular concordance, the ventriculo-arterial concordance that often co-exist with aortic or pulmonary subvalvular or valvular obstructions. Rhythm disturbances are not uncommon. Patients with heterotaxia may also have extra-cardiac comorbidities that complicate management in early life, like intestinal malrotation.

31.5 Postoperative Management of Neonatal Palliative Interventions

Management of HLHS, aortic coarctation, and anomalous pulmonary venous return are discussed in specific chapters in this book.

Pulmonary artery banding and modified Blalock–Taussig or central shunts that usually have an uneventful postoperative course but in some patients, particularly in low weight or premature newborns, the Q_p/Q_s balance may be difficult to achieve:

- Patients with high pulmonary resistances that may be a source on undercirculation (desaturation, oligemic lungs) may require specific management as described in the chapter dedicated to pulmonary hypertension (chapter 44), essentially with the adequate ventilation and the use of inhaled pulmonary vasodilators. Other causes for undercirculation to be addressed, may relate to significant systemic vasoplegia, to small pulmonary arteries or to partial shunt obstruction, which emergently needs to be elucidated.
- Patients with high pulmonary flow (overcirculation expressed by saturations above 80%, low diastolic pressures with a high pulse differential, radiological signs of pulmonary volume overload, progressive metabolic acidosis and hyperlactatemia), will require a “pharmacological banding” associating:
 1. Maintenance of high blood viscosity (hematocrit above 40–45%)
 2. Diuretics, usually furosemide or bumetamide eventually associated with hydrochlorotiazide or with spironolactone
 3. Systemic IV vasodilators to optimize afterload reduction (milrinone, sodium nitroprusside, nitroglycerine, phentolamine, phenoxybenzamine), followed by oral drugs (captopril, enalapril)
 4. Hypoxemic therapy may be required in some cases
 5. In refractory case, a comprehensive anatomic assessment by echocardiography should be undertaken in order to assess function and the presence of residual lesions (i.e., residual aortic coarctation)

A saturation of 80% reflects a Q_p/Q_s around 1/1 if pulmonary venous saturations are normal; nevertheless, caution has to be taken in patients with desaturated pulmonary veins, in which case the same 80%

of systemic saturation could reflect a much higher Q_p/Q_s .

The aim of this “pharmacological banding” is to decrease the Q_p/Q_s following the principles described in Poiseuille’s law: flow is directly proportional to the ratio of resistances and the diameter of the shunt and inversely proportional to the length of the shunt and blood viscosity.

Some patients achieve an adequate balance after a few weeks of ambulatory medical therapy, although those operated during the first few days of life may show signs of overcirculation around the 3–4 weeks of life, once pulmonary resistances decrease to physiological levels.

Pulmonary artery banding may sometimes be too loose, but may also be too tight inducing the development of acute or rapidly progressive cyanosis requiring further intervention. Pulmonary banding may also migrate peripherally, producing distortion of the pulmonary arteries or even total occlusion. When the banding is too close to the pulmonary valve it may also distort the annulus and induce pulmonary regurgitation that must be addressed, particularly in those patients in whom the pulmonary valve becomes a neo-aortic valve in the future.

Particular caution ought to be observed in patients with shunts, regarding the prevention of a hypercoagulability status predisposing to thrombosis of the shunt:

- Avoid dehydration or disproportionate negative hydric balance
- Use of heparin at 10 Units/kg/h as a continuous infusion, or a bolus of 50 Units/kg every 6 h, from the sixth postoperative hour, in the absence of bleeding
- Use of antiplatelet therapy once the patients resumes enteral feeding
- Avoid polycythemia

31.5.1 Monitoring

These patients require a peripheral arterial line, ideally inserted in the right radial artery if an aortic coarctation was repaired and a central venous line as indwelling catheters. Other signs to be monitored are cardiac and

respiratory rate, peripheral oxygen saturation, ECG and eventually cerebral and abdominal NIRS. New technologies by peripheral thermodilution (i.e., PiCCO® and Flo-Trac® catheters) may become essential tools for the appraisal and the follow-up of these patients.

31.5.2 Inotropic and Vasodilator Drugs

After a pulmonary artery banding or a shunt, these patients very seldom require inotropic support. Whenever necessary, elective drugs may be dopamine or dobutamine, this later offering the benefit of some degree of systemic vasodilation, although with the potential inconvenience of inducing tachycardia and increasing myocardial oxygen consumption. Patients in overcirculation do require more selective systemic vasodilators as described above. When an aortic coarctation is repaired, patients might have tachycardia and hypertension, needing aggressive therapy with systemic vasodilators and beta-blockers, usually sodium nitroprusside or IV nicardipine and esmolol (please see chapter 26, related to Aortic Coarctation).

31.5.3 Respiratory Management

Cardiopulmonary interactions are an essential aspect to be taken into account and are in favor of an early extubation policy in the operating room or throughout the first six postoperative hours (see chapter 4, on Heart–Lung interactions). Nevertheless, some patients (low weight, premature babies, syndromic patients, or else, patients with high pulmonary resistances or with overcirculation) may require a longer ventilation period. The need for positive pressures does not necessarily justify mechanical ventilation and may be overcome with CPAP or with BiPAP. In case of delayed chest closure, extubation ought to be achieved within 12–24 h after closure. Nitric oxide (12, 13) may be required in some circumstances.

31.5.4 Sedation and Analgesia

Most patients reach good analgesic levels with nonopioid therapy eventually associated with nonsteroidal anti-inflammatory drugs. Yet, the association of morphine

or fentanyl with benzodiazepines (midazolam, lorazepam) at minimal efficient doses may prove useful during the first 48 h, particularly in patients having required an intervention by thoracotomy. Dexmedetomidine has become an attractive alternative in these patients.

31.5.5 Anticoagulation

In case of systemic–pulmonary shunt it is important to administer IV heparin at 10 Units/kg/h as a continuous infusion, or a bolus of 50 Units/kg every 6 h, from the sixth postoperative hour, in the absence of bleeding.

Antiplatelet therapy (aspirin, dipyridamol or eventually clopidogrel) ought to be prescribed as soon as patient resumes enteral feeding, allowing to suspend the heparin.

31.5.6 Management of Specific Problems

Specific problems are mostly those associated with the balance of the ratio between the systemic and the pulmonary resistances as previously discussed.

Other complications to consider may be: diaphragmatic palsy or paresis, chylothorax, Horner's syndrome, by phrenic or recurrent-laryngeal nerve lesions.

31.6 Cavo-pulmonary Connections

Different techniques may be used: modified Glenn connection, bidirectional Glenn connection, Hemi-Fontan connection or cavo bipulmonary connection (or bicavo-bipulmonary, in the presence of a right and a left superior vena cava) followed by total intra or extracardiac connections.

Single ventricle physiology is shared by various heterogeneous situations. Their common characteristic is that there is a complete mixing of oxygenated and desaturated blood that will be distributed in both the systemic and the pulmonary circuits. The main objective of the univentricular type repair or palliation is to individualize the systemic and the pulmonary circulations in order to achieve almost normal systemic saturations with a more effective ventricular workload.

The cavo-pulmonary connection performed with the Glenn intervention is the first step toward this goal.

William E Glenn firstly described his technique in 1958. The classic Glenn procedure consisted in completely dividing the left from the right pulmonary branches, connecting the latter to the right superior vena cava while preserving the anterograde flow from the heart toward the left branch. Some of these patients have survived to adulthood, but many have developed left pulmonary hypertension, having therefore become cyanosed, as an equivalent to the Eisenmenger's complex. In case of surgical intervention, these patients would require a double lumen endotracheal tube allowing differential ventilation of the right and the left lung. The current modified Glenn connection (since the 1980s) allows passive flow from the superior vena cava to both pulmonary branches and any continuity with the ventricular mass is ceased by sectioning the pulmonary trunk, or restricted by further tightening the banding, in which case a degree of anterograde pulsatile flow will persist into the pulmonary arteries.

31.6.1 Preoperative Assessment

Most patients with single ventricle physiology have an unbalanced physiological pattern and need some type of palliation. Three main pathophysiological conditions may be identified. These general rules also apply to the neonatal approach previously described. Regardless of the functional type, a percutaneous atriseptostomy or an atrial septectomy may be required in order to ensure an adequate arteriovenous mixing or to avoid postcapillary pulmonary hypertension and obstruction to the systemic or the pulmonary venous return (Table 31.1).

1) Single ventricle with restricted pulmonary flow:

In case of obstruction to the pulmonary flow, a mandatory modified Blalock–Taussig or central arteriovenous shunt is indicated in the neonatal period early in life.

2) Single ventricle with excessive pulmonary flow:

An early pulmonary banding is the universal recommendation aiming to project the pulmonary vascular bed against the deleterious effect of excessive flow and pulmonary hypertension.

Table 31.1 Preoperative evaluation of candidates to cavo-pulmonary connections

Value	Low risk	High risk
IPVR (uwood)	<2	>4
PAPm (mmHg)	<15	>20
LVEDP (mmHg)	<8	>12
EF (%)	>60	<45

IPVR indexed pulmonary vascular resistances; PAPm mean pulmonary pressure; LVEDP left ventricular end-diastolic pressure; EF ejection fraction

3) Single ventricle with restricted systemic flow:

Systemic obstructions may be multiple and heterogeneous and may involve the bulboventricular foramen, the subaortic outflow tract, the aortic valve and/or the aortic arch varying from global hypoplasia, atresia and various forms of aortic coarctation or interruption. In any of these cases, the obstruction must be removed or palliated (i.e., aortic coarctectomy, repair of an interrupted arch, removal of a subaortic obstruction, Norwood or Sano intervention, Damus–Kaye–Stensel procedure).

Whatever neonatal surgery is performed, the persistent parallel circulation may induce a hemodynamic fragility in the midterm that requires a strict follow-up including clinical assessment, appraisal of weight gain, peripheral oxygen saturation, cardiac rhythm and an echocardiographic follow-up of the systemic ventricular function, the atrioventricular valve status, and the pulmonary pressures.

31.6.1.1 Subsequent Assessment and Management

All of the above patients will become candidates for cavo-pulmonary connections throughout the first months or years of life. To summarize, the required conditions (6) to indicate a cavo-pulmonary connection or the confirmation of the absence of any anatomical or functional obstructions throughout the future cavo-pulmonary circuit:

a) Anatomic criteria:

No significant stenosis or deformation of the pulmonary arteries

No pulmonary venous stenosis

Nonrestrictive communication between the atrial cavities (in case of stenosis or atresia of an atrioventricular valve)

No subvalvular or valvular aortic obstruction
 No residual aortic coarctation
 No thrombus within the vascular bed

b) Functional criteria:

Low pulmonary pressures and resistances
 No significant atrioventricular valvular regurgitation
 Normal ventricular function, both systolic and diastolic
 Normal sinus rhythm and no conductive disorders

The main general objectives of the cavo-pulmonary connection are as follows:

- To facilitate the diastolic unload of the systemic ventricle
- To prevent deformation of the pulmonary arteries
- To avoid the negative impact of the continuous diastolic “steal” on the myocyte which, associated to the diastolic volume overload may induce irreversible myocardial changes.

These objectives are attained by diverting venous blood from the superior vena cava toward the pulmonary artery with a modified Glenn connection, or else, with a Hemi-Fontan procedure. Once this intervention is performed, the shunt is ligated and/or sectioned and the pulmonary artery banding is further tightened, or alternatively a total section of the pulmonary trunk from the ventricular mass is performed.

Usually, this intervention is proposed when the pulmonary arteries have an adequate diameter and the pulmonary vascular resistances are low, around the age of 3 months and ideally before 6 months of age.

In the case of Hypoplastic Left Heart Syndrome, the trend is to perform the cavo-pulmonary connection at the earliest.

31.6.1.2 Cardiac Catheterization

Cardiac catheterization is a common procedure prior to the cavo-pulmonary connection (5–7, 14). The objectives of such procedure are as follows:

- a. To measure saturations and pressures in the pulmonary branches and to estimate the $Q_p:Q_s$ ratio and the pulmonary vascular resistances. In patients with borderline values, cardiac catheterization allows the performance of pharmacological tests aiming to reduce the pulmonary resistances (Fig. 31.2).

- b. To perform angiographies in the ventricular cavities, the innominate vein, the pulmonary arteries, and the aortic arch.
- c. To perform interventional procedures like dilatation and stent insertion in localized pulmonary stenosis or on residual obstructions of the distal suture of the neo-aorta and also to dilate or stent any residual aortic coarctation. It may also be instrumental for the percutaneous embolization of veno-venous pulmonary collateral vessels, arteriovenous malformations (AVM) or aortopulmonary collateral vessels. Last but not least, cardiac catheterization is useful to occlude fenestrations after completion of the total cavo-pulmonary connection.

31.6.1.3 Other Investigations

Magnetic Resonance Imaging has replaced cardiac catheterization to some extent (8) in selective cases and might become the tool of election for preoperative assessment of candidates for cavo-pulmonary connections in the near future. Computerized Tomography with angiography is also a useful complementary study.

31.6.2 Surgical Techniques

31.6.3 Partial Cavo-pulmonary Connections

31.6.3.1 The Glenn Procedure

The modified Glenn anastomosis may be performed on cardiopulmonary bypass with beating heart or without cardiopulmonary bypass in patients with antegrade flow who do not require any intracardiac intervention. The superior vena cava is sectioned from the atrial mass after ligation of the azygos return and its caudal portion is directly anastomosed onto the right pulmonary artery. Any previous aortopulmonary shunt is ligated and/or sectioned. When a previous pulmonary banding has been performed, some groups maintain a persistent antegrade flow from the ventricular mass, although tightening the banding, while others favor the section of the

pulmonary trunk and even the resection of the pulmonary valve in order to remove any pouches that would become a potential source of systemic thromboembolism. The theoretical advantage of the first approach is to provide the lungs with a hepatic angiogenesis inhibitor factor that would decrease the risk for pulmonary arteriovenous fistula formation. Arteriovenous fistula have a significant hemodynamic impact on the Fontan type circulation and become a source of persistent hypoxemia and are more common in patients with heterotaxia and with interrupted inferior vena cava and azygos continuation in whom a Kawashima procedure is performed. Potential disadvantages of preserving the pulmonary antero-grade flow are pulmonary diastolic overload and potential for distortion of the pulmonary artery anatomy by the banding, particularly if it migrates toward the pulmonary branches bifurcation. During the same operating time, other interventions might be indicated: atrioventricular valvular plasty, atrial septectomy, pulmonary artery plasty or patch enlargement, or repair of any residual aortic arch obstruction.

The Glenn anastomosis is more laborious and may carry an increased morbidity when performed in patients with HLHS and previous hybrid approach, in whom it is required to remove the ductal stent and perform an atrial septectomy, a plasty of the pulmonary arteries and a reconstruction of the aortic arch.

Like for many other cardiac surgeries, modified ultrafiltration (MUF) facilitates hemoconcentration and favors a more stable postoperative course.

31.6.3.2 The Hemi-Fontan Procedure

This is an alternative to the modified Glenn cavo-pulmonary connection. It might facilitate the second step toward the total cavo-pulmonary connection if the choice is an intracardiac tunnel. It consists in creating an anastomosis between the right atrium and the pulmonary artery by septalizing the atrial cavity with a Goretex® patch in order to divert the flow drained from the superior vena cava onto the pulmonary bed, while ensuring the drainage of the flow arriving from the inferior vena cava toward the ventricular mass, across the atrioventricular valve.

31.6.4 Postoperative Management

31.6.4.1 Monitoring

These patients should be monitored with the classical tools (cardiac rate and ECG, respiratory rate, oxygen saturation, arterial pressure both invasive and noninvasive) to which should be added a transthoracic right atrial catheter to appraise central venous pressure and an internal jugular indwelling catheter to assess the pulmonary artery pressure. This later catheter should be removed as soon as possible, once the hemodynamic profile shows to be adequate and stable, in order to minimize risks for thrombosis in the cavo-pulmonary circuit. NIRS and modern technology by thermodilution (i.e., PiCCO® and Flo-Trac® catheters) are becoming essential tools for the appraisal and the follow-up of these patients.

31.6.4.2 General Measures

After a partial cavo-pulmonary connection, general measures to be undertaken do not change significantly from the measures adopted for any postoperative case, with a few important details to be mentioned:

- Patients should be positioned in a 45° semifowler decubitus, to promote passive venous drainage by gravity
- Enteral feeding should be resumed as soon as possible
- Early mobilization is crucial
- Any indwelling lines, particularly those in the superior venous axis, should be removed as early as possible
- Caution should be taken with regards to the pleural drains; the trend is to be conservative and leave them in situ for at least 48 h, taking into account the accrued risk for pleural effusion and chylothorax

31.6.4.3 Inotropic and Vasodilator Therapy

Usually, these patients require low doses of inotropes (milrinone or amrinone). Target saturations should remain between 75 and 80%, central venous pressures around 5–6 mmHg, mean pulmonary pressures

should be below 15 mmHg with a low transpulmonary gradient. It is common to observe a transient systemic hypertension, quite likely of central origin.

31.6.4.4 Respiratory Management

Cardiopulmonary interactions are crucial in the context of the cavo-pulmonary connections. Ventilatory parameters should be rigorously monitored in order to preserve both the pulmonary and the cerebral blood flow. Hyperventilation should be avoided, since although facilitating pulmonary flow, it would decrease cerebral flow which ensures the main preload of the cavo-pulmonary system. As a matter of fact, an elevated $p\text{CO}_2$ should not preclude extubation as it increases the cerebral blood flow and therefore the Glenn flow. Also, positive intrathoracic pressures induce a reduction of both the pulmonary flow and the systemic ventricle preload with an increase of pulmonary vascular resistances. Therefore, most patients are extubated in the operating room or during the first six postoperative hours, once there is evidence of hemodynamic, neurologic, respiratory and homeostatic stability and controlled bleeding. Ventilation is better tolerated after the partial connection rather than the total connection because in the first case, flow from the inferior vena cava to the heart fills the systemic ventricle independently. Any respiratory complications like atelectasis, pneumothorax or pleural effusions should be promptly rectified.

31.6.4.5 Sedation and Analgesia

Postoperative sedation and analgesia should target proper levels of comfort while ensuring spontaneous breathing autonomy allowing early extubation. A balance must be established to avoid pain, allow proper cough and airway protection (to reduce risks of atelectasis), and reduce the typical irritability that characterizes these patients, secondarily to transient cerebral venous congestion and changes in cerebral flow patterns.

31.6.4.6 Anticoagulation

Prophylactic anticoagulation with heparin at 10 Units/kg/h as a continuous infusion, or a bolus of 50 Units/kg every 6 h, should be started from the sixth postoperative

hour, in the absence of bleeding. Then, on the 1 day, once feeding is resumed, it should be replaced by antiplatelet therapy with aspirin (3–5 mg/kg/day). Alternatively, dipyridamol or clopidogrel might be used although the latter still requires further clinical studies in the pediatric population.

31.6.4.7 Complications

The four main complications to be taken into account after the partial cavo-pulmonary connection are as follows:

1. Increased pressures in the cavo-pulmonary circuit
2. Hypertension and bradycardia
3. Low cardiac output syndrome (LCOS)
4. Hypoxemia

Increased Pressures in the Cavo-pulmonary Circuit

Immediately after surgery there may be a transient increase of pressures in the cavo-pulmonary circuit, secondarily to the inflammatory changes induced by the cardiopulmonary bypass, volume overload, and the mechanical ventilation with positive pressure. The clinical expression of this complication is the development of a superior vena cava syndrome, associated with increased pulmonary pressures, progressive cyanosis, and decrease in the systemic stroke volume.

It is therefore important to establish a spontaneous breathing pattern as early as possible, to aggressively manage any respiratory complication (atelectasis, pneumothorax or pleural effusions), to use pulmonary vasodilators as required, mostly Nitric Oxide (12, 13) and sildenafil, and to start loop diuretics to induce diuresis and a negative balance. When pressures persist high in spite of these measures (above 18 mmHg) a cardiac catheterization might be required to rule out stenosis at the anastomotic site or else, distally in the pulmonary arteries, thrombosis, or high pulmonary vascular resistances.

Hypertension and Bradycardia

The mechanism behind hypertension might be an inadequate pain control, stress response with release of catecholamines or a down-regulator effect to maintain

cerebral perfusion in the context of high venous pressure and congestion. This phenomenon is usually transitory and well controlled with angiotensin inhibitors, but during the acute phase, these patients might need the use of sodium nitroprusside or intravenous calcium inhibitors.

Bradycardia is usually a reflex response to the sudden unload induced by the Glenn connection, although in a small percentage of cases it may be due to a lesion of the sinus node, in which case it is unresponsive to drugs like atropine or isoproterenol.

Low Cardiac Output Syndrome (LCOS)

Significant LCOS is seldom observed after a partial cavo-pulmonary connection (Table 31.2), except in patients with previous ventricular dysfunction or with severe atrioventricular valvular regurgitation, in whom a sudden unload may have an impact in cardiac output. In patients with such documented conditions, cardiac transplant ought to be considered rather than a progression toward a univentricular repair pathway.

Hypoxemia

Hypoxemia is the most common short- and long-term complication after a partial cavo-pulmonary connection. Initial saturations should remain between 75 and 85%. Persistent saturations below 70% justify further investigations. Etiology of persistent hypoxemia is variable and heterogeneous and may include: decreased cerebral flow (hypocapnia, hypotension), ventilation/perfusion mismatch (pleural effusion, atelectasis, pneumothorax, pneumonia, AVM), increased oxygen consumption (sepsis, low cardiac output, ventricular dysfunction, anemia), or decreased pulmonary blood flow (increased pulmonary vascular resistances, stenosis of the

cavo-pulmonary anastomosis, veno-venous collateral vessels, restrictive intra-atrial communication).

Veno-venous collateral vessels between the superior and inferior venous territories induce a persistent desaturation by decreasing the effective pulmonary flow and some may be occluded by percutaneous interventional catheterization.

AVM are a common cause of late hypoxemia (15, 16) and are more frequently documented in heterotaxic syndromes with interrupted inferior vena cava and azygos continuation. They are thought to develop because of the absence of a hepatic angiogenesis inhibitor factor. Diagnosis is suggested by echocardiography with contrast test and ensured by angiography. AVMs tend to progress after the completion of the Fontan circuit. Patients having had a Kawashima intervention (17, 18) are more prone to develop AVMs and chronic hypoxemia.

Currently, partial cavo-pulmonary connections carry a very low morbidity and mortality is close to 0%.

31.6.5 Total Cavo-pulmonary Procedures

31.6.5.1 The Fontan and Modified Fontan Procedures

Francis Fontan originally described a procedure by which the right atrial cavity would be directly anastomosed onto the pulmonary artery (9). This technique lately showed to have a number of disadvantages, due to persistent blood stasis in the right atrium. Concomitantly, it was recognized in the early 1980s that to proceed with a total cavo-pulmonary connection in one surgical step would have a significant mortality due to a significant acute remodeling of the systemic ventricle. Since inception of the original Fontan's technique, three essential

Table 31.2 Low Cardiac Output Syndrome (LCOS) associated with cavo-pulmonary connections

Pressure monitoring (mmHg)	CVP–PAP <2 PAP–P _{la} <5 P _{la} <5	CVP–PAP >2 PAP–P _{la} <5 P _{la} = 5–10	CVP–PAP <2 PAP–P _{la} >5 P _{la} = 5–10	CVP–PAP <2 PAP–P _{la} <5 P _{la} >10
Diagnostic orientation	Hypovolemia	Restrictive SVC to PA anastomosis PA thrombosis	Increased pulmonary resistances Pulmonary venous stenosis	Ventricular dysfunction Left-sided obstruction Atrioventricular valve regurgitation

PA pulmonary artery; CVP central venous pressure; PAP pulmonary arterial pressure; P_{la} left atrial pressure; SVC superior vena cava

modifications were developed for patients who had already undergone the Glenn or the Hemi-Fontan connection as a first step intervention in order to avoid or limit the remodeling phenomenon (17, 18, 19–36). First, the anastomosis between the inferior vena cava, the hepatic veins, and the pulmonary artery was performed as an intracardiac shunt created with the wall of the right atrium and with Goretex® and diverting the blood draining from the inferior segment of the body toward the pulmonary artery. Second, a more recent modification was proposed by diverting the blood with an extracardiac conduit, a less traumatic surgery, and theoretically reducing the risks for arrhythmia, the latter not having been demonstrated so far. The third and probably the most important modification consists in the creation of a fenestration between the intra or the extracardiac conduit and the atrial mass. This fenestration acts like a “pop-off” structure that is functionally useful in patients in whom the pulmonary pressures and resistances are above the desired levels. Although inducing cyanosis, this fenestration allows a more stable and adequate hemodynamic profile and decreases the risk of persistent “right failure” with superior vena cava syndrome, peripheral edema, ascitis, and protein-losing enteropathy.

31.6.6 Postoperative Management

31.6.6.1 Monitoring

After a total cavo-pulmonary connection patients should be comprehensively monitored with cardiac rate and ECG, respiratory rate, oxygen saturation, arterial pressure both invasive and noninvasive and also have a transthoracic atrial catheter and an internal jugular indwelling catheter to assess the pulmonary artery pressure. Indwelling catheters should be removed as soon as possible to minimize risks for thrombosis in the cavo-pulmonary circuit. Near infra-red spectroscopy (NIRS) and modern technology by thermodilution (i.e., PiCCO® and Flo-Trac® catheters) may also be instrumental in taking therapeutic decisions with these patients.

31.6.6.2 General Measures

As for the partial cavo-pulmonary connections, general measures are the same as for any postoperative case,

but again, there are a number of specific details to cautiously follow:

- Patients should be positioned in a 45° semifowler decubitus with partly folded legs, to promote passive venous drainage from both the superior and the inferior segments of the body
- Enteral feeding should be resumed as soon as possible
- Early mobilization is crucial
- Any indwelling lines should be removed as early as possible
- Caution should be taken with regard to the pleural and mediastinal drains since these patients are prone to develop pericardial and pleural effusions and chylothorax, mostly when the pulmonary pressures are high or in the upper normal range.

31.6.6.3 Inotropic and Vasodilator Therapy

After a total cavo-pulmonary connection, patients often need low to moderate doses of inotropics or lusitropic drugs (milrinone). Target saturations should remain above 90%, central venous pressures that correspond to mean pulmonary pressures should be below 15 mmHg with a low transpulmonary gradient. As for the Glenn procedure, it is common to observe a transient systemic hypertension or transient peripheral and central edema.

31.6.6.4 Respiratory Management

As for the Glenn connection, cardiopulmonary interactions are fundamental. Ventilatory parameters should be rigorously monitored in order to preserve both the pulmonary and the cerebral blood flow. Hyperventilation should be avoided. Caregivers should keep in mind that positive intrathoracic pressures induce a reduction of both the pulmonary flow and the systemic ventricle preload with an increase of pulmonary vascular resistances. Ventilation is better tolerated after the partial connection rather than the total connection because in the first case, flow from the inferior vena cava to the heart fills the systemic ventricle independently. Consequently, most patients are extubated in the early phase of their postoperative course, once there is evidence of hemodynamic, neurologic, respiratory and homeostatic

stability and controlled bleeding. Any respiratory complications like atelectasis, pneumothorax or pleural effusions should be promptly rectified.

Patients with persistent low saturations (“right-to-left” shunt through the fenestration) and high pulmonary pressures may benefit from inhaled nitric oxide although its administration has to be cautious when the function of the systemic ventricle is borderline.

31.6.6.5 Sedation and Analgesia

Postoperative sedation and analgesia should target proper levels of comfort while ensuring spontaneous breathing autonomy allowing early extubation. A balance must be established to avoid pain, allow proper cough and airway protection (to reduce risks of atelectasis), and reduce the typical irritability that characterizes these patients, secondarily to transient cerebral venous congestion and changes in cerebral flow patterns.

31.6.6.6 Anticoagulation

There is no current consensus regarding the potential benefit of long-term anticoagulation versus antiplatelet aggregation therapy after a total cavo-pulmonary connection.

Nevertheless, acute prophylactic anticoagulation is universally ensured with heparin as previously described.

Once feeding is resumed, it may be replaced by antiplatelet therapy with aspirin (3–5 mg/kg/day), alternatively with dipyridamol or clopidogrel or by anticoagulation with anti-vitamin K agents as opposed to antiplatelet drugs.

Patients with dysfunctional Fontan physiology or with documented procoagulant status should be seriously considered for active anticoagulation (37) with oral anti-vitamin K agents and/or with subcutaneous heparin, taking into account their risk for thrombosis.

31.6.6.7 Complications

Main *anticipated complications* after the total cavo-pulmonary connection are as follows:

- 1) Increased pressures in the cavo-pulmonary circuit
- 2) LCOS
- 3) Hypoxemia

4) Other:

- Pleural effusions, chylothorax, pericardial effusion
- Arrhythmias
- Phrenic nerve palsy
- Thromboembolic events

Other *chronic complications*:

- a. Development of venous collaterals, pulmonary AVM, or systemic-to-pulmonary arterial collaterals
- b. Failure to thrive
- c. Protein losing enteropathy (PLE)
- d. Low functional capacity
- e. Plastic bronchitis
- f. Thromboembolic events

31.6.6.8 Acute Complications of Total Cavo-pulmonary Connections

Increased Pressures in the Cavo-pulmonary Circuit

As for the partial cavo-pulmonary connections, there may be a transient increase of pressures in the cavo-pulmonary circuit, secondarily to the inflammatory changes induced by the cardiopulmonary bypass, a volume overload and the mechanical ventilation with positive pressure. The clinical expression of this complication is the development of a superior vena cava syndrome, hepatosplenomegaly, ascitis and peripheral edema, associated with increased pulmonary pressures, and progressive cyanosis when there is a fenestration or decrease in the systemic stroke volume in the absence of the latter.

Although it is important to try to establish a spontaneous breathing pattern as early as possible, the decision to extubate needs to be weighted against the risks of low cardiac output and metabolic acidosis.

It is essential to aggressively manage any respiratory complication (atelectasis, pneumothorax or pleural effusions) and to use pulmonary vasodilators as required, mostly Nitric Oxide and sildenafil as well as loop diuretics to induce diuresis and a negative balance.

When pressures persist high in spite of these measures (above 18 mmHg), often associated with persistent hypoxemia and desaturation below 90%, a number of conditions need to be ruled-out:

1. Carefully assess pulmonary pressures and resistances
2. An ECG and eventually an atrial ECG should be performed to ensure that the patient has a normal sinus rhythm and normal atrioventricular conduction
3. An echocardiography should be performed to assess ventricular function, competence of the AV valves, the degree of shunting through the fenestration, and to rule out the presence of pericardial fluid
4. A chest X-ray should be requested to rule-out the accumulation of pleural fluid and any acquired intrapulmonary event (i.e., atelectasis, pneumothorax)

A cardiac catheterization might be required to rule out stenosis at the anastomotic site or else, distally in the pulmonary arteries, thrombosis, or high pulmonary vascular resistances.

Low cardiac output syndrome (LCOS)

Significant LCOS may be observed after a total cavo-pulmonary connection (Table 31.2), mostly in patients with previous ventricular dysfunction, with severe atrioventricular valvular regurgitation or with a tenuous hemodynamic stability. Treatment is based on the use of inotropic, vasodilator or lusitropic drugs, induced hypothermia, diuretics and eventually resynchronization strategies. Patients with refractory LCOS may require mechanical assistance and may be considered for cardiac transplant.

Hypoxemia

Hypoxemia is rather common in patients with fenestrations and moderately or severely increased pulmonary resistances. Persistent saturations below 90% justify further investigations as described above for patients with increased pulmonary pressures, situation that usually co-exists with the hypoxemia.

A cardiac catheterization may also be necessary to rule-out anatomic or functional obstructions, thrombosis (38) or high pulmonary vascular resistances. It may also identify veno-venous or arterial-venous fistula requiring embolization (39). In some circumstances, it is useful to transiently occlude the fenestration and

reassess hemodynamics. When the pulmonary pressures remain below 18 mmHg, systemic saturations increase significantly and there is no impact in the cardiac function, a definite occlusion of the fenestration with an intravascular device may be considered.

Acute Effusions

Acute and chronic effusions confined to the thorax (pleural or pericardial effusions, chylothorax) or extrathoracic (ascitis, peripheral edema) are common after total cavo-pulmonary connections. Supposedly, the use of a fenestration is a favorable preventive factor. These patients may require intrathoracic drains for long periods of time. In case of chylothorax, and adequate diet with middle chain triglycerides and the use of parenteral feeding is indicated. In refractory cases, somatostatin or octreotide followed by pleurodesis with or without thoracic duct ligation may be considered (40). The partial hepatic vein exclusion reported by Yves Lecompte is not currently performed since most patients develop intrahepatic venous collaterals with significant right-to-left shunts (17, 41).

Arrhythmias

By definition, patients with total cavo-pulmonary connections tolerate very poorly any arrhythmia or conductive disorder and must be aggressively managed (42–44). Atrioventricular synchrony is probably vital in these patients.

Atrial flutter is the most common arrhythmia in this context and is often associated with sinus node dysfunction, which complicates its management. It often gives a sign of alert for serious hemodynamic complications. As previously mentioned, the use of extracardiac conduits has not reduced the incidence of arrhythmias or sinus node dysfunction. Atrial flutter may be preceded by sinus bradycardia in which case the use of a prophylactic epicardial pacemaker may be a benefit although this has yet to be demonstrated. Technical complications for the use of mono or dual chamber pacemakers are related to the fact that these can only be epicardial, in patients who often have chronic adhesions secondary to multiple surgeries.

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Chapter 32

Anomalous Pulmonary Veins

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32.1 Introduction

This chapter discusses different types of anomalous pulmonary venous returns, but concentrates on total anomalous pulmonary venous return (TAPVR).

TAPVR is a condition in which all the pulmonary veins drain into one or several systemic veins instead of the left atrium (LA). The most important determinant of immediate postnatal stability of newborns with TAPVR is the presence or absence of pulmonary venous obstruction. Obstructed TAPVR is an undeniable emergency in neonatal cardiac surgery. TAPVR is frequently associated with small left-sided cardiac structures due to underfilling of the left heart, atrial septal defects (ASD; essential to allow systemic cardiac output), and abnormal systemic venous drainage in patients with heterotaxy syndromes. Infants presenting with TAPVR in the context of a heterotaxy syndrome are more likely to have other major cardiac congenital anomalies, such as Tetralogy of Fallot, double outlet right ventricle, hypoplastic left heart, and hypoplastic aortic arch. Any degree of pulmonary venous obstruction may be accompanied by pulmonary venous fibrosis, abnormal pulmonary arterial muscularization, and pulmonary lymphangiectasia. Four types of TAPVR exist based on the location of the anomalous pulmonary venous drainage: supracardiac (~50%), cardiac (~25%), infradiaphragmatic (~15%), and miscellaneous or mixed (~10%) [1].

Partial anomalous pulmonary venous drainage (PAPVR) is a condition in which one or more, but not all, of the pulmonary veins drain anomalously into the systemic veins. This is a range of condition in which almost every imaginable combination of pulmonary–systemic connection has been observed. Left pulmonary veins commonly connect anomalously to structures derived from the left cardinal system, such as the coronary sinus or the left innominate vein. Similarly, the right veins commonly connect anomalously to structures derived from the right cardinal system, such as the superior vena cava (SVC) or the inferior vena cava (IVC) [2, 3].

32.2 Anatomy and Embryology

Anomalous pulmonary venous return can result from a number of deviations of the pulmonary venous development, so understanding of the origin of anomalous pulmonary venous drainage requires a review of the developmental biology of the systemic and pulmonary veins.

A major forerunner of the systemic veins is the cardinal system, which develops at 24–28 days of gestation and initially consists of the paired anterior and posterior cardinal veins. These primitive veins connect to the left and right horns of the sinus venosus, the cavity of the embryologic heart. Eventually, the posterior cardinal veins are replaced by the subcardinal and the supracardinal venous systems. The anterior cardinal vein and the two posterior systems form parts of IVC and its main branches as well as the azygous and the hemiazygous systems. The paired vitelline veins, which originally drain the yolk sack, are other major contributors to the venous system. As the embryo matures, the

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vitelline veins give rise to the hepatic sinusoids, the portal system, parts of the IVC, and the ductus venosus. Ultimately, in the course of normal development, the left-sided cardinal and vitelline veins regress, while the right-sided ones persist and give rise to the great veins, which, in turn, connect to RA.

The development of the pulmonary veins trails that of the systemic veins by about a week. Initially the lung buds are drained by the splanchnic plexus, which interconnects extensively with the cardinal and the vitelline systems, but does not reach the heart. By the end of the first gestational month, the common pulmonary vein buds off the posterior wall of the LA and soon connects the pulmonary venous plexus to the sinoatrial portion of the heart. By 38–40 days of gestation, the pulmonary–splanchnic connections disappear, leaving four major pulmonary veins that empty into the common pulmonary vein, which in turn drains into LA. As the cardiac development continues, the common pulmonary vein is incorporated into LA, while the four pulmonary veins connect separately and directly to the LA [4, 5]. However, maldevelopment of the common pulmonary vein may lead to persistent pulmonary–splanchnic connections and abnormal drainage of the pulmonary veins into the systemic venous or right-heart circulation, resulting, as mentioned above, in TAPVR or PAPVR.

The four anatomic subtypes of TAPVR are described next.

Supracardiac: In the most common supracardiac pattern the four pulmonary veins join at a venous confluence behind the LA (remnant of the common pulmonary vein) and drain up the left side of the chest as the vertical vein (Fig. 32.1). Usually this vein passes in front of the pulmonary artery as well as the mainstem bronchus, but it may pass between them, which creates an obstruction to the pulmonary venous outflow. This vertical vein connects to the left innominate vein which, in turn, joins the SVC. Other possible supracardiac patterns include a direct connection between the vertical vein and either the right SVC, the azygous system, or the left SVC.

Cardiac: All four pulmonary veins drain into the common pulmonary vein which connects to either the coronary sinus or the right atrium (Fig. 32.2). The connection to the coronary sinus occurs in the region of the AV groove. The coronary sinus follows its normal path to the right atrium where it is either normally placed between the orifices of the venae cavae or dis-

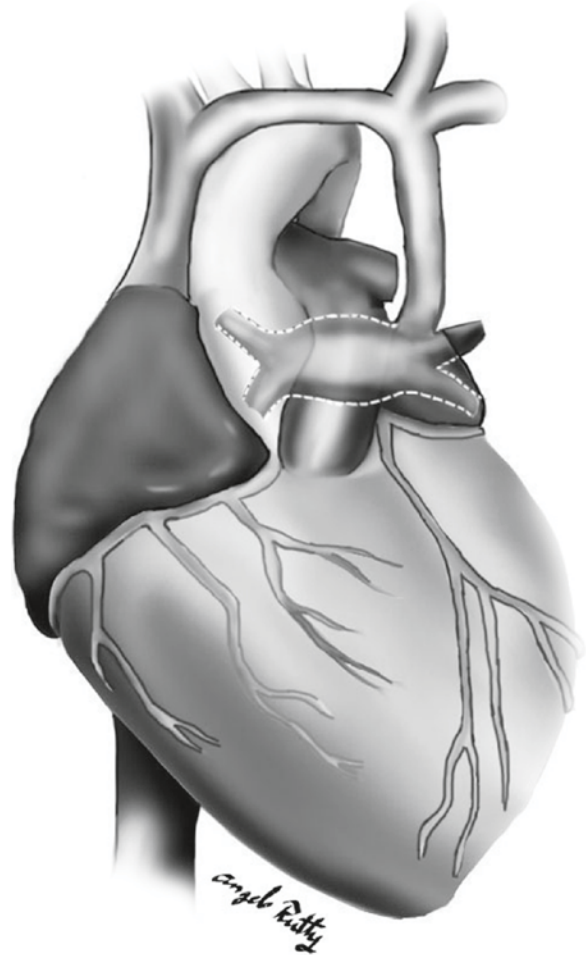


Fig. 32.1 Supracardiac type total anomalous pulmonary venous return (TAPVR). The vertical vein drains the pulmonary vein confluence into the innominate vein

placed posterior to the IVC opening. The direct connection of the common pulmonary vein to the right atrium is most frequently seen in cases of right isomerism.

Infracardiac: After the pulmonary venous blood is collected by a common pulmonary vein behind the heart, it passes down a venous channel through the esophageal hiatus of the diaphragm and connects to the portal vein (most commonly), the ductus venosus, the hepatic vein, or, rarely, directly to IVC (Fig. 32.3). The pulmonary venous blood then reenters the heart through the IVC.

Miscellaneous or Mixed: In this situation, anomalous connections of the pulmonary veins are seen at two or more of the above levels.

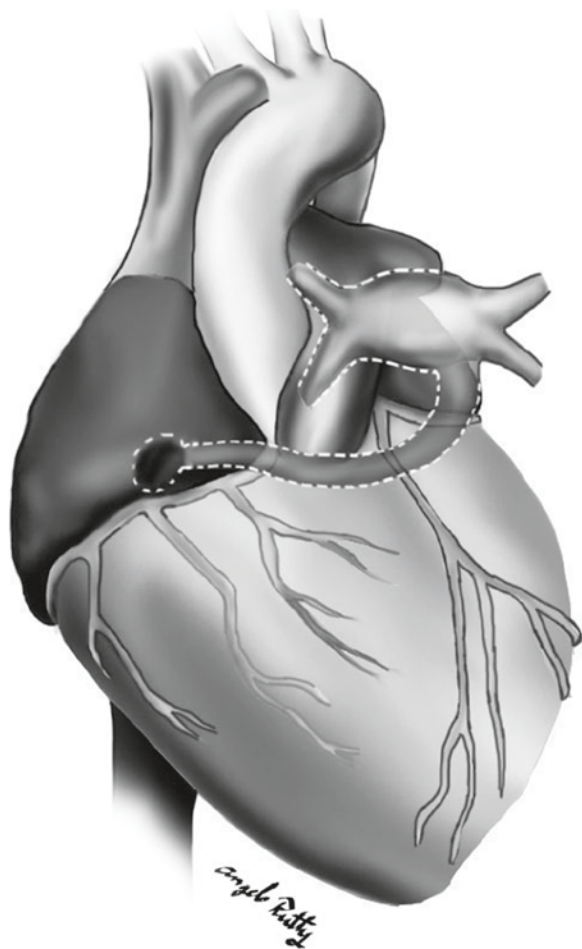


Fig. 32.2 Cardiac type TAPVR. The pulmonary vein confluence drains into the coronary sinus

In all the above situations, the presence of an interatrial communication is necessary to sustain life and, therefore, an ASD or patent foramen ovale (PFO) is considered part of the complex of TAPVR. In addition, the left-sided cardiac structures are diminished in size as the failure to incorporate the common pulmonary vein into the LA decreases the size of the atrium as well as the flow into (and thus the size of) the LV [6].

The cause of TAPVR is unknown, but the condition has been associated with exposure to paint or paint-stripping chemicals, lead, or pesticides. The genetic pattern of transmission of the abnormality is also unknown; however, a number of family studies have suggested a monogenic inheritance. Polysplenia, asplenia, and cat's eye syndrome are the most noteworthy syndromes associated with TAPVR [7].

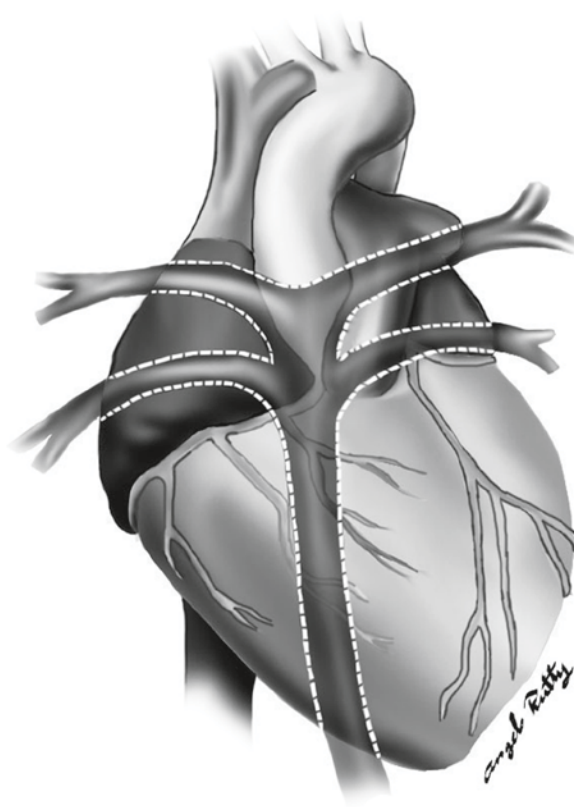


Fig. 32.3 Infracardiac type TAPV. The descending vertical vein drains into the portal vein

PAPVR involves a large spectrum of anatomic connections between one or more pulmonary veins and the systemic venous drainage. The most common *PAPVR* pattern is the drainage of the left upper pulmonary vein into the left innominate vein, which subsequently drains into the coronary sinus or the LA. This type of drainage is commonly associated with an ASD. The second most common abnormality is the connection between a right pulmonary vein and the IVC. This is associated with the Scimitar syndrome, which includes bronchial anomalies, dextrocardia, hypoplasia of the right lung and of the right pulmonary artery, and anomalous aortic blood supply to the right lung (pulmonary sequestration). A third common situation involves anomalous drainage of the right pulmonary vein(s) into the SVC or right atrium. In this condition, unroofing of the right pulmonary veins is present as well as a sinus venosus ASD. Morphologically, the patients exhibit right atrial, right ventricular, and pulmonary artery dilation. Due to the right ventricular dilation, the intraventricular septum is deviated toward

the left ventricle, and the left ventricle appears “small-ish”. Connections between a left pulmonary vein and the right SVC (part of the sinus venosus defect), the coronary sinus, or the hemiazygous vein have also been reported. PAPVR is associated with a number of other cardiac defects and syndromes including heterotaxy and Turner syndrome [8, 9].

32.3 Pathophysiology

In all forms of TAPVR the pulmonary venous blood completely mixes with systemic venous blood and returns to right atrium via the systemic veins (obligatory left-to-right shunt). To provide LV preload (and cardiac output), there must be an obligatory right-to-left shunt. This shunt most frequently occurs at the atrial level, via either a PFO or an ASD. Oxygen saturations in all cardiac chambers are identical and dependent on the amount of pulmonary blood flow. The pulmonary blood flow, in turn, is mostly governed by the degree of pulmonary venous obstruction. So, if the pulmonary venous return is unobstructed, the pulmonary blood flow is significantly increased, the oxygen saturations in all cardiac chambers are relatively high, and the infant soon develops congestive heart failure with minimal levels of cyanosis. Although these infants appear pink, their pulmonary vascular resistance is labile and they can experience episodes of pulmonary arterial hypertension, with associated cyanosis. In infants with TAPVR and a severe obstruction to pulmonary venous return, pulmonary venous hypertension and pulmonary edema are always present. Moreover, their pulmonary arterioles constrict, adding a component of pulmonary arterial hypertension. The overall result is severe RV and PA hypertension, poor pulmonary compliance, high bronchial resistance to airflow, and, ultimately, hypoxemia, right ventricular failure, and cardiogenic shock. The physiology of these infants resembles that of persistent pulmonary hypertension. Most infants born with TAPVR present with some degree of pulmonary venous obstruction, and their individual physiologic state falls between the two extremes described above.

The pathophysiology of PAPVR is that of an ASD with right ventricular volume overload secondary to left-to-right shunt, resulting in progressive right ventricular dilation. In addition, certain anatomic types of PAPVR are associated to the presence of ASDs. This is

the case of PAPVR to the SVC associated to sinus venosus ASDs. If PAPVR is left unrepaired for decades in patients with a long-standing left-to-right shunt, these patients may develop pulmonary hypertension [9, 10].

32.4 Preoperative Assessment and Management

32.4.1 Assessment

32.4.1.1 Obstructed Pulmonary Veins

Clinical Presentation

Infants with obstructed TAPVR present soon after birth with severe cyanosis and respiratory distress, and the acuity of their presentation is proportional to the degree of pulmonary venous obstruction. The cyanosis may worsen when infants with infradiaphragmatic drainage feed, as the food-filled esophagus compressed the vertical vein. On physical examination, signs of pulmonary edema and pulmonary hypertension (loud P2, the murmur of tricuspid regurgitation, or a gallop rhythm) are present, and hepatomegaly is not uncommon.

Chest Radiography

The chest X-ray of these infants typically shows gross pulmonary edema without cardiomegaly. Findings may be misinterpreted as surfactant deficiency, severe neonatal pneumonia, or lymphangiectasia. It may also reveal the presence of pleural effusion, which can be confirmed by chest ultrasound.

ECG

ECG shows RVH (which may be dismissed as “physiologic”), and occasionally *appulmonale* is present.

Echocardiography

Echocardiography demonstrates large right-sided and small left-sided structures, dilated pulmonary arteries, features of pulmonary hypertension, and an intraatrial

communication with a pure right-to-left shunt. The dilated vertical vein and its connections to the anomalous pulmonary veins are best visualized behind the LA from the suprasternal notch. Determining which type of TAPVR is present is very important. The features of the supracardiac type are best imaged in the short axis through the suprasternal notch using color mapping and Doppler interrogation to define the left SVC flow. The large coronary sinus (characteristic of the cardiac type of TAPVR) may be imaged in the apical four-chamber and parasternal short-axis views. Subcostal views may demonstrate a dilated vein descending through the diaphragm in the infradiaphragmatic type. The possibility of the mixed type of TAPVR is only eliminated conclusively if all four pulmonary veins are visualized connecting to the confluence.

Other Imaging

MRI imaging may supplement echocardiographic findings, especially if adequate echocardiographic images cannot be obtained [11].

32.4.1.2 Unobstructed Pulmonary Veins

Clinical Presentation

Infants with unobstructed TAPVR present later than their obstructed counterparts. They are not severely ill, but may have a history of failure to thrive and frequent pneumonias. On physical exam, mild cyanosis and mild hepatomegaly may be seen. Cardiac findings include a fixed-split S2 with a loud P2 and the soft systolic murmur of relative pulmonic stenosis (similar to a large ASD).

Chest Radiography

Chest X-ray of these infants typically shows cardiomegaly (the characteristic “Snowman heart” is present after a few months of age) and features of increased pulmonary blood flow, but not severe pulmonary edema.

ECG

ECG demonstrates RVH and the RSr' configuration, and appulmonale is present in some cases.

Echocardiography

Echocardiographic findings in unobstructed TAPVR are similar to those in the obstructed type, except for the signs of obstruction (engorged vertical vein) and the relative frequency of the specific anatomic subtypes found (i.e., features of subdiaphragmatic drainage are less likely to be present in an infant with unobstructed TAPVR).

Cardiac Catheterization

Preoperative diagnostic angiography is only occasionally needed. Pulmonary artery wedge injections demonstrate the anatomy of the pulmonary venous drainage on levophase (Fig. 32.4a, b). Systemic venous balloon-occlusion angiography can also be performed within the vein to which the pulmonary veins drain.

Other Imaging

MRI imaging may supplement echocardiographic findings, especially as a means to rule out small intrapulmonary veins (poor surgical outcome), and if adequate echocardiographic images cannot be obtained.

32.4.2 Preoperative Management

32.4.2.1 Stabilization

The preoperative management of severely ill infants with obstructed TAPVR is very challenging. The goal should be to quickly improve oxygenation and cardiac output, and to avert end-organ damage in order to allow for emergent TAPVR repair. Occasionally, due to intractable hypoxemia and acidosis, this is unachievable without resorting to extracorporeal membrane oxygenation (ECMO). Such infants are stabilized on ECMO for 1–2 days and then taken to the operating room for repair.

32.4.2.2 Respiratory Management

All severely ill infants with obstructed TAPVR should be emergently intubated, preferably with a cuffed

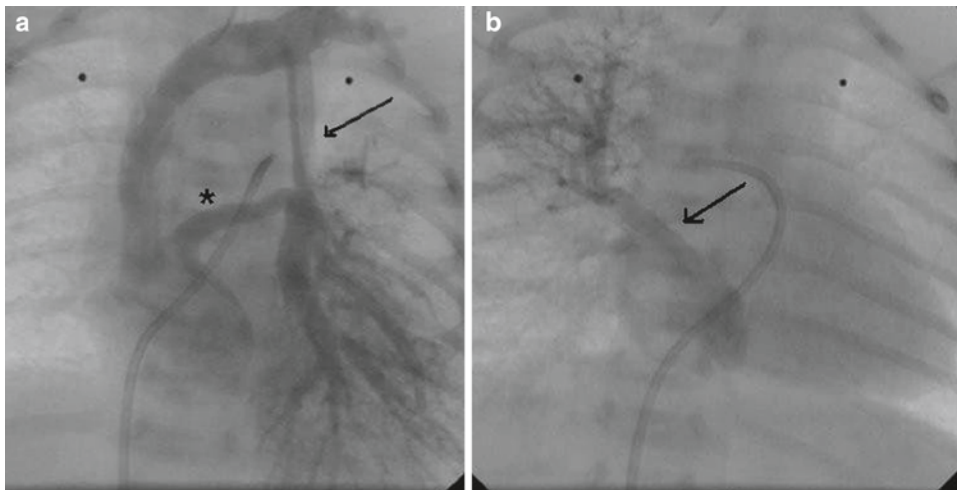


Fig. 32.4 (a) Following a left pulmonary artery wedge injection on levophase the complex anomalous pulmonary venous connection is demonstrated. The left pulmonary veins drain dually into the innominate vein via a vertical vein (arrow), as well to the pulmonary venous confluence

which drains to the coronary sinus via a horizontal vein (*). (b) Following wedge injection in the right pulmonary artery the levophase demonstrates the right pulmonary veins (arrow) returning to the coronary sinus with a large unobstructed confluence

endotracheal tube in anticipation of poor pulmonary compliance and high airway pressures.

The mechanical ventilation strategy includes aggressive titration of positive end-expiratory pressure (PEEP), to as high as 10–12 mmHg and peak inspiratory pressure (PIP) to, as high as 35–40 mmHg if necessary to minimize pulmonary edema and to maximize oxygenation and ventilation in the face of significant decrease in pulmonary compliance and increase in airway resistance.

The use of high supplemental oxygen fraction (FiO_2) (usually 100%) is indicated to maximize systemic O_2 delivery; however, since high FiO_2 also increases pulmonary blood flow, it may worsen pulmonary edema in the context of obstructed pulmonary venous drainage.

For similar reasons, the utilization of the pulmonary vasodilator nitric oxide (NO) in this setting is controversial, but some advocate its judicious use to acutely reduce PAH and optimize ventilation/perfusion matching.

32.4.2.3 Cardiovascular Management

Cardiac support for these infants involves expedient initiation of inotropic medications (epinephrine and norepinephrine) and possibly cautious volume loading and blood transfusion to maintain cardiac output and systemic oxygen delivery.

Most cardiac intensivists advise against the use of PGE_1 in this setting because it may worsen pulmonary edema and systemic hypotension.

To decrease pulmonary hypertension, alkalemia may be induced with bicarbonate or THAM. However, it is important to remember that, just like for O_2 , NO, and PGE_1 , this may lead to worsening pulmonary status.

32.4.2.4 Other Important Issues

Serum electrolytes should be normalized, with special attention paid to ionized Ca^{++} , Mg^{++} , K^+ , and glucose. Careful sedation and muscle relaxation should be used acutely to reduce oxygen consumption in these infants. Ultimately, expedient repair as soon as the infant is reasonably stable is crucial. Some non-critically ill infants who are less severely obstructed may need no preoperative intensive care; others may benefit from mild inotropic support and decongestive therapy [12].

32.5 Surgical Management

Repair of TAPVR requires the use of cardiopulmonary bypass. A period of circulatory arrest is frequently

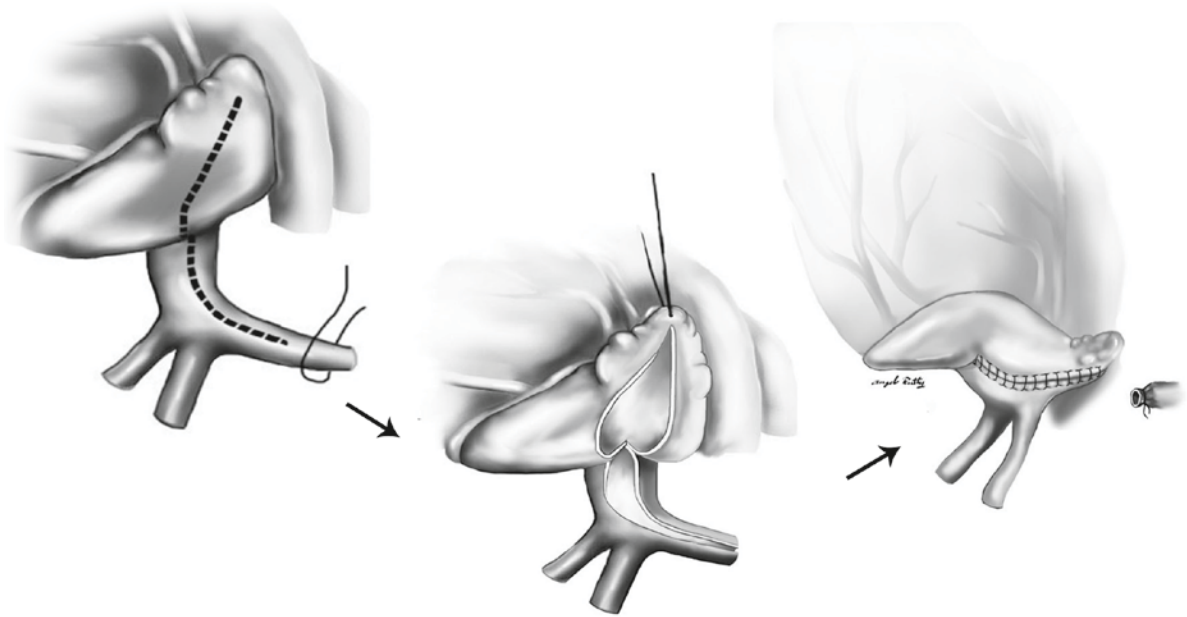


Fig. 32.5 Supracardiac TAPVR repair. With the apex of the heart elevated and retracted rightward, the left atrium (LA) and the pulmonary vein confluence are opened. The anastomosis is then performed with a running suture, and the vertical vein is ligated and divided

utilized when performing the repair in neonates and small infants, but in older patients it can be avoided with the use of bicaval cannulation.

The surgical management of patients with *supracardiac* (Fig. 32.5) and *infracardiac* TAPVR is similar, requiring an anastomosis between the pulmonary vein confluence and the LA. The ASD is routinely closed through the left atriotomy or a right atriotomy. It is our practice to always ligate the vertical or decompressing vein in order to prevent a postoperative left-to-right shunt at this level, although this is not a universal routine.

In the *cardiac type*, the veins drain into the right atrium either directly or via the coronary sinus. If draining directly, the repair consists of funneling the pulmonary venous return into the LA through the ASD, which frequently needs enlargement. A piece of pericardium is used to create the pulmonary venous channel. If draining via the coronary sinus, then unroofing of the coronary sinus into the LA and patch closure are required (Fig. 32.6).

The *mixed type* TAPVR usually requires a combination of the previously mentioned techniques as dictated by specific anatomy. On occasion, a single

anomalous pulmonary vein can be left uncorrected without a major hemodynamic consequence.

32.6 Postoperative Management

32.6.1 TAPVR

32.6.1.1 Monitoring

Postoperative pulmonary hypertension and low cardiac output are frequently seen in infants with TAPVR due to young age at repair, exposure to cardiopulmonary bypass, medial muscularization of the pulmonary arterioles leading to labile PA pressures, and small left-sided structures. Infants who were not obstructed preoperatively are at a lesser risk for postoperative pulmonary hypertension. On the other hand, patients with residual postoperative pulmonary venous obstruction are at an increased risk for it. Therefore, obtaining an early postoperative echocardiographic study of the pulmonary venous gradients

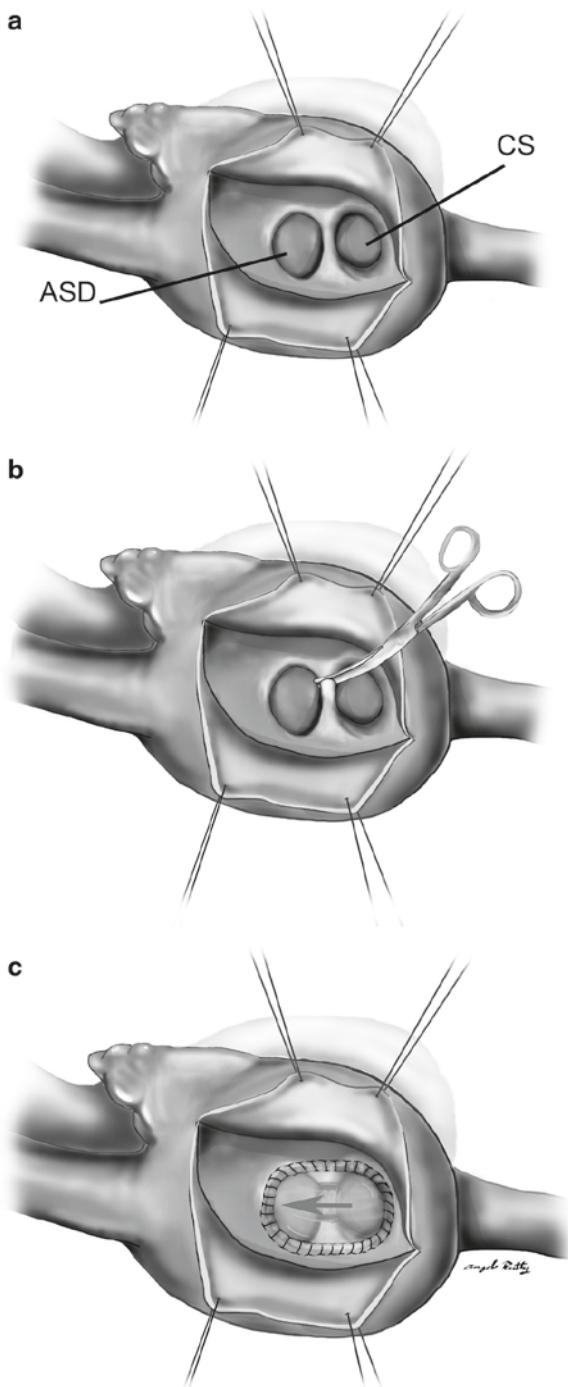


Fig. 32.6 Cardiac TAPVR repair. (a) Via a right atriotomy the large coronary sinus (CS) and the interatrial communication (atrial septal defect (ASD)) are visualized. (b) The coronary sinus is unroofed into the LA. (c) The coronary sinus and the ASD are closed with a single patch, creating a new pulmonary venous channel

and RV pressures is important, as may be the use of transthoracic PA or LA lines in addition to the standard monitoring.

32.6.1.2 Sedation and Analgesia

The post-TAPVR repair patients at high risk for pulmonary hypertension may be sedated and muscle-relaxed during early recovery, with a combination of opioids, benzodiazepines, and muscle relaxants, until hemodynamic stabilization.

32.6.1.3 Respiratory Management

The chest may be left open for 24–48 h after repair (especially in neonates).

The ventilatory strategy is chosen to minimize PA pressures. Thus, optimal PEEP is used to avoid atelectasis and pulmonary edema as well as hyperexpansion and other ventilatory settings are adjusted to produce a V_t of 10–12 cc/kg and normocarbica or mild respiratory alkalosis. It is important to remember that alveolar underinflation and overdistention increase pulmonary vascular resistance and worsen pulmonary hypertension.

NO should be used at the first sign of PA hypertension and weaned very slowly as improvement occurs. However, care must be taken to first rule out residual pulmonary venous obstruction as a cause of persistent pulmonary hypertension unresponsive to NO.

32.6.1.4 Cardiovascular Management

Hemodynamic support may include low-dose inotropes, especially milrinone, which has been shown to decrease PA pressures and to attenuate the development of low cardiac output syndrome in infants after cardiac surgery. ECMO and NO support may be necessary for several days postoperatively. Supraventricular arrhythmias are common after TAPVR repair (5–10%, with a higher incidence among patients with a history

of the cardiac type TAPVR) and are treated in the standard fashion.

32.6.1.5 Fluid Management

Fluid management should initially be very conservative (total fluids at half maintenance on postoperative day one, slowly liberalized to full maintenance over 3–4 days) in order to avoid overloading the small left-sided structures and causing pulmonary edema.

32.6.2 PAPVR

The postoperative care of the PAPVR is usually uncomplicated.

Patients with PAPVR draining to in the SVC may develop SVC obstruction and potential obstruction of the baffle which reroutes the right veins into the LA.

In Scimitar syndrome, the repair involves redirection of the right veins using a baffle to the LA, and special attention again must be taken to avoid potential obstruction of the baffle. In addition, pulmonary hypertension may be a complicating factor during the postoperative period.

Chest X-ray is useful in the postoperative care of both TAPVR and PAPVR repair, as bilateral or unilateral opacification alerts the intensivist to the existence of a localized pulmonary vein/veins obstruction [12, 13].

32.7 Long-Term Outlook

The long-term outlook for patients with repaired TAPVR is very good, with an operative mortality rate of 10–15% (now closer to 10%) and long-term survival approaching 85% [14]. Stenosis of the individual pulmonary veins or the pulmonary venous confluence is common postoperatively (around 15% after 1–2 years), especially in the infradiaphragmatic and miscellaneous types. However, with successful neonatal repair, the outlook for these patients is very good [14].

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Chapter 33

Dextro-Transposition of the Great Arteries

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33.1 Introduction

Transposition of the great arteries (d-TGA) is the most common cyanotic congenital heart lesion that presents in neonates [1, 2]. In this condition, the systemic and pulmonary circulations are in parallel rather than in series. The defect occurs more frequently in males of normal birth weight. The precise embryologic nature of this defect is not completely elucidated. In general terms, rotation of the myocardial wall of the outflow tract is arrested or fails to initiate in hearts with transposition of the great arteries. However, in particular, the anomaly appears to be related to an underdevelopment or abnormal absorption of the subpulmonary conus or infundibulum in d-TGA (see below for anatomical description). Normally, the subpulmonary infundibulum (conus) is present and the subaortic conus is absent [3]. This anatomic set up allows a normal alignment of the great vessels with the correspondent ventricle. Also, a recent study in the mouse suggests that some congenital heart defects involve a failure of outflow tract formation during development [4].

33.2 Anatomy

The hallmark of TGA is ventriculoarterial discordance, in which the aorta arises from the morphologic right ventricle and the pulmonary artery arises from the morphologic left ventricle (Fig. 33.1). Based upon the

anatomic relationship between the atria, ventricles, and great vessels, there are several anatomic arrangements of TGA:

- 1) S, D, D: (where S – atrium situs solitus, D – d-loop ventricle where the RV is right sided and LV is left sided, and D – dextroposition of the aortic valve relative to the pulmonary valve). Essentially, there is atrioventricular concordance with ventriculoarterial discordance. Due to the presence of a sub-aortic conus or infundibulum, the aorta is aligned with the right ventricle.
- 2) S, D, A or S, D, L: An “antero” or “levo” position of the aortic valve relative to the pulmonary valve exists.
- 3) S, L, L: (where S – atria in situs solitus, L – ventricular l-loop where LV is right sided and RV is left sided, and L – aortic valve is in “levo” position relative to the pulmonary valve). There is atrioventricular discordance with atria-arterial concordance; the segmental arrangements support the concept of congenitally physiologically corrected TGA.
- 4) I, L, L: (where I – inverted atria (right sided left atrium), L – l-loop ventricle (right sided LV), and L is levo version of the aortic valve). Atrioventricular concordance exists with ventriculoarterial and atrioarterial discordance. There is a viscerotrial situs inversus.
- 5) I, D, D: (where I – inverted atria, a right sided left atrium-viscerotrial situs inversus, D – d-loop ventricle where the RV is right sided and LV is left sided, and D – dextroposition of the aortic valve relative to the pulmonary valve). Atrioventricular discordance and atria-arterial concordance are present. It is a physiologically corrected TGA [5].

Upon arrival to the intensive care unit, the caregiver must be aware of the patient’s coexistent heart defects and the existence and status of a patent foramen ovale/

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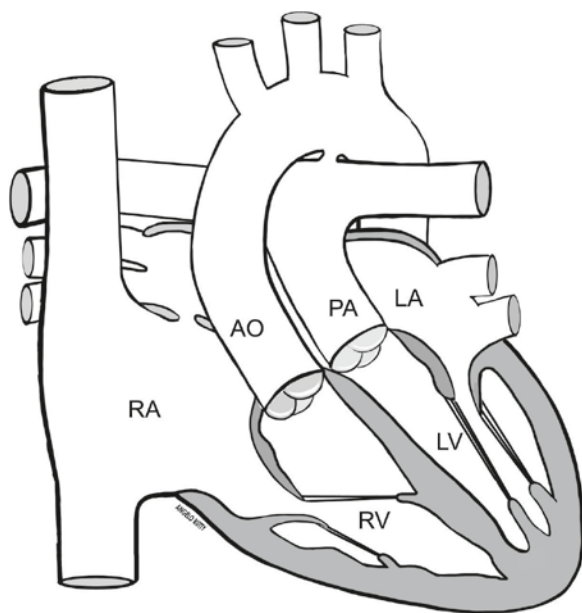


Fig. 33.1 Transposition of the great arteries

atrial septal defect and/or ventricular septal defect and patent ductus arteriosus, as these are needed to ensure proper intracardiac mixing. Other coexistent heart defects must be ruled out, including coronary artery anomalies, coarctation of the aorta, hypoplastic or interrupted arch, pulmonic stenosis, right ventricular outflow tract obstruction, mitral or tricuspid valve abnormalities, hypoplasia of the right ventricle and left ventricular outflow tract obstruction. In the setting of uncorrected transposition physiology, right ventricular pressure is higher than left ventricular pressure (septum may be bowing towards the LV). Therefore, the gradient across the left ventricular outflow tract (connected to the low pressure pulmonary tree) may be overestimated and may disappear after the arterial switch operation (disappearance of septal bowing). Also, some patients may have attachments of mitral valve cords into the left ventricular outflow tract; this anatomic variation may be a challenge to release the left ventricular outflow tract obstruction [6].

The other important anatomic aspect to define in TGA is the orientation of the great vessels as either side by side, oblique, or antero-posterior. The facing sinuses are rotated as a result of the mentioned orientations of the great vessels. The coronary arteries will follow the shortest pathway to the aortic sinuses in the aortic root. These anatomic landmarks are of paramount importance

in determining the degree of difficulty of surgical intervention and the intensivist must understand the clinical implications of each arrangement on potential postoperative morbidity and mortality [7, 8].

Summary of aortic sinuses in the aortic root /the coronary artery location and great vessel orientation:

- 1) Side by Side: Aortic valve rightward position, anterior and posterior facing sinus.
- 2) Oblique: Aortic valve anterior /rightward, left anterior facing sinus and right posterior facing sinus.
- 3) Anterior–Posterior: Aortic valve in anterior position, right facing sinus and leftward facing sinus.

The coronary artery anatomy in TGA is quite variable; common coronary patterns are shown in Fig. 33.2. The coronary arteries are described from the vantage point of a person sitting in the non-facing sinus, looking toward the pulmonary artery, sinus one represents the right hand facing coronary sinus and sinus two the left hand facing coronary sinus.

33.3 Physiology

33.3.1 Fetal Physiology

In general, the fetus tolerates the resulting physiology of TGA well. In a simple complete TGA, a change in ventricular afterload is seen. The low resistance of the umbilical-placental system receives the right ventricular output and, conversely, the left ventricle faces the high pulmonary vascular resistance and placental vascular resistance. The effect of this physiology on both ventricles may affect the distribution of flow from the superior and inferior vena cavae. Normally, the superior vena cava carries lower oxygenated blood which is directed to the right ventricle and pulmonary tree. In the setting of complete TGA, the lower oxygenated blood will be delivered to the aorta, especially the ascending aorta (supplying the coronaries and the carotid arteries). The effects of the decreased oxygen delivery to the coronary system and brain (neurological outcomes) are still unknown.

The inferior vena cava carries more oxygenated blood from the placenta and, in the normal fetus, this blood is preferentially directed through the foramen ovale to the aorta; in TGA this blood will be delivered

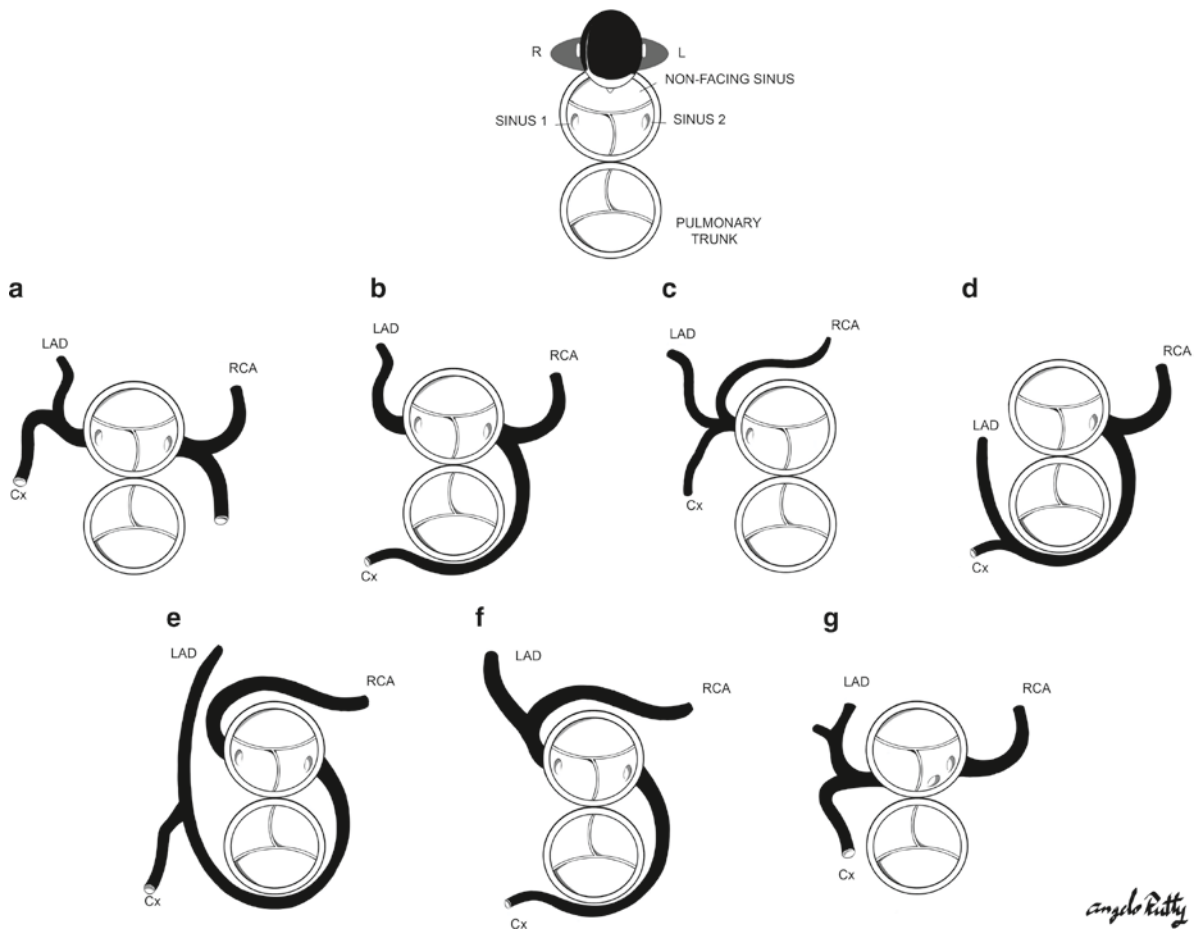


Fig. 33.2 Frequent coronary patterns in TGA. (a) Normal anatomy, (b) circumflex artery from the RCA, (c) single left coronary artery, (d) single right coronary artery, (e) inverted coronary pattern, (f) RCA from LAD and circumflex from sinus 2, (g) intramural left main from sinus 2

to the pulmonary tree and perhaps lower the pulmonary vascular resistance. At the post-ductal level (due to the PA-Aorta shunt through the PDA) oxygen levels are seen to return to “normal” post-ductal levels in fetuses without TGA [9].

33.3.2 Postnatal Physiology

As stated above, the circulations in TGA exist in parallel rather than in series. Assuming a normal gas exchange, the oxygenated blood from the left atrium will be ejected by the left ventricle into the pulmonary circulation without reaching the systemic circulation. In addition, de-oxygenated blood returning from the

superior and inferior vena cavae do not reach the left sided structures for oxygenation. The physiologic consequence of this anatomic arrangement is a profound hypoxemia incompatible with life unless intracardiac (PFO/ASD or VSD) or extracardiac (patent ductus arteriosus-bronchial circulation) communications are appropriately patent.

To understand the preoperative physiology of the disease it is crucial to define key concepts which are relevant to the pre and postoperative management. To avoid confusion it is important to differentiate between anatomic and physiologic shunts:

The anatomic left-to-right shunt represents the amount of blood crossing from left side of the heart to the right side of the heart.

The physiologic left-to-right shunt is the amount of oxygenated blood that returns to the left side of the heart through the lungs.

The anatomic right-to-left shunt is the amount of blood passing from the right side of the heart to the left sided structures (left atrium, left ventricle and pulmonary artery).

The physiologic right-to-left shunt is the amount of de-oxygenated blood that reaches the systemic circulation without passing through the lungs.

Inefficient effective systemic or pulmonary blood flow as a result of inappropriate intracardiac or extracardiac communications is incompatible with survival. Clinically, these infants arrive in the intensive care unit with cyanosis, systemic hypoperfusion, cardiogenic shock, metabolic acidosis, oliguria and multiorgan dysfunction.

The degree of mixing can be assessed by identifying the combination of ventricular filling, size of communications, pulmonary vascular resistance, and other coexistent anomalies such as ventricular outlet obstructions. If there is effective mixing with pulmonary stenosis, the effective pulmonary blood flow will be low (poor oxygenation). Conversely, if there is a significant left ventricular outflow obstruction or coarctation of the aorta (closing PDA), the effective pulmonary blood flow would be sufficient with “appropriate” oxygenation, but the infant will experience systemic hypoperfusion [10].

33.4 Diagnosis

33.4.1 *D-TGA, Intact Ventricular Septum, and Inadequate Intra and Extracardiac Shunts*

33.4.1.1 Clinical Presentation

Initially the patient is robust a few hours after birth as clinical stability is given by the patent foramen ovale and patent ductus arteriosus. However, clinical symptoms appear after PDA closure or even sooner if the patent foramen ovale is very restrictive. Profound cyanosis, tachypnea without retractions, and prominent cardiac impulse are commonly present. Murmurs

are not usually heard and pulses are normal until cardiogenic shock appears.

Arterial oxygen saturation will indicate values between 50–70% and arterial blood gases show oxygen values in the low and mid 20s (unresponsive to oxygen administration) with metabolic acidosis and usually normal CO₂.

33.4.1.2 Chest X-Ray

Chest X-ray (antero-posterior view) shows no significant cardiomegaly and the lungs are clear. The shape of the heart is described as “egg on a side.” A narrow superior mediastinal shadow is seen with no evidence of the main pulmonary artery.

33.4.1.3 ECG

Electrocardiogram is essentially normal with prominent right ventricular voltages.

33.4.2 *DTGA, Ventricular Septal Defect*

33.4.2.1 Clinical Presentation

Cyanosis may not be prominent in this subset of patients. Nevertheless, in some group of infants, the VSD does not guarantee sufficient mixing and patients may require balloon atrial septostomy. The physical exam shows an apparently normal infant with comfortable tachypnea. Cardiac activity may be normal with a normal first sound and a loud second sound with a narrow split. There is 2–3/6 systolic ejection murmur best heard over the left lower sternal border.

Arterial oxygen saturations range between 75–low 90 % and arterial oxygen level is approximately in the 40s with normal pH and pCO₂. Without surgical repair, these patients eventually develop heart failure due to increased pulmonary blood flow.

33.4.2.2 Chest X-Ray

Chest-X ray shows a narrow superior mediastinal area, cardiomegaly, and prominent vascularity.

33.4.2.3 ECG

Electrocardiogram may be normal or may demonstrate RVH.

33.4.3 D-TGA and Pulmonary Stenosis

33.4.3.1 Clinical Presentation

Cyanosis is a prominent finding once the PDA constricts and a harsh 2–3/6 systolic ejection murmur best heard at the mid left sternal border is ascertained on physical exam. The first sound is normal and the second sound is loud. The right ventricular impulse is not hyperactive and there are no signs or symptoms of congestive heart failure.

33.4.3.2 Chest X-ray

Chest X ray shows no significant cardiomegaly with decreased pulmonary vascular markings.

33.4.4 D-TGA, Coarctation of the Aorta or Interrupted Aortic Arch

33.4.4.1 Clinical Presentation

The clinical presentation may not necessarily differ from the isolated DTGA, especially when the PDA is open. Nevertheless, the combination of DTGA, VSD and arch hypoplasia/ interrupted aortic arch increases the risk of augmenting pulmonary blood flow and these patients may experience tachypnea and respiratory failure. If the neonate develops pulmonary hypertension with high pulmonary vascular resistance, reverse differential cyanosis might be present. Absent or diminished femoral pulses and systemic hypo-perfusion may be evident when the PDA becomes restrictive.

33.4.4.2 Chest X-ray

Chest X-Ray shows increased pulmonary vascular markings and cardiomegaly.

33.4.4.3 ECG

The electrocardiogram may be normal or may show biventricular hypertrophy. Left axis deviation can occur with TGA and inlet VSD. Isolated left ventricular hypertrophy suggests TGA/VSD and an associated hypoplastic right ventricle [11].

33.5 Preoperative Management

Essentially, these patients can be transferred to the intensive care unit with two clinical presentations:

1. Unstable patient with cyanosis and cardiogenic shock.
2. Stable infant who had prenatal diagnosis made

Unstable neonates must have the ABC of resuscitation completed along with a brief echocardiogram for diagnosis, assessment of ventricular function, and evaluation of patency of ductus arteriosus and foramen ovale. A more detailed echocardiogram should be completed once the infant is stable. PGE₁ must be initiated (0.03–0.1 µg/kg/min, dose could be adjusted according to the clinical picture) and inotropic support and fluid and bicarbonate administration should be titrated according to the acid-base status, ventricular function, and hemodynamic status. Some of these patients require “generous” fluid administration to maintain appropriate mixing. The fundamental cause of the cardiovascular instability is insufficient mixing due to PDA closure or restrictive foramen ovale. If the constricting PDA is the only problem, prostaglandin infusion should rapidly compensate the infant. If a restrictive PFO is the main cause of insufficient mixing, an emergent balloon atrial septostomy (BAS) must be done (Fig. 33.3). This procedure can be completed at the bedside in the intensive care unit [12] or in the cardiac catheterization laboratory. In our experience (Children’s Hospital of Pittsburgh of UPMC) the intensive care unit is the place of choice, especially if there is an umbilical catheter placed reaching the heart. However, if the echocardiogram is not able to clearly define the coronary artery anatomy and the surgeon needs that information prior to intervention, angiography of the aortic root is needed to define the coronary anatomy. In such case it is preferred to take the patient

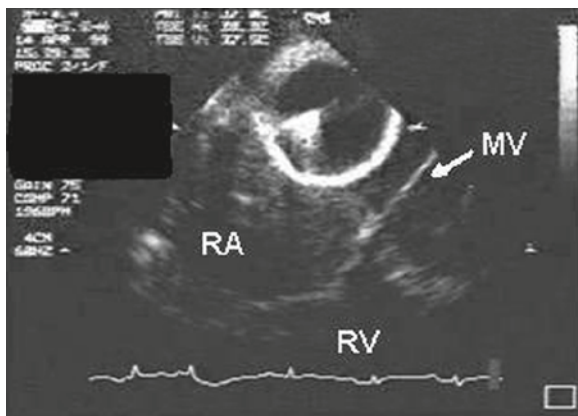


Fig. 33.3 Balloon atrial septostomy under echocardiographic guidance. The image demonstrates echocardiographic frame obtained during bedside balloon atrial septostomy, in a modified apical four chamber view. The balloon is inflated in the left atrium, away from the mitral valve. After the septostomy is performed, the balloon will then be seen in the right atrium (RA). *RV* right ventricle; *MV* mitral valve

to the catheterization laboratory and perform both the septostomy and angiography during the same procedure. If a patient is being transferred for an emergent balloon septostomy it is best directly to have the patient go to the catheterization laboratory, as, if there were any access problems fluoroscopy can be helpful. In addition, if any difficulties were encountered with the balloon procedure, alternative options would be readily available (static balloon dilation, ASD creation, etc). In addition, if the umbilical venous line cannot be advanced into the heart, it is best to perform the procedure in the catheterization laboratory, as catheter manipulation and visualization with echocardiography is easier in the short catheter course from the umbilicus, while it can be quite difficult from the groin without fluoroscopy.

Prior to starting the BAS, blood must be available and a stable airway must be guaranteed (not necessarily all neonates must be intubated for the procedure). The preferred approach is the umbilical access, although the procedure can be easily done via the femoral vein. If the child has an umbilical vein line in place, and it reaches the heart, then it can be safely exchanged in the ICU over a wire (J tipped or floppy tipped are preferred). If instead the line ends in the liver, it is best to either go to the catheterization laboratory and perform a venogram of the hepatic vein to assure the ductus venosus is open, following which the

catheter can be advanced through it into the heart, or a floppy tip 0.018" wire can be used to facilitate reaching the heart, under fluoroscopic guidance. A sheath can then be placed from the umbilical vein into the right atrium, and the septostomy catheter advanced.

The set up for a septostomy includes the following:

1. Umbilical catheter (if the umbilical vein is to be accessed)
2. 0.018" 40–60 cmm floppy tip wire
3. 6 F and 7F sheaths
4. Septostomy catheter (either of the following, or 2 different ones ideally available):
 - a. Braun septostomy catheter (fits via a 6 F sheath and has an end-hole which allows to draw back and to inject saline solution): This is the preferred one for bedside septostomies, since it allows for sampling to help assure the tip is in the left atrium and also allows injection of saline which can be visualized by echocardiography. Takes up to 2.5 cc.
 - b. Miller–Edwards balloon (Baxter) (fits via a 7 F sheath): can take up to 4 cc, although 2.5–3 cc is all that is needed for a term baby.
 - c. Traditional Rashkind balloon (fits via a 6 F sheath)

The echocardiographer is positioned on the left side of the patient, while the interventional cardiologist is on the right side and feet of the patient. All septostomy catheters have a "hockey stick" type of curve that facilitates reaching the left atrium via the patent foramen ovale. If there is an intact septum, the patient has to go to the catheterization laboratory where a transeptal puncture can be performed, although this instance is extremely rare in TGA.

If angiography is indicated for definition of coronary arteries, the best approach is using the "laid-back" view, as described by Mandell et al. [13], which involves extreme caudal angulation in the AP camera (Fig. 33.4). A Berman 5F catheter is advanced antegrade into the ascending aorta and angiography is performed in this biplane (extreme caudal in the AP and straight lateral in the lateral cameras) with transient balloon occlusion of the flow. Transient complete heart block can occur as a complication associated with catheter manipulation out the right ventricular outflow tract in these patients, such that if at all possible it is best to avoid angiography and delineate the coronary anatomy by echocardiography. For many surgeons,

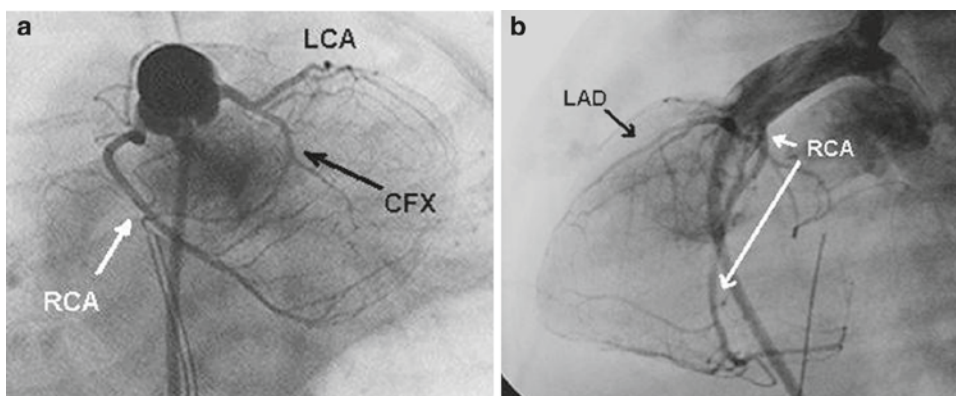


Fig. 33.4 Aortography for coronary artery definition. Laid back aortogram performed in anteroposterior (a) and lateral projection (b) demonstrates normal coronary anatomy. The balloon is inflated transiently to force contrast into the

coronary arteries, and deflated towards the end of the injection. RCA right coronary artery; LCA left coronary artery; CFX circumflex coronary artery; LAD left anterior descending coronary artery

perfect definition of coronary anatomy is not essential, as this can be determined in the operating room, and an ASO is performed for almost every anomaly anyway.

Once the BAS is completed, prostaglandin E_1 can be stopped, although some neonates may need to have the medication re-started due to poor mixing and persisting significant hypoxemia ($pO_2 < 30\text{mmHg}$ and acidemia). Prior to reinitiating the prostaglandins in these cases, an echocardiogram must be requested to assess the atrial communication and ductus arteriosus. The goal is to optimize the patient's volume status and to discontinue inotropic support as soon as the infant is hemodynamically stable after BAS. Stable patients after BAS can be fed until surgical repair. Cultures are obtained and antibiotics started when sepsis is suspected. In addition, head ultrasound, renal ultrasound, and genetic tests may be routinely done prior to surgical intervention.

Patients with arch hypoplasia, coarctation of the aorta, or interrupted aortic arch along with VSD and d-TGA deserve special attention to avoid pulmonary over-circulation syndrome and systemic hypoperfusion with the resultant multiorgan failure (refer to these conditions' specific chapters in the section titled "Preoperative Management"). Patients with d-TGA, interrupted aortic arch, and pulmonary hypertension (concomitant lung disease) will present as critically ill with severe cyanosis. [14] ECMO may be required until pulmonary hypertension improves. The caregiver should be aware that during the ECMO run, the left ventricle may "de-condition" and may cause complications

in the postoperative care of the arterial switch operation (ASO) [15].

Associated medical problems such as respiratory distress, meconium aspiration syndrome, and CNS ischemic and hemorrhagic events should be identified and addressed appropriately. If the patient is extremely premature or other associated conditions are present, an early ASO should be delayed. If intracranial hemorrhage is present, it is advisable to wait for two weeks before the ASO. As a consequence of the delay of the procedure, the left ventricle needs to be re-trained to handle the high systemic vascular resistance after the ASO.

Retraining the LV implies placement of a pulmonary band with or without a shunt (if patient continues to be very cyanotic). In addition, daily echocardiograms must be done to evaluate the left ventricular mass (if greater than 35 g/m^2 , the patient is likely to be suitable for ASO) [16]. The LV training process should not take more than 1–2 weeks, especially in infants. During the training period patients may require a fair amount of inotropic support due to LV failure and low cardiac output syndrome [17, 18].

33.5.1 Surgical Management

The *arterial switch* operation is the procedure of choice for the surgical management of transposition of the great arteries. It is performed via a median sternotomy

incision with cardiopulmonary bypass and moderate to severe hypothermia. A period of deep hypothermic circulatory arrest is frequently utilized for the closure of the atrial and/or ventricular septal defects. Technically (Fig. 33.5), it involves the transection of both great vessels, the translocation of the pulmonary arteries anterior to the aorta (Lecompte maneuver) and the suturing of the distal aspect of both great vessels to the proximal arterial roots attached to the “correct ventricles,” the distal ascending aorta to the arterial root attached to the left ventricle (neoaortic root, native pulmonary root) and the distal main pulmonary artery to the arterial root attached to the right ventricle (neopulmonary root, native aortic root). Very importantly, the coronary arteries need to be harvested from the native aorta and reimplanted in the neoaorta. The neopulmonary root is reconstructed with a patch of pericardium. When present, the atrial septal defect

and/or the ventricular septal defect are closed through a right atriotomy. The operative mortality associated with the arterial switch operation is approximately 5%.

In cases with delayed diagnosis (greater than 6–8 weeks of age) a two stage approach is recommended. It consists of an initial pulmonary artery band (to train the left ventricle) followed by an arterial switch operation. Occasionally, a systemic to pulmonary artery shunt is needed if the patient develops significant cyanosis after pulmonary artery banding. Frequently, the left ventricle can be trained in a relatively short period of time (days) allowing for a complete repair within the same hospitalization [19, 20]

For complex TGA with left ventricular outflow tract obstruction and a ventricular septal defect there are three surgical options. The *Rastelli* repair is frequently utilized and involves the creation of an interventricular tunnel, funneling the left ventricular blood into the

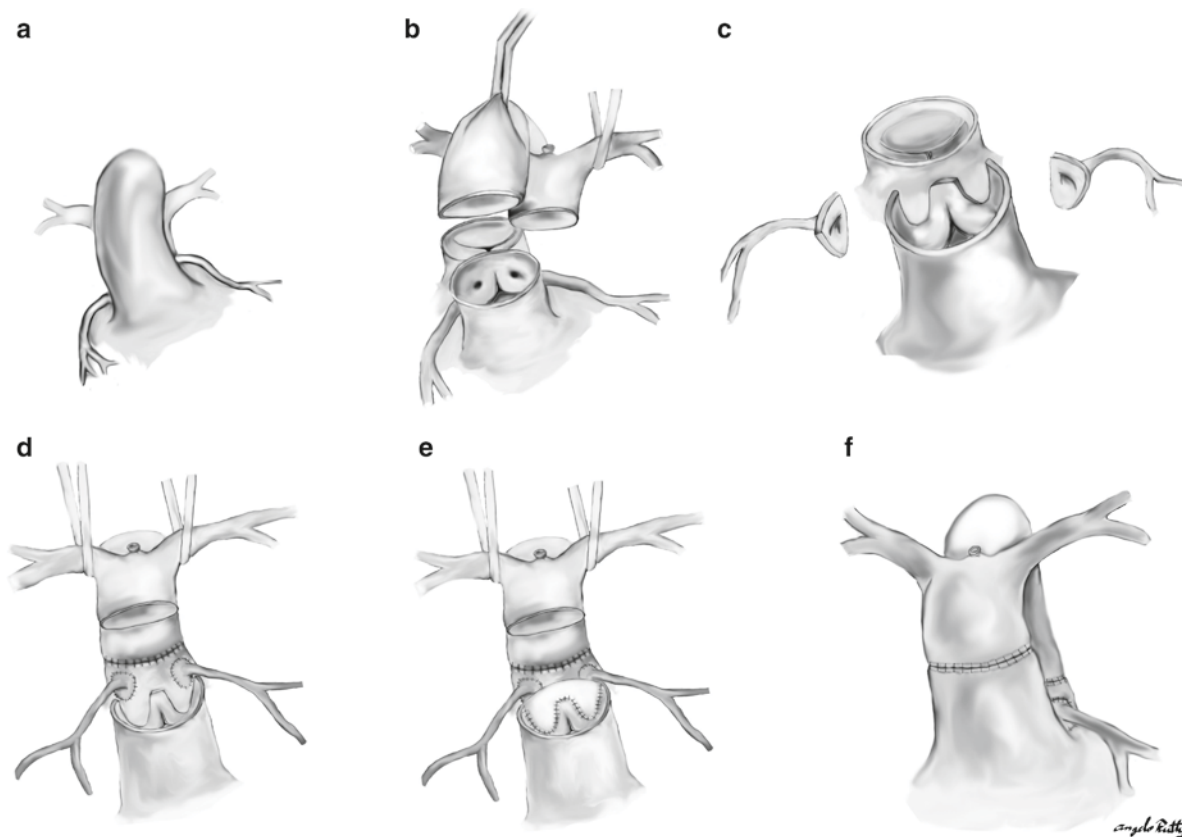


Fig. 33.5 The arterial switch operation. (a) The ascending aorta is anterior to the main pulmonary artery in transposition of the great arteries, (b) both great vessels are transected, (c) the coronary buttons are harvested from the native aorta, (d) after

performing the Lecompte maneuver, the distal aorta is anastomosed to the neoaortic root and the coronary arteries are reimplanted, (e) the neopulmonary root is reconstructed with a pericardial patch, (f) the pulmonary artery anastomosis is performed

anterior aorta; a conduit is used to establish right ventricle to pulmonary artery continuity (Fig. 33.6). Another alternative is the *R.E.V.* (*Réparation à l'Étage Ventriculaire*) procedure, it involves the enlargement of the ventricular septal defect to create a more direct communication between the left ventricle and the aorta and a direct anastomosis between the right ventricle and the pulmonary arteries, avoiding the use of a conduit (Fig. 33.7). Finally, in the *Aortic Translocation* procedure (*Nikaidoh* procedure) the aortic root is

moved into the pulmonary position, closer to the left ventricle, avoiding the creation of an interventricular tunnel (Fig. 33.8). The right ventricular outflow tract can be repaired with or without a conduit. This procedure results in a more “normal” anatomic result which could result in better long-term outcomes.

Patients who present later in life with an infra-systemic left ventricle may also be candidates, in some circumstance, to an *atrial switch* operation (a *Mustard* or a *Senning* procedure).

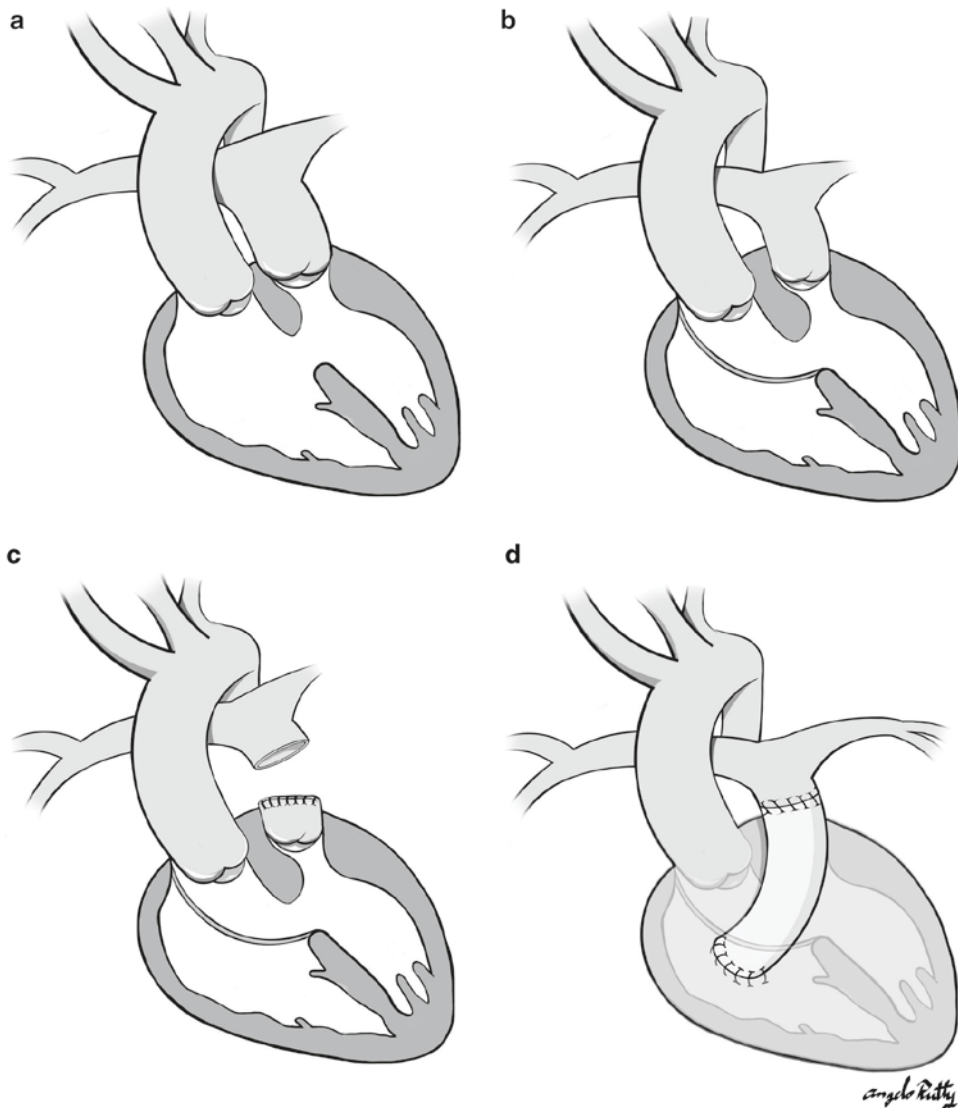


Fig. 33.6 Rastelli repair. (a) Transposition with a ventricular septal defect and pulmonary stenosis, (b) the interventricular tunnel is created with a prosthetic patch, funneling the left ventricular

blood into the aorta, (c) the main pulmonary artery is transected, (d) after performing a right ventriculotomy, a conduit is placed between the right ventricle and the pulmonary arteries

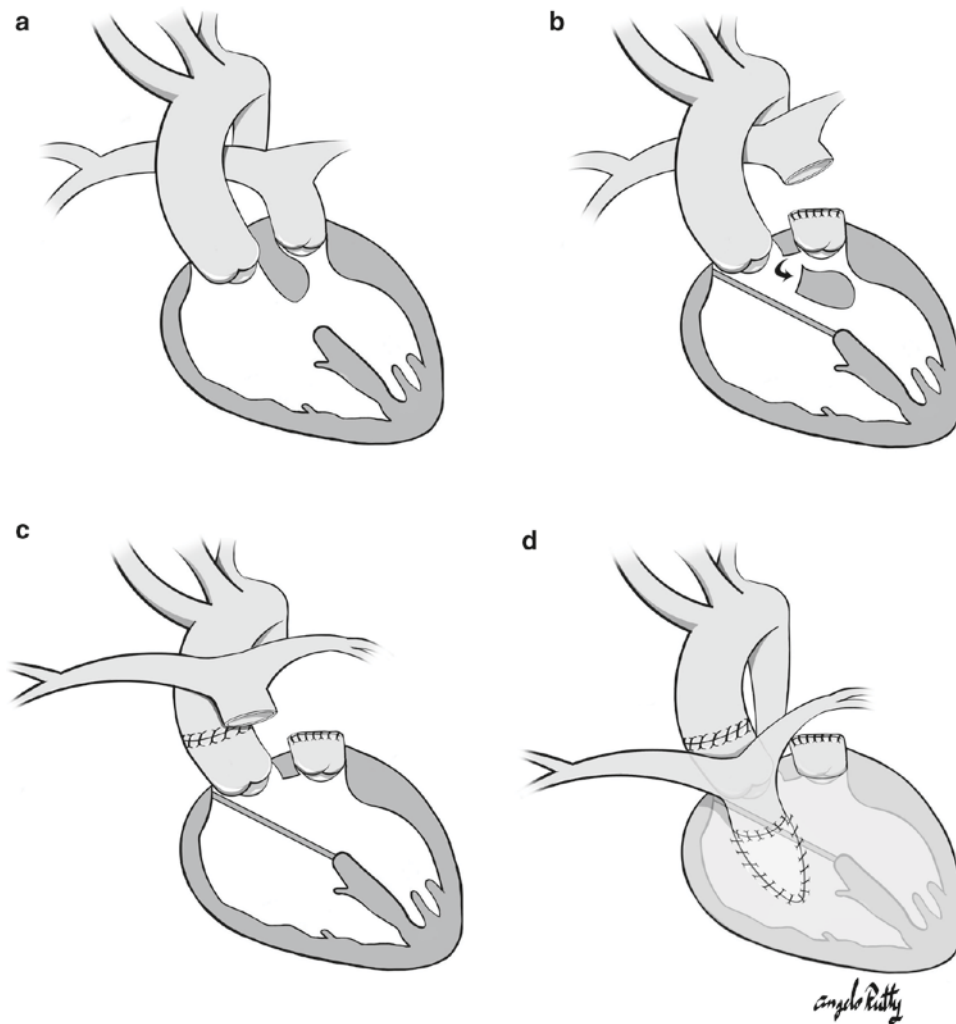


Fig. 33.7 R.E.V. Procedure (Lecompte procedure). (a) Transposition with a ventricular septal defect and pulmonary stenosis, (b) the outlet septum is resected, enlarging the VSD, and the interventricular tunnel patch is placed; it results in a more

direct communication between the left ventricle and the aorta, (c) the main pulmonary artery is transected and the Lecompte maneuver performed, (d) a direct anastomosis between the right ventricle and the pulmonary arteries is created

33.6 Postoperative Management

33.6.1 D-TGA and Intact Ventricular Septum

The corrective surgical procedure of this constellation includes ASO and post balloon ASD closure. The main complications following the ASO include: low cardiac output syndrome, mitral regurgitation, coronary insufficiency and/or ischemia, supra-ventricular aortic stenosis (AS) and pulmonary stenosis (PS), and bleeding along

multiple suture lines [21]. To better organize the postoperative management in a more didactic manner, it is divided by system:

33.6.1.1 Cardiovascular Management

The infant may or may not arrive with the chest open into the intensive care unit. The current trend is chest closure in an uncomplicated ASO. Details of TEE must be immediately available to the intensive care physician. Typical inotropic support includes low dose

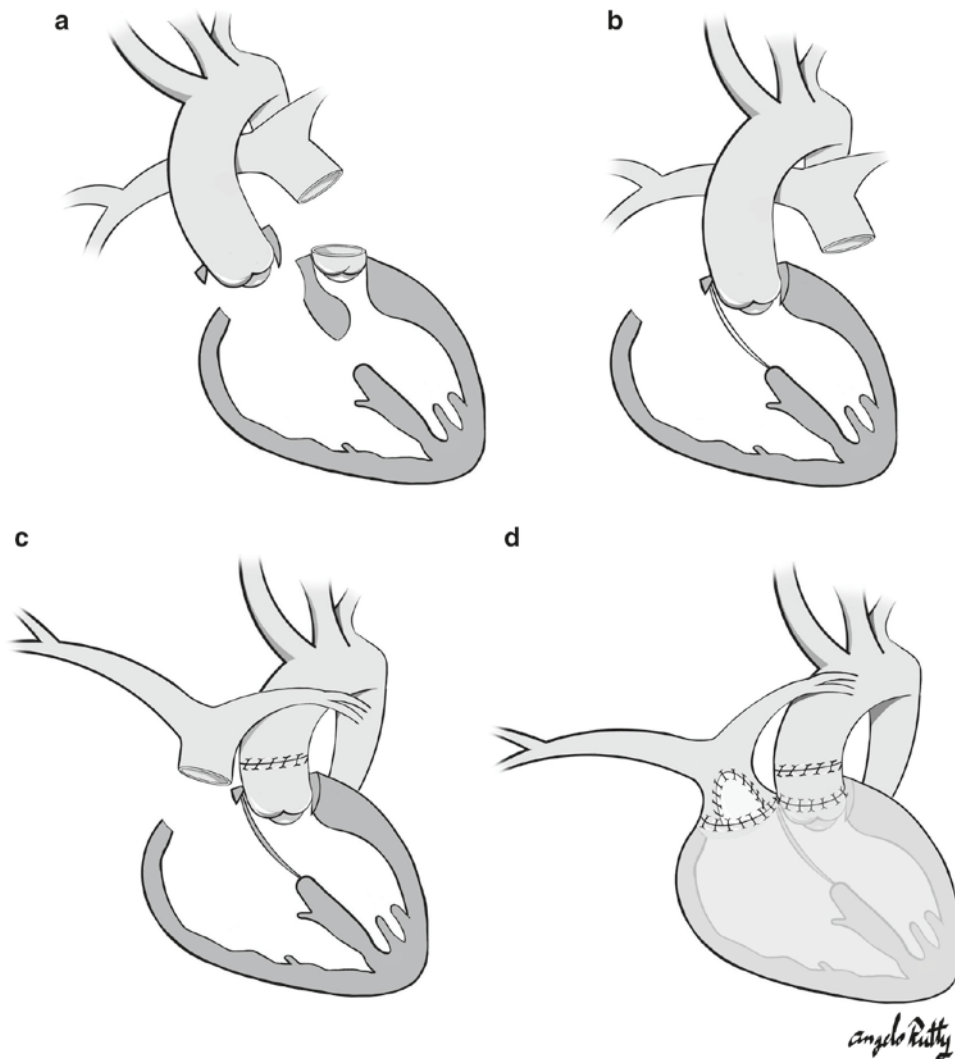


Fig. 33.8 Aortic translocation procedure (Nikaidoh procedure). (a) The aortic root is harvested from the right ventricle, with or without the coronary arteries attached, and the proximal main pulmonary artery is transected, (b) after dividing the outlet septum the aortic root is moved and sutured in the pulmonary

position and the ventricular septal defect is closed, (c) the Lecomte maneuver is performed. (d) a direct right ventricle to pulmonary artery anastomosis is performed; a patch of pericardium is used to augment the usually hypoplastic main pulmonary artery

dopamine (3–5 $\mu\text{g}/\text{kg}/\text{min}$), low dose epinephrine (0.05–1 $\mu\text{g}/\text{kg}/\text{min}$), milrinone (0.75 $\mu\text{g}/\text{kg}/\text{min}$), and sodium nitroprusside (1–3 $\mu\text{g}/\text{kg}/\text{min}$). Some institutions may routinely use nicardipine as an afterload reducing agent. The doses will be titrated according to the clinical condition and patient's hemodynamic status. It is of paramount importance that the intensivist avoids high inotropic support. If a particular infant requires high inotropic support to maintain borderline hemodynamics, the best approach is to use ECMO until the ventricular function recovers. Likewise, it is

important to remember that ECMO is only a transient support and an exhaustive search for potential underlying pathology to rule out residual surgical lesions, suboptimal myocardial preservation, and/or excessive tissue stretching/damage during the repair must be completed. After repair, the echocardiogram, CVP, and left atrial pressure are monitored routinely. In addition, lactate levels, mixed venous saturations, and NIRS values as well as basic physical exam findings are checked to ensure sufficient cardiac output.

The electrocardiogram is crucial for monitoring potential arrhythmias, coronary insufficiency, and/or infarct. The ECG must be compared to the pre-operative ECG. If coronary insufficiency is suspected, IV nitroglycerine drip may be started. Atrial arrhythmias can be seen due to ASD closure; however, ventricular arrhythmias should alert the intensivist to coronary anastomosis problems. At this time, a diagnostic echocardiogram (looking for regional wall abnormalities) and a cardiac catheterization must be requested as soon as possible.

High left atrial pressure usually is indicative of LV dysfunction and mitral regurgitation. Atrial wave form should be analyzed; prominent V wave is most likely consistent with significant mitral regurgitation (MR). Additionally, the pulmonary venous pressure and pulmonary pressure will be elevated secondary to LV dysfunction. Nitric oxide is contraindicated in this setting and, thus, patients may benefit from a generous after-load reduction, low atrial "tolerable" rates for age, and careful fluid administration. In general, once ventricular dilation and function improves, the mitral regurgitation improves. In cases of MR, the left ventricular systolic function may be overestimated by echocardiography due to the unloaded ventricle.

33.6.1.2 Respiratory Management

Once patients are hemodynamically stable without significant residual anatomic lesions, extubation should be promptly administered following the universal ICU criteria. Extubation failure in the setting of no residual heart disease and no significant lung disease should alert the clinician to the presence of diaphragmatic paralysis. During chest closure the intensive care physician must closely monitor lung volumes, compliance, and flow ventilator curves as, not infrequently, surgeons may press on the ETT during surgical intervention and respiratory deterioration may occur following cardiovascular collapse. Prior to chest closure patients must have the endotracheal tube suctioned and a pacemaker must be at the bedside with the pacing wires connected. If the infant has the chest closed after the ASO, patient should be ventilated with tidal volumes of 10–12 cc/kg, peak pressure sufficient to expand the lungs (avoid over-distention and collapse), PEEP

5–6 cm/H₂O, and FIO₂ to maintain saturations of 98–100% in patients without intracardiac shunts.

33.6.1.3 Fluid, Electrolytes and Nutritional Management

Twenty four hours after surgical repair parenteral nutrition is begun with Dextrose concentration between 20–25%, protein intake around 3 g/day, and fat intake around 3–3.5 g/kg/day. Enteral nutrition is commenced once the infant reaches hemodynamic stability.

33.6.1.4 Hematologic Management

Bleeding is a common complication after ASO and occurs more commonly when the procedure involves a long CPB time and cross clamp time. In addition, the ASO procedure involves placement of multiple suture lines which are potential sources of bleeding. One method which could possibly be used to treat this complication includes transfusion of either platelets, fresh frozen plasma, or cryoprecipitate. If bleeding persists above 7–10 ml/kg/h, chest re-exploration should be considered at the bed side. It is not unusual that blood clots may compress some coronary branches causing ischemia and cardiovascular collapse.

33.6.1.5 Gastrointestinal Management

Liver and pancreatic function tests such as amylase and lipase should be monitored. PO intake is encouraged after 24 h of extubation. Careful attention must be paid to changes in the quality and quantity of the chest and peritoneal drainage after enteral feeds are started (chylothorax and chyloperitoneum).

33.6.1.6 Renal Management

Furosemide and thiazides are the most commonly used diuretics. Furosemide is frequently started within 6–12 h after repair (dose 0.1–0.4 mg/kg/h). The aim is to achieve negative fluid balance within 24–48 h after

repair; this will facilitate chest closure and the extubation process. It is frequently observed that as the peritoneal drainage decreases urine output reaches its maximal volume.

33.6.1.7 Neurologic Management

Some centers routinely perform EEG 12–24 h post repair to detect seizure activity. Although this practice is controversial (low yield), it may be advisable to request an EEG at least 1–2 h post repair and, if abnormalities are seen, the test is extended as long as it is clinically necessary. The most important issue for this practice is to select a group at risk that deserves close follow up. Following the same principle complete head ultrasounds may be performed post repair.

33.6.1.8 Infectious Disease Management

At Children's Hospital of Pittsburgh, vancomycin and third generation cephalosporins are routinely used until the chest is closed. Following closure, a first generation cephalosporin is used until the chest tubes are removed. The incidence of mediastinitis is almost nonexistent in this institution. Central lines must be discontinued as soon as possible to decrease the risk of nosocomial infections. If patients need long term intravenous access, a Broviac catheter or a peripherally inserted central catheter (PICC) may be placed [21].

33.6.2 D-TGA and Ventricular Septal Defect

In addition to the postoperative care issues mentioned in d-TGA with intact ventricular septum, VSD closure represents an additional challenge [22]. Patients in this category are at higher risk for ventricular dysfunction including low cardiac output syndrome, conduction abnormalities, and other co-morbidities (related to CPB time) than patients with simple transposition. Transesophageal or trans-thoracic echocardiogram must be completed to assess function, AV valve regurgitation, and residual VSD. Transient/complete heart block and/or junctional ectopic tachycardia can be

seen as complications of VSD closure (see specific chapters for management).

33.6.3 D-TGA With Ventricular Septal Defect and Pulmonic Stenosis

33.6.3.1 Rastelli Repair

In this repair, an intraventricular baffle across the VSD is used to connect the left ventricle with the aorta. To connect the right ventricle to the pulmonary artery, a conduit is placed between the two structures. Potential complications during the postoperative period include: low cardiac output syndrome, biventricular dysfunction, conduction abnormalities, arrhythmias, baffle obstruction (murmur, decreased systemic perfusion, weak pulses, renal failure, etc), baffle leak, and/or RV-PA conduit obstruction/compression by the sternum (murmur, RV hypertension, cyanosis, and RV dysfunction).

33.6.3.2 Nikaidoh Operation

The Nikaidoh operation and its modifications involve harvesting the aortic root (separating it from the RV), extensive dissection and individual transfer of the coronary arteries, and reconstruction of the right ventricular outflow tract establishing an anatomic connection between the RV and the pulmonary tree. This operation allows a better alignment of the right and left ventricular outflow tracts. It is especially useful in the presence of an inlet or restrictive ventricular septal defect, a hypoplastic right ventricle, a straddling atrioventricular valve, and an anomalous coronary artery course interfering with the right ventricular outflow tract. The postoperative period can be complicated by low cardiac out syndrome, ventricular dysfunction, and coronary ischemia.

33.6.3.3 Physiologic Correction: Senning and Mustard Procedure

The objective of atrial switch operations involving either a Senning (use of the atrial wall and septal tissue) or Mustard (use of the autologous pericardial

tissue) procedure is to create an atrial arterial concordance and atrio-ventricular discordance (physiologically corrected transposition of the great arteries). Currently, these procedures are performed as part of the double switch operation for l-TGA and they are not the procedures of choice for DTGA. There are two intracardiac baffles to reroute the systemic venous blood across the mitral valve and the pulmonary venous return across the tricuspid valve. A number of short and long term complications have been published including systemic and pulmonary venous baffle obstruction and leaks, tricuspid and mitral valve regurgitation, right ventricular dysfunction, and dysrhythmia [23]. Obstruction of the systemic venous pathway is manifested by upper extremity plethora, chylothorax, anasarca, and low cardiac output syndrome. Pulmonary venous baffle obstruction is manifested by white-out lungs, air-space disease, pulmonary hypertension, and left ventricular dysfunction. Baffle leak from the pulmonary venous blood to the pulmonary ventricle would cause a left-to-right shunt with ventricular overload. Conversely, baffle leak from the systemic venous blood to the systemic right ventricle would result in right-to-left shunt with oxygen desaturation and ventricular volume overload.

33.7 Long Term Outcome

The long term outcome after the arterial switch procedure has been satisfactory in most patients; however, results are strongly influenced by the surgical learning curve of each institution [24, 25]. The re-operation free survival rate including late death in one study was 82.2% at 10 years and 75.7% at 15 years in patients who had the arterial switch procedure. Several publications have documented evidence of neurologic abnormalities after the ASO; [26, 27] nevertheless, this is a moving target and the future care of these patients implies not only an improvement in survival in simple and complex TGA, but also ensures that these infants have a good quality of life [28, 29]. Abnormal CNS has been documented in patients with congenital heart disease even prior to surgery. Regarding the Nikaidoh operation, since 1996, 21 patients have undergone aortic translocation at Children's Hospital of Pittsburgh and at the Congenital Heart Institute of Florida. There was only one early

death and one patient required heart transplantation due to left ventricular dysfunction [30].

Late complications of d-TGA after repair include supra-aortic stenosis, supra-aortic pulmonary stenosis, development of neo-aortic root dilation and neo-aortic regurgitation, sinus node dysfunction, arrhythmias, coronary artery abnormalities, and, rarely, sudden death.

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Chapter 34

Congenitally Corrected Transposition of the Great Arteries (ccTGA) or Levo-Transposition of the Great Arteries (l-TGA)

Rukmini Komarlu, Victor O. Morell, Michael Tsifansky, and Ricardo Muñoz

The congenitally corrected aortopulmonary transposition (ccTGA), also called l-TGA, is characterized by atrioventricular discordance and ventriculoarterial discordance (Fig. 34.1). The right atrium is connected to the morphologic left ventricle, which, in turn, is connected to the pulmonary artery. The morphologic left atrium is connected to a morphologic right ventricle, which pumps blood into the aorta. The aorta is anterior and leftward of the pulmonary artery. Therefore, in ccTGA deoxygenated blood passes from the right atrium into the pulmonary artery, and the oxygenated blood returns to the left atrium and is ultimately distributed to the body through the aorta [1, 2], and, in contrast with the D-TGA, results in normal physiology of blood flow. This anomaly is extremely rare, comprising 0.6–1.4% of all congenital heart defects, with the male-to-female ratio of 1.3:1 [3].

About 94% of ccTGA cases are associated with other cardiovascular lesions [1], with the most common abnormalities involving the tricuspid valve (in up to 91% of patients) [4]. When ccTGA and Ebstein's anomaly coexist, the tricuspid valve and right atrial morphology is different from the "classical" Ebstein's in that the anterior leaflet is not sail-like, and the atrialized part of the right ventricle is relatively small [23]. A ventricular septal defect, usually perimembranous, is found in up to 79% of patients, and in some of them, the tricuspid valve straddles the ventricular septum, forbidding biventricular repair. Some patients may

have a common ventricle [1, 4], and in them an associated aortic outflow obstruction is common [1]. Pulmonary outflow tract obstruction occurs in up to 44% of cases [4], and is often due to subvalvar obstruction by fibrous tissue tags (57%) [2], but valvular pulmonary stenosis or atresia also occurs. In the presence of a VSD, the degree of cyanosis is directly proportional to the amount of pulmonary stenosis. Abnormalities of the AV node, including dual AV node with an abnormal His bundle, are quite common in patients with ccTGA, and many ultimately develop complete heart block [5], which can occur spontaneously at any point during intra- or extra-uterine life. The risk of natural onset AV block is approximately 2% per year after diagnosis [6]. Tricuspid valve and VSD surgery also frequently precipitate complete heart block. The mitral valve is abnormal in 39–55% of patients [1, 7], showing more than two cusps, abnormal chordae and papillary muscles, dysplasia, or a cleft [7]. The coronary arteries show the so-called "mirror image distribution." The right coronary artery distributes like the morphologic left coronary artery, giving rise to the circumflex and anterior descending branches. A larger arterial branch crosses the morphologically right ventricular outflow tract in 61% of cases, which is important for the planning of the right ventriculotomy, and a main coronary arterial branch crosses the pulmonary artery in 96% of cases [8]. Other cardiac anomalies in patients with ccTGA include dextrocardia (24–32%), situs inversus (3%) [1, 4], right aortic arch, anomalous pulmonary venous return, atrial septal defects (46%), complete AV canal, and patent ductus arteriosus. Patients with Ebstein's anomaly and ccTGA can also have coarctation of the aorta (1.4%) or aortic atresia [9].

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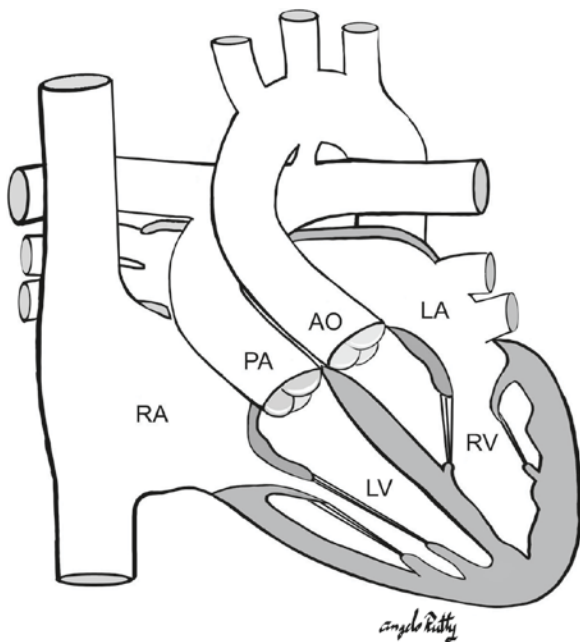


Fig. 34.1 Congenitally corrected transposition of the great arteries

34.1 Embryology

Corrected transposition in viscerotransposition develops when the primitive heart tube loops to the left instead of the right, resulting in the lack of spiral rotation of the conotruncal septum [22]. Therefore, the aorta is connected to the morphologic right ventricle, and the pulmonary artery is connected to the morphologic left ventricle. The ventricles are attached to the normally positioned atria, making this abnormality physiologically corrected. Based on fetal diagnosis and follow-up, survival from the in utero diagnosis to birth is 75–80% [10, 11].

34.2 Clinical Presentation

Patients with ccTGA may seek medical advice at any age, depending on the presence and severity of associated cardiac anomalies. Infants with a large ventricular septal defect, severe tricuspid regurgitation, aortic coarctation, or aortic arch defects are early to experience congestive heart failure. They may be cyanotic, if the pulmonary blood flow is decreased. Atrial and ventricular arrhythmias, and varying degrees of AV block can also bring these patients to medical attention

[3]. In the absence of associated cardiac anomalies, some patients may remain functional and seek medical advice only as adults [12]. The condition may go undiagnosed until late adulthood, when it is found on echocardiogram done for an abnormal ECG, atypical chest pain, or signs of RV failure [13].

On physical exam, left parasternal lift and a systolic murmur akin to mitral regurgitation can be heard at the left sternal border in the presence of tricuspid regurgitation. A systolic impulse can be felt in the second or third left intercostal space with a loud and single second sound. A murmur of pulmonic stenosis may be heard at the mid left sternal border. The cardiac impulse may be maximal on the right side of the chest in the presence of dextrocardia.

34.3 Chest X-ray

Chest X-ray may show dextrocardia, mesocardia, or levocardia; the vascular pedicle may be narrow due to the loss of the normal arterial relationship. Cardiomegaly may be evident.

34.4 ECG

Electrocardiographically, the presence of Q waves in the right, but not left, precordial leads suggests the diagnosis of ccTGA. Because of the ventricular inversion, the right and left bundles are inverted, resulting in septal activation from right to left. Varying degrees of AV block can occur.

34.5 Echocardiography

Echocardiography allows an easy assessment of the interatrial and interventricular septa, the atrioventricular, aortic and pulmonary valves, and the global biventricular function, although the presence of dextrocardia may make structure identification challenging. Subcostal views demonstrate the atrial situs and the position of the cardiac apex. Short-axis and apical four-chamber views show the ventricular morphology, mitral-pulmonary fibrous continuity and ventriculoarterial discordance. High parasternal short-axis view demonstrates the

abnormal arterial relationship, with the aorta anterior and leftward of the pulmonary artery. The aortic arch should be carefully interrogated for the presence of coarctation, interruption, or PDA. Coronary artery anatomy should be identified, although it is often easier to do by cardiac MRI or by high-resolution CT scan. Transesophageal echocardiography is extremely helpful in making the diagnosis in adults, especially for the determination of atrial situs and presence of tricuspid regurgitation [14].

34.6 Cardiac Catheterization

Cardiac catheterization can assess systemic AV valve regurgitation, systemic ventricular function, the hemodynamics of any associated anomalies, the left and the right heart pressures and the pulmonary vascular resistance. Transient or complete heart block can occur due to catheter manipulation during the procedure. In older patients, coronary angiography is important prior to surgical intervention.

34.7 Preoperative Management

Congestive heart failure in patients of any age is managed with diuretics, inodilators or other afterload reducers, and sodium restriction. Complete heart block is common, but placement of an endocardial pacemaker can precipitate deterioration in RV function and worsening of tricuspid regurgitation.

Cyanotic neonates with severe PS, right ventricular outflow tract obstruction, or pulmonary atresia benefit from PGE₁ infusion and optimization of Q_p/Q_s in preparation for a systemic-to-pulmonary artery shunt. Cyanotic infants and children with ccTGA beyond the neonatal period tend to be more stable, and their surgical outcomes are less compromised by poor preoperative status [15]. Patients should always receive prophylaxis for bacterial endocarditis.

34.8 Timing of Surgery

Patients in need for surgery usually have either significant cyanosis or significant pulmonary overcirculation. Cyanotic neonates and small infants commonly undergo

a systemic-to-pulmonary artery shunt before proceeding with a complete repair. At Children's Hospital of Pittsburgh we prefer to perform the double switch procedure at about 1 year of age. The timing of tricuspid valve repair or replacement in these patients remains uncertain. The mid and long-term outcomes may improve if tricuspid valve replacement is performed in patients with a right ventricular ejection fraction greater than 44% [13]. An exercise stress test may help assess impaired exercise tolerance even before functional limitations occur, indicating the need for a tricuspid valve procedure. In patients under 10 years with right ventricular dysfunction, with or without tricuspid insufficiency, a double switch surgery after left ventricular retraining using a pulmonary artery band is an option. Patients with significant tricuspid regurgitation may benefit from a pulmonary banding that would decrease the regurgitation by increasing the LV (subpulmonary ventricle) pressure, therefore partially compressing the RV (systemic ventricle) inducing remodeling and a decrease of the tricuspid annulus.

34.9 Surgical Techniques

The approaches to surgical management of patients with ccTGA can be grouped into two options: a *physiologic repair* and an *anatomic repair*.

After physiologic repair, the right ventricle remains the systemic ventricle, and any other associated lesion is repaired. Although simpler, this approach results in a right ventricle dependent systemic circulation, which has negative long-term implications, mainly RV failure and tricuspid regurgitation.

After anatomic repair, the left ventricle becomes the systemic ventricle, and the outcomes should be better. Nevertheless, the repair involves some form of a technically challenging double switch procedure.

34.9.1 The Double Switch procedure

The "double switch operation" encompasses several techniques depending on the associated lesions, including:

1. An atrial switch with an arterial switch
2. An atrial switch with a Rastelli procedure
3. An atrial switch with an aortic translocation

All of these require cardiopulmonary bypass and cardioplegic arrest. Figures 34.2 and 34.3 depict the two atrial switch procedures, the Mustard and the Senning interventions. The arterial switch, the aortic translocation, and the Rastelli procedure have been described in the chapter 33 related to d-TGA. The operative mortality of the double switch is reported around 10% [16, 17].

34.9.2 VSD Closure

It is important to recognize that in patients with atrioventricular and ventriculoarterial discordance the conduction tissue runs anterior and cephalad to the pulmonary valve and then descends along the anterior margin of the

VSD before diverging into the bundle branches [3]. Division of the outlet septum (required during the aortic translocation procedure) does not result in complete heart block, but closure of the VSD may injure the conduction tissue (Fig. 34.4). Not surprisingly, a significant number of patients will develop postoperative or spontaneous heart block and require pacemaker placement.

34.9.3 Single Ventricle Repair

Patients with straddling atrioventricular valves, multiple ventricular septal defects or associated ventricular hypoplasia should be considered for univentricular palliation [18].

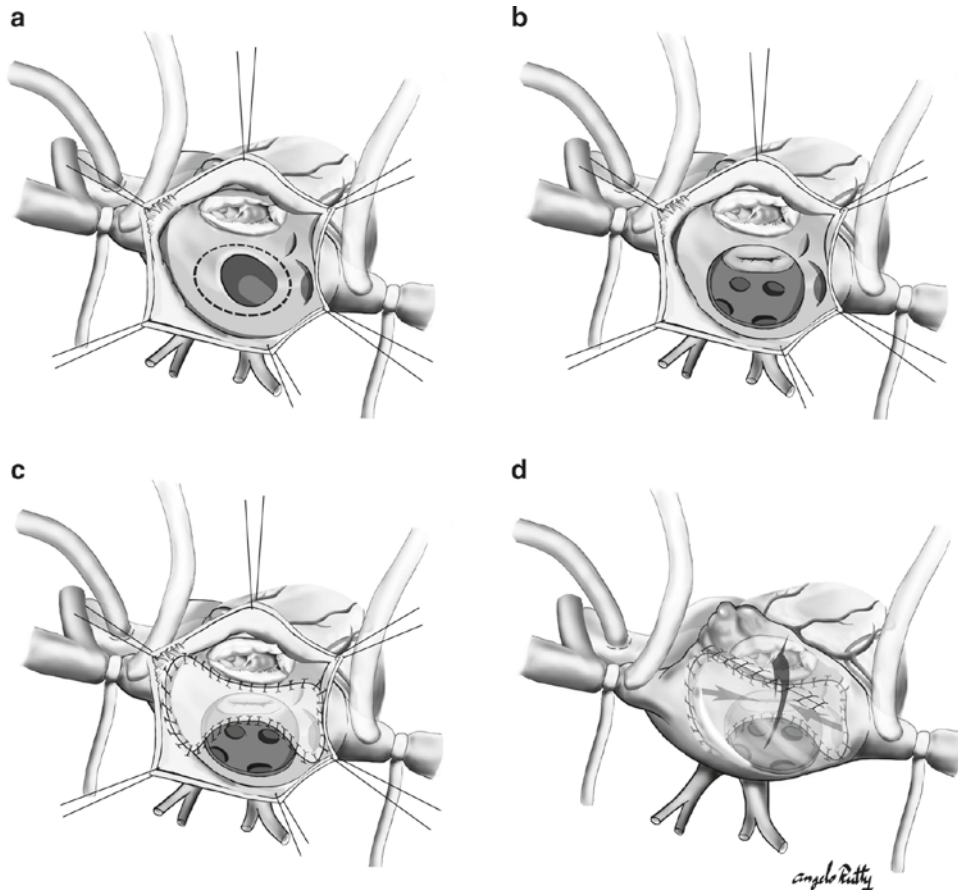


Fig. 34.2 The Mustard procedure. (a–b) A right longitudinal atriotomy is made, and the atrial septum is aggressively resected, preserving the medial ridge. (c) A dumbbell-shaped patch of autologous pericardium is used to redirect the systemic venous

return into the right ventricle via the posteriorly located tricuspid valve. (d) The right atriotomy is closed; now the pulmonary venous return drains into the left ventricle via the anteriorly located mitral valve

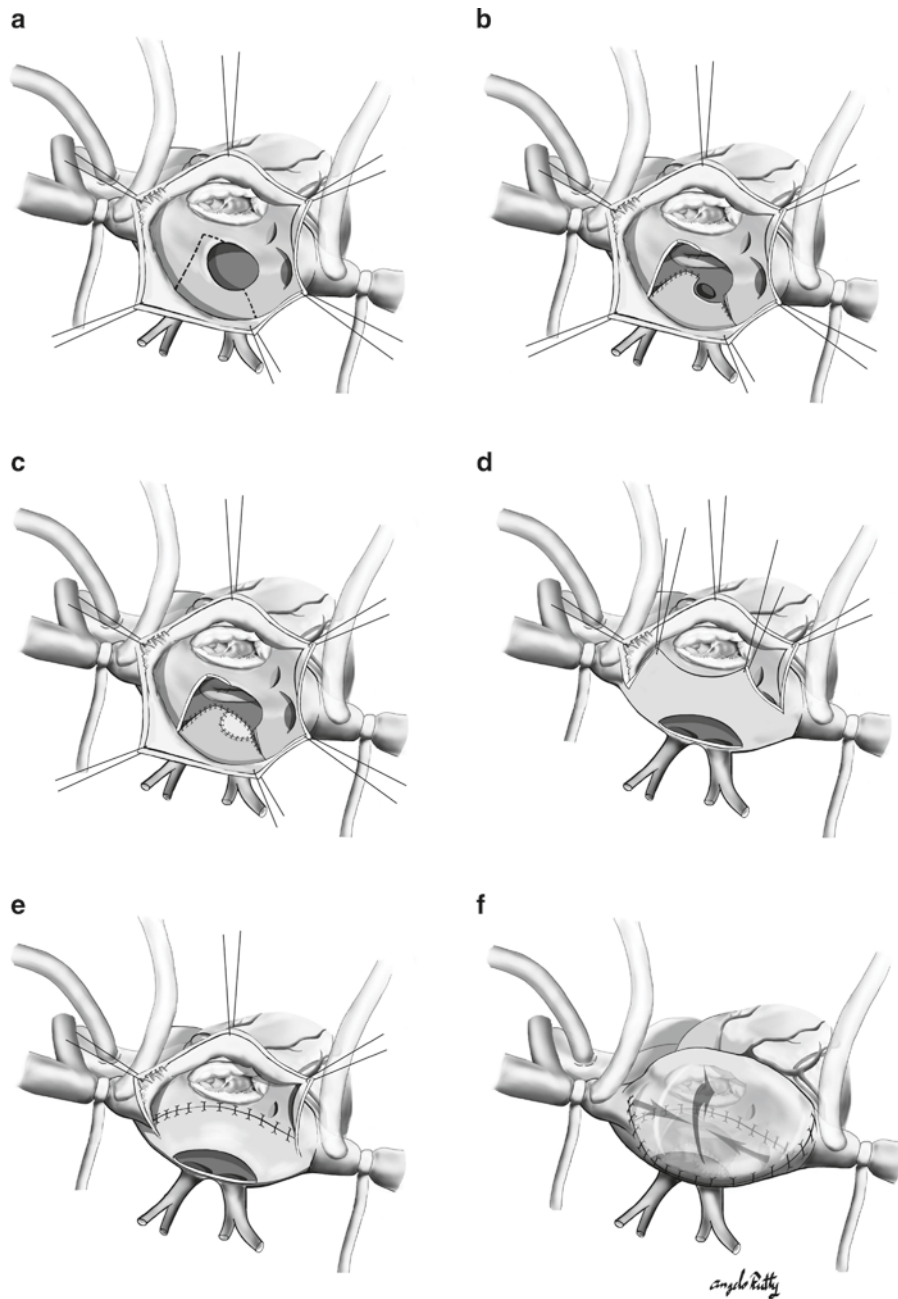


Fig. 34.3 The Senning Procedure. (a-b) Via a right atriotomy, a laterally based flap of atrial septum is created and moved posteriorly, over the orifices of the pulmonary veins, becoming the roof of the pulmonary venous baffle. (c) Frequently, a segment of pericardium is needed to augment the flap. (d) A separate incision is made in the left atrium, just anterior to the right-sided pulmonary veins.

(e) The systemic venous baffle is created by suturing the posterior edge of the right atrial incision to the medial rim of the atrial septum. (f) The pulmonary venous channel is created by suturing the anterior edge of the right atrial incision along the external surface of the systemic venous baffle (around the superior and inferior cava) and to the lateral edge of the left atrial incision

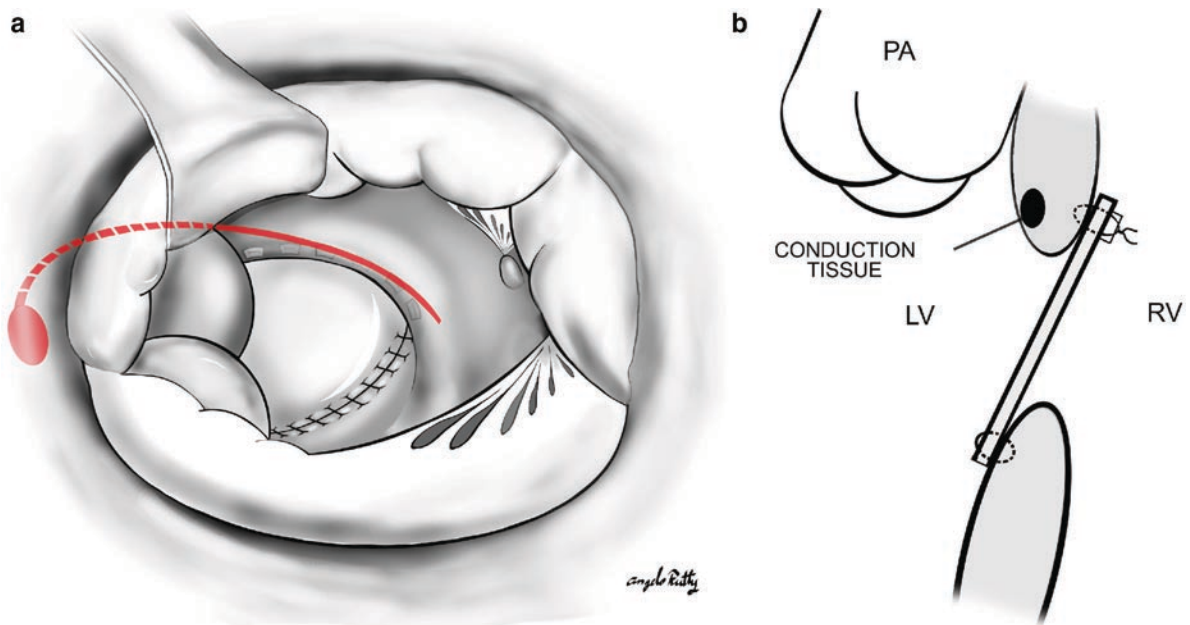


Fig. 34.4 (a) The atrioventricular conduction bundle (in red) runs in the anterosuperior margin of the defect. (b) Along the anterosuperior margin of the VSD, interrupted sutures are placed along the RV side in order to avoid injuring the conduction system

34.10 Postoperative Management

The postoperative management depends on the repair of the associated lesions, including pacemaker placement, release of right ventricular outflow tract obstruction, Blalock–Taussig shunt placement, tricuspid valve repair, ventricular septal defect closure, conventional Rastelli, double switch operation, atrial switch and intraventricular rerouting, and a Fontan type surgery [17]. With the exception of the double switch, specific postoperative care of associated lesions is described in their respective chapters.

34.10.1 Double Switch Operation (Atrial and Arterial Switch)

The postoperative care addresses the potential complications of the atrial switch (Senning or Mustard operations) and the arterial switch operations.

34.10.2 Complications of the Atrial Switch

- Systemic venous baffle obstruction: These patients can have SVC syndrome, plethora, anasarca, and low cardiac output syndrome. Rapid bedside echocardiographic diagnosis of the obstruction must be made and decision taken to proceed with cardiac catheterization or surgical reintervention.
- Pulmonary venous baffle obstruction: These patients show clear signs of pulmonary edema. Gas exchange worsens and high ventilatory settings are often needed (increased PEEP, tidal volumes and FiO_2). Pulmonary venous return falls leading to a decrease in systemic cardiac output. Echocardiogram, cardiac catheterization and/or surgical reintervention may be indicated.
- Baffle leaks may lead to ventricular volume overload and systemic desaturation may be present and may, depending on the severity, require interventional catheterization or surgical reintervention.

- Atrial arrhythmias, conduction disturbances or sick sinus syndrome are managed according to the specific electrophysiologic disturbance.

Postoperative management of the arterial switch operation has been described elsewhere, in the chapter dedicated to d-TGA. It is noteworthy, however, that patients after a double switch operation are at risk of significant ventricular dysfunction requiring generous inotropic support or ECMO.

34.11 Long-Term Outcomes

The main long-term complication of ccTGA is failure of the systemic right ventricle, especially in the presence of tricuspid regurgitation. RV dysfunction usually becomes clinically significant by 17 years of age [18]. About 50% of patients with associated defects and about 30% without them develop RV dysfunction by 45 years of age [19]. The prevalence of complete heart block and tricuspid regurgitation also increases with age.

Historically, patients undergoing conventional repair have shown survival rates of 61% at 15 years [20] and 48% at 20 years [21] after the initial repair. Slightly more than half of the patients have required reoperation within 16 years, and 35% required placement of a pacemaker. Nearly half have required tricuspid valve surgery by the age of 40 years. The most common cause of death was reoperation (36%); other causes included sudden death, progressive myocardial failure, and documented arrhythmias [21]. Risk factors for death included RV end-diastolic pressure >17 mmHg and RV dysfunction before surgery, complete heart block after surgery, subvalvular pulmonary stenosis, and Ebstein malformation of the tricuspid valve [20]. A recent study found that more than moderate tricuspid regurgitation and cardiopulmonary bypass time longer than 240 min increased the risk of in-hospital mortality, while persistent tricuspid valve regurgitation was a risk factor for late mortality [17].

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Chapter 35

Truncus Arteriosus

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Truncus Arteriosus (TA) is a rare congenital cardiac malformation, firstly described by Wilson in 1798 and reported with an incidence between 0.006 and 0.043 per 1,000 live births. It accounts for 0.7% of all congenital cardiac malformations [1] and for 1–2% of congenital heart diseases identified at autopsies. This disease occurs with equal frequency in male and female gender and it has no racial preference.

TA has been defined as an anomaly in which the aorta, the coronary arteries and the pulmonary arteries arise from a single vessel (common truncus) originated from the cardiac chambers. There is no remnant or rudimentary pulmonary artery arising separately from the heart.

TA may be an isolated anomaly or associated with chromosomal anomalies. The most commonly associated condition is the 22q11· deletion [2, 3]. This deletion may have an impact on the complications associated with the surgical correction of the TA.

35.1 Anatomy

Persistent TA is a conotruncal anomaly that consists of a unique arterial trunk that leaves the heart giving rise to the coronary arteries, the pulmonary, and the systemic arteries. This anomaly is usually diagnosed in a context of situs solitus with a ventricular D-loop.

The truncal valve is located in the normal aortic valve position, with a fibrous continuity between

truncal and mitral valves, but it presents with a larger annulus. Leaflets are most often dystrophic resulting in stenosis and/or regurgitation. This unique semilunar truncal valve is in most cases tricuspid (69%), but may also be quadricuspid (22%) or bicuspid (9%). Uni-, penta-, and hexacuspid valves have been rarely described [4]. No other semilunar valve is found in these cases. The function of this valve has to be precisely analyzed before surgery to decide if it can be preserved or not. Usually, the truncal valve overrides equally the ventricular septal defect over right and left ventricle. But quite often, the truncal valve is deviated on the right and may result in a narrowing of the left ventricle outflow after repair of the ventricular septal defect.

The partial or complete failure of the aortopulmonary septation results in the common arterial trunk and the absence of infundibular septum results in the ventricular septal defect under the truncal valve. The ventricular septal defect is large and juxta truncal. Its inferior part is usually muscular (posterior limb of the trabecula septomarginalis) and remote from the tricuspid valve. Occasionally, this muscular part does not exist or is very thin, and the lower limit of the ventricular septal defect can be very near the tricuspid valve and the conduction system, which can be injured during repair.

Pulmonary arteries arise from the common trunk, close to the truncal valve, from a short posterior pulmonary trunk, separately from the posterior wall, or in a random fashion often associated with an interrupted aortic arch.

Many associated anomalies have been reported:

- There is a left superior vena cava in 4–12% of patients.
- In most cases coronary arteries distribution is normal, but anomalies may occur in around 15% of patients [4–6]

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- A big infundibular artery or even a left descending artery originating from the right coronary artery can cross the infundibulum (prominent conus branch of the right coronary artery supplying the right ventricular outflow tract) and have to be respected by the infundibulotomy.
 - A small leftward-displaced left anterior descending coronary artery may be present.
 - An origin of the posterior descending artery from the circumflex artery may be seen in 27% of patients.
 - Anomalies of coronary ostial origin are documented in 37–49% of patients.
 - Some coronary arteries may also arise from variable level of the TA and have to be identified not to be injured during surgery.
- The aortic arch on the right in 21–36% of patients [4, 5, 7].
 - In 11–19% of patients, there is an interrupted aortic arch, most commonly a type B (in Van Praagh's type 4 TA) [4, 5, 7, 8].
 - Hypoplasia of the aortic arch with or without coarctation occurs in 3% of patients [8].
 - In 16% of patients, one pulmonary artery is absent on the side of the aortic arch [9].
 - The mitral valve may be dysplastic.
 - Other associations:
 - A secundum atrial septal defect in 9–20% of patients.
 - An aberrant subclavian artery in 4–10% of cases.
 - Mild tricuspid stenosis in 6% of cases.
 - Partial anomalous pulmonary venous connection, tricuspid atresia, mitral atresia, ventricular inversion, and an asplenia complex [9–13] have been described as rare.

Patients with TA may also have extracardiac anomalies in 21–30% of cases. The most common association is the 22q11 deletion or DiGeorge sequence. This anomaly has been documented in one-third of all TA and in two-thirds of patients with a type B interrupted aortic arch and may have a significant impact in the postoperative course and in the long-term prognosis of these patients. Other described associated anomalies include skeletal deformities, hydrourter, bowel malrotation, and multiple complex anomalies [6].

35.2 Classifications

Two classifications are commonly used. The classification from *Collet and Edwards*, described in 1949 [14], is based on the origin of the pulmonary arteries (Fig. 35.1). *Type I* is defined by the presence of a main pulmonary trunk, arising from the ascending aorta giving the two pulmonary arteries. In *Type II*, the pulmonary arteries arise from close but separated ostia on the common arterial trunk, whereas these ostia are widely separated in *Type III*. *Type IV*, where pulmonary arteries are coming from the descending aorta is now considered like a form of tetralogy of Fallot with pulmonary atresia in which pulmonary blood supply is achieved by aortopulmonary arteries (pseudo TA).

In the *Van Praagh* classification, defined in 1965 [4], differences in the types of TA are based on the embryological septation (Fig. 35.2). *Type A* is defined by the presence of a ventricular septal defect and *Type B* by its absence. These types are completed by four extracardiac patterns for the aorta and pulmonary arteries

- *Type 1* presents a partially formed aortopulmonary septum resulting in a segment of main pulmonary trunk. It is the most frequent type (about 60%) and corresponds to Collet's Type I.
- *Type 2* has no aortopulmonary septum and thus no main pulmonary trunk, pulmonary arteries originating directly from the TA (about 30%, corresponding to Collet's types II and III).
- *Type 3* is very rare and defined by a unique pulmonary artery originating from the TA, the second one coming from the ductus arteriosus or from an aortopulmonary artery (hemitruncus).
- *Type 4* corresponds to an aortic arch interruption downstream the left common carotid artery. After the pulmonary bifurcation, a large patent ductus arteriosus supplies the descending aorta and the left subclavian artery.

35.3 Pathophysiology

Since the common trunk receives blood from both ventricles, a VSD is almost always present [15, 16]. This ventricular septal defect is usually large. The predominant physiological characteristic of this disease is

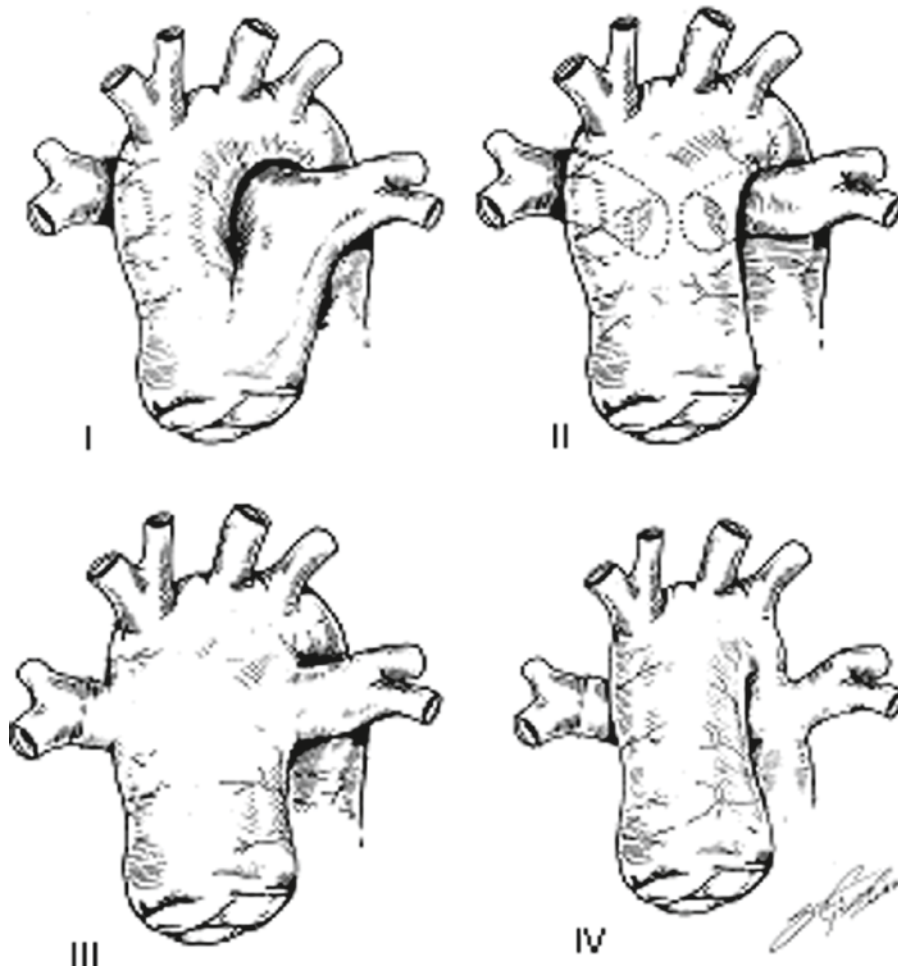


Fig. 35.1 Truncus Arteriosus (TA), classification of Collet and Edwards

therefore a significant left-to-right shunt, unless the pulmonary arteries are hypoplastic or stenotic or the pulmonary vascular resistances are elevated. In fact, like for any other left-to-right shunt, the degree of shunting depends to a great extent on the ratio of resistances between the systemic and the pulmonary circulations. As pulmonary vascular resistances decrease over the first few weeks of life, patients develop signs of cardiac failure.

Truncal valve regurgitation and stenosis are seen in 10–15% of patients each. If truncal insufficiency is severe, signs and symptoms of heart failure may also appear shortly after birth.

In the uncommon situation in which infants have stenosis of the pulmonary arteries, obvious cyanosis may be present at birth and intensify with age [6], although these patients have less cardiac failure.

If an interrupted aortic arch is associated, patients become very symptomatic early in life, associating pulmonary overcirculation with pulmonary hypertension and cardiac failure, with signs of low cardiac output and left obstruction. Nevertheless, in type 4 TA, the pulmonary arteries often are stenotic, protecting the patients against overcirculation.

35.4 Diagnosis

- *Clinical presentation:*

Most patients present in the neonatal period. Clinical presentation depends on the Q_p/Q_s , hence, patients with stenosis of the pulmonary arteries are essentially

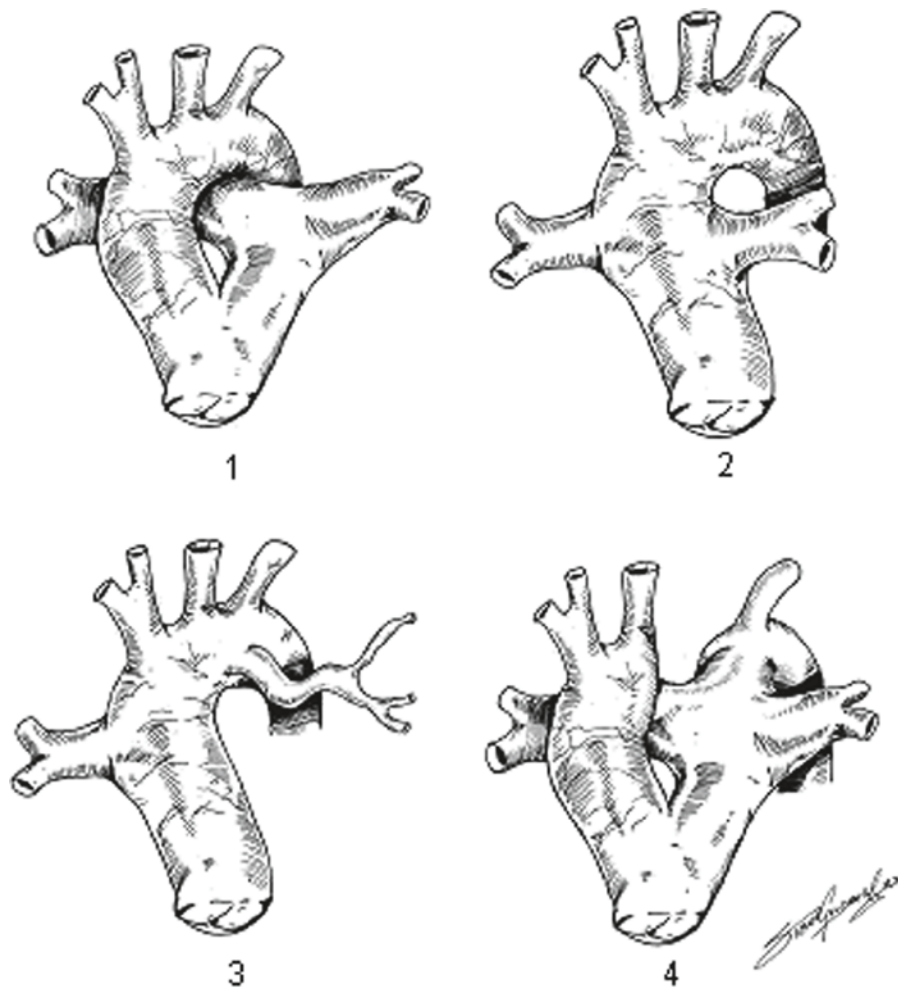


Fig. 35.2 TA, classification of Van Praagh

cyanotic, whereas patients without pulmonary protection develop signs of cardiac failure and failure to thrive over the first 2–4 weeks of life. Neonates may also appear mildly cyanotic because of high pulmonary vascular resistances. Feeding difficulties may be secondary to the TA, but caregivers must pay attention to the association with 22q11 deletion, which may also have an impact on the feeding capacities. Patients with very high Q_p/Q_s may ultimately associate cyanosis to the signs of cardiac failure, due to pulmonary interstitial edema.

Patients with excessive pulmonary flow present with clinical signs of cardiac failure and of diastolic steal from the truncal vessel towards the lungs, namely failure to thrive, tachycardia, tachypnea, excessive sweating, bounding pulses, and significant systemic systolo-diastolic pressure differential. These patients

also have a hyperdynamic precordium, a left precordial bulge, and cardiac auscultation may reveal a gallop rhythm and the presence of murmurs. A dysplastic and stenotic truncal valve may be the source of a pansystolic murmur and also of a diastolic high-pitched murmur, directly proportional to the degree of the associated regurgitation, if any. Stenotic pulmonary arteries will explain the presence of a systolic murmur, irradiated towards the side of the affected artery. A thrill is present in patients with increased Q_p/Q_s . The first sound is normal and the second sound may be unique and loud. An ejection click may also be heard.

- *ECG*

The ECG findings in the neonate may be varied and even normal. It usually shows a sinus rhythm and signs

of biventricular hypertrophy. ECG is useful to rule-out the exceptional scenario of myocardial ischemia and as a baseline study for any eventual postoperative event.

- *Chest X-ray:*

Chest radiography shows a cardiomegaly frequently present since birth. The aortic arch may be right-sided. In patients with high Q_p/Q_s , as the pulmonary vascular resistances decrease, cardiomegaly as well as pulmonary vascular markings increases progressively, reflecting the excessive blood flow. With the increased venous return to the left heart, the left atrium may be enlarged and compress the left bronchus. Venous congestion may also be noted as the left ventricle dilates – with both the increased left return and the truncal valve regurgitation – and fails in more aged patients. In patients with stenotic pulmonary arteries or in late survivors with elevated pulmonary resistances, pulmonary vascular markings will be normal or decreased and the cardiomegaly is mild unless induced by severe truncal regurgitation. The absence of thymus suggests the association with 22q11- deletion.

- *Echocardiography*

Echocardiography is the cornerstone reference for diagnosis and follow-up of patients with TA (Figs. 35.3–35.6). It has significantly reduced the need

for cardiac catheterization for diagnostic purposes, since it comprehensively shows:

- The conotruncal anomaly, with the ventricular balance, the ventricular function, and the interventricular septal defect.
- The origin and configuration of the pulmonary arteries allowing the definition of the type of TA.
- The anatomic and functional characteristics of the truncal valve.
- The origin and distribution of the coronary arteries.

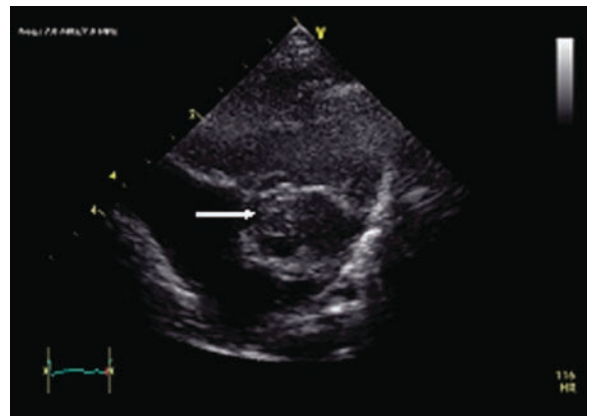


Fig. 35.3 Echocardiography showing a TA with a dysplastic truncal valve (arrow)

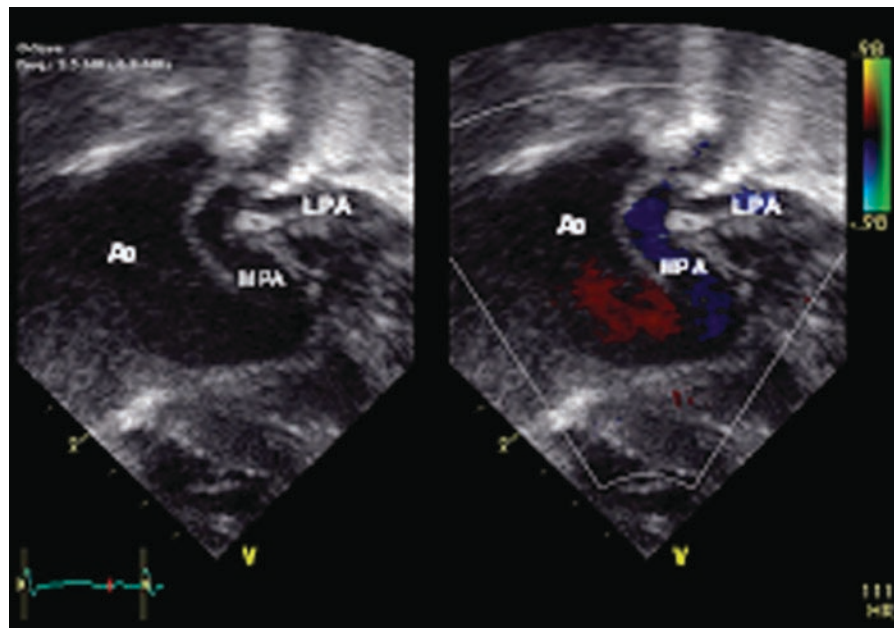


Fig. 35.4 Echocardiography showing a type 1 TA (*Ao* aorta; *MPA* main pulmonary artery; *LPA* left pulmonary artery)

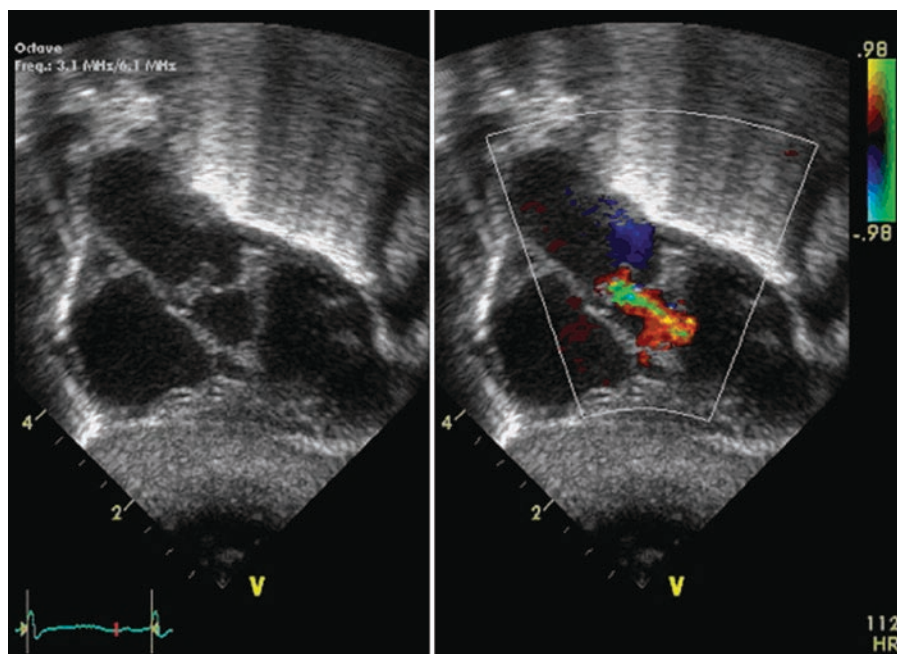


Fig. 35.5 Echocardiography showing a TA with a moderate regurgitation of the truncal valve

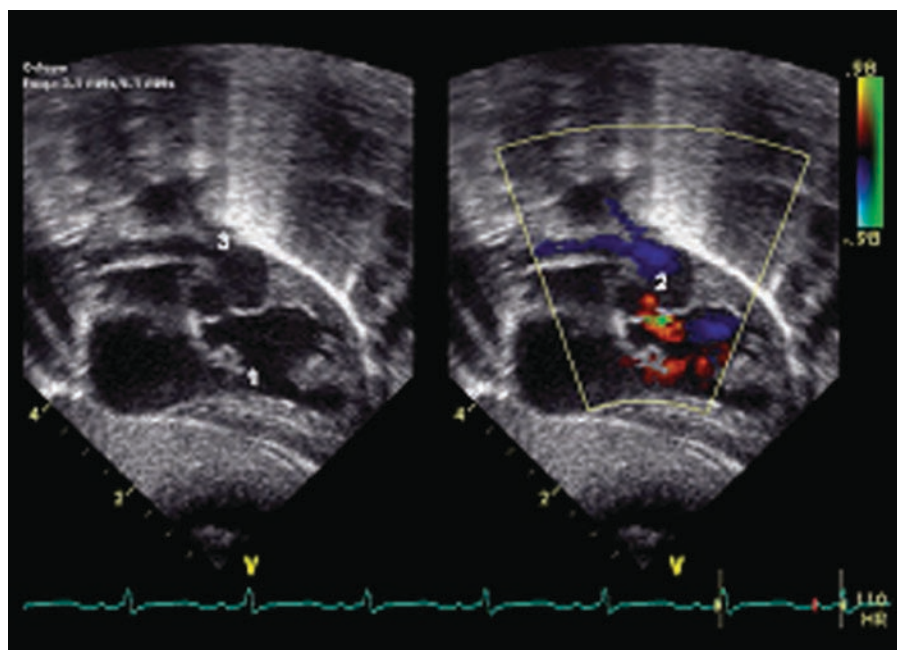


Fig. 35.6 Echocardiography showing a type 1 TA (1: ventricular septal defect; 2: mild to moderate regurgitation of the truncal valve; 3: pulmonary artery bifurcation)

- The anatomy of the aortic arch; elucidates the association with interrupted aortic arch and aberrant retroesophageal right subclavian artery.
- Any other associated anomaly.

Echocardiography also facilitates the immediate perioperative evaluation of the surgical repair using transesophageal techniques. The main differential diagnosis prior to intervention is to be established with tetralogy of Fallot and pulmonary atresia with ventricular septal defect.

- *Cardiac catheterization*

Cardiac catheterization is still performed to confirm anatomic and physiologic details whenever the echocardiography is not elucidative or if there is suspicion of multiple ventricular septal defects or complex associated anomalies. It is particularly useful in late survivors who present with severe pulmonary arterial hypertension and in whom there is a need to study pulmonary vascular resistances and their response to therapy. Patients with TA who have pulmonary artery resistances above 8 Wood units/m² have higher operative and postoperative mortality [9, 17].

In patients who have been previously operated and require reintervention (i.e., right ventricle to pulmonary artery conduit replacement), cardiac catheterization may be useful in identifying coronary artery anatomy that can be obscured by the presence of pericardial adhesions when assessed by echocardiography.

- *Other studies*
- *MRI*

MRI is a useful noninvasive method that enables a noninvasive anatomic diagnosis of TA and can in some cases replace cardiac catheterization, particularly in aged patients. MRI is currently recognized by pediatric cardiologists and cardiac surgeons as an inevitable technique for the preoperative and postoperative evaluation of some heart diseases [18]. It provides information about the anatomic characteristics of the vascular anomalies and their relation to the bronchial system. It also allows a reliable functional evaluation of the ventricular performance and provides flow information determining the degree of truncal valve stenosis or regurgitation.

- *CT scan*

CT scans are useful for the evaluation of anomalies of the aortic arch and anomalies of vascular structures like the

aberrant origin of the right retroesophageal subclavian artery. It may also help defining systemic and pulmonary venous connections, anomalies of the origin and course of the coronary arteries, and the spatial relationship between vascular and airway structures.

35.5 Management

Total repair of TA should be performed in the early life, unless contraindicated by prematurity of extracardiac morbidity. However, some patients require preoperative management of specific problems to optimize conditions for the surgical procedure.

35.6 Preoperative Medical Management

35.6.1 Cardiovascular Management

Patients with significant truncal valve regurgitation or cyanosis due to pulmonary edema may benefit of a milrinone infusion until surgery. Milrinone improves myocardial contractility, reduces the afterload of the ventricular mass, and the left atrial pressure. Nevertheless, particular care must be taken with excessive systemic vasodilation that might compromise coronary perfusion.

In patients with elevated Q_p/Q_s , O₂ ought to be carefully administered since, by inducing pulmonary vasodilation, it may facilitate further pulmonary overcirculation and increasing of the pulmonary edema with systemic low cardiac output. In exceptional cases, subatmospheric therapy may be needed.

Diuretics are indicated in these patients in order to decrease the preload and the degree of pulmonary edema. Loop diuretics may be administered in boluses or as a continuous infusion.

Fluid restriction should be avoided because of the impact on the caloric input.

35.6.2 Respiratory Management

Symptomatic patients may require noninvasive positive pressure in the form of CPAP or BiPAP. It improves

pulmonary edema and reduces systemic afterload, hence improving the stroke volume. When mechanical ventilation is required, caregivers should provide conditions to reduce or limit pulmonary vascular flow. Hyperventilation should therefore be avoided. The objective is to provide low respiratory rate, tidal volume, peak pressures and FiO_2 , keeping oxygen saturations in the range of 75–85%. When the excessive Q_p/Q_s is refractory to these measures, patients may need deep sedation, the use of muscle relaxants and subatmospheric gases.

35.6.3 Nutritional Management

Preoperative nutrition is crucial and may have an impact in the postoperative course. Early enteral feeding is therefore recommended. Patients in whom enteral feeding is contraindicated or limited should be started on parenteral feeding as soon as possible.

35.6.4 Other

Patients with excessive Q_p/Q_s improve with measures that optimize systemic flow. This includes, other than the use of systemic vasodilators, diuretics, and adequate ventilation, the increasing of blood viscosity with transfusion of red blood cells.

Taking into account the high incidence of 22q11 deletion, a sample for genetic analysis (FISH) should be systematically sent to the laboratory.

35.7 Surgical Management

As previously discussed and to summarize, TA induces cyanosis due to blood mixing at the level of the VSD, and a left-to-right shunt at the arterial level, responsible for heart failure and quick development of a severe pulmonary vascular obstructive disease, frequently after 6 months. Survival after surgical repair has greatly improved by early repair, and most authors recommend treating these children before 1 month of age. Surgical repair is always indicated except for late survivors with high pulmonary vascular resistances (Eisenmenger's syndrome).

For the large majority of TA (about 90%), in the absence of truncal valve dysfunction or aortic arch interruption, surgical repair consists in the separation of the pulmonary arteries from the truncal vessel, the closure of the ventricular septal defect, and the reconstruction of the right ventricular outflow tract with the placement of a valved conduit towards the pulmonary arteries. In cases with truncal valve dysfunction, although techniques of repair have been described, replacement by a homograft is often indicated. Last, for TA with aortic arch interruption, a reconstruction of the aorta is mandatory.

The type of surgical repair depends on the anatomic form:

- Repair of isolated TA

Isolated forms of TA (nearly 90% of cases) correspond to Van Praagh's types A1 and A2 and to Collett's types I, II, and III.

After sternotomy and fixation of a pericardium patch in glutaraldehyde, cardiopulmonary bypass is established between the distal ascending aorta and both vena cava. The procedure may nowadays be achieved under continuous high flow, high hematocrit normothermic cardio pulmonary bypass. After pulmonary artery control, aortic cross clamping, and cardioplegia, the common TA is open, a pulmonary trunk or an aortic patch including the two pulmonary arteries is harvested. This defect on the ascending aorta is generally repaired only by termino terminal anastomosis between the aortic root and the distal ascending aorta. Both pulmonary branches are well mobilized. Through a right ventriculotomy starting immediately under the truncal valve, the ventricular septal defect is exposed and closed by a pericardial or prosthetic patch. The patch must be large to avoid narrowing of the left ventricular outflow and its lower fixation has to preserve the conduction system. The right ventricle outflow tract is then reconstructed with a small size pulmonary or aortic homograft or with a valved prosthetic conduit, placed between the pulmonary bifurcation and the right ventriculotomy (Fig. 35.7). All these materials are unable to grow and will undergo degradation requiring iterative replacement.

To avoid such material, surgical techniques have been developed using autologous tissues [19]. These techniques consist in a mobilization of the pulmonary trunk or bifurcation towards the right ventriculotomy and the anastomosis of its posterior wall to the top of

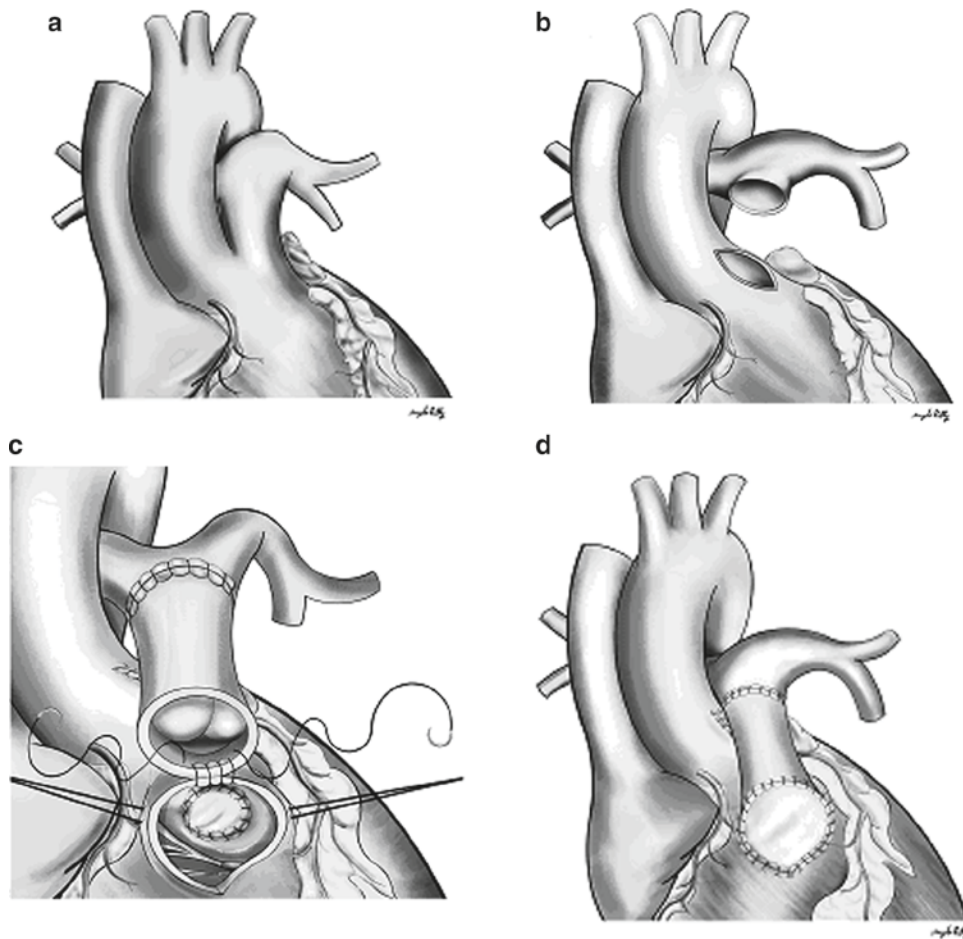


Fig. 35.7 *Truncus Arteriosus Type I repair:* (a) Type I TA. (b) First, the pulmonary trunk is separated from the truncus. (c) Then through a right ventriculotomy the VSD is closed and a valved conduit is used to establish RV to PA continuity. (d) The completed repair

the ventriculotomy, directly or using the left atrial appendage. An anterior hood is made of pericardium to complete the anterior part of the right outflow tract. To avoid dramatical consequences of postoperative pulmonary hypertension, a monocuspid valve is implanted in the right outflow tract, but ultimately pulmonary regurgitation appears as the main drawback of this technique.

Finally, although it is not the author's policy, some surgeons may preserve a small (5 mm) atrial septal defect as a security in case of pulmonary hypertensive crisis or right ventricular failure [20].

- Repair of TA with truncal valve dysfunction

Truncal valve stenosis is rare and often overestimated preoperatively because of the increased blood flow.

Intraoperative commissurotomy is sufficient in most cases and must be conservative to avoid postoperative regurgitation.

Preoperative regurgitation is frequent, due to the dystrophic truncal valve leaflets. Mild to moderate regurgitation may be respected. For severe regurgitation a valvuloplasty should be attempted (Fig. 35.8).

If a valvuloplasty is not possible, the truncal valve is replaced by a cryopreserved aortic homograft. The truncal valve is removed, the ventriculotomy is prolonged through the truncal annulus, and the superior edge of the patch used for the ventricular septal defect closure becomes the anterior part of the new annulus where the homograft is sutured. Coronary arteries are then implanted in the homograft before distal anastomosis to the distal ascending aorta.

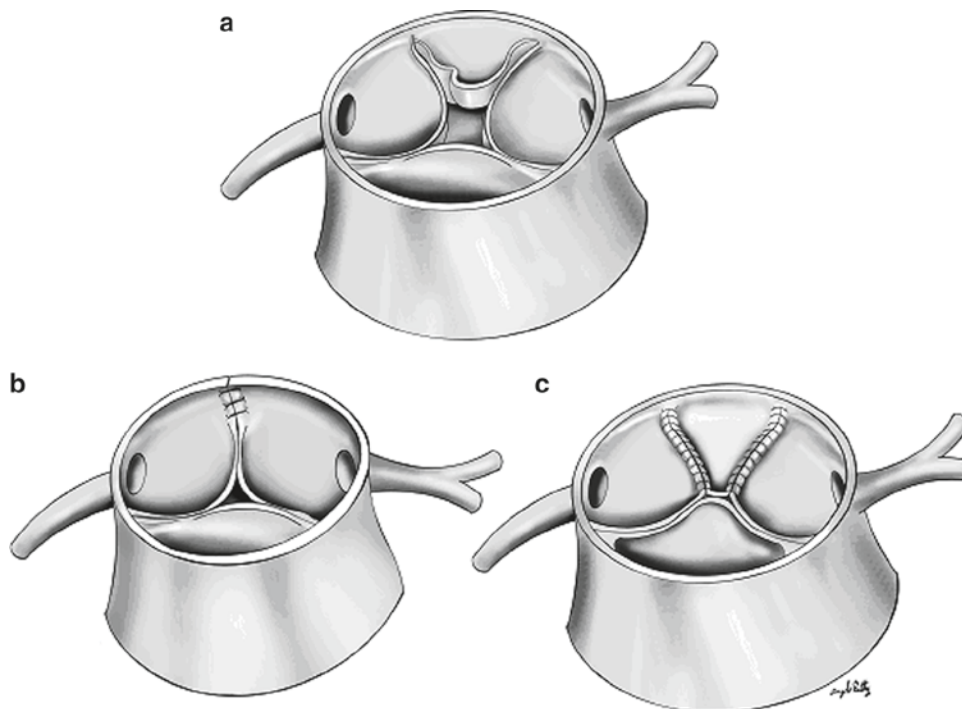


Fig. 35.8 *Truncal valve repair.* (a) Options for valve repair in the presence of a quadricuspid truncal valve with a prolapsing leaflet include: (b) leaflet and aortic sinus resection or (c) commissural closure

- Repair of TA with aortic arch interruption

TA with aortic arch interruption corresponds to Van Praagh's type A4 TA. For this repair, cardiopulmonary bypass is modified to avoid circulatory arrest. The authors use a PTFE prosthetic tube anastomosed to the brachiocephalic arterial trunk for the arterial cannulation in order to achieve a continuous antegrade cerebral perfusion during partial circulatory arrest necessary for the reconstruction of the aortic arch.

After section of the pulmonary trunk from the TA, all the ductal tissue is resected. The descending aorta is mobilized as far as possible, and in most cases, its posterior wall can be sutured to the longitudinal incision of the ascending aorta. The large anterior and inferior defect of the ascending aorta and aortic arch is reconstructed with a patch of autologous aorta or vascular homograft. Cerebral perfusion is then converted to total, and conventional cardiopulmonary bypass is initiated. The VSD is closed followed by the right ventricular outflow tract reconstruction towards the pulmonary arteries, following the procedure described for other types of TA (Fig. 35.9).

- Repair of hemitruncus

For hemitruncus repair, the pulmonary artery originating from the ductus arteriosus or the descending aorta is detached and then branched on the pulmonary arterial tract forming a new pulmonary bifurcation.

35.8 Postoperative Management

Postoperative management after TA repair varies with the anatomic form and may be impacted by the duration of CPBP, the aortic cross-clamp and the circulatory arrest time. Residual lesions will also complicate postoperative course and must absolutely be ruled-out in patients who do not progress uneventfully. Most of the potential complications develop essentially during the peak of the inflammatory process throughout the first 48 h. The main complications to be anticipated and prevented if possible are pulmonary hypertensive spells and low cardiac output syndrome (LCOS).

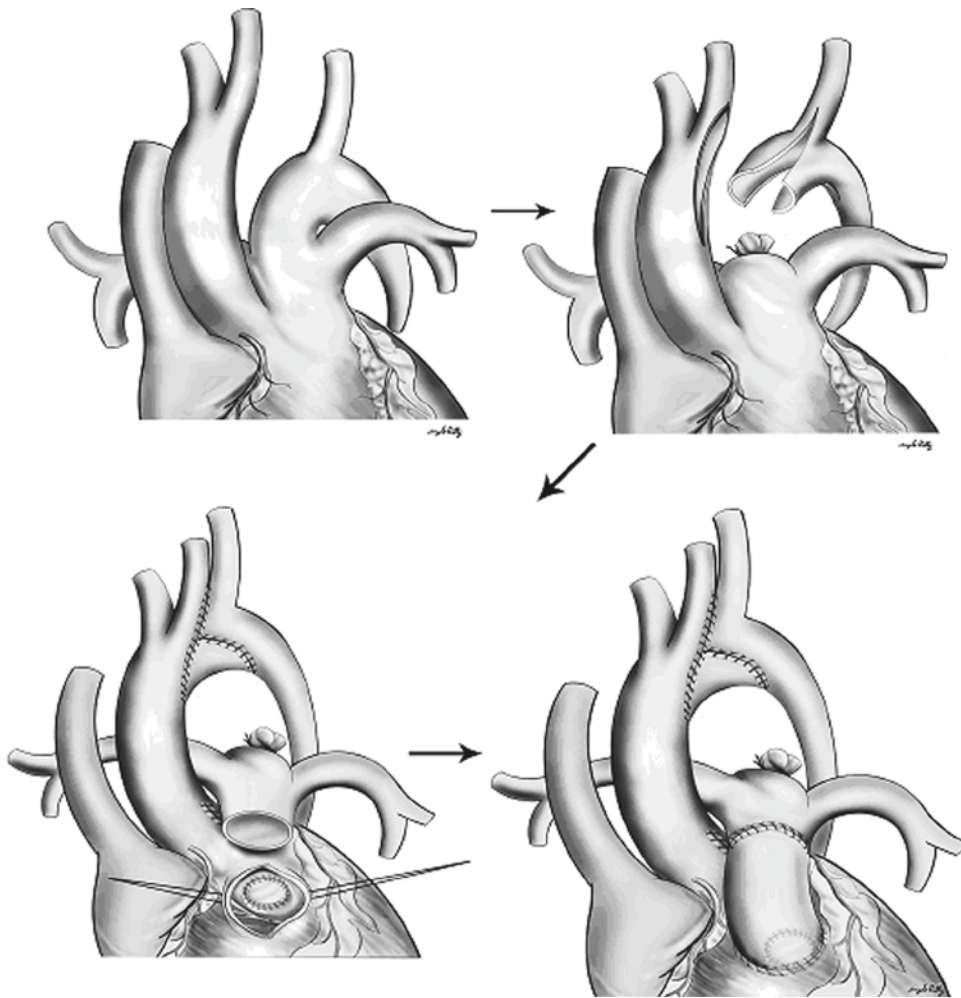


Fig. 35.9 Repair of TA with aortic interruption. The technique utilized to repair the aortic interruption involves a direct anastomosis (superiorly) with patch augmentation (inferiorly). After

separating the pulmonary trunk from the truncus and closing the VSD, a valved conduit is used to establish RV to PA continuity

35.8.1 Monitoring

Taking the above information into account, and although this varies with the institutions, most patients require indwelling pulmonary and left atrial catheters, as a complement to the central and the arterial lines. Noninvasive monitoring is based on heart rate with ECG, respiratory rate, and peripheral oxygen saturation, as a minimal requirement. Transcutaneous CO_2 and NIRS are also important tools to use, although this is not a generalized practice.

35.8.2 General Measures

During the acute phase, patients should be mobilized and manipulated as minimum to decrease the risks for pulmonary hypertensive spells.

With the same goal, potential triggers for pulmonary hypertension ought to be prevented. These include volume overload, pain or agitation, fever, metabolic or respiratory acidosis, hypoxia, and anemia to mention some.

Patients should be kept in an anabolic status for which early nutrition is crucial.

Caregivers must pay attention to risks related to the presence of a 22q11⁻ deletion, particularly with regards to metabolic disturbances, airway complications, and sepsis.

35.8.3 Fluid Management

After total repair of TA on CPBP, patients must be restricted to 50% of their requirements on day one, followed by 75% on day two and 100% from day three. Obviously, these recommendations must be individualized and adapted to the patient's hemodynamic, respiratory, and metabolic status.

35.8.4 Sedation and Pain Control

After total repair, TA patients are under risk of developing pulmonary hypertensive crisis and should be maintained well sedated and under analgesia for at least 12–24 h or until there is confirmation of a consistent hemodynamic stability, with a combination of opioids and benzodiazepines to be titrated to the minimal efficient dose. Titration and length of treatment with these drugs also depends on the type of intervention and characteristics of the patients. Infants with 22q11⁻ deletion are often more difficult to wean from the ventilator due to associated anatomic or functional airway anomalies. Delayed chest closure is also a factor that might determine the length and strength of sedation and analgesia.

Muscle relaxants may be required in patients who remain unstable and who have refractory pulmonary hypertensive crisis, however should not be used systematically.

Dexmedetomidine, propofol, ketamine, or clonidine drips may be used in specific cases.

35.8.5 Respiratory Management

These patients are very sensible to cardiopulmonary interactions. Provided an adequate and consistent hemodynamic stability is documented and in the absence of bleeding, neurologic, respiratory, or metabolic concerns,

patients should progress towards spontaneous breathing and extubation as soon as possible, although consideration has to be taken for the risks of pulmonary hypertension. The latter factor is more prevalent in patients' repaired later in life or who have had a complex repair. Sometimes, extubation is deferred by a systematic delayed sternal closure. All respiratory collateral complications (pleural effusion, atelectasis, or pneumothorax) should be aggressively managed.

Minimal manipulation of the airways is also essential to prevent pulmonary hypertension.

It is important to ensure an adequate oxygenation and to maintain pH levels between 7.40 and 7.45, with pCO₂ around 30–35 mmHg.

During pulmonary hypertensive crisis, patients may be managed with hyperoxygenation and hyperventilation and often require a supplemental dose of sedation, analgesia, and muscle relaxants.

The use of inhaled nitric oxide has been an outstanding tool to manage these patients. Some institutions promote the use of preventive nitric oxide, although there is no evidence-based data supporting this practice. Patients who require nitric oxide or remain dependent of it may be candidates for the use of sildenafil.

Patients who remain unstable and refractory to the medical management of severe pulmonary hypertension may require mechanical assistance (ECMO).

35.8.6 Cardiovascular Management

Hemodynamic management also depends on the type of repair.

The recommended association consists on drugs with inotropic effect (milrinone, dopamine, dobutamine) and systemic vasodilators (milrinone, phentolamine, phenoxybenzamine, sodium nitroprusside, nitroglycerine). In fact, lusotropic drugs like milrinone are the most common choice, sometimes associated with low dose epinephrine as required.

If the right ventricle is hypertrophic and poorly compliant, higher filling pressures may be required and beta-blockers may be useful to decrease the cardiac rate thus optimizing the ventricular filling (diastolic) time. Esmolol is, in this scenario, a good compromising since easy to titrate and its short half-life offers an advantage in patients who poorly tolerate it.

Loop diuretics are usually initiated throughout the first day.

After total repair of a TA, a number of scenarios may occur, requiring more specific or aggressive hemodynamic management:

a) *Right ventricular dysfunction*

Right ventricular dysfunction, both systolic and diastolic may be secondary to multiple causes: elevated pulmonary pressures, residual left-to-right shunts, coronary compression by the conduit, and also the impact of the ventriculotomy. The consequence of this is an inadequate forward flow and the development of right-sided failure with venous congestion, hepatomegaly, and ascitis. This will also result in the increase of afterload for vital organs like the kidneys and the gut. Echocardiography is essential to rule-out residual shunts, assess the ventricular function and also to define the anatomy of the reconstructed outflow tract and pulmonary arteries. Significant obstruction and/or regurgitation may be documented and require a reintervention. Nevertheless, in most cases of right dysfunction, progressive improvement is observed overtime. In case of doubt or whenever echocardiography is not able to completely elucidate the hemodynamic conditions, a cardiac catheterization is indicated and may also allow percutaneous intervention.

These patients require higher right filling pressures and the use of lusitropic drugs. Ventilatory measures and eventually inhaled nitric oxide may be used to try to optimize the reduction of the right ventricular afterload that would promote an increase in the stroke volume and the reduction of the conduit regurgitation.

b) *Left ventricular dysfunction*

This situation, reflected in a LCOS, is the most common complication after pulmonary hypertension. It may be secondary to: pulmonary hypertension, right ventricular failure, the presence of residual defects or the intrinsic changes induced by the CPBP, the stress-response, and the inflammatory syndrome. Patients may persist with relatively adequate blood pressure but their stroke volume and tissue oxygen delivery will be suboptimal. The consequence will be the progressive development of low peripheral perfusion, reduced urine output, metabolic or lactic acidosis, decreasing of the sVO_2 and of the NIRS values.

Management is based upon the use of milrinone, low dose of dopamine and epinephrine, and compensation of

all identified metabolic disturbances. Particular attention must be paid to the calcium, magnesium, potassium, and sodium levels in these patients.

Refractory cases need ECMO and this strategy should be utilized sooner than later when the trend does not show an adequate response to the medical treatment.

c) *Residual lesions*

Patients who do not progress well, need to be evaluated for residual lesions. Clinical examination remains important to develop a pathophysiological assessment. Echocardiography is the main tool used for this purpose but complementary investigations may be required. In patients with a pulmonary catheter, a Q_p/Q_s estimation may also reveal important data.

The main lesions to rule-out are:

- Residual ventricular septal defects
- Residual aortic arch obstruction
- Residual stenosis or significant regurgitation of the truncal valve
- Right ventricular outflow tract obstructions
- Pulmonary obstructions or conduit regurgitation
- Coronary compression
- Poor ventricular function

Prognosis in these patients depends on anticipation. Early identification of these problems and their rectification by medical or surgical measures is essential.

d) *Arrhythmias and conductive disorders*

Arrhythmias are not uncommon after total repair of a TA. The most common disturbances are supraventricular tachycardias and junctional ectopic tachycardia. Ventricular arrhythmia should induce urgent assessment of the coronary arteries and myocardial perfusion.

Conductive disorders may also be identified. The incidence of complete heart block for this anomaly is around 3–5% (please consult chapter 53 related to Arrhythmias).

Right bundle branch block is almost constantly documented after TA repair.

35.8.7 Management of Electrolytic and Acid–Base Status

Acidosis is a potential trigger for pulmonary hypertensive crisis and should be avoided. Meticulous correction of

metabolic acidosis with sodium bicarbonate or with THAM is recommended. Ventilatory parameters must also be adapted to the blood gases in order to preserve an adequate acid–base status. Electrolytic disturbances should also be systematically rectified. Calcium chloride may be required on a regular basis as a bolus or as a continuous infusion in patients with 22q11 deletion.

35.8.8 Management of Renal Function

Urine output may remain marginal during the first 48–72 h. The early use of loop diuretics in boluses or as a continuous infusion is recommended, provided that an adequate renal preload and circulatory volume is ensured. It is common to insert a peritoneal catheter in the perioperative phase that helps palliating a deficient urine output. Some teams recommend the systematic replacement of fluid losses through the peritoneal catheter with albumin during the first 24 h. Peritoneal catheters should be removed as soon as possible, when patients are deemed to have normal urine productivity.

35.8.9 Neurologic Management

A preoperative brain ultrasound is recommended as a baseline evaluation and should be controlled after the intervention. Management of neurologic complications is discussed in a specific chapter in this book (chapter 61).

35.8.10 Management of Infectious Issues

Protocols concerning antibiotic prophylaxis vary within countries and even institutions. Cefazolin remains probably the most widely used antibiotic for this purpose and Vancomycin replaces the former in MRSA positive patients.

Patients with 22q11 deletion, those with an open chest and on ECMO require close monitoring of the infectious markers. Early broad-spectrum antibiotic cover should be indicated in case of suspected sepsis.

35.8.11 Management of Gastrointestinal Issues

Early enteral feeding, at least for trophic stimulation is not contraindicated, unless patients course with LCOS that predisposes to splanchnic hypoperfusion and increases the theoretical risk for necrotizing enterocolitis. NIRS may be a useful tool to assess risks and tolerance to feeding in these neonates and infants. Patients who cannot be enterally fed, should be started on early total parenteral nutrition. H₂-antagonists or proton-pump inhibitors are recommended during the acute phase. Hepatic and pancreatic function should be carefully monitored, particularly once feeding is resumed.

35.9 Results

Reported perioperative mortality for children operated on for TA in neonate period varies from 10 to 15% [21–23]. This rate is higher for older children with augmented pulmonary vascular resistances, interruption of the aortic arch, or truncal valve insufficiency.

All patients with a valved conduit will need reoperation for stenosis and/or pulmonary regurgitation. Age for these reoperations is variable according to the size of the first conduit or homograft and its alteration.

The evolution of a truncal valve dysfunction may also lead to reoperation for truncal valve replacement.

Long-term survival is about 80–85% at 20 years [24], with, for most patients a normal quality of life.

Without treatment, the natural history courses towards death, with a survival described around 20% at 1 year of age. Nevertheless, some patients have been reported to survive until their third, fourth, or fifth decade [25, 26].

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Chapter 36

Double Outlet Right Ventricle

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36.1 Introduction

Double Outlet Right Ventricle (DORV) is a mode of ventriculo-arterial connection that can express several “phenotypes.” This conotruncal anomaly that represents 0.5–1.5% of congenital cardiac defects, presents with a wide spectrum of anatomical forms depending on the location of the ventricular septal defect, the relationship between the great vessels and the ventricular cavities and the presence of a pulmonary flow obstruction. This wide variation has led to many controversies over the anatomical definition and the optimal surgical management. DORV is frequently associated with hypoplasia of one ventricle. The most complex forms remain a surgical challenge for biventricular repair, many centers still preferring the Fontan option.

DORV is often associated with a 22q11 deletion. This is important to diagnose as this chromosomal abnormality may influence the postoperative course and be a source of significant complications.

36.2 Anatomical Definition

If first described by Lev [1], the anatomical definition has evolved with time. The basic definition states that a DORV has more than 50% of the two great vessels outlet arising from the right ventricle. Nevertheless, definitions have been multiple and somewhat debatable, as expressed in the following examples:

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- Robert H. Anderson [2] created the above described “50% rule,” which is the most frequently used.
- Richard Van Praagh [3] defined DORV as essentially a mitro-aortic discontinuity in relation with the persistence of the subaortic conus.
- Yves Lecompte [4] defines DORV as a malposition of the great vessels.
- Daniel Sidi’s definition focuses on the presence of double conus.
- François Lacour-Gayet [5, 6] introduced the “200% rule,” recognizing the “real surgical” DORV as those with the entirety of the two great vessels arising from the right ventricle.

Depending on the location of the VSD, four anatomical types are usually considered [2]:

- DORV with subaortic VSD
- DORV with doubly committed VSD
- DORV with subpulmonary VSD (Taussig–Bing anomaly)
- DORV with uncommitted or remote VSD

Associated abnormalities are the rule. This anomaly may be correlated to complex subvalvular obstructions (i.e., by a conal septum), with pulmonary or aortic valvular stenosis or with aortic coarctation or interrupted aortic arch.

Anomalies of the origin and the course of the coronary arteries are also common.

In the most complex cases, some of these associated anomalies may contraindicate a total biventricular repair.

Follows a list of different possibilities:

- Pulmonary valvar or subvalvar obstruction is the most frequent association and can be seen in the four types, although exceptional in the Taussig–Bing anomaly.

- Subaortic obstruction is frequent, due to the presence of a subaortic muscular infundibulum.
- The restriction of the VSD is frequent and represents a major problem because the left ventricular outflow may be obstructed.
- Multiple VSDs and “Swiss-cheese” interventricular septum are common.
- Aortic arch obstruction is quite specific of the Taussig Bing anomaly.
- Associated atrioventricular valve malformations include tricuspid and mitral valve straddling.
- The most complex form is due to the association of a complete atrioventricular canal with usually a right isomerism and the frequent presence of total anomalous pulmonary venous return.
- The hypoplasia of one ventricle as well as mitral valve atresia are frequent.
- The presence of a large left superior vena cava without bridging vein is frequent and has been considered as potentially responsible for the hypoplasia of the left ventricle.
- Pulmonary valve atresia is possible in DORV; the definition is then questionable as there is only a single outlet, even though there are two infundibular areas in the right ventricle.
- Truncus arteriosus with the truncal valve arising from the right ventricle may be called a “double outlet” right ventricle by extension of the definition.

36.3 Pathophysiology and Functional Classification

The pathophysiology of DORV depends on the anatomical associations. The position of the VSD with regards to the great vessels and the eventual association with pulmonary stenosis plays an essential role in this pathophysiology.

Therefore, the spectrum of clinical presentation may vary from a situation of *increased pulmonary flow* (VSD physiology) when there is no subvalvular or valvular pulmonic stenosis, to a situation of *cyanosis* (physiology of TGA or physiology of tetralogy of Fallot if there is a severe stenosis of the right outflow tract of the pulmonary valve).

In three-fourth of the cases, the *VSD is subaortic* and therefore the aorta receives preferential oxygenated blood from the left ventricle. As a consequence, the

degree of cyanosis may be mild and pulmonary arterial pressure is elevated, except in the presence of pulmonary obstruction.

If a *pulmonary stenosis* is associated, the degree of cyanosis is proportional to the severity of the obstruction and pulmonary pressures are obviously low. The degree of cyanosis also depends on the quality of intracardiac mixing.

When there is a transposed aorta with a *subpulmonary VSD and no pulmonary stenosis*, the anomaly is also called a Taussig-Bing complex (10% of cases) and its pathophysiology corresponds to that of a TGA with VSD. These patients therefore have cyanosis and also cardiac failure: the oxygenated blood arriving from the left ventricle is steered towards the pulmonary artery and desaturated blood from the right atrium is ejected onto the aorta.

In case of *doubly committed VSD*, clinical presentation may mimic a Tetralogy of Fallot or a VSD, depending on the presence or the absence of pulmonary obstruction.

The same pathophysiological scenario occurs when there is a *non-committed VSD*, which means the interventricular communication is far from the great vessels, by a distance greater than the aortic valve diameter.

The spatial relation of the VSD with the arterial outlets and the eventual association with a pulmonary stenosis allow the definition of various *functional types*, with common clinical presentation and more importantly, similar surgical repair.

This *functional classification* (Fig. 36.1) that follows has been adopted together by the nomenclatures of the Association for the European Paediatric Cardiology (AEPC), the European Association of Cardiothoracic Surgery (EACTS) and the Society of Thoracic Surgery (STS) [7–9]:

1. *VSD-type DORV*:

This variant represents 24% of cases and includes the DORV with subaortic or doubly committed VSD and no pulmonary stenosis. The pathophysiology of this association is that of a VSD with a large left-to-right shunt and pulmonary hypertension. In more than one-third of the cases [5, 6, 10] the VSD is restrictive. The great vessels are not always “200%” displaced towards the RV.

2A. *Fallot-type DORV*:

This anatomic form that represents 64% of cases includes DORV with subaortic or doubly committed

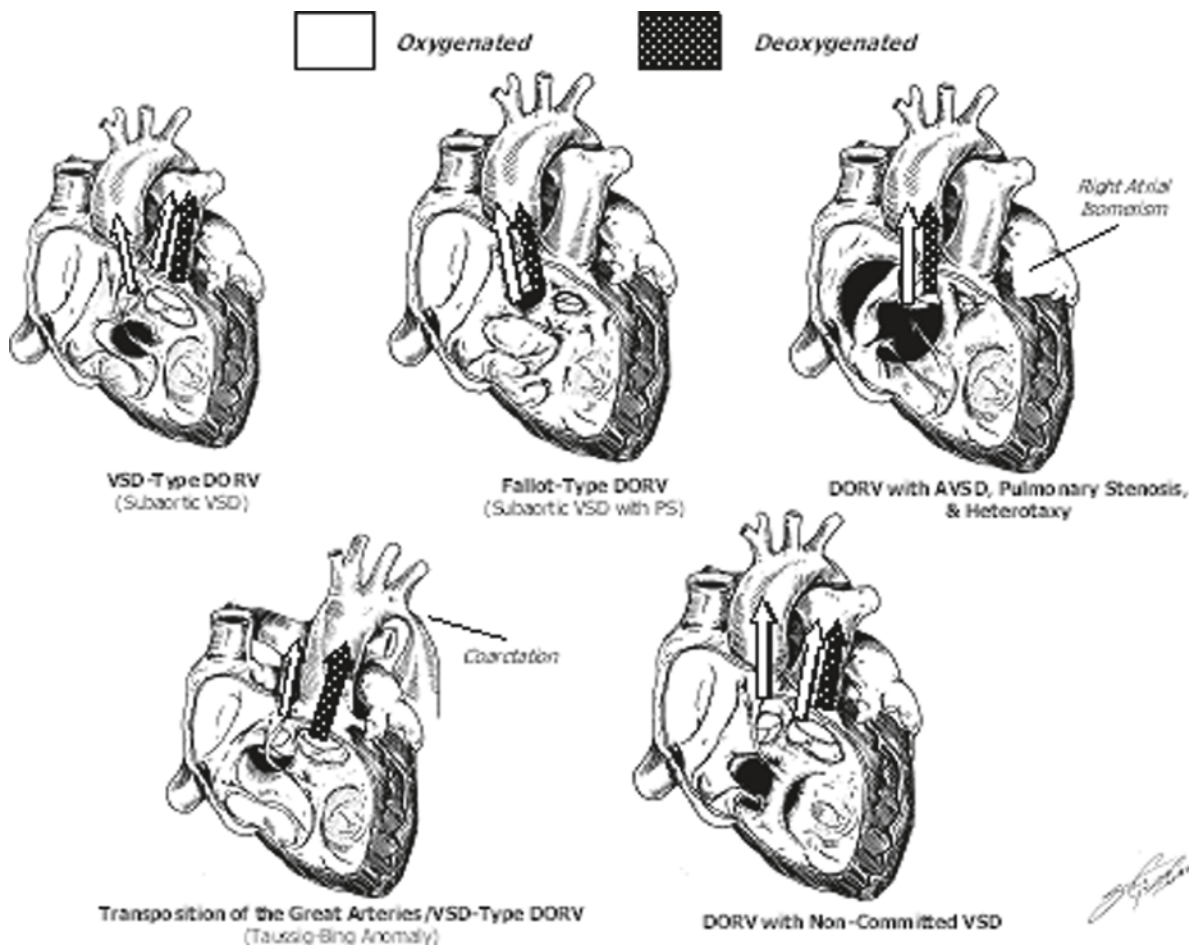


Fig. 36.1 Functional classification of the double outlet right ventricle (DORV)

VSD with pulmonary stenosis. The pathophysiology is the equivalent of a Tetralogy of Fallot. It is often quite difficult to differentiate these forms from a real Tetralogy of Fallot as the overriding of the aorta may be partial. In more than one-third of these cases [5, 6, 10] the VSD is restrictive. The great vessels seldom arise “200%” from the RV.

2B. DORV with Atrioventricular septal defect, pulmonary stenosis and heterotaxy:

The pathophysiology of this association is the same as in an AVSD with Tetralogy of Fallot. Clinical progression may be complicated by anomalies present in heterotaxy, usually a right isomerism. Pulmonary stenosis is the rule and pulmonary atresia is also possible. The AVSD anatomy is usually a

Rastelli type C. In most cases, the VSD is an AVSD-Fallot type, with a large superior component, close to the aortic valve [5, 6, 10]. Total anomalous pulmonary venous return is a frequent association. Most cases are not associated with Down’s syndrome. An intestinal malrotation is also common and should be ruled out. In this form, the great vessels arise “200%” from the RV.

3. TGA/AVSD- type DORV (Taussig Bing anomaly):

The pathophysiology of this anomaly corresponds to that of a TGA with VSD. There is no pulmonic stenosis and the VSD is exceptionally restrictive. Aortic arch obstruction and subaortic obstruction are frequent. The right ventricle is usually slightly small but not hypoplastic, unless there is an associated

organic tricuspid valve stenosis. The great vessels almost never originate “200%” from the RV.

4. DORV with a non-committed VSD:

In this anatomic form, the VSD is distant from the arterial valves by a distance greater than a diameter of the aortic annulus [11]. The VSD is located below the trabecula septo marginalis [12], in contact with the tricuspid annulus [10]. The great vessels arise “200%” from the right ventricle. In the absence of pulmonary stenosis, the pathophysiology is that of a single ventricle with unprotected pulmonary blood flow. With pulmonary stenosis, the pathophysiology is that of a single ventricle with restricted pulmonary blood flow.

36.4 Clinical Presentation

The clinical presentation depends on the following aspects:

- The position of the VSD with regards to the great vessels
- The position of the great vessels
- The presence or the absence of pulmonary obstruction
- The presence or the absence of anomalies of the aortic arch

If the VSD is subpulmonary, patients usually present in their first 3–6 weeks of life with cyanosis and signs of cardiac failure secondary to an elevated Q_p/Q_s (pulmonary overcirculation): failure to thrive, breathlessness on feeding, tachycardia, tachypnea and diaphoresis. Clinical examination reveals a cyanotic patient with a hyperdynamic precordium, a thrill on palpation, a gallop rhythm and hepatosplenomegaly. A soft systolic murmur due to excessive flow may be heard at the pulmonary foci.

When the VSD is subaortic, patients are diagnosed in the same age range once pulmonary resistances decrease. These patients present with predominant signs of cardiac failure and excessive pulmonary flow with some degree of cyanosis. Clinical presentation depends to a great extent on the presence and severity of pulmonary obstruction which is often associated with this type of DORV: the degree of cyanosis will be proportional and the degree of cardiac failure will be inversely proportional to the severity of the obstruction.

The cardiac murmur also depends on this factor and tends to increase in intensity as the degree of obstruction increases. In patients with predominant cardiac failure and no pulmonary protection, a thrill will be present.

When the VSD is doubly committed there will be mild cyanosis and signs of cardiac failure.

36.5 Chest X-ray

The chest X-ray reveals cardiomegaly and plethoric lungs in case of subaortic VSD or subpulmonary VSD without pulmonary stenosis. In case of pulmonary obstruction, cardiomegaly is mild or absent and lung vascularity may be normal or decreased depending on the severity of the stenosis.

36.6 Echocardiography

Echocardiography is the cornerstone of diagnosis allowing a detailed definition of the anatomic associations (Figs. 36.2 and 36.3) and is also instrumental for the follow up of operated patients.

36.7 Cardiac Catheterization

Cardiac catheterization (Figs. 36.4 and 36.5) is not systematically performed in the neonatal period although it is sometimes indicated in complex forms or to elucidate coronary anatomy and the suspicion of multiple VSD. In older patients or in patients with significant residual lesions, this technique is very useful and often provides the possibility of percutaneous intervention as a complement to cardiac surgery.

36.8 Other

MRI, 3D echo and CT angio scan may be indicated in some cases and are evolving techniques that might become a referente for noninvasive diagnosis in the near future.

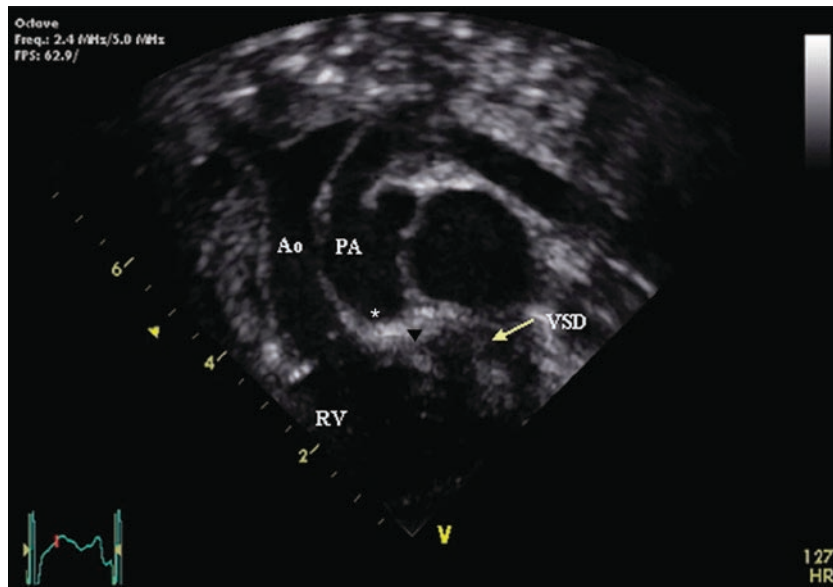


Fig. 36.2 DORV with a non-committed VSD, transposed aorta, pulmonary stenosis (*) and a large conal septum (▼)

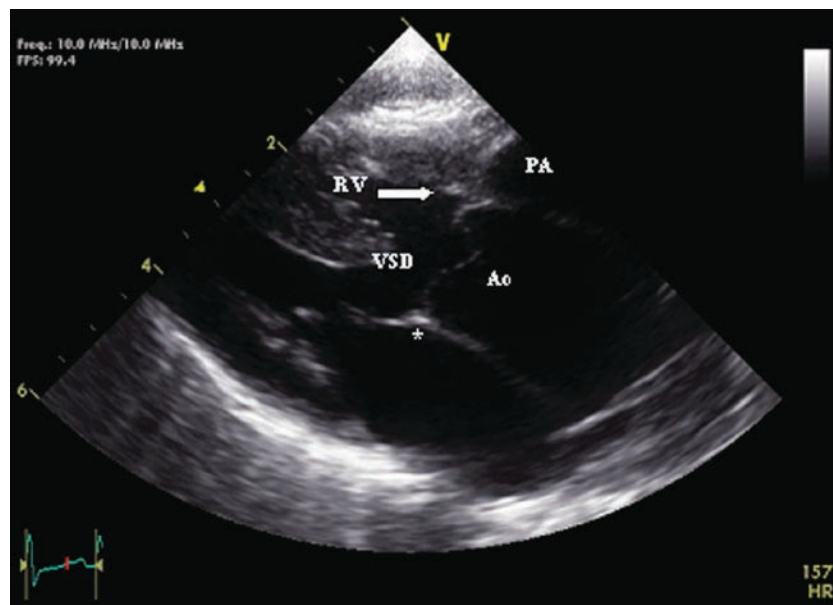


Fig. 36.3 Fallot-type DORV. The VSD is subaortic. Notice that the aorta is not fully arising from the RV and that there is a subpulmonary obstruction (full arrow). There is a mitro-aortic discontinuity (*)

36.9 Preoperative Management

Preoperative medical management depends on clinical presentation. In the neonatal phase, there are three main scenarios:

1. *In the absence of pulmonary protection* (no valvular or subvalvular pulmonary stenosis): neonates present as if they had a large unrestrictive VSD. In the neonatal phase, these patients are usually asymptomatic until the age of 3–6 weeks when they present in

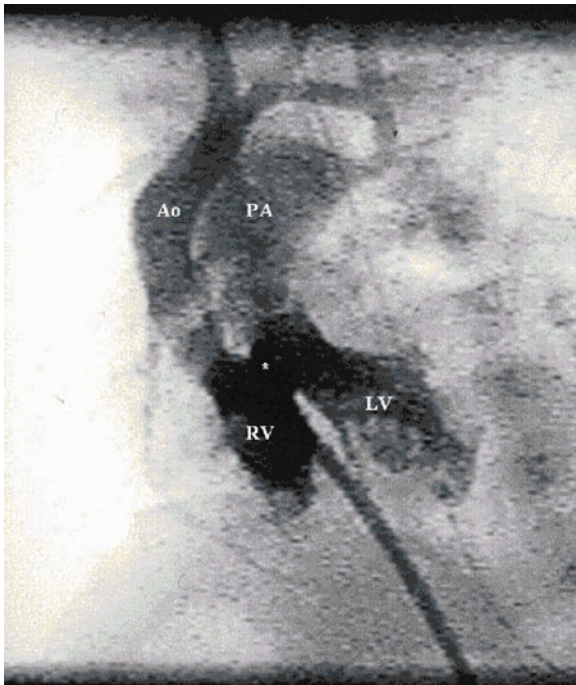


Fig. 36.4 DORV with TGA, VSD and obstructed aortic arch (Taussig-Bing anomaly). PA pulmonary artery; Ao aorta; RV right ventricle; LV left ventricle; * VSD

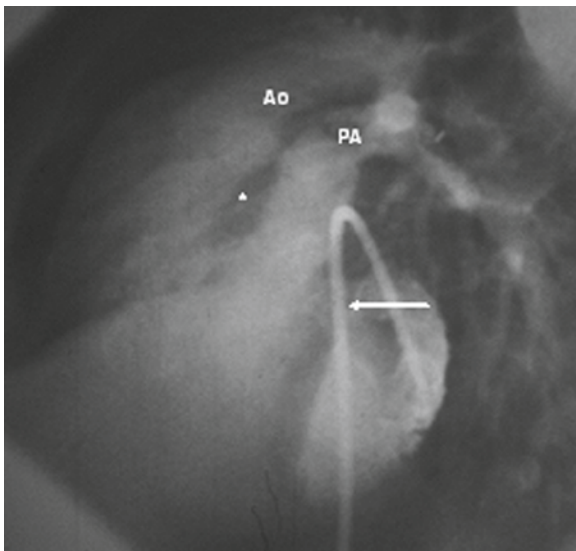


Fig. 36.5 cardiac catheterization documenting a DORV with a non-committed VSD (filled arrow). Both great vessels (PA pulmonary artery; Ao aorta) arise “200%” from the RV. Notice that the conal septum (*) is part of the RV and unrelated to the ventricular septation

cardiac failure. Medical treatment is based upon the association of loop diuretics with peripheral vasodilators and, in some institutions, with digoxin which is controversial. Anemia must be prevented or treated if identified since it may increase the severity of the left-to-right shunt by lack of viscosity. In case of persistent signs and symptoms of cardiac failure a surgical intervention is indicated. A total repair is usually indicated. Nevertheless, depending on the patient's characteristics and the presence of associated extracardiac anomalies, palliation is sometimes required in the form of a banding of the pulmonary artery.

2. *In the presence of valvular or subvalvular pulmonary stenosis:* clinical tolerance should be assessed once the ductus arteriosus closes. If the right obstruction is severe, patients become progressively cyanosed and may even reveal a ductal-dependency justifying the administration of endovenous E_1 prostaglandins (PGE_1). In this case, the indication of a modified Blalock–Taussig shunt or a percutaneous dilatation of the right obstruction will be mandatory; stenting of the ductus arteriosus has arisen as another interesting alternative. On the other side of the spectrum, patients with mild pulmonary stenosis may need medical management similar to those with a VSD physiology, although these patients tend to progressively become more obstructive until reaching a balance. They may also develop severe stenosis throughout the first few months of life, requiring palliation.
3. *In the presence of associated complex anomalies:* treatment depends on the malformative complex: the most common situation is that of patients who require PGE_1 for a severe pulmonary or systemic obstruction. Anomalous pulmonary venous return is a significant complicating factor that may need to be rectified in the neonatal period.

36.10 Medical Interventions

Interventional catheterization: cardiac catheterization may be useful to perform palliative percutaneous pulmonary valvulotomy in case of obstruction, as an

alternative to surgical shunts. This seems quite challenging because of the right ventricular outflow tract could well have a severe muscular obstruction by malalignment of the conal septum. As described above, stenting the ductus arteriosus is also an option. In patients in whom the intracardiac mixing is inadequate in spite of the VSD, cardiac catheterization allows to perform a Rashkind atrioseptostomy in the neonatal period or throughout the first few weeks of life.

36.11 Surgical Management

36.11.1 Biventricular Repair

Provided that there are two viable ventricles, biventricular surgical repair is nowadays the best option even though more technically demanding than a cavopulmonary palliation.

1. VSD-type DORV:

Patients present with clinical signs of overcirculation due to the association of an unrestrictive VSD and unprotected pulmonary blood flow. For this reason, these children usually require a one-stage biventricular repair within the first 3 months of life. A pulmonary artery banding may be considered in selected cases, in the absence of flow restriction across the VSD. During the total repair, the VSD is baffled towards the aorta through the tricuspid valve, although a right ventriculotomy may be necessary. It appears in literature that VSD enlargements are required in more than one-third of the cases [13, 14]. The frequent requirement for VSD enlargement and a right ventricular approach distinguishes this lesion from other anomalies requiring VSD repair.

2A. Fallot-type DORV:

These patients present like a Tetralogy of Fallot and therefore surgical repair is very similar. Nevertheless, a modified Blalock–Taussig shunt may be considered in the neonatal period. The total repair involves closing the subaortic VSD with a larger patch and the right ventricular outflow tract obstruction is repaired accordingly. The VSD can be restrictive and may need to be enlarged in nearly one-third of the cases [5, 6, 10].

2B. DORV with atrioventricular septal defect, pulmonary stenosis and heterotaxy:

These patients are repaired like patients with a Tetralogy of Fallot associated with an AVSD. The right ventricular outflow tract is most often stenotic and sometimes atretic. For this reason, the repair is undertaken beyond the age of 6 months, requiring a previous modified Blalock–Taussig shunt if the cyanosis is severe. The AVSD is a Rastelli type C. The VSD has a superior component close to the aortic annulus [10]. The real challenge of this form is the association with a total anomalous pulmonary venous return that needs to be repaired in the neonatal period. As for the association AVSD-Fallot, efforts should be undertaken to maintain pulmonary valve continence. Hence, the use of a valved conduit may be necessary. The patch required to baffle the VSD to the aorta may sometimes reduce the right ventricular size and a one-and-a-half ventricle repair may be needed. This form of DORV clearly requires a technically demanding and challenging repair.

3. TGA/VSD- type DORV (Taussig Bing anomaly):

Neonatal total one stage repair consisting in an arterial switch, VSD to PA baffle and aortic arch reconstruction when needed, is the best option [15–17]. The Kawashima operation has been abandoned by most of the teams. A right ventriculotomy is often needed. A previous palliation with PA banding with coarctation repair is rarely undertaken nowadays and is reserved to neonates with extracardiac disorders contraindicating surgery on cardiopulmonary bypass. It remains also an option in less experienced centers, but it requires the absence of subaortic obstruction. The frequent associated subaortic obstruction needs to be corrected by division of the parietal band of the right ventricle and often by right ventricular outflow tract patch enlargement. The technical challenge of this neonatal arterial switch is due to the side-by-side relationship of the great vessels, the complex coronary anatomy, the associated subaortic obstruction and a weight lower than 2.5 kg. Due to the frequent hypoplasia of the neopulmonary annulus, these patients are at risk for late right ventricular outflow tract obstruction [15].

4. DORV with non-committed VSD:

These patients present with a remote VSD and the two great vessels arising “200%” from the RV [18, 19].

This form illustrates, from a surgical standpoint, the real DORV. Importantly, the VSD lies at a distance from both the aortic and pulmonary annulus greater than the aortic diameter [15]. Pulmonary blood flow obstruction and a restrictive VSD may also be present.

There are different surgical options for these patients depending on the presence of a pulmonary obstruction and the possibility of constructing a tunnel between the VSD and the aorta:

1. in the absence of pulmonary obstruction:

The tunnelization from the left ventricle towards the aorta using a large patch or multiple patches [20] requires the resection of the parietal band. It may additionally require the reimplantation of the conal tricuspid papillary muscle on the baffle patch and a resection of the subaortic conus. When the VSD is very remote from the aorta, it is usually close to the pulmonary annulus. This allows a surgical repair like in the case of a Taussig Bing anomaly, with a tunnelization of the VSD to the PA and an arterial switch (Fig. 36.6) [15].

2. in the presence of pulmonary obstruction:

This rare anatomical form raises the most difficult surgical issues.

When the right ventricular outflow tract obstruction is purely muscular, an arterial switch with VSD to PA baffle and infundibular patch is a good option.

When the right ventricular outflow tract obstruction is valvular, a Rastelli [21] type operation or a R.E.V. [22, 23] operation (Réparation à l'Etage Ventriculaire or Lecompte intervention) is indicated when the VSD to aorta tunnel can be safely performed. This requires closure of the pulmonary outflow and a RV to PA conduit (Rastelli) or a Lecompte maneuver (R.E.V.).

The Nikaidoh [24] operation has exceptionally been reported successfully in DORV with non-committed VSD, as it implies doing a left ventriculotomy and a very long aortic translocation with a high risk for the coronary transfer.

36.11.2 Univentricular Repair

The major controversy between biventricular and univentricular repair in some forms of DORV lies in the reluctance of several teams to enlarge a restrictive VSD or to resect the conal septum. Nevertheless, several

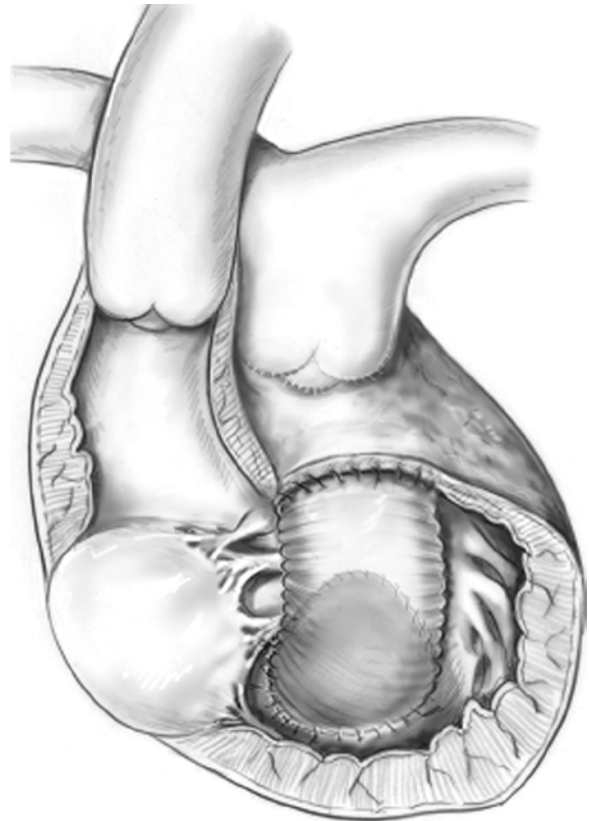


Fig. 36.6 DORV with a non-committed VSD and a very remote aorta. The patch is tunneling the LV towards the pulmonary artery across the VSD. This technique will be complemented with an arterial switch

reports currently in press [6] tend to prove that the enlargement of the VSD does not increase the risk of complete heart block nor does it impact on the long term myocardial function.

Univentricular repair is *mandatory* in specific circumstances:

- a) Significant hypoplasia of one of the ventricles
- b) Severe atrioventricular valve straddling or overriding
- c) Multiple (“swiss-cheese”) ventricular septal defects
- d) Surgical learning curve

Also, the tunnelization to the aorta may sometimes reduce too much the right ventricular size, leading to a one-and-a-half ventricular repair by associating a partial cavo-pulmonary connection. Some authors consider that in such cases, the total cavo-pulmonary connection is a better indication than the one-and-a-half ventricular repair.

Cardiac transplant may be contemplated as an alternative in some circumstances.

36.12 Postoperative Management

Postoperative management varies depending on the anatomic and physiologic form and also on the type of intervention. Thus, principles discussed in specific chapters dedicated to the management of VSD, Fallot's tetralogy and TGA with VSD are applicable to a great extent (see chapters 16, 19 and 33 in this book).

The most specific problems concern rhythm and conductive disturbances (persistent atrial tachycardia, ventricular ectopy, third degree atrioventricular heart block), myocardial ischemic changes and persistent subvalvular obstructions (secondary to a prolapse of the VSD patch onto the left ventricular outflow tract or to a VSD with restrictive dimensions).

36.12.1 Monitoring

Invasive monitoring includes an arterial line (to be inserted on the right radial artery in case of associated coarctectomy), a central venous catheter and a left atrial line. A transthoracic pulmonary catheter may be inserted if the patient is considered at risk of developing acute pulmonary hypertensive spells.

Non-invasive monitoring is based on heart rate with ECG, respiratory rate and peripheral oxygen saturation, as a minimal requirement. Transcutaneous CO₂ and NIRS are also important tools to use.

36.12.2 Sedation

Postoperative sedation after palliative interventions may be superficial although an adequate pain control ought to be ensured. Patients should be kept comfortable and free of pain, while care is taken to protect their airways and breathing spontaneously, allowing early extubation. This can be achieved by associating non-opioid analgesia with low dose morphine or fentanyl and benzodiazepines (in boluses or as a continuous infusion). Dexmedetomidine is now published as a

drug with an interesting potential for the pediatric cardiovascular population.

After total repair of a DORV, patients are maintained sedated and under analgesia for at least 12–24 hours or until there is confirmation of a consistent hemodynamic stability, with a combination of opioids and benzodiazepines to be titrated to the minimal efficient dose. Titration and length of treatment with these drugs also depends on the type of intervention and patients' characteristics: usually, a VSD closure or a Rastelli type intervention progress more rapidly than an arterial switch with VSD closure and coarctectomy or a R.E.V. repair. Delayed chest closure is also a factor that might determine the length and strength of sedation and analgesia.

Muscle relaxants may be required, however should not be used systematically.

Dexmedetomidine, propofol, ketamine or clonidine drips may be used in specific cases.

36.12.3 Fluid Management

Fluid management is based upon the type of intervention. Palliative surgery does not require fluid restriction unless the patient is deemed to be volume overloaded. Nevertheless, after total repair on CPBP, patients must be restricted to 50% of their requirements on day one, followed by 75% on day two and 100% from day three. Obviously, these recommendations must be individualized and adapted to the patient's hemodynamic, respiratory and metabolic status.

36.12.4 Respiratory Management

After a total repair of a DORV, patients are very sensible to cardiopulmonary interactions. Provided an adequate and consistent hemodynamic stability is documented and in the absence of bleeding, neurologic, respiratory or metabolic concerns, patients should progress towards spontaneous breathing and extubation as soon as possible. Sometimes, extubation is deferred by a systematic delayed sternal closure. All respiratory collateral complications (pleural effusion, atelectasis or pneumothorax) should be aggressively managed.

36.12.5 Hemodynamic Management

Hemodynamic management also depends on the background defect and on the type of repair. Further details are discussed in the chapters related to the management of VSD, TGA with VSD and Tetralogy of Fallot, diseases that share pathophysiological characteristics.

The recommended association consists on inotropic drugs (dopamine) and systemic vasodilators (phen-tolamine, phenoxybenzamine, sodium nitroprusside, nitroglycerine) or lusitropic drugs – like milrinone – with low dose epinephrine as required.

If the right ventricle is hypertrophic and poorly compliant, higher filling pressures may be required and beta-blockers may be useful in order to decrease the cardiac rate therefore optimizing the ventricular filling (diastolic) time. Esmolol is, in this scenario, a good compromising since it is easy to titrate and its short half life offers an advantage in patients who poorly tolerate it.

Loop diuretics are usually initiated throughout the first day.

36.12.6 Morbidity and Mortality

Morbidity and mortality of DORV repair depend on the anatomic associations, the surgical technique and the general conditions of the patients and interrelated noncardiac anomalies. Patients with 22q11⁻ deletions have a higher incidence of metabolic, respiratory and infectious complications.

Mortality reported on literature varies from around 5% in the “simple” forms with subaortic VSD, to 10–15% in Fallot type repair or arterial switch with interventricular repair and may increase significantly when the VSD is uncommitted, very distant from the left ventricle and requiring a complex and long tunnelization to establish continuity between the left ventricle and the aorta.

Anatomic forms requiring a univentricular repair share the same morbidity and mortality as other anomalies with univentricular physiology.

Overall long-term survival is estimated between 80 and 95%.

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Chapter 37

Ebstein's Disease

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Ebstein's disease is a congenital cardiac anomaly that occurs with an incidence of approximately 1–5 in every 20,000 live newborns, therefore representing 1% of congenital cardiac defects. It is the most common etiology for congenital tricuspid regurgitation in the neonatal period as well as later in life. The etiology of Ebstein's anomaly is unknown, however, a number of environmental factors have been implicated, namely maternal exposure to varnishing substances and maternal use of benzodiazepines and lithium ingestion during the first trimester of pregnancy.

37.1 Anatomy

In Ebstein's disease, there is a displacement of the septal and posterior tricuspid leaflets towards the apex of the right ventricle (Fig. 37.1). These leaflets are usually dysplastic and aberrantly adherent to the ventricular wall by multiple, short, anomalous chordae and the anterior component may be redundant. The result of this anomalous anatomy is the reduction of the right ventricular volume because the inlet portion between the plane of the annulus and the plane of the valvular closure is integrated onto the right atrium. This is the so-called atrialized portion that is often diskynetic. The tricuspid annulus and the right atrium are usually dilated and can become quite large. Depending on the severity of the disease, tricuspid regurgitation will develop and the right ventricle may

be deprived of its inlet portion. Functional right obstruction is therefore a common finding.

Ebstein's disease may have various degrees of severity that have been classified in 1988 by Alain Carpentier [1] as follows (Fig. 37.2):

1. *Type A*: this is a mild form of the disease in which valvular dysplasia is discrete, the leaflet displacement is mild and consequently, the right ventricular volume and functionality are barely affected. Tricuspid regurgitation is usually trivial if not absent.
2. *Type B*: in this form, leaflet dysplasia and caudal displacement are moderate and the atrialized portion of the right ventricle is larger. The anterior leaflet is redundant and mobile and tricuspid regurgitation is usually mild or moderate. The size of the right ventricle is still rather adequate, although in the lower acceptable range.
3. *Type C*: the atrialized portion of the right ventricle is large, the anterior tricuspid leaflet is redundant but has a limited motion, restricted by the short chordae. Since the volume of the right ventricle is reduced, the anterior leaflet may be a source of right ventricular outflow tract obstruction.
4. *Type D*: the right ventricle is almost completely atrialized, hence the cavitory volume is confined to the outlet portion. The anterior leaflet, although redundant, is immobile since the aberrant chordae are too short and rigid. The only path between the right atrium and the pulmonary artery, through the small ventricle, is ensured by the tricuspid antero-septal commissure.

Concomitant anatomic abnormalities are present in 39% of patients with Ebstein's anomaly.

Atrial septal defects are often found in Ebstein's disease; 42–60% of cases have an ASD that plays an important role in the pathophysiology.

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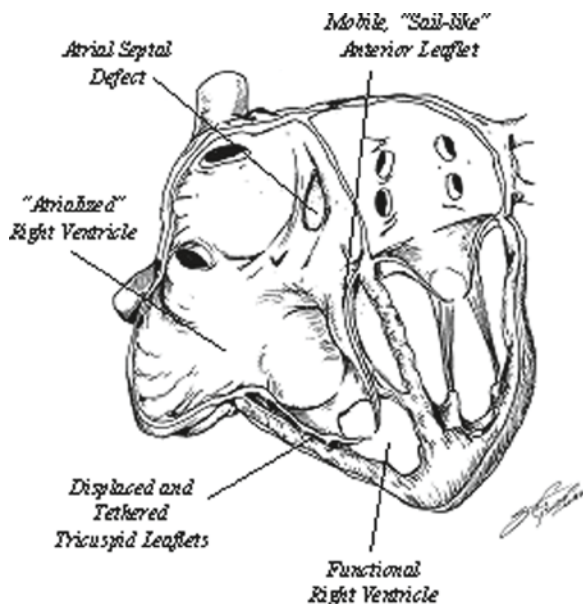


Fig. 37.1 Ebstein's anomaly

Severe pulmonary stenosis or atresia is also a common association. This obstruction may be functional in approximately half of the cases and anatomical in a fourth of cases. Both types of obstruction significantly increase mortality in these patients.

Anomalous conduction pathways may be associated with Ebstein's disease. Wolff-Parkinson-White syndrome has been described in 10–25% of patients. In 6% of cases there are multiple aberrant pathways, the majority localized around the tricuspid annulus.

Ventricular septal defects, transposition of the great arteries, tetralogy of Fallot and mitral valve abnormalities have also been described as infrequent associations with the disease.

37.2 Pathophysiology

This disease includes a large spectrum of varied grades of valvular dysplasia with caudal displacement of the valvular leaflets, the septal and the posterior leaflet being often adherent to the wall and restricted in their motion.

Hemodynamic consequences of the anomaly are associated with the following factors:

1. The degree of displacement of the tricuspid leaflets and the degree of atrialization of the right ventricle
2. The severity of the tricuspid regurgitation
3. The functional capacity of the reduced right ventricle

4. The degree of functional or anatomic right obstruction
5. The presence of an atrial septal defect and the degree of right-to-left shunt
6. The presence and the nature of arrhythmias
7. The degree of left ventricular compression by the right cavities in older patients

Although the atrialized portion of the right ventricle is anatomically integrated into the right atrium, it contracts with the right ventricle, causing a backward flow into the right atrium.

The functional capacity of the right ventricle is affected by the lack of volume and of diastolic preload, the functional or anatomic right ventricular outflow tract obstruction and to significant anomalies of its geometry. The right cavities may also distort the geometry of the left ventricle and have an impact in both the diastolic and the systolic function of the later.

The presence of an atrial septal defect plays an important pathophysiological role and defines the degree of cyanosis due to a mandatory right-to-left shunt. This shunt may be dependent on the degree of tricuspid regurgitation, right atrial pressure as well as right ventricular size and compliance.

37.3 Diagnosis

37.3.1 Background

Symptoms in patients with Ebstein's anomaly depend on the anatomical associations, on the functional characteristics and on the association with arrhythmia or conductive disorders.

Cyanosis is a common feature, secondary to the right-to-left shunt across an atrial septal defect and to the functional right ventricular obstruction. Cyanosis is enhanced by the presence of cardiac failure. In the neonatal period, this cyanosis may improve as the pulmonary vascular resistances decrease throughout the first few weeks of life. In the older patient, cyanosis tends to be progressive and to worsen, particularly when an arrhythmia arises.

In older patients, progressive right ventricular failure with decrease of cardiac output, leads to the development of *dyspnea*, *fatigue*, *ascites* and *peripheral edema*.

Cardiac arrhythmias and conductive disorders significantly add to the symptoms and may be a cause of sudden

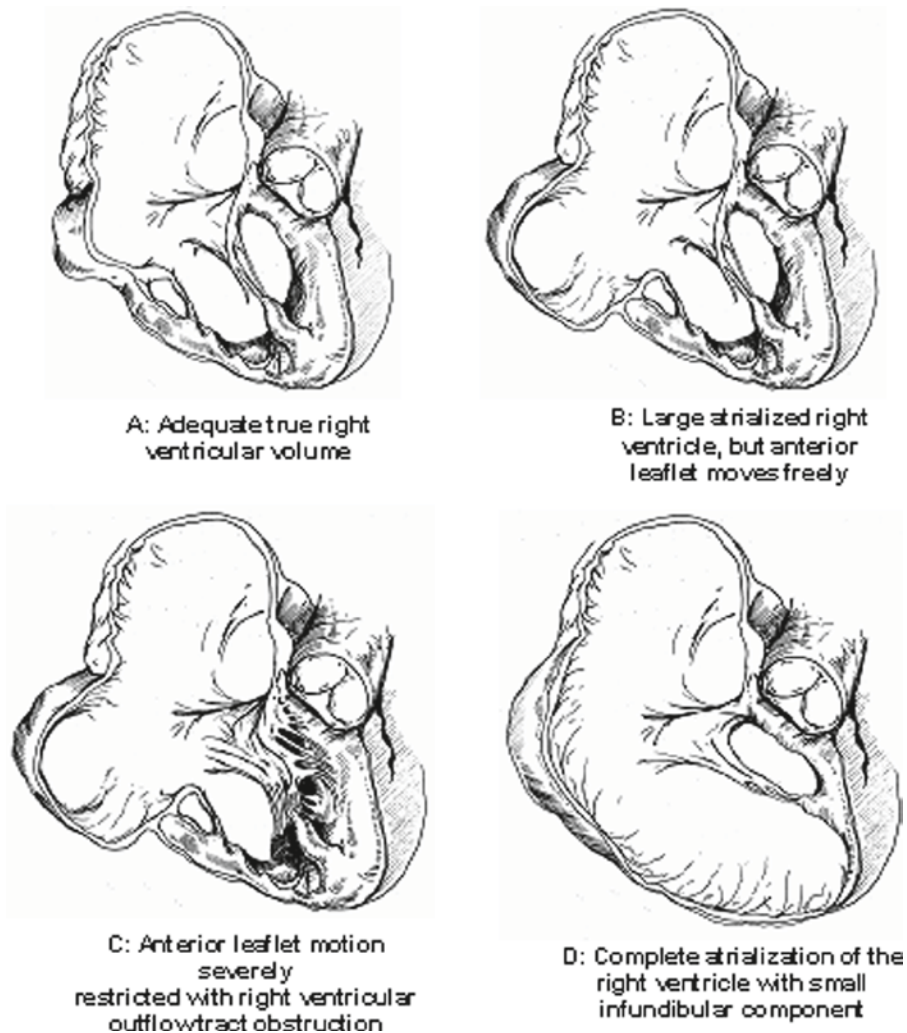


Fig. 37.2 Carpentier's classification of Ebstein's disease

death. As many as one third of patients may have paroxysmal supraventricular tachycardia spells. Ventricular arrhythmias, although less frequent, may also occur.

Patients with Ebstein's anomaly and atrial septal defects have an accrued risk of developing paradoxical embolism, brain abscess and bacterial endocarditis.

37.3.2 Clinical Presentation

There is a large spectrum of clinical signs, ranging from the severe neonatal form to asymptomatic cases that may present in the middle teenager years or in young adulthood.

This varied clinical presentation depends on the anatomic and functional individuality.

Ebstein's disease may be incidentally diagnosed in-utero and can be the cause for *fetal* cardiomegaly, hydrops and arrhythmia. Doppler analysis of blood flow in the hepatic vein and the ductus venosus may show a reverse-flow pattern, providing an early sign of dysfunction.

In the *neonate*, increased pulmonary vascular resistances (PVR) are the main cause of a functional right obstruction that, in association with the right-to-left shunting at the atrial level, account for the degree of cyanosis. Clinical signs depend on this factor and evolve with the PVR modifications during the first few weeks of life. 50% of neonates present with cyanosis

and a cardiac murmur during the first week of life. As PVR decreases, unless there is a significant anatomic right obstruction or severe tricuspid regurgitation with a significant shunt at the atrial level, cyanosis improves and may even disappear. Nevertheless, patients with severe forms of Ebstein's or with associated right outflow tract obstruction may persist cyanotic and develop early signs of cardiac failure. In the absence of an adequate medical or surgical management, 20–40% of these patients may die in the neonatal phase and less than 50% survive beyond the age of 5 years. Patients seldom fail to thrive.

In some neonates, in the presence of a patent ductus arteriosus – that might be vital if the pulmonary stenosis is significant – a “circular shunt” may develop. This shunt consists in a significant retrograde flow from the main pulmonary artery towards the right, ventricle and then, by the tricuspid regurgitation, towards the right atrium. This phenomenon will induce a lack of perfusion towards the peripheral pulmonary arteries and may also be a source of further right cardiac failure and of a massive right-to-left shunt, if there is an associated ASD.

Older patients may remain asymptomatic until adolescence or adulthood. They are usually diagnosed upon the presence of progressive cyanosis, fatigue on exertion and arrhythmia.

Potential risks in chronic patients include the following:

1. Paradoxical embolism
2. Transient ischemic spells
3. Stroke
4. Brain abscess, related to chronic cyanosis
5. Infective endocarditis
6. Sudden cardiac death
7. Cardiac arrhythmias

37.3.3 Description of the Main Clinical Signs

Cyanosis has varying degrees of severity, may worsen with arrhythmia and may induce the development of clubbing in untreated patients.

As cardiomegaly develops, precordial examination may show a significant *asymmetry and right parasternal prominence*.

Right cardiac failure is a common pathophysiological feature. These patients may display *congested jugular veins*, although right atrial pressure may be

low in which case this sign is not present. As the right dysfunction increases, caregivers may identify the presence of large *a* and *v* waves.

On auscultation, the *first heart sound is split* and loud on the tricuspid foci and mitral component may be soft or even absent. This is due to the delayed closure of the elongated tricuspid anterior leaflet. The second sound is usually normal but may also be split in the presence of right bundle branch block. In the presence of cardiac failure and distended right atrium, a *third and fourth sounds* may be present. Tricuspid regurgitation is a source of a *holosystolic murmur*, the *intensity and duration of* which vary with the severity of the regurgitation and may increase during inspiration.

Arrhythmias, mostly supraventricular tachycardia, atrial fibrillation or flutter, are common: 5–10% of neonates, 10–20% of infants and as high as 50% in grown-up patients.

37.3.4 ECG

Most patients with Ebstein's anomaly have an abnormal ECG. Common ECG patterns are:

1. A normal sinus rhythm
2. Abnormal p waves compatible with right atrial enlargement
3. Prolonged PR interval (first degree AV block) in 42% of patients. PR may be short in the presence of WPW syndrome
4. Low QRS voltage
5. Right Bundle Branch Block with RSR' in the right precordial leads
6. Presence of arrhythmias:
 - a. paroxysmal supraventricular tachycardia
 - b. atrial fibrillation
 - c. atrial flutter
 - d. ventricular tachycardia

37.3.5 Chest X-Ray

Chest radiographs can reveal a number of anomalies:

1. In the majority of cases, there is a very significant cardiomegaly. This cardiomegaly may be impressive (Fig. 37.3) and occupy most of the thoracic cavity, This is the so-called “wall-to-wall heart.”

2. The right atrium is distended
3. Lung vascular markings may be normal or decreased, depending on the presence and the degree of right outflow tract obstruction
4. The aortic root and the main pulmonary artery shadow may be small

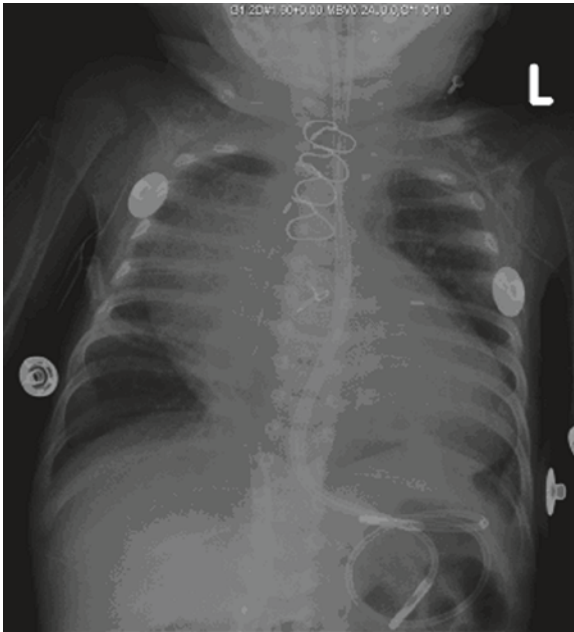


Fig. 37.3 Chest X-ray showing the characteristic massive cardiomegaly in a newborn with Ebstein's anomaly

37.3.6 Echocardiography with Color Doppler

Echocardiography is the first choice diagnostic tool [2–4], even in the antenatal period (Fig. 37.4). It allows a comprehensive evaluation of the tricuspid anatomy (Figs. 37.5 and 37.6), the ventricular characteristics, the degree of right outflow tract obstruction and of right-to-left atrial shunt, if present. Echocardiography also allows categorizing the type of anomaly and help defining the adequate surgical options.

The main echocardiography findings are as follows:

1. An apical displacement of the tricuspid septal leaflet greater than 8 mm/m² of body surface
2. Anomalous aspect of the leaflets, with dysplasia, thickening, redundant aspect, anomalous motion and aberrant attachments to the ventricular wall. This anatomy leads to an eccentric or absent coaptation.
3. A dilated right atrium and atrialized portion of the right ventricle. An atrialized to functional right ventricular ratio greater than 0.5 is associated with unfavorable prognosis.
4. A right ventricle with reduced volume and altered contractility. A functional right ventricular area of less than 35% of the total right ventricular area is associated with poor prognosis.
5. Some patients may have an aneurismal dilatation of the right ventricular outflow tract (right ventricular outflow tract : aortic root \geq 2:1)

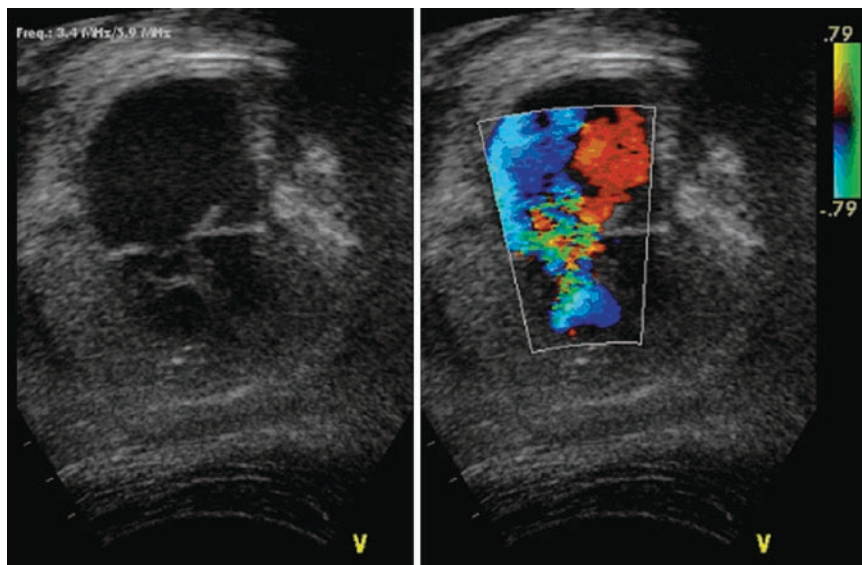


Fig. 37.4 Prenatal echocardiography showing a severe Ebstein's anomaly with significant tricuspid regurgitation

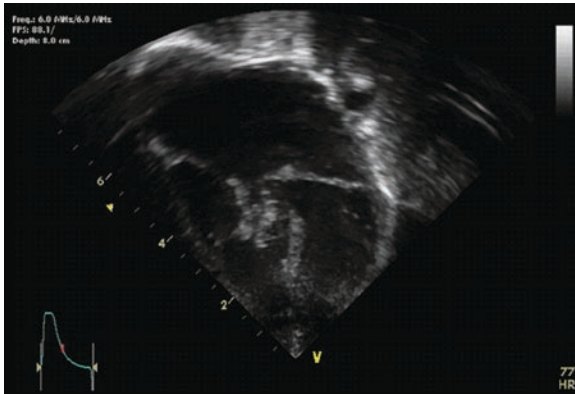


Fig. 37.5 Trans-thoracic echocardiography showing a type A Ebstein's anomaly

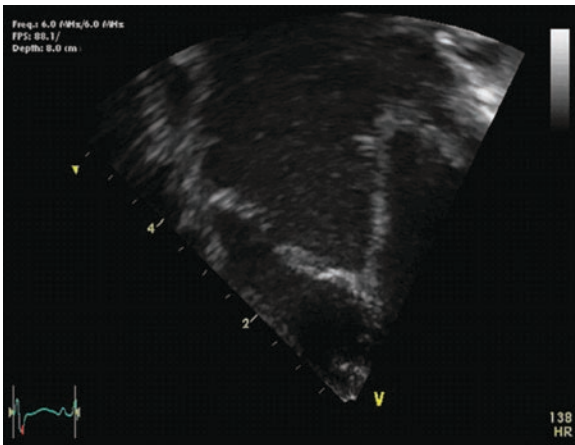


Fig. 37.6 Trans-thoracic echocardiography showing a type D Ebstein's anomaly

6. The left ventricle may be distorted, compressed by the right cavities and may have abnormal diastolic and systolic function
7. Doppler assessment shows varying degrees of tricuspid regurgitation and gives evidence of the right-to-left shunt at the atrial level
8. M-mode assessment reveals a paradoxical inter-ventricular septal motion and confirms the above described ventricular anomalies
9. Other associated anomalies

In neonates, a score may be applied in order to identify those with higher mortality risk. This evaluation is performed in the four-chamber view:

Right atrial area + area of the atrialized portion/ area of the functional right ventricle + left ventricular area

A value above 1.5 is associated with 100% of early mortality. A ratio between 1.1 and 1.4 is associated with an early mortality of 10% and a late mortality of 45%.

Other echocardiographic signs correlated with mortality below 3 months of age are:

1. Right ventricular dysplasia
2. The presence of a compressed left ventricle by the right cavities
3. Insertion of the anterior leaflet on the right ventricular free wall

37.3.7 Cardiac Catheterization

Cardiac catheterization is seldom performed in patients with Ebstein's anomaly, because echocardiographic techniques are elucidating.

Moreover, the incidence of arrhythmias during the procedure can reach 25% with a 14% mortality associated with such events.

Yet, cardiac catheterization may be useful when the anomaly is associated with other complex malformations or else to perform electrophysiologic studies that can identify anomalous accessory pathways and guide ablative therapy.

In cases of anatomic right outflow tract obstruction, pulmonary valvuloplasty may be performed in the cardiac catheterization laboratory. In the setting of significant tricuspid regurgitation and pulmonary regurgitation, attention must be paid to the potential development of a circular shunt complicating pulmonary valvuloplasty.

37.3.8 Other Diagnostic Techniques

Magnetic Resonance Imaging may be useful to assess the volume and the function of the right ventricle and is particularly interesting in grown-up patients in whom the echographic window is limited.

37.4 Preoperative Medical Management

Medical treatment of Ebstein's anomaly may be complex and difficult. Age and symptoms at presentation are variable and determine a broad therapeutic spectrum.

37.4.1 Neonatal Period

In the neonatal period, and while PVR are labile and decreasing over time, the two main problems faced by clinicians are cyanosis with hypoxemia and congestive cardiac failure. Clinical expression depends on the anatomic and functional aspects. Arrhythmias are seldom observed in this period of life. One important ingredient for success is patience. Indeed, neonates with Ebstein's disease should be allowed time to transition towards a steady physiological state, particularly with regards to the stabilization of PVR.

Patients with Ebstein's disease and cyanosis may require the use of PGE₁ to maintain ductal patency and induce pulmonary vasodilation.

In case of persistent and significant circular shunt, caregivers might need to stop PGE₁ infusions in order to reduce the size or abolish the flow through the ductus arteriosus. This might be problematic when there is an anatomic pulmonic stenosis, justifying a cardiac catheterization to relieve the obstruction.

Caregivers may need to employ further medical strategies to decrease pulmonary vascular resistances. These strategies include:

1. Mechanical ventilation
2. The use of NaHCO₃⁻ or THAM for blood pH alkalinization
3. The use of inhaled nitric oxide (iNO)

Patients in cardiac failure may benefit from the use of low dose Dopamine and Milrinone. Milrinone may also play a role in reducing pulmonary resistances. Dobutamine is utilized in some centers, although it may be pathophysiologically inadequate to choose this drug in such a context.

Induction of diuresis with loop-diuretics may be necessary, particularly in the presence of neonatal anasarca.

Early and aggressive nutrition is a benefit for these patients.

37.4.2 Infants, Children and Grown-Up Patients

Infants, children, teenagers and young adults may require treatment for three major problems that are often inter-related:

1. Progressive cyanosis
2. Progressive cardiac failure
3. Cardiac arrhythmias and conductive disorders

Medical therapy usually relies upon the use of systemic vasodilators (mostly Angiotensin-Converting Enzyme inhibitors), diuretics and digoxin. Antibiotic prophylaxis for bacterial endocarditis may be considered. Patients with persistent or recurrent arrhythmias may need the use of anti-arrhythmic drugs and may require electrophysiological studies and radiofrequency ablation of accessory pathways.

37.4.3 Surgical Management

Surgical treatment may be corrective or palliative. Correction means repairing the underlying tricuspid valve displacement and regurgitation, trying to rehabilitate the functional right ventricle and repairing any associated anomalies. However, in the very young patient, palliation may be the best, compromising as a bridge to later definitive repair. The general trend, although no consensus exists, is to perform surgery sooner than later once signs of heart failure begin to appear.

In *neonates*, surgical treatment is reserved to those severely symptomatic and refractory to medical treatment, or else with obstructive anatomic forms. Neonates who are refractory to the above described medical measures have a higher mortality and should be considered for a surgical approach.

The choice of the surgical technique depends on the anatomic form and has been controversial. There is no evidence-based data showing that neonatal total repair offers advantages when compared to the conservative medical therapy.

Persistently cyanotic patients, with functional or anatomic right obstruction, may require a modified Blalock-Taussig shunt. When a pulmonary stenosis or atresia is associated, some authors [5] have proposed a reconstruction of the right ventricular outflow tract with tricuspid repair and partial closure of the atrial septal defect. Nevertheless, clinical experience is still very limited and inconclusive.

Patients with persistent cardiac failure due to severe tricuspid regurgitation, massive right atrial dilatation and right-to-left shunt at the atrial level may need a Starnes procedure [6], which excludes the right ventricle by partially closing the tricuspid valve, placating the right atrial wall and enlarging the atrial septal defect (Fig. 37.7).

In *older and adult patients*, surgery has been reserved for those with:

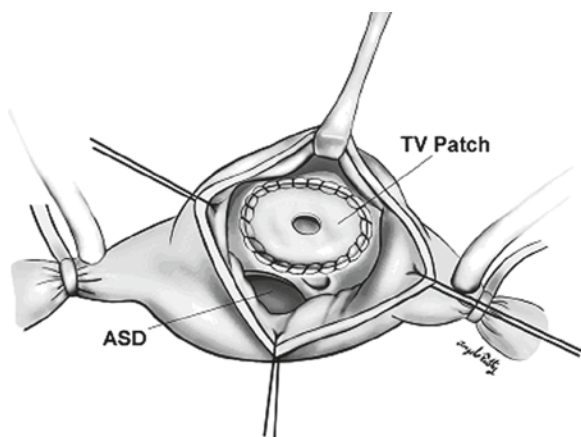


Fig. 37.7 The Starnes technique. With cardiopulmonary bypass support and under cardioplegic arrest, the right atrium is opened. The interatrial communication (ASD) is enlarged and the tricuspid valve is closed with a fenestrated patch (TV patch). Also, a reduction atrioplasty is performed

1. Significant functional limitation:
 - a. NYHA class I or II with worsening symptoms or with a cardiothoracic ratio greater than 0.65
 - b. NYHA class III or IV
 - c. Background of paradoxical embolism
2. Progressive cyanosis (saturation lower than 80% and/or significant polycythemia)
3. De novo, recurrent or refractory arrhythmias.

The different degrees of anatomic severity determine technical aspects of the surgical management, including tricuspid valve repair and replacement. As previously described, Ebstein's anomaly is characterized by an apical displacement of the septal and posterior leaflets of the tricuspid valve, resulting in a division of the right ventricle to a proximal atrialized chamber and a distal functional cavity. The degree of displacement of the septal and posterior leaflets determines the different types of functional anomalies described by Carpentier [1]. To summarize, in type A, the displacement of the septal leaflet is minimal and the atrialized right ventricle is small. In type B, the displacement of the septal leaflet is moderate and the atrialized chamber is larger. In type C, the displacement of the septal and posterior leaflets is important, and associated with a dyskinetic or akinetic atrialized chamber; the anterior leaflet's motion is restricted because of short chordae and muscular attachments to the right ventricular wall. In type D, the atrialized chamber is

enormous, creating a tricuspid sack with practically no functional right ventricle.

Conservative surgery to restore competent tricuspid function and preserve right ventricular contractility is preferable to valve replacement whenever repair is feasible, particularly in type A, B and the vast majority of type C cases. Tricuspid valve repair avoids the risks of prosthetic valve dysfunction, thromboembolism, endocarditis, and patient-prosthesis mismatch resulting from the child's somatic growth. Durability of bio-prostheses in patients with Ebstein's anomaly compares favorably with that in other cardiac valve positions and also with that in patients suffering from other tricuspid valve diagnoses [7]. Aims of the conservative approach are:

1. To reduce the paradoxical motion of the atrialized portion by plication
2. To close the interatrial septal defect
3. To map and section the accessory pathways (Maze procedure)

Successful repair of the tricuspid valve has been reported by Danielson and collaborators in around 58% of cases, where as in 36% a valvular replacement has been required [8].

The feasibility of conservative surgery depends on the size and mobility of the anterior leaflet, the tethering of its free edge and the number of its fenestrations.

Transesophageal echocardiography is essential to define these elements, the size of the atrialized chamber, and other intracardiac anomalies, as well as for evaluating left and right ventricular function the competency of the tricuspid valve repair, and detecting residual intracardiac shunts [9].

The most frequently associated cardiac anomalies include atrial and ventricular septal defects, hypoplastic pulmonary artery and pulmonary valvular stenosis, and should be corrected at the same time as Ebstein's anomaly.

Despite the variety of Ebsteins' repair techniques described in the literature [10–12], after that published by Carpentier in 1988 [1], only a few of them are reproducible and have become standardized (Fig. 37.8). These techniques include mobilization of the displaced leaflets and/or the anterior leaflet, longitudinal or horizontal plication of the atrialized right ventricle, and plication of the tricuspid valve annulus with clockwise rotation and reattachment of the mobilized leaflets on to the right atrioventricular groove [13]. In type A and B, the conservative approach could only be focused on the tricuspid valve by repairing it

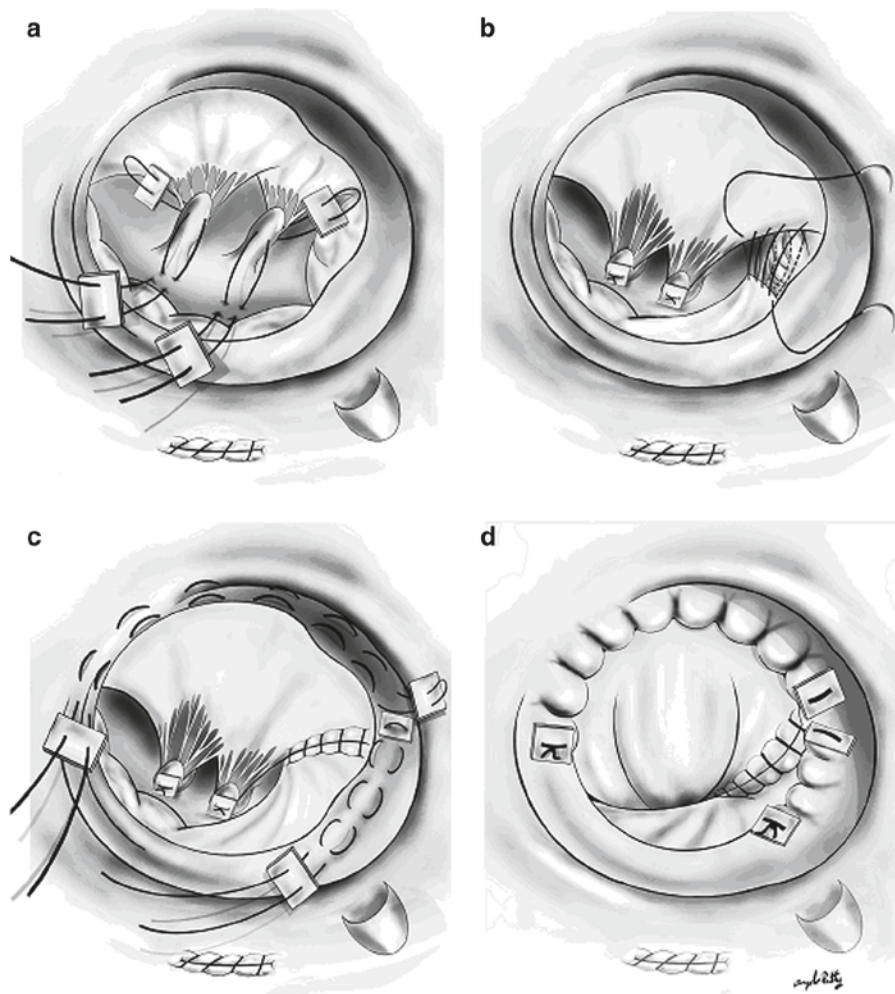


Fig. 37.8 The Mayo Clinic technique. (a) The papillary muscles supporting the anterior leaflet are moved toward the ventricular septum with pledgetted sutures and the atrial septal defect is closed, (b) the right edge of the anterior and septal

leaflets is approximated, plicating the posterior leaflet in the process, (c) anterior and posterior annuloplasty sutures are placed, (d) Once repaired, the tricuspid valve function depends on the ability of the anterior leaflet working as a monocusp valve

and preserving the level of the functional tricuspid annulus. Plication or limited resection of the atrialized chamber should be selectively considered in cases of large dyskinetic atrialized chambers, usually present in types C and D. Right reduction atrioplasty should be routinely performed in cases of dilated right atrium. Patients with accessory conduction pathways should undergo electrophysiological mapping for identification and ablation [14]. A concomitant right-sided Maze procedure should be performed in patients with a history of intermittent or chronic atrial flutter or fibrillation [15, 16].

Concomitant bi-directional cavo-pulmonary shunt, translating into a one-and-a-half-type ventricular repair, significantly reduces the operative mortality for Ebstein's anomaly in high risk patients with massive tricuspid insufficiency (associated hepatomegaly and / or ascites), a voluminous atrialized chamber, poor right ventricular contractility (as assessed by echocardiography and/or visually during surgery), or long-standing atrial fibrillation [17]. Bi-directional cavopulmonary shunt results in lower preload, reducing strain on the compromised right ventricle, hence preventing postoperative ventricular dilatation.

Orthotopic cardiac transplantation may be a pertinent indication in selected patients, particularly in neonates with severe forms of Ebstein's anomaly.

37.5 Postoperative Management

Univentricular, one-and-a-half or biventricular repair of patients with Ebstein's anomaly, mostly in the neonate population, anticipates right ventricular dysfunction. General principles of management focus on the reduction of right ventricular afterload by decreasing the pulmonary resistances. This protects right ventricular strain and reduces the risks of hemodynamically significant tricuspid regurgitation. General principles concerning management of univentricular repair are specifically discussed in the chapter related to single ventricle (chapter 31).

37.5.1 Sedation and Analgesia

Pain control and sedation are crucial after palliative or corrective surgery. The common association combines benzodiazepines with opioids, usually fentanyl in the neonatal period or morphine in the older patients. Some patients may require the association of alpha-2 agonists (i.e., dexmedetomidine or clonidine). Early administration of non-opioid analgesia reduces the risks for undesirable side-effects of opioid drugs. Neonatal patients who tend to develop pulmonary hypertension or maintain high PVR may need the use of muscle relaxants in combination with the above, until stable.

37.5.2 Fluid Management

Fluid management of patients with Ebstein's anomaly who have undergone a CPBP procedure, should follow the general guidelines, with a restriction of 30–50% on day 1, followed by 50–75% on day 2 and 100% from day 3. Closed heart palliative surgery does not require a restricted fluid administration. These principles must be individualized and adapted to the patients' characteristics, aiming for a negative fluid balance whenever possible.

37.5.3 Inotropic and Vasodilator Therapy

As previously described, inotropic support and afterload reduction are crucial for these patients. Dopamine and milrinone are the most commonly utilized vasoactive medications. Drug-induced sinus tachycardia should be avoided since it may decrease the filling of an abnormally compliant right ventricle, hence reducing the stroke volume.

37.5.4 Respiratory Management

Cardiopulmonary interactions are essential and PVR must be kept in the lower range. For this, it is important to provide an adequate oxygenation and to maintain pH levels around 7.45 with controlled hyperventilation. This may also be achieved by using alkalinizing drugs. Inhaled nitric oxide is an essential tool to optimize PVR.

Early extubation may be achieved in stable patients. However, particularly in the neonatal group, sternal closure may be voluntarily delayed for an average of 48 h, which sets back elective extubation.

37.5.5 Management of Specific Problems

Postoperative arrhythmias are a frequent occurrence. These anomalies have been reported in 42% of post-surgical patients in the neonatal period and significantly account for morbidity and mortality. The most common disorders are supraventricular tachycardia, transient atrioventricular heart block, ventricular arrhythmias and junctional ectopic tachycardia.

37.6 Prognosis

Natural progression of Ebstein's disease varies with the degree of tricuspid and right ventricular compromising. Symptomatic neonatal forms are worrisome and yield a more unfavorable prognosis. Nevertheless, most of patients present with symptoms in their middle teenage years and around 5% of them survive beyond the age of 50 years. Previous collaborative studies from the years 70 describe the follow-up of more than

500 patients between 1 and 25 years of age, documenting the following data:

1. Seventy-two percent of infants below 1 year of age develop cardiac failure
2. Seventy-one percent of children and adolescent, as well as 60% of adults are in NYHA class I and II
3. The high mortality at a young age declines significantly later in life

Prognosis depends greatly on the severity of the disease, the available treatment options and the surgical results. The main residual lesion of concern that influences mortality is the right ventricular obstruction. Other prognostic factors have been described in literature:

1. Male gender
2. Early age at presentation as described above
3. Cardiothoracic ratio greater than 0.65
4. Septal leaflet attachment ratio of more than 0.45
5. Increasing ratio of the combined area of right atrium and atrialized right ventricle to that of the functional right ventricle (see echocardiography section) from grade 1 (less than 0.5) to grade 4 (more than 1.5)
6. Higher NYHA class

Based on several clinical studies, Ebstein's anomaly in children can be repaired with low mortality and satisfactory long-term durability, with approximately 90% of late survivors in NYHA functional class I or II.

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Chapter 38

Anomalous Coronary Arteries

Eduardo M. da Cruz, Jonathan Kaufman, Steven Goldberg, Thomas Fagan, Christina Phelps, Cécile Tissot, Deborah Kozik, Max Mitchell, David Campbell, and Victor O. Morell

Coronary artery anomalies in the pediatric population are essentially related to congenital defects or secondary to inflammatory, immunological or vasculitic processes.

Their classification is complex and biased by the significant anatomical variability in normal individuals.

Anomalies of coronary arteries may involve coronary ostia, the position of the Valsalva sinuses or the origin and the distribution of the coronary branches.

Incidence of aberrant coronary arteries is lower than 1% in the adult population. Nevertheless, the incidence of anomalous coronary arteries is significantly higher in young individuals with sudden death (4–15%); as a matter of fact, they represent the second most common cause of sudden death in youth, after the hypertrophic cardiomyopathy [1–5].

Anomalous coronary arteries may be diagnosed as an isolated defect (i.e., the ALCAPA or anomalous left coronary artery arising from the pulmonary artery and the isolated coronary fistulas) or in association with complex cardiac malformations (i.e., conotruncal anomalies like the Fallot's tetralogy and the pulmonary atresia with ventricular septal defect, some forms of pulmonary atresia with intact interventricular septum or the transposition of the great vessels).

These anomalies may also be associated with ventricular septal defect, atrioventricular septal defect (endocardial cushion defect), aortic coarctation or complex cardiac malformations with single ventricle physiology and heterotaxia.

Many of the coronary anomalies are “silent” and asymptomatic and therefore diagnosed as a casual

finding in medical autopsies. When associated with cardiac anomalies acting as a source of significant left-to-right shunt, coronary anomalies may also be silent until surgical correction of the other defects that may trigger an abrupt myocardial ischemia [6, 7].

Patients with coronary anomalies may be admitted with heart failure, ischemia, cardiac arrhythmias or in a status post syncope or post cardiac arrest.

38.1 Classification

The most common coronary anomalies identified in the pediatric population may be classified as follows:
A. Congenital:

- ALCAPA (also called the Bland–White–Garland syndrome) (Fig. 38.1).
- Isolated coronary fistulas
- Ostial atresia or stenosis
- Anomalies of the origin, the trajectory or the distribution of coronary arteries isolated or in the context of congenital cardiac defects:

Transposition of the great arteries

Pulmonary atresia with intact interventricular septum

Conotruncal anomalies (i.e., tetralogy of Fallot, pulmonary atresia with ventricular septum defect, Double Outlet Right Ventricle)

Anomalous course: interarterial, retroaortic, pre-pulmonic, septal, intramural

“Other:”

Left coronary artery myocardial bridging

Right coronary artery arising from the coronary sinus

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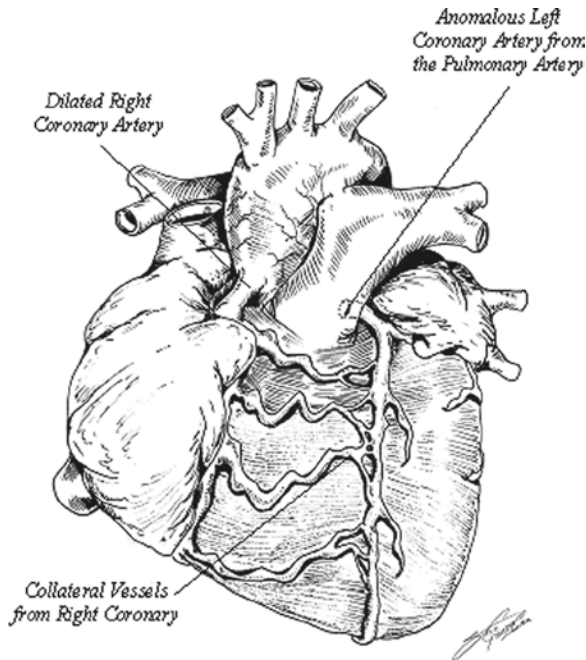


Fig. 38.1 Anomalous left coronary artery arising from the pulmonary artery (ALCAPA)

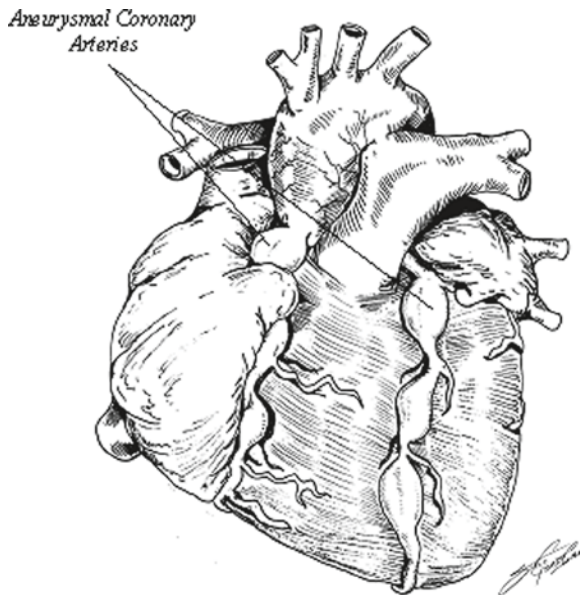


Fig. 38.2 Kawasaki's disease with multiple coronary aneurysms

B: Acquired:

- Kawasaki's disease (Fig. 38.2)
- Homozygote familial hypercholesterolemia

38.2 Pathophysiology

Anomalous coronary origin or distribution may be well tolerated and asymptomatic and clinical expression varies depending on the etiology, the associative lesions and the compensatory mechanisms.

Congenital defects like the ALCAPA or coronary fistulas may cause acute or chronic ischemia respectively progressing towards myocardial infarct and a dilated hypokinetic cardiomyopathy with secondary ischemic mitral regurgitation or recurrent ischemia because of a diastolic “steal.” An analogous phenomenon may be observed when coronary arteries have a right ventricular-dependent circulation like in the case of pulmonary atresia with intact interventricular septum and severe right ventricular hypoplasia with embryonic sinusoids and coronary fistula. Coronary fistulas may drain onto the right atrium, the right ventricle, the pulmonary artery, the left ventricle or the cava system and their impact varies with the pathophysiological implications. Other than ischemia, this anomaly may be associated with heart failure, pulmonary hypertension of arrhythmias.

In the case of transposition of the great arteries and in conotruncal anomalies, coronary anatomy must be adequately identified in order to avoid inadvertent surgical injuries by a section of important coronary branches or rhythm disturbances by ischemia of the sinus node.

In acquired coronary anomalies, the main pathophysiological pattern is acute or chronic ischemia.

38.3 Diagnosis

38.3.1 Clinical

Clinical symptoms and signs of coronary problems in the pediatric population may be heterogeneous and even unspecific, depending on the etiology:

- Myocardial ischemia and infarct
- Cardiogenic shock
- Malignant rhythm disorders
- Ventricular dysfunction and dilated cardiomyopathy
- Syncope
- Sudden death or “near-miss” syndrome

Clinical presentation may mimic a bronchiolitis-like syndrome [8], but a detailed clinical examination encompassed by radiological evaluation should document signs of left or global cardiac failure, a cardiac murmur secondary to ischemic mitral regurgitation or signs of shock and a moderate to severe cardiomegaly on the chest X-ray.

Symptoms: in newborns and toddlers, symptoms may be unspecific: diaphoresis, irritability, feeding problems, pallor, failure to thrive, respiratory wheezing and dyspnea. Older patients usually complain of angina, precordial pain or have a syncopal episode.

Signs: in case of progressive ischemia, clinical examination will reveal signs of left or global cardiac failure and low cardiac output. Usually, there is tachycardia and a galop rhythm. Frequently, a systolic murmur is found, characterizing an ischemic mitral regurgitation. This later might be an isolated clinical sign. When ischemia progresses to myocardial infarct, clinical appraisal will identify signs of cardiogenic shock. In the specific case of coronary fistula, the cardiac murmur will be continuous in nature and may coexist with signs of cardiac failure.

Some phenotypic patterns should motivate further studies in patients with suspected coronary anomalies: for example, patients with Williams–Beuren syndrome may have a coronary ostial stenosis associated with supraaortic stenosis.

38.3.2 Chest X-ray

Chest X-ray shows signs of cardiac failure with cardiomegaly and pulmonary vascular stasis. As mentioned above, radiological findings may mimic a bronchiolitis-like syndrome in young infants.

38.3.3 ECG

ECG is a useful diagnostic and follow-up tool in showing the affected territories in case of ischemia or infarct. Some electric patterns suggest specific diagnosis like

in the case of the ALCAPA. A Q wave on DII and aVL leads should raise suspicion.

38.3.4 Echocardiography

Echocardiography remains one of the cornerstone diagnostic tools. It is instrumental in identifying the coronary anatomy, origin and distribution (Fig. 38.3), it allows documentation of the segmental anomalies induced by ischemia and it may also show indirect signs of ischemia such as acquired mitral regurgitation and subendocardial hyper-echogenicity [9].

38.3.5 Cardiac Catheterization

Nearly all patients with anomalous coronary arteries will require a cardiac catheterization (Fig. 38.4) at some point in their lives, for both diagnostic and interventional purposes [10, 11]. Please consult the chapter on Cardiac Catheterization (chapter 5) for more details.

38.3.6 Other

Cardiac enzymes (troponin, CPK and CPK MB, LDH) are useful for the diagnosis and the follow-up of patients who have undergone an ischemic event. Pro-BNP levels should also be systematically controlled and followed, particularly in patients who remain symptomatic after a significant ischemic insult.

MRI and CT angiography are important supplementary tools to ensure a comprehensive noninvasive assessment and follow-up of the coronary lesions, their impact in the myocardial function and on the atrioventricular valve regurgitation [10, 11].

Positron Emission Tomography scan is sometimes indicated in order to appraise potential for myocardial recovery (hibernated myocardium). This is a useful complementary tool to distinguish between ischemia without or with ongoing or established infarct.

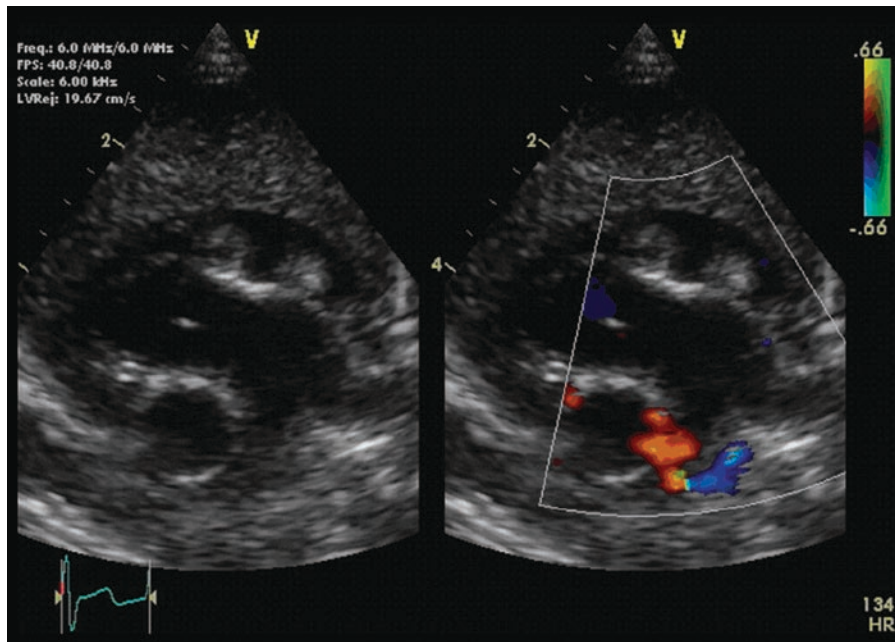


Fig. 38.3 2D echocardiography showing an ALCAPA arising from the right pulmonary artery

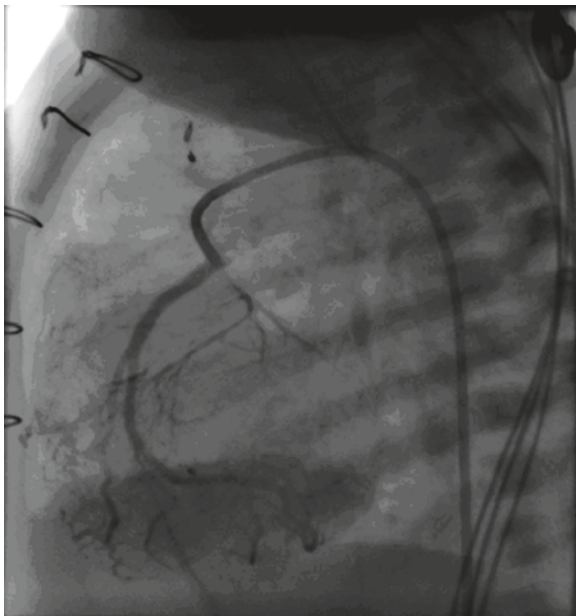


Fig. 38.4 Right coronary angiography showing an ostial atresia of the left coronary artery with retrograde flow from the right coronary artery

38.4 Preoperative Management

Preoperative management must be individualized. Once the anomaly has been identified, prevention of progressive lesions is crucial. Such management concentrates on therapy of cardiac failure and of any multi-systemic compromising in case of shock. In this later scenario, unless the circulatory failure is refractory to medical therapy or if the patient is deemed to rapidly progress towards further deterioration, any surgical indication should be delayed until a multi-organ stability is attained.

Symptomatic patients should be comprehensively monitored with an arterial catheter and an indwelling central catheter. A Swan–Ganz catheter is a useful tool for a comprehensive hemodynamic assessment and may be a good indication in patients who progress inadequately or whenever a differential diagnosis of the type of shock is required. However, in many pediatric centers this is uncommon and therefore fraught with potential complications.

Near Infra-Red Spectroscopy (NIRS) and modern technology by thermodilution (i.e., PiCCO® and Flo-Trac® catheters) are also utilized as tools for the appraisal and the follow-up of these patients.

38.4.1 General Measures

- Oxygen administration
 - Initiate inotropic drugs if necessary. As for the oxygen, these drugs must be administered very cautiously since they may trigger malignant arrhythmias by reperfusion. Phosphodiesterase inhibitors are particularly useful in this context because of their effect in reducing ventricular afterload. Other alternatives are dopamine, dobutamine and the nitric derivatives (IV nitroglycerin and isosorbide dinitrate). In case of severe and refractory ventricular dysfunction, Levosimendan is a potentially interesting drug although pediatric experience is still limited. Epinephrine (adrenaline) and norepinephrine (noradrenaline) are frequently utilized in association with dopamine, milrinone and vasodilators.
 - Administration of loop diuretics (furosemide, bumetamide) as boluses or in continuous IV infusions
 - Rectify all metabolic, electrolytic or acid-basic disorders
 - Optimize hematocrit levels (>35%)
 - Attempt to minimize oxygen consumption and respiratory work; in case of low cardiac output in patients with limited reserves, it is reasonable to electively mechanically ventilate patients. Positive pressure ventilation by CPAP, BiPAP or assisted ventilation is essential for patients in established or eminent cardiogenic shock. During the intubation process, rapid sequence drugs should be used (i.e., etomidate and rocuronium). Intubation may lead to cardiac arrest and cardiovascular collapse and it is therefore advisable to alert the surgical team to the potential need for ECMO. Some patients with ventricular hyperexcitability may benefit with a dose of lidocaine on induction, to reduce the risks for ventricular arrhythmias during the intubation. In patients with ALCAPA, it is important to avoid hyperventilating and hyperoxygenating the patients since these maneuvers may aggravate coronary ischemia by decreasing pulmonary vascular resistances.
- In case of refractory shock, rapidly progress towards mechanical assistance (extracorporeal life support)
 - Aggressively treat all multi-organ dysfunction (peritoneal dialysis or continuous veno-venous hemofiltration or hemodiafiltration in case of renal failure, compensation of coagulation disorders and administration of vitamin K in case of hepatic dysfunction, cerebral and splanchnic protective measures, to mention some)
 - Symptomatic treatment of all intercurrent infections is crucial; prevention also plays an important role with regards to Respiratory Syncytial Virus (Polivizumab) and Influenza virus (Anti-Flu vaccination)
 - Optimization of enteral and/or parenteral caloric intake is also vital

38.4.2 Specific Measures

1. ALCAPA:

- a. Start a continuous intravenous heparin infusion
- b. Administer anti-arrhythmic drugs as required; in case of ventricular hyperexcitability, lidocaine, bretilium or amiodarone may be indicated and very cautiously administered
- c. Initiate assisted ventilation in case of shock or unstable hemodynamic status
- d. Initiate ECLS as required, sooner than later in cases refractory to medical therapy
- e. Perform an urgent cardiac catheterization for diagnostic and eventual interventional purposes
- f. Urgent surgical repair: this applies to the anatomical reimplantation of the anomalous coronary artery or to an intrapulmonary tunnelization of the anomalous artery towards the aorta (Takeuchi procedure). Ligation of the ALCAPA is nowadays very seldom the technique of choice. Ostial stenosis or atresia represent a surgical challenge with inconsistent results; tolerance to this condition relies on the type of collaterality patients may develop from the right coronary artery
- g. Some deemed inoperable cases may become candidates for an orthotopic cardiac transplant,

eventually bridged with a ventricular assistance device.

2. Coronary fistula:

- a. Same indications as described above for the ALCAPA in case of ischemia or complications
- b. Schedule an elective or urgent cardiac catheterization – depending on the clinical scenario – for diagnostic and eventual interventional purposes. Many coronary fistula are occluded by percutaneous interventions.
- c. Surgical ligation of the fistula if not feasible by cardiac catheterization

3. Anomalies of the origin, the trajectory or the distribution of coronary arteries in the context of congenital cardiac defects:

- a. There are no specific measures, except for the importance of the iconographic documentation of the anomaly in order to provide surgeons with a maximum of anatomical information. This may be achieved by echocardiography, cardiac catheterization and in older patients with a high resolution Computerized Tomography Angiography [9, 10].

4. Kawasaki disease:

Monitoring is limited to noninvasive techniques (ECG, noninvasive blood pressure, peripheral oxygen saturation) except in presence of acute ischemia when an arterial catheter and a central venous line are indicated. Current management protocols are based upon an international taskforce [12–32].

a. Clinical and biological suspicion based upon internationally recognized criteria:

- A minimal of 4/5 classic clinical signs are required in the presence of high fever refractory to medications:
- Polymorphic cutaneous rash (80%)
- Non-purulent bilateral conjunctivitis (85%)
- Limb modifications: palmo-plantar erythema, diffuse edema of hands and feet, peri-ungueal desquamation (75%)
- Oropharyngeal modifications: cheilitis, pharyngeal hyperemia, «raspberry» tongue (90%)
- Cervical adenopathies: at least one node >1.5 cm (70%)

This situation is a clear indication for the administration of immunoglobulin at a single dose of 2 g/kg in slow IV (caution should be taken with potential anaphylactic reactions) over 6 h and aspirin at anti-inflammatory doses (80–100 mg/kg/day), even in the absence of demonstrated coronary or cardiac lesions by echocardiography. Taking into account this aspirin dose, it is recommended to administer a local (i.e., sucralfate) or systemic (i.e., ranitidine, proton pump inhibitors) medication for gastric protection. The aspirin dose will be decreased to 3–5 mg/kg/day (antiplatelet dose) once the inflammatory syndrome improves or in case of persistent thrombocytosis.

b. Persistent clinical symptoms and signs or persistent inflammatory syndrome:

- b1. Persistent or recurrent fever 48 h after the initial administration of IV immunoglobulins (signs or persistent vasculitis with increased risk for coronary aneurysm development):

- Administer a second dose of IV immunoglobulins at 2 g/kg

- b2. Persistent fever after the second dose of immunoglobulin:

- Administer a third dose of IV immunoglobulins at 2 g/kg
- Initiate IV methylprednisolone at 30 mg/kg, for 1–3 days

- b3. Other therapies:

- Pentoxifyllin (anti-TNF, vasodilator and antiplatelet effect)
- Infliximab (anti-TNF monoclonal antibody)
- Plasmapheresis
- Immunosuppressive therapy

c. Added therapy in case of complications:

- c1. Coronary dilatation or aneurysm: treatment depends on the severity of coronary compromising:

Antiplatelet therapy:

- a. Aspirin
- b. Dipyridamol or clopidogrel

Anticoagulation:

- a. Heparin, followed by Oral anticoagulation (target INR of 2.0–2.5)

- b. Abciximab (monoclonal antibody, inhibitor of the platelet glycoprotein receptor type IIb/IIIa)

c2. Coronary thrombosis:

Control of vascular inflammation:

- a. Immunoglobulins
- b. Corticosteroids

Thrombolysis:

- a. Urokinase
- b. Streptokinase
- c. rTPA

Anticoagulation:

- a. Heparin, followed by Oral anticoagulation

c3. Myocardial ischemia (particularly in presence of ventricular dysfunction):

- Continuous infusion of nitroglycerin and inotropic drugs
- Urgent coronary artery bypass graft
- Orthotopic cardiac transplant (in case of malignant arrhythmia, severe ventricular dysfunction, coronary disease not deemed repairable by surgery or by interventional catheterization): these patients may require ECLS while awaiting a donor.

c4. Severe ventricular arrhythmias:

Administer anti-arrhythmic drugs: IV lidocaine at 1 mg/kg, followed by a drip at 15–50 µg/kg/min

Invasive management consists in a surgical coronary artery bypass graft if ischemia persists in spite of medical measures. Alternatively, in some cases, cardiac catheterization may also be a therapeutic option. In case of severe cardiogenic shock with massive myocardial infarction, mechanical assistance (ECLS) is indicated while awaiting recovery of myocardial function after intervention, or else, as a bridge to cardiac transplantation.

5. *Homozygote Familial Hypercholesterolemia:*

Prophylactic therapy:

- a. Statins
- b. LDLH-apheresis
- c. Hepatic transplantation
- d. Antiplatelet therapy in case of documented coronary lesions

38.5 Surgical Management

There are two commonly used operative techniques in the management of patients with an ALCAPA [33–36]; they both require cardiopulmonary bypass and cardioplegic arrest. In the *coronary artery reimplantation procedure*, the anomalous artery is reattached to the aorta (Fig. 38.5); and in the *Takeuchi procedure* a tunnel is created from the aorta to the origin of the anomalous coronary in the pulmonary artery, allowing aortic blood flow into the anomalous coronary (Fig. 38.6). Older patients with preserved ventricular function can be managed with a simple ligation of the anomalous coronary artery.

In the presence of significant ischemic mitral valve regurgitation, a mitral valvuloplasty might be required at the time of surgery.

Coronary artery fistula ligation or suture closure can be performed with or without cardiopulmonary bypass support, depending on the location of the fistula.

Patients with an anomalous aortic origin of a coronary artery from an incorrect sinus of Valsalva are usually managed by one of the following procedures: coronary unroofing, coronary reimplantation, or in some cases coronary bypass. They all require cardiopulmonary bypass and cardioplegic arrest.

Not infrequently, patients may require mechanical circulatory support preoperatively or postoperatively because of significant ventricular dysfunction. The reported operative mortality associated with ALCAPA repairs is less than 8% and the long-term outcomes are excellent [37, 38].

38.6 Postoperative Management

Postoperative requirements depend to a great extent on the preoperative conditions. Generally, if the patient was well balanced prior to the intervention, no significant complications are anticipated. Nevertheless, patients must be cautiously monitored for persistent or recurrent acute ischemia, ventricular dysfunction, low cardiac output syndrome and arrhythmias due both to the ischemic event or to reperfusion injuries. A significant echocardiographic improvement may be documented over the first 48 h of postoperative course, although total recovery is not expected before weeks or months of progression, if ever.

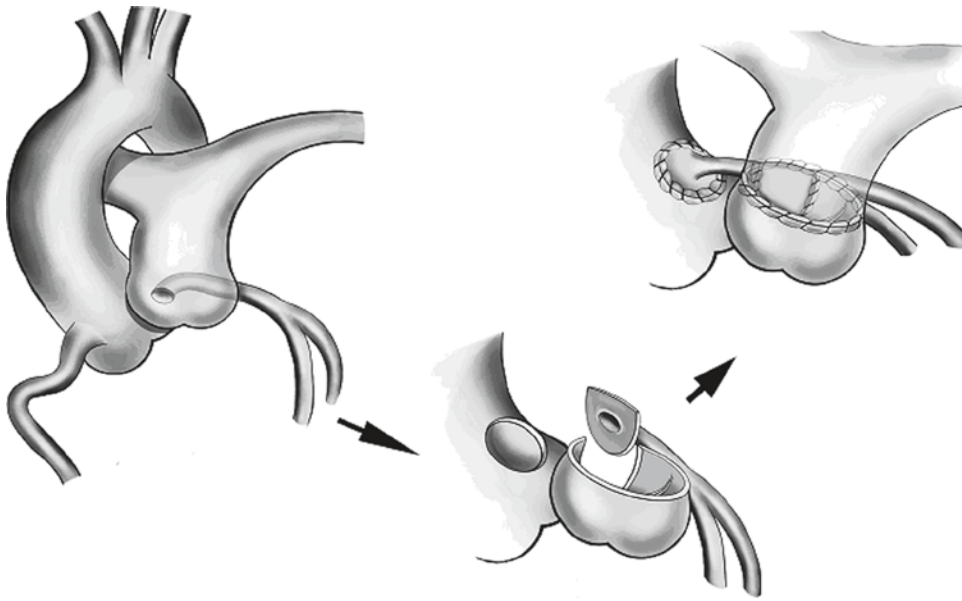


Fig. 38.5 *Anomalous coronary artery reimplantation.* Once on cardiopulmonary bypass, the heart is arrested by delivering cardioplegia via the ascending aorta and the main pulmonary artery in order to perfuse the myocardium supplied by the anomalous

coronary. Then, the anomalous coronary artery is harvested from the pulmonary artery and reimplanted into the aorta. The pulmonary artery is repaired with a patch of pericardium

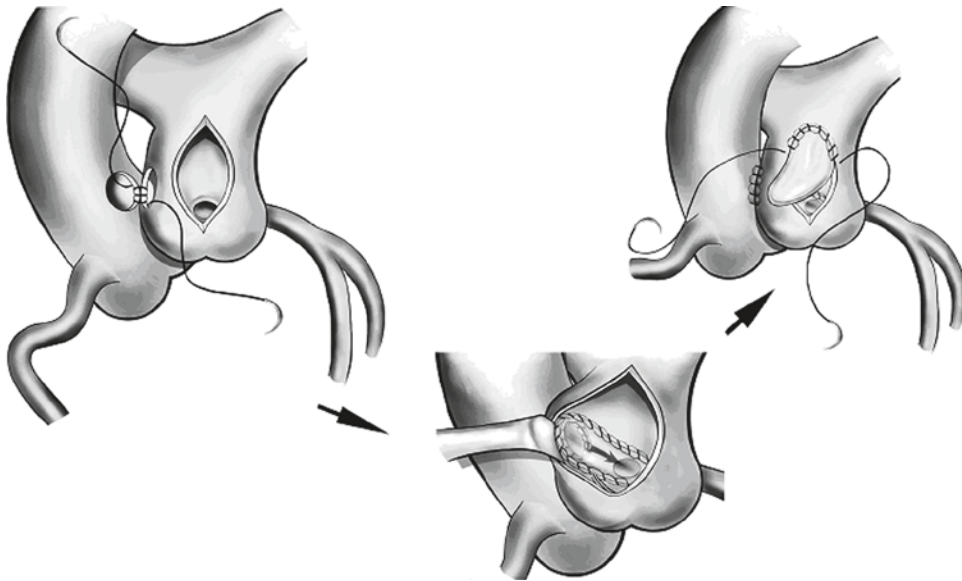


Fig. 38.6 *Takeuchi Procedure.* First, a side-to-side connection between the aorta and the pulmonary artery is created. Then an intrapulmonary artery tunnel is created with a patch,

tunneling the oxygenated aortic blood into the origin of the anomalous coronary. Finally, the pulmonary artery is repaired with a patch

Anticipated postoperative complications may be as follows:

- *Ischemia:* a continuous ECG monitoring will immediately identify any recurrent ischemic event. Serial

control of cardiac enzymes (CPK, CPK MB, LDH, troponin) and pro-BNP may also be useful. *Any ventricular arrhythmia should be taken as an expression of ischemia until otherwise demonstrated.* Ischemia may occur as a consequence of a

spasm of the coronary graft, particularly if an internal mammary artery was used, in which case the use of IV Diltiazem may prove very useful.

- *Arrhythmias*: as mentioned above, any ventricular arrhythmia should motivate further investigations in order to identify sources of residual or recurrent ischemia. In any doubtful situation, a surgical revision should be proposed. Potentially, any other arrhythmia and conductive disorders are possible in this context. A strict metabolic control and rectification of documented disorders regarding potassium, sodium, calcium and magnesium levels is required.
- *Persistence of a severe myocardial dysfunction*: these patients may require mechanical assistance until recovery or as a bridge to cardiac transplant

38.6.1 Monitoring

Monitoring of these patients should include an arterial catheter, a central venous catheter, and in case of surgery on cardiopulmonary bypass in patients with significant left ventricular dysfunction, a left atrial catheter and eventually a Swan–Ganz catheter. NIRS is currently used as a systematic method to assess regional perfusion.

38.6.2 Sedation and Analgesia

Sedation and pain control is ensured by the association of midazolam, morphine or fentanyl and seldom muscle relaxants. Alternatively, dexmedetomidine or propofol may be used. Propofol may have an hemodynamic impact in these already fragile patients and must be handled by very experienced practitioners, ideally as a continuous infusion and by avoiding boluses. Etomidate is a drug to consider for rapid sequence procedures, although considerations ought to be taken with regards to the potential adrenocortical dysfunction. Once the hemodynamic status is stable, multi-organ function is deemed adequate, and in the absence of bleeding or residual ischemia, patients are allowed to breathe spontaneously in order to progress towards extubation. If the surgery was a simple ligation of a coronary fistula, patients may be extubated in the operating room or very early on the intensive care unit.

38.6.3 Fluid Management

With the exception of the ligation of coronary fistula without ventricular compromising, in which case no fluid restriction is necessary, patients should receive a total of 30–50% of physiological requirements on the first day, 50–75% on the second day and 75–100% on the third day. As in the case of all other surgeries on cardiopulmonary bypass, caregivers should aim for a negative or neutral fluid balance. Excessive volume load should be optimized with a titration of furosemide as a continuous infusion.

38.6.4 Inotropic and Vasodilator Drugs

These patients benefit from the universal approach to postoperative cardiac patients associating inotropic and vasodilator drugs, or else, using lusitropic drugs, the aim being to support the myocardial function and to reduce ventricular afterload. The combination of milrinone with low doses of epinephrine (adrenaline) is very efficient for this purpose. In patients with conserved ventricular function, the alternative may be the association of dopamine and dobutamine. This latest should be carefully used though in order to avoid unnecessary myocardial oxygen consumption. Many other vasodilators might be used depending on the institutional protocols: phentolamine, phenoxybenzamine, hydralazine, nitroglycerine or sodium nitroprusside. Nitroglycerine is an interesting drug for this cohort of patients for its effect in reducing the transmural pressure, therefore optimizing myocardial perfusion. Epinephrine (adrenaline) is a clear indication in patients with ventricular dysfunction, although it should be used with caution considering the increase in oxygen consumption and the potential for induction of arrhythmias. Levosimendan has arisen as a drug with a high interest in patients with persistent ventricular dysfunction and may become a rescue drug in the future; however, further clinical studies are required in the pediatric population.

Extracorporeal life support techniques should be indicated in patients who are refractory to inotropic and vasodilator drugs.

38.6.5 Respiratory Management

In the absence of surgical or postoperative complications, respiratory weaning is started after 12–24 h.

Positive ventilatory pressures are a favorable cardiopulmonary interaction in patients with left ventricular dysfunction and therefore extubation to a CPAP or to BiPAP should be considered.

38.6.6 Specific Management

Left ventricular dysfunction, low cardiac output syndrome and arrhythmias are managed as further described elsewhere in this book.

All ventricular ischemia must be considered as an emergency. Clinical manifestation of ischemia may vary from an acute left ventricular dysfunction with low cardiac output to ventricular arrhythmias. If general conditions allow it, a cardiac catheterization should be performed. Otherwise, the patient should be taken back to the operating room for surgical revision. While awaiting the intervention, nitric derivatives should be increased and IV Diltiazem ought to be considered for the possibility of a vascular spasm of the graft.

Anticoagulation: with the exception of the ligation of a coronary fistula, all patients should be on a continuous infusion of heparin at 10 units/kg/tour, from the sixth postoperative tour, in absence of active bleeding. From day one, once feeding has resumed, antiplatelet therapy should be started. Some groups recommend the use of low molecular weight heparin (enoxaparin, fraxiparin, calciparin) for a few days, followed with levels of anti-Xa factor.

Arrhythmia: management of arrhythmia and conductive disorders is discussed in detail in a specific chapter (chapter 53). In patients with ventricular hyperexcitability, lidocaine, bretilium or amiodarone as a continuous infusion may be considered. Use of amiodarone requires great caution for its negative chronotropic effect.

38.7 Results

Prognosis of these anomalies is very heterogeneous and individual. Preventive measures remain crucial. In patients with ischemic injuries and no myocardial

necrosis, the potential for total recovery is significant once the anatomic anomaly is rectified [39].

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Chapter 39

Aortic Valve Regurgitation

Michael Tsifansky, Victor O. Morell, and Ricardo Muñoz

Aortic regurgitation (AR) may be caused by valve disease or aortic root anomalies, but it is rare in children without other congenital or acquired heart disease. It is more commonly associated with aortic stenosis, but may also be seen in patients with Tetralogy of Fallot (ToF), D-transposition of the great arteries (DTGA), coarctation of the aorta (CoA), endocardial cushion defect, single ventricle, truncus arteriosus (TA), infective endocarditis, and mitral valve disease. Systemic diseases associated with AR include rheumatic fever, systemic lupus erythematosus, and Takayasu arteritis. AR related to significant dilation of the ascending aorta is seen in patients with Marfan syndrome, bicuspid aortic valve, osteogenesis imperfecta, and rheumatoid arthritis. Significant ascending aortic dilation may, in turn, worsen the AR and lead to aortic dissection.

39.1 Pathophysiology

Both preload and afterload are increased in AR. The effective forward stroke volume is initially well maintained at the expense of high end-diastolic volume and increased LV mass. However, eventually the left ventricular wall thickening fails to manage the excessive regurgitant stroke volume, and the end-systolic wall stress rises [1]. Thus over the course of its natural history, AR leads to a spectrum of anatomic and physiologic changes, including dilation and hypertro-

phy of the left ventricle, dilation of the mitral apparatus and mitral regurgitation, dilation of the left atrium, pulmonary venous hypertension, and eventually global ventricular dysfunction.

39.2 Physical Examination

The vital signs are remarkable for wide pulse pressure. The pulses are bounding with abrupt distension and fast collapse, especially over the carotids. This coincides with a marked systolic–diastolic differential. There is a prominent apical cardiac impulse. On auscultation there is an early (immediately after A2) blowing decrescendo diastolic murmur best heard along the left sternal border.

39.3 Preoperative Management

Patients with AR rarely require ICU admission preoperatively, with the exception of those in whom acute AR develops after balloon dilation of the aortic valve or in the context of infective endocarditis. Acute AR is poorly tolerated, and the development of congestive heart failure (CHF) is rapid and overwhelming. Patients with AR who exhibit signs of CHF, arrhythmias, syncope, or chest pain are candidates for surgical intervention.

In the setting of acute AR and CHF, admission echocardiogram, electrocardiogram, and chest X-ray should be obtained, and a central venous line and arterial line should be placed.

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A milrinone infusion (0.25–1 $\mu\text{g}/\text{kg}/\text{min}$) may help to improve myocardial contractility and decrease afterload. Because these patients usually have low diastolic and mean blood pressure, it is prudent to start milrinone at a low dose and titrate upwards to effect under close hemodynamic monitoring.

Diuretics and careful fluid restriction are indicated.

Ventricular arrhythmias are ominous signs of significant ventricular dysfunction, and surgery should be promptly undertaken.

If infective endocarditis is suspected, serial blood cultures must be drawn, and antibiotics must be started immediately.

A transthoracic echocardiogram should be done looking for endocardial vegetations and, if found, they should be assessed for size and mobility. If a transthoracic echocardiogram is unrevealing and endocarditis is suspected on clinical grounds, a transesophageal echocardiogram should be strongly considered. These patients are at high risk of thromboembolic events [2].

39.4 Surgical Management

There are two surgical strategies for the management of patients with aortic insufficiency: *aortic valve repair and*

replacement. Both procedures require cardiopulmonary bypass and cardioplegic arrest, and are usually performed under mild to moderate hypothermia. Lately, reparative techniques are being used more frequently with moderate success [3–5]. Commonly used techniques are shown below (Figs. 39.1–39.3).

39.5 Postoperative Care of Aortic Regurgitation Repair

The care of patients after surgery for AR is relatively simple. Unless they present preoperatively with pulmonary edema, they are usually extubated on admission to the ICU.

Arterial and central lines are usually left in place at least for the first postoperative day.

Chest X-ray and ECG are obtained on admission; it is important to compare them with the preoperative studies [6, 7].

The majority of patients require postoperative afterload reduction, which should be optimized by the physical examination and the results of the TEE.

Electrolytes should be closely monitored and corrected to avoid arrhythmias.

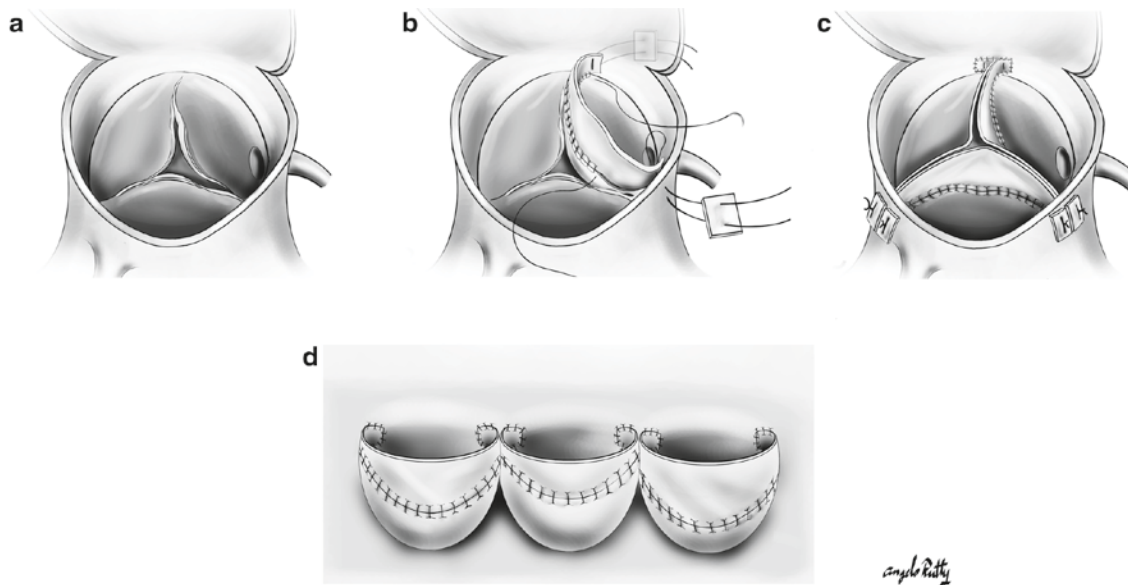


Fig. 39.1 Pericardial Leaflet Extension Technique. (a) Abnormal trileaflet aortic valve with poor coaptation. (b) The pericardial extension is sutured to the left aortic cusp. (c) All three aortic cusps

are augmented with pericardial patches, creating a competent valve. (d) Note that the size of the pericardial patch extension varies for each cusp

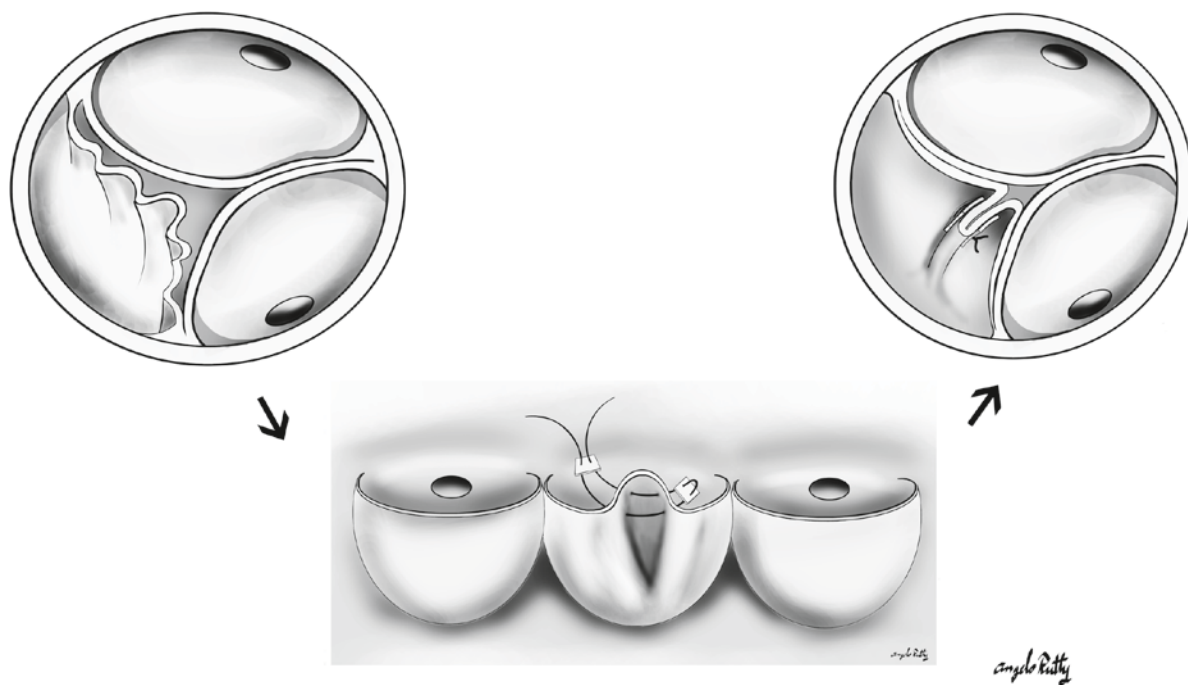


Fig. 39.2 Aortic Leaflet Plication. In the presence of a redundant and prolapsing aortic cusp, a centrally placed plicating suture improves valve coaptation, reducing regurgitation

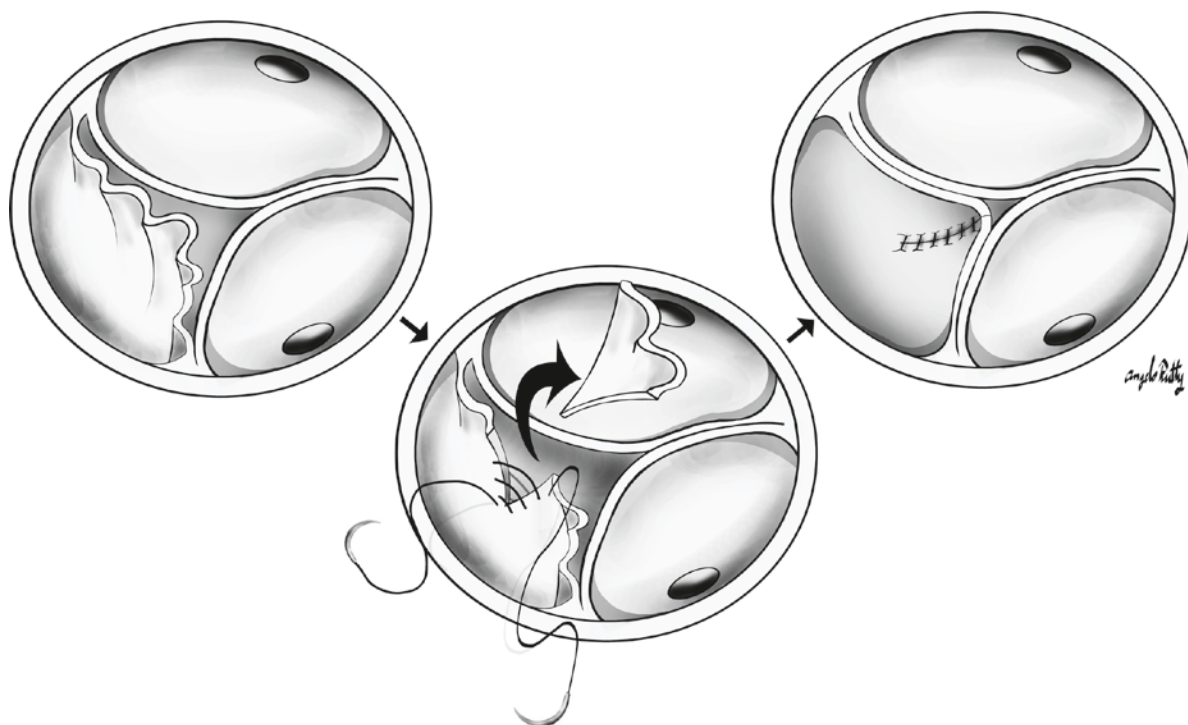


Fig. 39.3 Partial Aortic Leaflet Resection. The redundant central section of the prolapsing cusp is resected in order to improve valve coaptation

For the purposes of sedation, we prefer to use dexmedetomidine supplemented as needed with low-dose narcotics and benzodiazepines.

If a prosthetic valve has been placed, anticoagulation should start once the bleeding is controlled, typically on postoperative day 2. Initially, regular heparin infusion is used. When oral intake is stable, and after at least 2–3 days on heparin, warfarin is started, and heparin is continued until warfarin is therapeutic. The values of PT (for warfarin) and, the PTT (for heparin) should be closely monitored, and a diet consistent in vitamin K content should be adhered to (please see the chapter on prosthetic valves for further details).

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Chapter 40

Vascular Rings and Pulmonary Sling

Yuliya A. Domina, Sang Park, and Victor O. Morell

40.1 Anatomy

Aortic arch anomalies are not uncommon and result from embryologic derangements during the development of the aortic arches and their branches [1]. Early in gestation there are both right and left aortic arches, but the right normally atrophies and disappears. Vascular rings occur when certain structures persist rather than involute or involute rather than persist, resulting in the encirclement and compression of the trachea and esophagus. From 3 to 5 % of cases of stridor in infancy are due to vascular rings.

The following vascular abnormalities can cause airway obstruction and, occasionally, esophageal symptoms.

1. *Double aortic arch* (Fig. 40.1) is the most common vascular ring, and results when the right arch fails to involute. Both arches may be patent: the right arch is dominant in 70% of cases, the left in 20% and the arches are almost equal in size in 10% of cases. One arch, usually the left, may be present but often atretic.
2. *A right aortic arch with an aberrant left subclavian artery and left ligamentum arteriosum* (Fig. 40.2) is a rather common anomaly, but the ring is a loose one in most cases and causes no symptoms. If the left subclavian artery arises from a diverticulum of Kommerell, a remnant of the left descending aorta, the ring may be tighter and cause symptoms.
3. *A left aortic arch with an aberrant right subclavian artery* (Fig. 40.3) is also common and usually asymptomatic. Rarely, there is an associated

right-sided descending aorta and then the ring tends to be tighter and more symptomatic [2].

4. *A pulmonary artery sling* (Fig. 40.4), also known as distal origin of the left pulmonary artery, occurs when the left pulmonary artery originates abnormally from the right pulmonary artery and courses between the trachea and esophagus, resulting in encroachment on the distal trachea and the right main stem bronchus. Associated intracardiac abnormalities are present in 10–15% of cases [3].
5. *Anomalous innominate artery* (Fig. 40.5). This anomaly occurs when the innominate artery arises unusually distally from the aortic arch, then courses tangentially anterior to the trachea. The degree of tracheal compression is variable but occasionally is severe.

40.2 Pathophysiology and Clinical Presentation

Despite variability in anatomy of these anomalies, they are all influenced by a common pathophysiologic mechanism; symptoms are due to compression of large airways and/or the esophagus. Patients with severe compression tend to present early in life. In others, symptoms appear later in life or do not occur at all. Long standing compression of the trachea and main-stem bronchus by the high pressure arterial system tends to cause tracheo-bronchomalacia, with airway collapse on exhalation and consequent air trapping. A barking cough and stridor that is expiratory and/or inspiratory are common signs. In infants and children with severe obstruction from innominate artery compression, symptoms commonly worsen during respiratory infections [4]. Compression of the esophagus

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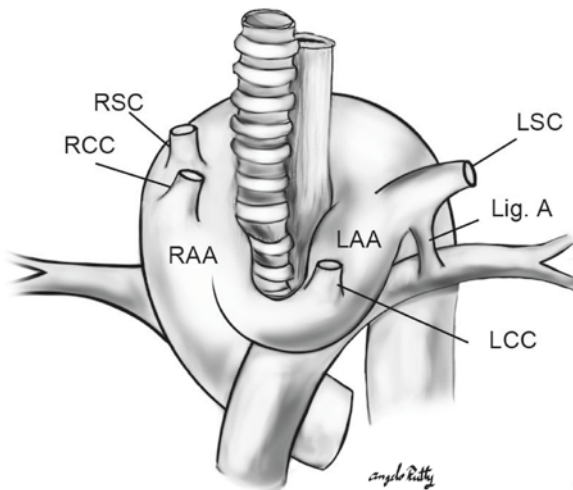


Fig. 40.1 Double aortic arch. (RAA right aortic arch; LAA left aortic arch; RCC right common carotid artery; LCC left common carotid artery; RSC right subclavian artery; LSC left subclavian artery; Lig.A ligamentum arteriosum)

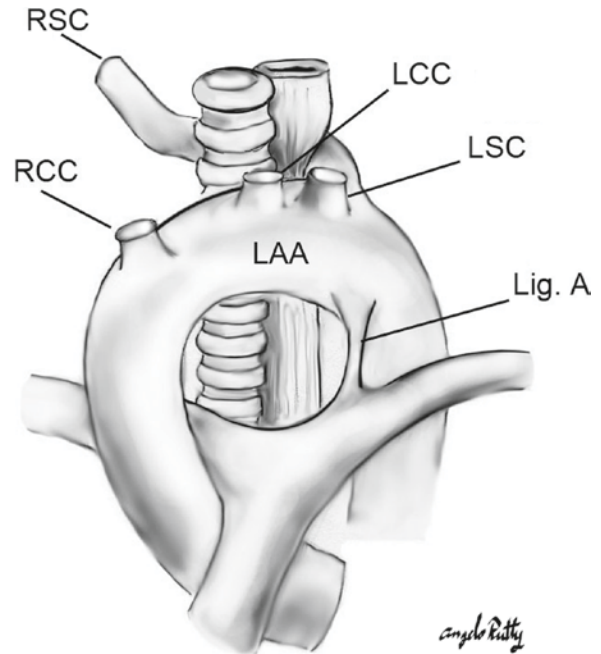


Fig. 40.3 Left aortic arch (LAA) with an aberrant right subclavian artery (RSC). (RCC right common carotid artery; LCC left common carotid artery; LSC left subclavian artery; Lig.A ligamentum arteriosum)

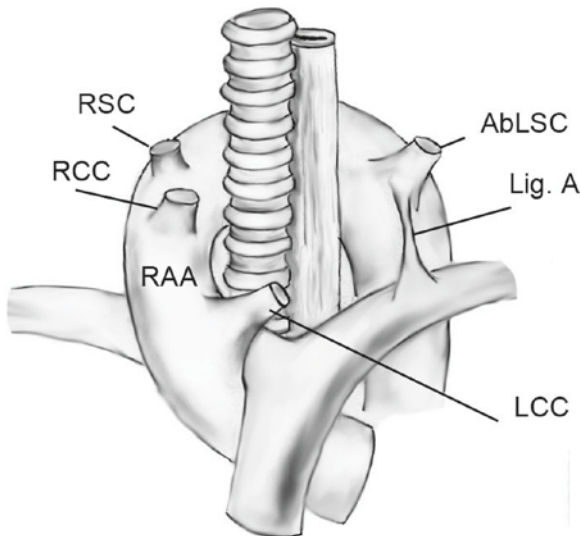


Fig. 40.2 Right aortic arch (RAA) with an aberrant left subclavian artery (AbLSC) and a left ligamentum (Lig.A). (RCC right common carotid artery; LCC left common carotid artery; RSC right subclavian artery)

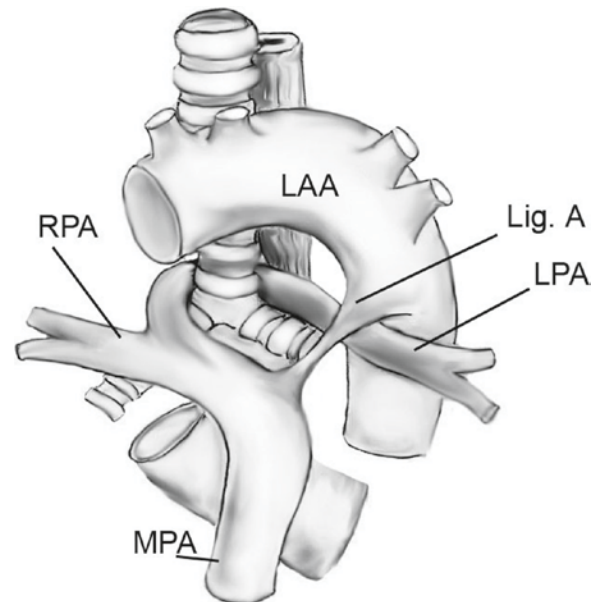


Fig. 40.4 Pulmonary artery sling. (MPA = main pulmonary artery, RPA = right pulmonary artery, LPA = left pulmonary artery, LAA = left aortic arch, Lig.A = ligamentum arteriosum)

may cause dysphagia, but rarely in infancy when diet is largely liquid. However, severely affected infants may show slow feeding, regurgitation, aspiration, and failure to thrive. Infants with a double aortic arch typically present in the newborn period and often have severe symptoms with the classic “barky” cough and nearly constant stridor. Children with a right aortic

arch and left ligamentum frequently present somewhat later in life (3–9 months of age) because the ring is

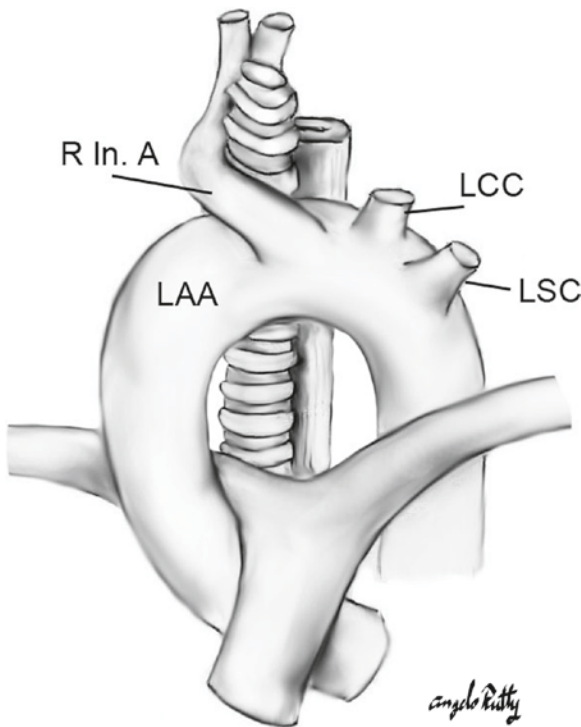


Fig. 40.5 Innominate artery tracheal compression caused by an anomalous origin of the innominate artery (RIn.A) from the aortic arch. (LAA left aortic arch; LCC left common carotid artery; LSC left subclavian artery)

“looser,” being formed partially by the low pressure pulmonary artery and the ligamentum arteriosum [5].

Other congenital anomalies, including intra-cardiac defects, should always be sought in patients with aortic arch anomalies. A right aortic arch is common in patients with tetralogy of Fallot and truncus arteriosus, but a vascular ring is rarely seen in this group. Tracheal anomalies including tracheal rings, absence of the membranous trachea and tracheal stenosis have been reported in infants with pulmonary sling (ring–sling complex) [6].

There is no definitive medical therapy for vascular rings or pulmonary sling, and symptomatic patients should undergo surgical correction as soon as feasible, especially if symptoms are severe. Preoperatively, the patient should be given adequate nutritional support as well as general respiratory care and appropriate treatment of any respiratory tract infection. Usually, surgery should not be unduly delayed because of a respiratory tract infection, since surgical correction of the ring allows more adequate and complete clearing of respiratory secretions.

40.3 Diagnostic Studies

There are a few diagnostic modalities available for evaluation of the child suspected of having a vascular ring.

Barium esophagram used to be the only important tool for diagnosing a vascular ring. The retroesophageal indentation by the abnormal vessel is persistent in all views, differentiating it from a peristaltic wave. Pulmonary sling is the only vascular abnormality which causes an anterior rather than posterior esophageal indentation. Barium esophagram is normal in patients with an anomalous innominate artery. Other more definitive modalities are now available and it is less frequently used.

Bronchoscopy is a very important diagnostic tool for infants and young children with stridor, and in the presence of a vascular ring, shows an extrinsic, often pulsatile, compression of the trachea. Bronchoscopy is also the diagnostic procedure of choice for infants with complete tracheal rings and innominate artery compression syndrome, where there is a pulsatile oblique anterior compression of the trachea. When the bronchoscope is pressed onto the pulsatile area the right brachial pulse may diminish or disappear.

Echocardiography is useful for making the diagnosis of most of vascular rings and pulmonary artery sling, but is limited because a vascular segment without a lumen and the trachea cannot be visualized. Nonetheless, the sidedness of the aortic arch and direction and origins of the brachiocephalic arteries provide useful information,

Computed tomography (CT) and *magnetic resonance imaging (MRI)* are useful as they identify both the vascular structures and the tracheo-bronchial anatomy. It is a vital part of preoperative assessment and planning for congenital tracheal stenosis [6]. These studies are employed if the diagnosis is not clear from the other procedures listed above.

Angiography is rarely needed for the diagnosis of a vascular ring, but in unusual cases it can offer information not available from any other modalities.

40.4 Surgical Management

In general, vascular rings are approached through a left lateral thoracotomy and do not require cardiopulmonary bypass. In a double aortic arch the smaller of

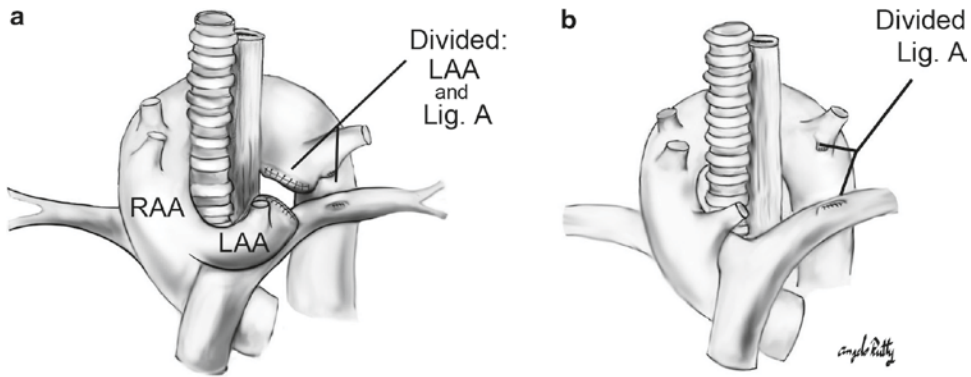


Fig. 40.6 (a) Repaired Double Aortic Arch; the smaller left aortic arch (LAA) and the ligamentum arteriosum (Lig.A) have been divided. (b) Repaired right aortic arch with aberrant LSCA; the ligamentum arteriosum has been divided

the two arches is divided (Fig. 40.6). Arch division should always be done between vascular clamps with oversewing of the divided stumps, because simple ligation and division has been associated with ligature slippage and subsequent catastrophic hemorrhage. In patients with a right aortic arch and an aberrant left subclavian artery the ligamentum arteriosum requires division (Fig. 40.6). If there is an associated Kommerell's diverticulum, it is either resected and oversewn or pexed to the fascia of the vertebral column to prevent compression of the trachea and/or esophagus from the diverticulum itself.

Our approach to patients with innominate artery compression involves an aortopexy via a right parasternal incision, affixing the proximal innominate artery to the posterior aspect of the sternum (Fig. 40.7). Another option involves division and re-implantation of the innominate artery through midsternal approach instead of above mentioned suspension technique.

Patients with a pulmonary artery sling are repaired via a median sternotomy approach and with the use of cardiopulmonary bypass. The left pulmonary artery is transected at its origin from the right pulmonary artery and re-implanted on the left lateral aspect of the main pulmonary (Fig. 40.8). Also, if the patient has complete tracheal rings (50% of patients) it is best managed at the same time.

40.5 Postoperative Management

The postoperative course is usually benign and in the absence of severe tracheomalacia most of the patients

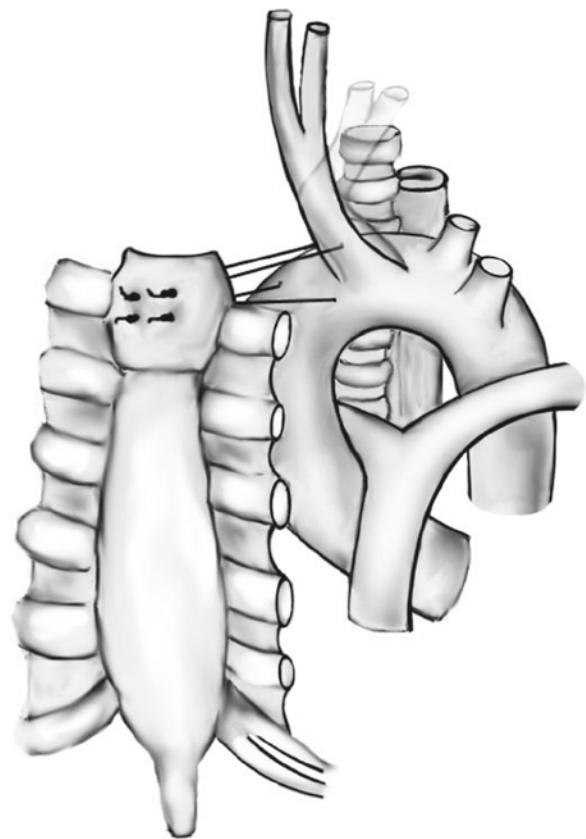


Fig. 40.7 Aortopexy. Suspension sutures are placed at the origin of the innominate artery and then advanced through the sternum. Once on tension, the sutures will reposition the proximal aortic arch and innominate artery in a more anterior position in the mediastinum, relieving the tracheal compression

usually do not require admission to the pediatric critical care unit. The majority of them are extubated in the operating room, monitored in the hospital for 24–48 h,

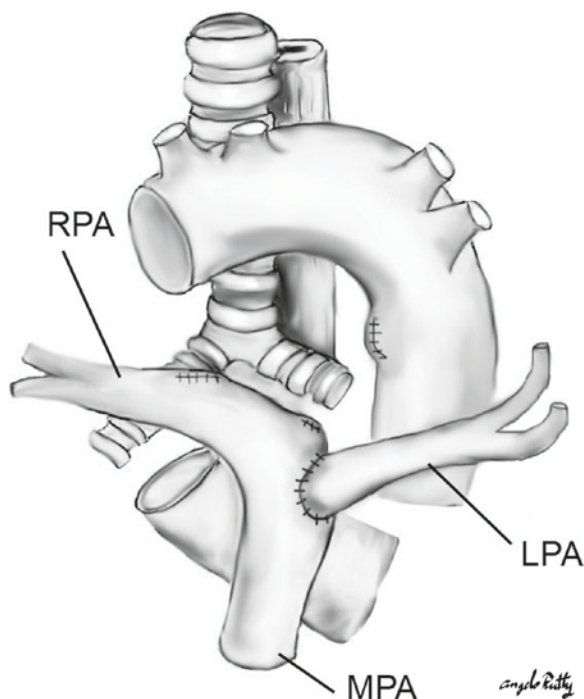


Fig. 40.8 Repaired Pulmonary Artery Sling. The left pulmonary artery (LPA) has been separated from the right pulmonary artery (RPA) and then anastomosed to the main pulmonary artery (MPA); the ligamentum arteriosum was divided.

and then discharged. Invasive monitoring in the form of arterial catheter and central venous catheter is usually used intra-operatively and discontinued upon transfer to the postoperative care area.

Pain from the thoracotomy incision could interfere with breathing efforts and lead to atelectasis and pneumonia.

Injuries to the phrenic and recurrent laryngeal nerve are uncommon.

Excessive bleeding is also a rare postoperative complication.

However, disruption of the thoracic duct may rarely occur.

40.6 Long-term Outlook

Long-term results of the patients operated for vascular ring spectrum are generally favorable. Most infants experience significant improvement in respiratory status

immediately after relieving from the compression caused by vascular ring. However, complete resolution of the symptoms may take a few weeks to months with gradual resolution of tracheo-bronchomalacia. Nonetheless, 92–95% of them are expected to be free of their respiratory symptoms by the end of first postoperative year [7].

Among those with less optimal long-term results are patients with a pulmonary sling with and without complete tracheal rings and those with severe associated congenital cardiac defects. In patients with a severely deformed trachea or tracheomalacia, additional reconstruction procedures such as a tracheal graft with autologous rib may be required to alleviate life threatening respiratory problem [8]. A number of patients continue to show evidence of some pulmonary function abnormalities years after surgery [9]. In Baker's series of patients with pulmonary sling, the patency of the left pulmonary artery re-anastomosed through median sternotomy and while using cardiopulmonary bypass was 100% with the mean blood flow to the left lung by nuclear scan being 42% [7].

The majority of institutions performing surgeries for vascular anomalies on infants with no intra-cardiac or extracardiac defects report virtually no mortality.

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Chapter 41

Takayasu Arteritis

Yuliya A. Domnina and Ricardo Muñoz

41.1 Anatomy

Takayasu arteritis (TakA), described by Mikito Takayasu in 1908, is a chronic, large-vessel vasculitis of unknown etiology that primarily affects the aorta, the proximal portions of its branches, and the pulmonary arteries. In this illness, progressive and sustained inflammation of involved vessels leads to stenotic lesions and aneurysm formation. TakA, also known as “Pulseless disease,” is a rare disorder with an incidence of 1.2–2.6 cases/million/year and occurring most frequently in the Far East and Africa [1]. Strong association with tuberculosis was found in patients afflicted with TakA in those parts of the world. Lower rates are observed among white European and North American descendants. This disease usually affects young patients with a female-to-male ratio of 9:1. The peak incidence occurs in the third decade of life; however, the disease has been identified in patients as young as 6 months old [2].

41.2 Pathophysiology

The cause of TakA is unknown, but immunogenetic factors appear to play a major role in pathogenesis. TakA has been reported in identical twins, leading to hypotheses of a hereditary basis for the disease. In Japan and Korea, TakA has been found to be associated with human leukocyte antigens HLA-A10, B5,

Bw52, DR2, and DR4, although these associations have not been confirmed in Western studies. In the US, TakA has been found to be connected with HLA-B22 [3]. The initial acute phase, or the prepulseless or active inflammatory stage, of vasculitis is characterized by the thickening of the aortic wall with or without alterations in the arterial lumen. Microscopic studies reveal pan-arteritis involving all layers of the artery, particularly the media. The destruction of the elastic membrane and infiltration of all layers by lymphoid and plasma cells are pronounced. The intima is thickened due to proliferation of the endothelium as well as edema. In the second phase of the disease, the progressive inflammatory process manifests through the formation of granulomas composed of macrophages, epithelioid, and giant cells. Finally, the pulseless end-stage sclerotic phase demonstrates alterations in the arterial lumen and is characterized by stenosis (seen in 90–100% of TakA patients), occlusion/thrombosis, atypical coarctation, dilation and/or aneurysms. Frequently, stenosis and obstruction predominate, but dilation and aneurysms are not rare [3].

41.3 Clinical Presentation and Diagnostic Tools

During the acute phase of TakA, constitutional symptoms such as headaches, dizziness, fever, fatigue, weight loss, myalgia, arthralgia, abdominal pain, nausea, cough, lymphadenopathy, anemia, and transient skin rashes are prevalent. Due to the nonspecific nature of these signs, the diagnosis of the disease is difficult and frequently delayed for months to years.

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Elevated erythrocyte sedimentation rate (ESR) has been used as a marker of disease activity. Other acute phase reactants have also been used as good activity markers, including alpha-1 acid-glycoprotein, C-reactive protein, electrophoretic alpha-2-globulin, and haptoglobin levels. However, normal acute phase reactants do not assure complete disease remission [4].

During the early presentation of the disease the aortography may demonstrate only thickening of the walls of the aorta and its major branches.

CT angiography and magnetic resonance arteriography have proven to be more reliable tests to detect the presence of TakA at this point.

Progression of the disease into the late sclerotic phase adds symptoms related to ischemia: transient ischemic attack, seizures, ischemic stroke, visual disturbances, abdominal angina, extremity claudication, large vessels bruits, absent pulses, and renovascular hypertension. The symptoms of cardiac involvement are related to aortic dilation and may present as aortic insufficiency, congestive heart failure, and arrhythmia. Aortic aneurysms, thrombus formation, and rupture are the common causes of death in TakA.

Criteria for the classification of TakA were developed by comparing 63 patients with the disease versus 744 control patients with other forms of vasculitis. Six criteria were selected for the traditional format classification: onset at age ≤ 40 years, claudication of an extremity, decreased brachial artery pulse, >10 mmHg difference in systolic blood pressure between arms, a bruit over the subclavian arteries or the aorta, and arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities. The presence of three or more of these six criteria demonstrated a sensitivity of 90.5% and a specificity of 97.8% [5].

Arteriography is the gold standard of radiologic diagnosis of TakA as well as an intermittent test to monitor the progression of the disease and pre-intervention. Sequential imaging evaluations have revealed disease progression (as determined by the presence of new vascular lesions) in over 60% of patients with clinically stable profiles and normal ESRs [4]. However, renal toxicity from the use of contrast dye and radiation exposure are negative aspects of angiography and could be avoided by the use of magnetic resonance arteriography. Arteriography often demonstrates long, smooth, tapered narrowings or occlusions. Echocardiography can aid in the evaluation

of the ascending aorta and transverse arch. Duplex color-flow Doppler may reveal thickening of the intima, stenosis, and thrombi in the carotid, subclavian arteries, and the abdominal aorta and its branches.

41.4 Treatment

The treatment of TakA in the active phase consists of the control of inflammation with the use of steroids alone or in combination with other immunosuppressive agents. In the pulseless phase, aneurysmal dilatation and multiple stenotic lesions with resultant ischemia in the cerebral, coronary, peripheral arterial, and renal territories could lead to severe physiologic consequences and require surgical or endovascular intervention. Currently, daily high-dose *corticosteroid* administration 1–2 mg/kg for 4–6 weeks is the accepted initial therapy with remission attained in 50% of patients. High-dose therapy is subsequently weaned over 4–6 weeks while monitoring for signs of relapse. Forty percent of patients will relapse on steroid taper. In these patients or in patients with steroid-resistant disease, treatment with weekly intravenous *methotrexate* (adult dose 15–25 mg/week; pediatric 5–15 mg/m²/week) or oral *cyclophosphamide* (1–2 mg/kg/day) have allowed remission to be achieved and maintained [4]. *Cyclosporine* could be used as an alternative therapy offering an improved toxicity profile. Treatment of glucocorticoid resistant or relapsing TA with *anti-TNF therapy* (Etanercept and/or Infliximab) has demonstrated promising results. In one study, 14 of 15 patients with relapsing disease treated with anti-TNF therapy showed improvement and four patients were able to achieve $>50\%$ reduction in the glucocorticoid requirement. Sustained remission was reported in 10 of 15 patients, who subsequently were able to discontinue glucocorticoid therapy [6]. *Mycophenolate mofetil* (MMF) is another agent used to treat individuals with glucocorticoid resistant disease. MMF therapy has been seen to reduce clinical disease activity and to improve laboratory parameters in patients already treated with another immunosuppressive agent (methotrexate, azathioprine, or chlorambucil) who relapsed during steroid taper. MMF as a first line immunosuppressive drug has also been shown in studies to be well tolerated for an average of 23.3 months in a dose of 2 g/day [7].

41.5 Surgical Management

Clinical presentation of TakA is multifaceted and patients with this disease require a coordinated multidisciplinary approach for optimal care and outcome. In the chronic phase, the objectives of the clinical treatment are not always achieved by medical therapy alone. Surgical and percutaneous interventions, including bypass procedures, percutaneous transluminal angioplasty, stent placement, aortic valve replacement, and aortic root repair, are frequently performed in the chronic phase.

Aortic valvular regurgitation due to progressive aortic root dilation and resultant congestive heart failure may occur in patients with TakA. Surgical management of this condition may involve placement of a prosthetic valve, but is often complicated by occurrence of prosthetic valve detachment or formation of a pseudoaneurysm at the suture line. Postoperative morbidity includes continued progressive dilatation of the aortic root. Hence, aortic root replacement with a composite graft for aortic regurgitation associated with aortitis is indicated in view of the propensity for development of prosthetic valve detachment [8]. Active inflammation confirmed in intraoperative specimens was found to be a significant risk factor for valve or graft detachment [9].

Diffuse, multifocal, and ostial vessel involvement in TakA makes the surgical revascularization with bypass grafting difficult and is also associated with a high rate of restenosis [10]. The percutaneous correction of vessel obstructions at multiple sites emerged as a viable alternative therapeutic possibility with no contraindications even in the presence of active arterial inflammation. Restenosis is a known complication of the percutaneous procedure as well and repeated interventions are frequently necessary. A lower restenosis rate is observed when the vascular interventions are performed in the stable stage and when postinterventional immunosuppressive treatment is implemented. Percutaneous balloon angioplasty of the aorta and stent implantation in children with TakA has been reported to normalize systolic and diastolic blood pressures with improvement in exercise tolerance, congestive heart failure, and no complications up to 3 years [11, 12]. Short segment stenoses were found to restenose less frequently than long segment aortic stenoses. Percutaneous balloon angioplasty of renal artery stenoses in children with TakA has been found

to be a safe procedure with a significant decrease in arterial blood pressure and decreased requirements for antihypertensives. However, a 25% rate of restenosis has been seen on the 4–72 months follow up [13]. The restenosis rates have been improved by stent implantation. A possible alternative yet to be evaluated in a larger population of patients with TakA is the use of immunosuppressant-eluting stents (sirolimus, paclitaxel), which inhibit endothelial proliferation and endovascular inflammation and, thereby, decrease rates of restenosis.

41.6 Management in the Intensive Care Unit

TakA patients are rarely admitted to the intensive care unit unless the admission is related to complications of the disease, such as dehydration, hemoptysis, neurological deficits, seizures, single or multiple vessel occlusions, extremity claudication, rupture of aortic aneurysm, systemic hypertension, congestive heart failure, angina, side effects of immunosuppressive agents, and postinterventional catheterization.

41.7 Long-Term Outlook

Morbidity and mortality in patients with TakA are directly correlated with the vascular territories involved, complications (Takayasu's retinopathy, hypertension, aortic regurgitation, aortic root dilation, aneurysm, carotid artery stenosis, seizures, and stroke), and the progressive course of the disease. Currently, immunosuppressive agents added to corticosteroids can bring TakA into remission in majority of patients. However, significant morbidities are associated with these immunosuppressive therapies and are particularly seen in patients using high-dose steroids (diabetes, osteoporosis, hypertension, cataracts, and systemic infections). New drugs that target intimal hyperplasia, as well as drug-eluting stents, deserve to be studied for possible utility as adjuncts to present treatments [14]. Persistent inflammation and endothelial dysfunction place patients with TA at risk for premature

atherosclerosis. Despite these potential life-threatening complications, 5–10 year survival rates have been reported to be 70–90% [15].

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Chapter 42

Aortic Dissection

Yuliya A. Domnina and Victor O. Morell

42.1 Anatomy

Spontaneous aortic dissection (AoD) is a rare, life-threatening disease, yet it is the most common catastrophe of the aorta with a high mortality rate reported around 22–24%. It has a higher prevalence in a population with risk factors such as dilation of the aorta, connective tissue disorders, vasculitis, certain congenital heart diseases, age, hypertension, and dyslipidemia. However, even in the absence of risk factors, non-traumatic rupture of a dissecting aorta may occur. Patients at particular risk for aortic dissection could be classified as belonging to one of the following groups:

- *Congenital heart disease* (e.g., d-TGA, post-Ross procedure, Tetralogy of Fallot (TOF), Bicuspid Aortic Valve)
- *Non-syndromic aortopathies* (Familial Thoracic Aortic Aneurysm, Familial Aortic Dissection, Aortic Dilation/Adult Polycystic Kidney Disease, Hypertension-related Aortopathy)
- *Syndromic aortopathies* (Marfan Syndrome, vascular Ehlers-Danlos Syndrome, Loeys-Dietz Syndrome, Turner Syndrome, Noonan Syndrome)
- *Other systemic conditions* leading to aortic dilation (Osteogenesis Imperfecta, Homocystinuria, Familial Hypercholesterolemia, increased incidence was found in pregnancy, tertiary syphilis, cocaine abuse).

In a study by Januzzi et al of cohort of 951 patients diagnosed with AoD, younger patients <40 years old

compared with older patients >40 years old, had unique risk factors for dissection including Marfan syndrome, bicuspid aortic valve, and larger aortic dimensions. The mortality in the younger group of patients was similar to that of an older group [1]. The most common site of dissection was the first few centimeters of the ascending aorta, with 90% occurring within 10 cm of the aortic valve. The second most common site was just distal to the left subclavian artery. Five to ten percent of dissections do not have an obvious intimal tear. Dissections of the thoracic aorta have been classified anatomically according to De Bakey's classification (Fig. 42.1):

- *Type I*: The dissection involves the ascending aorta, aortic arch, and descending aorta.
- *Type II*: The dissection is localized to the ascending aorta.
- *Type III*: The dissection involves the descending aorta distal to the left subclavian artery, with further subdivision based on the extension of the dissection: – subtype IIIa: extension of the dissection proximally and distally. – subtype IIIb: extension of the dissection only distally [2].

A simplified classification has been introduced by the Stanford group (Fig. 42.2) and is based on the presence (Type A) or absence (Type B) of dissection of the ascending aorta. Type A involves the ascending aorta and type B does not.

42.2 Pathophysiology

Ascending aortic aneurysms and dissections have a distinctive pathophysiology reflected by a bimodal age distribution (presenting between the fourth and the

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Fig. 42.1 DeBakey's Classification of the aortic dissection

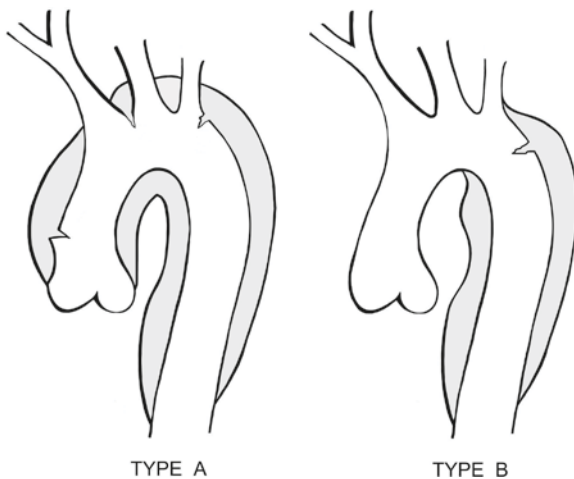
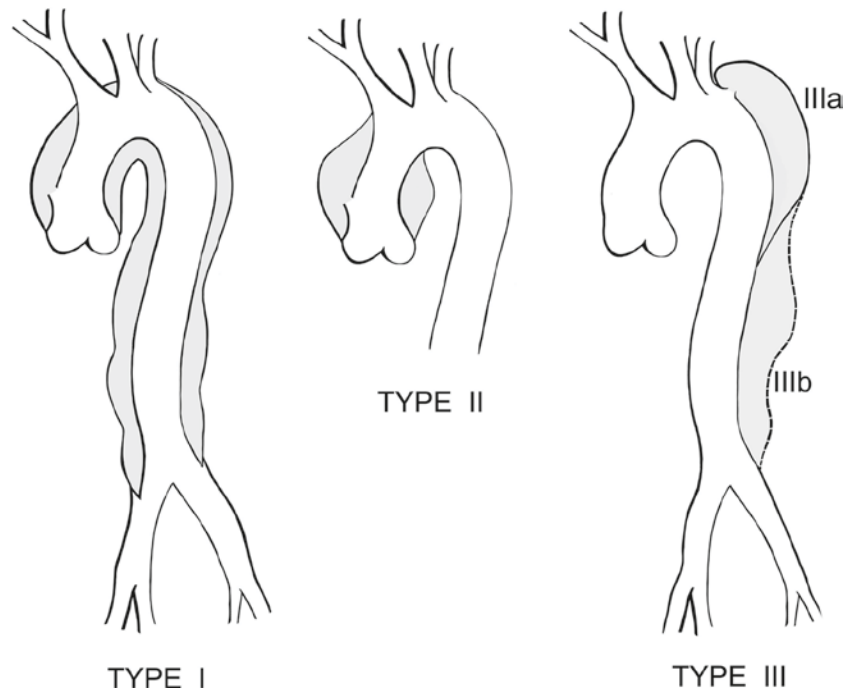


Fig. 42.2 Stanford Classification

sixth decades of life) and by hereditary predisposition. Patients with syndromic aortopathies tend to have dissection earlier and frequently have an atypical clinical picture at presentation. All ascending aortic aneurysms have similar histopathologic changes as reported by Gleason, and include: (a) elastolysis (or fragmentation of elastic fibers), (b) noninflammatory smooth muscle cell loss and dedifferentiation, (c) mucoid degeneration and medial degeneration – collectively termed cystic medial

degeneration (cystic medial necrosis). Degenerative aneurysms of the descending and abdominal aorta tend to present and dissect in patients over 65 years of age, and have more typical characteristics of an atherosclerotic process [3]. The initiating event of aortic dissection is a tear in the intimal layer, followed by the formation and propagation of a sub-intimal hematoma. The propagating hematoma creates a false lumen or double-barreled aorta. It can reduce blood flow to the major arteries arising from the aorta and results in a varied symptomatology. The intimal tear is more likely to occur in the ascending aorta (65%) or in the descending thoracic aorta (20%) with a fewer cases originating from the transverse arch (10%) and 5% from the descending aorta [4].

42.3 Clinical Presentation

Sudden, severe chest pain is the most common presenting symptom in patients with an aortic dissection. Aortic dissection should always be considered in the differential diagnosis of all patients presenting with chest pain and in particular in patients with known conditions or high risk factors for AoD. Location of pain and irradiation

usually corresponds to the affected area of the aorta and the vessels originating from the aorta that might be involved in the dissection. Sub-sternal chest pain frequently mimics chest pain of acute myocardial infarction and is associated with ascending aorta or aortic root dissection. Dissection in this area could cause interruption of coronary flow and result in myocardial ischemia. Pain that is described in the neck, jaw, or inter-scapular area may indicate that the dissection involves transverse arch with head and neck vessels or descending thoracic aorta. Aortic dissection could be painless. Painless dissection is more common in patients with syndromic aortopathies. Other physical findings may include: hypotension or hypertension, wide pulse pressure and new diastolic murmur with aortic insufficiency, tachycardia, muffled heart sounds, dyspnea, orthopnea, dysphagia, hoarseness, pericardial or pleural effusion, and ECG changes. Neurologic symptoms are common at presentation such as syncope and seizures, altered mental status, focal motor, or sensory neurologic deficits (paresthesias, hemiparesis, and paraplegias).

42.4 Preoperative Management

The armamentarium of tests used to diagnose aortic dissection includes CT and CT-angiogram of the chest with iodinated contrast material (Fig. 42.3), transthoracic and transesophageal echocardiogram, magnetic resonance angiogram (MRA) of the aorta and aortogram. Medical treatment is recommended for uncomplicated distal dissection, stable patients with

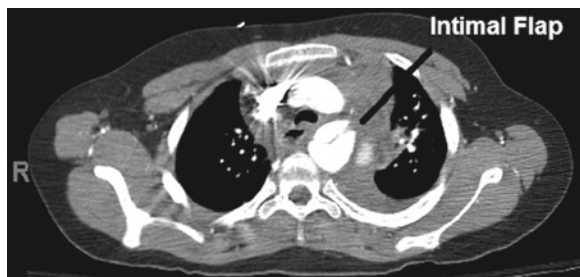


Fig. 42.3 Type B Aortic Dissection. A 13 year-old presented to the emergency room with severe back pain. A CT-scan of the chest revealed an intimal flap (arrow) in the thoracic descending aorta. Also, there is a large mediastinal hematoma and a left pleural effusion

isolated arch dissection, and chronic dissection (2 weeks or later after onset) [4].

An ECG must be obtained in all patients.

In the international registry of aortic dissection (IRAD), the first diagnostic test was *transthoracic* (TTE) and *transesophageal* (TEE) *echocardiography* in 33% of patients suspected to have AoD, *CT* in 61%, *MRI* in 2%, and *angiography* in 4% [5]. The demonstration of the intimal flap separating two lumina is the basis for diagnosis of aortic dissection. If the false lumen is completely thrombosed, central displacement of the intimal flap, calcification or separation of intimal layers can be regarded as definitive signs of aortic dissection. The other diagnostic goals include:

1. Localization of the intimal tear.
2. Evaluation of the extent of dissection.
3. Assessment of side branch involvement.
4. Definition between communicating and noncommunicating dissection.
5. Assessment of aortic regurgitation.
6. Detection of extravasation (periaortic or mediastinal hematoma, pleural or pericardial effusion) [6].

While arranging for appropriate diagnostic confirmatory test, patients should be *admitted to the intensive care unit* for monitoring and treatment. *Two large bore IV lines* should be placed for volume resuscitation and medication administration. An *arterial line* should be placed in the right radial artery as the involvement of the brachiocephalic trunk is rarely seen. *Periodic pressure monitoring of all four extremities* is indicated to rule out pseudo-hypotension due to obstruction of the aortic branches.

It is of paramount importance to provide *pain relievers* as severe pain of aortic dissection in itself stimulates sympathetic output and could lead to elevation of blood pressure, in turn stimulating propagation of dissection. Morphine sulfate in the age and size appropriate doses is a drug of choice in hemodynamically stable patients.

Blood pressure needs to be maintained slightly under normal values for age as long as all organs receive adequate perfusion. Beta-blockers as a class seem to be the agents of choice for hypertension associated with AoD due to its most prominent effect on the reduction of the force of left ventricular ejection dP/dt . Esmolol, propranolol, or labetalol could be administered as continuous or intermittent intravenous infusions. If beta-blockers are contraindicated, calcium

channel blockers may be considered. In general, it is advisable to combine beta-blockers (titrating dose to achieve physiologic bradycardia) and vasodilators. The use of only a vasodilator such as sodium nitroprusside can increase the dP/dT and potentially exacerbate the dissection. The goal of lowering of systolic blood pressure must be modified if oliguria or neurologic symptoms develop. The combination of fenoldopam and beta-blockers is a good choice in the setting of renal insufficiency good choice. It is important to be aware that in cases of refractory hypertension, the aortic dissection flap could have extended into the renal arteries, hypertension may be renin-related and careful administration of an intravenous angiotensin-converting enzyme inhibitor should be planned [4].

Hemodynamically unstable patients need to be intubated and mechanically ventilated and the transfer to the operating room (OR) should occur as soon as possible. TTE or TEE could be performed as the sole diagnostic procedure in the intensive care unit or in the OR in the interest of time. *Careful volume repletion* should be performed if blood sequestration in the false lumen, pleural or pericardial space is suspected [6].

42.5 Surgical Management

Type A dissections require prompt surgical intervention in order to prevent aortic rupture and death. The principles of the surgical repair include the following:

- (a) The elimination of the proximal extension of the dissection, to prevent rupture.
- (b) The reestablishment of intimal continuity, usually requiring resection or exclusion of the intimal tear.
- (c) The elimination of aortic insufficiency, with aortic valve resuspension or valve replacement.

The repair is performed via a median sternotomy incision and with cardiopulmonary bypass. An important technical aspect during the establishment of the extracorporeal circulation is the cannulation of the true arterial lumen to provide adequate end-organ perfusion; femoral artery cannulation is the preferred approach. A period of deep hypothermic circulatory arrest might be required if the repair involves aortic arch.

An interposition tube graft is used to replace the ascending aorta up to the level of the proximal arch (Fig. 42.4). In the presence of significant aortic root

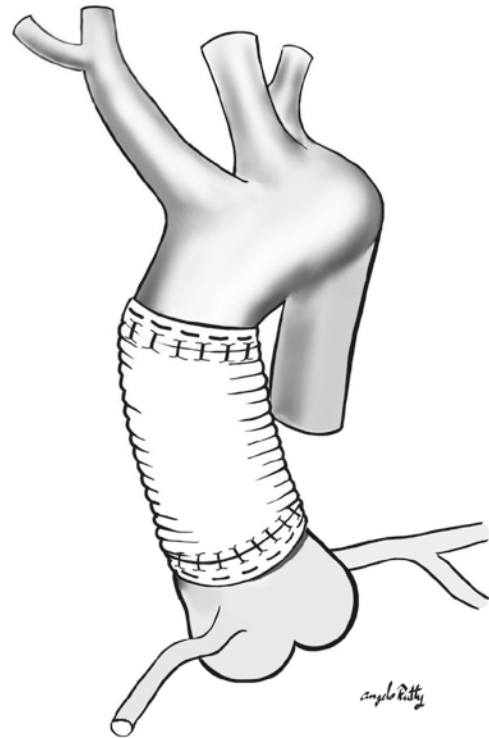


Fig. 42.4 Interposition Graft. The ascending aorta is replaced with a prosthetic conduit; the native aortic root is preserved

damage, especially in patients with Marfan's syndrome or with annulo-aortic ectasia, the recommended surgical repair includes a root replacement, either with a valve-sparing procedure or with placement of a valve-conduit (Bentall procedure) (Fig. 42.5). The hospital mortality rate associated with this type of surgical repair is between 5 and 30% [7, 8].

Type B dissections, in general, do not require acute surgical intervention, except for patients who present with, or develop aortic rupture, persistent pain, or end organ ischemia (renal, hepatic, intestinal, spinal cord, or lower extremities). The surgical approach is through a left thoracotomy and it requires a period of aortic cross-clamping. The repair involves the replacement of the descending thoracic aorta with an interposition graft. In order to prevent spinal cord ischemia (5–20% incidence), some form of distal perfusion technique (partial femoral artery to femoral vein bypass, left atrial to femoral artery bypass, shunt) is frequently utilized. It is also important to reimplant the intercostal arteries. The operative mortality associated with a type B dissection repair is approximately 20% [9].

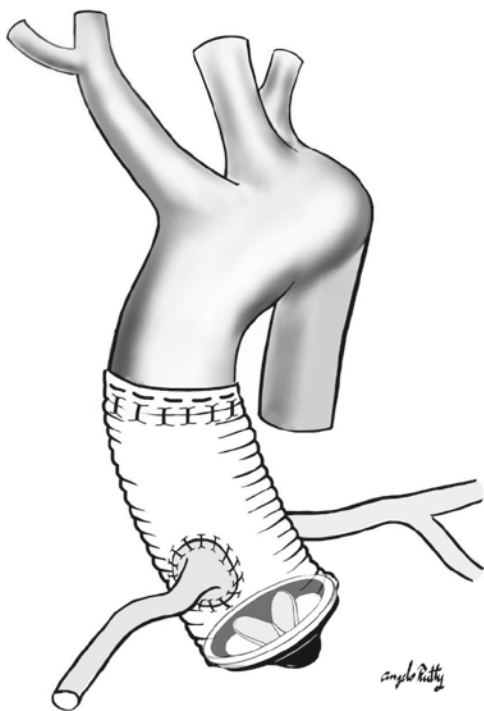


Fig. 42.5 Bentall Procedure. The aortic root is replaced with a mechanical valve-conduit, it requires coronary reimplantation

42.6 Postoperative Management

Postoperative care should be provided in the intensive care unit by the providers experienced in care of cardiac patients.

42.7 Monitoring

Central intravenous line and arterial line are usually placed during the preoperative care or in the OR. Post-repair TEE is frequently obtained in the OR to ascertain quality of the repair: residual valvar insufficiency or stenosis, residual gradient across the anastomosis, coronary flow, and postoperative cardiac function.

42.8 Respiratory management

If the patient was relatively asymptomatic before the surgery, early extubation could be considered, but

it is of a paramount importance that proper analgesia be provided.

42.9 Sedation and pain control

A dexmedetomidine infusion (central sympatholytic, sedative, analgesic, and anxiolytic) at 0.3–1 $\mu\text{g}/\text{kg}/\text{h}$ is an excellent and a safe alternative for a well established regimen of morphine boluses of 0.05–0.1 mg/kg and midazolam 0.05–0.1 mg/kg IV every 1–2 h. Inadequate pain control could lead to stimulation of sympathetic output and hypertension, hence increasing the risk of bleeding.

42.10 Cardiovascular management

Hypertension is a common problem after repair, especially if it was present in the preoperative period. Patients with syndromic aortopathies frequently manifest with aortic dissection without evidence of hypertension. Systolic hypertension usually occurs within the first 24–72 h, associated with carotid baroreceptor stimulation and frequently resistant to arterial vasodilators like nitroprusside. It is not infrequent that doses of nitroprusside as high as 10 $\mu\text{g}/\text{kg}/\text{min}$ to control blood pressure are required. If nitroprusside is used in high doses (6–10 $\mu\text{g}/\text{kg}/\text{min}$), concentrations of methemoglobin, should be monitored closely at least every 12 h. Cyanide levels should also be measured, especially when higher doses are used for more than 48 h, or if renal impairment is present. Arterial vasodilators are frequently supplemented with intravenous beta-blockers. Esmolol in a continuous infusion form is a drug of choice. A loading dose of 100–500 $\mu\text{g}/\text{kg}$ IV should be administered carefully over 10–20 min, especially if the patient has a history of decreased cardiac function. A maintenance dose of 25–250 $\mu\text{g}/\text{kg}/\text{min}$ is administered as a continuous infusion under strict monitoring conditions. Esmolol could cause bronchospasm, nausea and vomiting, congestive heart failure in the patient with decreased cardiac function and rate dependent cardiac output. Once enteral intake is resumed, ACE inhibitors such as captopril or enalapril could be used for the long-term blood pressure control.

42.11 Long-term Outlook

A dramatic improvement has been observed in survival rates of patients with Aortic dissections due to increased awareness, improved diagnostic modalities, and advances in operative repair and postoperative surveillance. The IRAD study reported a mortality of 27 and 29% for type A and type B dissection in 464 patients after surgical therapy and 53% and 9% after medical therapy respectively [10]. The best prognosis is reported for noncommunicating and type B dissection limited to the descending aorta, with 80 and 86% 2 year survival rate [6]. Close follow up is indicated for the patient with aortic dissection and it includes the assessment of signs of aortic expansion, aneurysm formation, signs of leakage at anastomoses, and organ malperfusion. The single most important factor is the excellent blood pressure control to bellow or at age appropriate norms or <135/80 mmHg for an adult patient. After discharge, regular outpatient visits at 1, 3, 6, and 12 months every year thereafter is recommended. Regular imaging with TTE echocardiography at follow up visits is indicated. If more detailed imaging is required, MRI is a well-accepted first choice [6].

All patients with dilated aorta and Marfan syndrome, vascular EDS, Loyez-Dietz syndrome, bicuspid aortic valve, or a family history of dissection or thoracic aortic aneurysm, need regular aortic surveillance with cross-sectional imaging and echocardiography, biannually after the initial meeting and then at least yearly thereafter. All patients with a thoracic aortic diameter at any level that exceeds an aortic index (measured/predicted diameter indexed to body surface area) of 1.3 or an absolute diameter of 40 mm require vigilant thoracic aortic surveillance. Elective aortic replacement should be considered for Marfan patients with a maximal aortic root diameter over 43 mm, and for the patients

with BAV or familial aneurysm/dissection patients with a maximal ascending aortic diameter of 45 mm [3]. Elective repair should also be strongly considered in patients with annual growth of ascending aorta >1 cm in diameter. Recent medication trials of ACE inhibitors and Angiotensin II receptor blockers may help control aortic dilation in Marfan patients.

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Chapter 43

Tracheal Reconstruction

Nick Pigott and Martin Elliott

43.1 Introduction

Tracheal reconstruction in children is usually performed for various types of congenital or acquired stenoses. This chapter concentrates principally on these and not on sub-glottic stenosis.

The incidence of severe tracheal stenosis requiring intervention in childhood is low (in the United Kingdom, perhaps 1.3 patients per million children aged <16 per year), but this patient group has consumed disproportionate resources and, until recently, short and long term results were poor. Over the last 10 years there have been significant improvements in all aspects of care for these patients and the outlook is now considerably improved.

43.2 Development and Anatomy of the trachea

Three-and-a-half into weeks in the development of a human embryo, a shallow laryngo-tracheal groove develops along the mid-ventral floor of the foregut endoderm near the level of the last pharyngeal arch. This groove deepens and, by the fourth week, becomes a blind outgrowth (the laryngo-tracheal bud) extending caudally and anteriorly to the esophagus. As the bud grows, it differentiates into the future larynx and the

lower respiratory system. The middle portion of this bud becomes the trachea. The distal end divides into two lung buds which develop into the right and left bronchi and lungs.

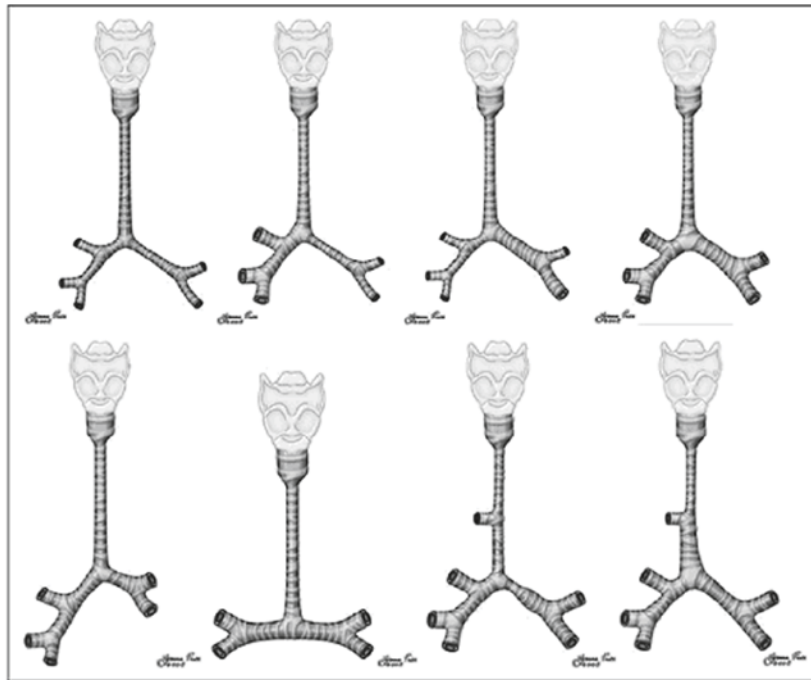
During the eighth week of gestation, the splanchnic mesoderm surrounding the respiratory diverticulum of the endodermal foregut begins to differentiate into primitive cartilage and smooth muscle. By the 10th week, this cartilage migrates around the primitive trachea forming segmented, C-shaped tracheal rings [1].

43.3 Morphology and associated lesions

Tracheal stenosis is generally described as short, medium, or long segment. Short segment tracheal stenosis is usually either a tracheal web or one or two isolated complete tracheal rings, and occasionally post-intubation stenosis. A tracheal web consists of a layer of tissue draped across the tracheal lumen [2]. While the thickness of the web varies, no deformity or abnormality of the underlying cartilage framework exists (in contrast to tracheal stenosis). Treatment consists of rupturing the web, usually by balloon dilatation, although laser dilation was used in the past. For isolated complete tracheal rings, local resection and end-to-end repair is preferred.

Congenital tracheal stenosis may affect varying proportions of the trachea and is usually associated with complete tracheal rings [3]. There is no agreed explanation for the origin of complete tracheal rings. It has been proposed that the formation of complete tracheal rings arises from disproportionate growth of the cartilage relative to the posterior tracheal pars membranacea [4]. It has also been suggested that

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The wide variation was seen at the Great Ormond Street Hospital for Children in London over the last decade. The drawings demonstrate the importance of both clear descriptions and the value of diagrams in the classification of these anomalies.

Fig. 43.1 Variation in morphology of congenital tracheal stenosis (From 25)

an intrinsic field defect in the cervical splanchnic mesenchyme may account for the presence of complete tracheal rings and the frequent association with abnormal vasculature [5]. There is a wide variety of tracheal stenotic morphology (see Fig. 43.1), but no agreed classification. However, long segment stenosis is usually defined as comprising $>50\%$ of the length of the trachea. Accurate description of the morphology is important when planning treatment and comparing outcomes. The degree and length of the narrowing should also be recorded, either from quantitative imaging or at surgery. The narrowing can be severe and self-evidently life-threatening. In a series of 52 of our own patients with tracheal stenosis managed by slide tracheoplasty [6], the median diameter of the trachea was 1.8 mm. It takes little imagination to appreciate the consequences of even minor degrees of mucosal edema in these circumstances.

Congenital tracheal stenosis is frequently associated with other congenital anomalies, most commonly left pulmonary artery sling (60% in our own center), but also including other vascular and intracardiac lesions of varying severity.

43.4 Clinical presentation

The symptoms observed with major tracheal abnormalities are a consequence of reduction in airway diameter. In general, severe narrowing leads to earlier presentation. Some children start off well, but either outgrow their stenotic airway, or present with a minor upper respiratory tract infection that causes mucosal edema and sudden obstruction of the already narrow airway. The narrow segment may also act as a source of positive end-expiratory pressure for more distal airways, disguising malacia which may present after repair as a problem in its own right.

A minority of patients referred for investigation and management of congenital tracheal stenosis have only inspiratory and, usually, a dominant expiratory stridor as their primary symptoms. Such patients can often be investigated as outpatients. Sometimes, complete tracheal rings can grow, and if the airway is not critically narrow one may be able to follow these patients without surgical intervention. However, the decision to leave them alone can be difficult and careful monitoring is required, especially during the winter (because of

increased frequency of upper respiratory infections and thus mucosal edema) or periods of somatic growth when the complete rings may not keep pace. We and others have small numbers of such patients under surveillance [7]

The timing of presentation varies with the severity of both the stenosis and the associated cardiovascular lesions. Those that present in the neonatal period have the most severe problems, and the respiratory demands of heart failure make early presentation even more likely. Others present later, as they outgrow the stenosis, develop mucosal edema or vascular compression from a pulmonary artery sling progresses. This is often towards the end of the first year of life.

“Near death” episodes (severe acute airway obstruction, often with peripheral air-trapping) are common, and many parents have had the distressing experience of having had to resuscitate their own children. Frequently, this is precipitated by a more severe upper respiratory tract infection as mucosal swelling that further restricts an already critically narrow airway.

43.5 Initial management

The primary management must be to establish a secure airway accompanied by a stable respiratory pattern. In the collapsed infant, intubation and ventilation are likely to be necessary. While laryngoscopy is often straightforward, the position, length, and diameter of the tracheal narrowing may make the passage and optimal positioning of an endotracheal tube extremely challenging. Intuitively, the use of Heliox as an inspired gas might be expected to reduce the need for intubation. This has the potential advantage of minimizing instrumentation of an already narrowed airway. Heliox can be used to overcome the resistance to airflow in a narrow tube because of the low density of helium [8–11]. However, published data to support this strategy are lacking. Since many affected children require high inspired oxygen concentrations, Heliox, with its fixed oxygen content, may fail to provide adequate flexibility.

In mild cases, it is sometimes possible to pass an endotracheal tube through the stenosis by accepting a significantly smaller tube size than that is ideal for the patient. However, this should not be done if significant force is required. A traumatized airway is more likely

to become edematous and complicate later surgical repair. Once placed, it is imperative that the tube is well secured. Excellent sedation is essential with a low threshold for neuromuscular blockade.

Routine monitoring should include capnography, oximetry, and regular arterial blood gas analyses. If adequate ventilation proves impossible (progressive respiratory acidosis and/or hypoxemia refractory to ventilatory manipulation), ECMO should be considered [12–18] pending investigation and definitive repair.

In our experience, it is almost never necessary to perform a preoperative tracheostomy. Indeed, we believe every effort should be made to avoid it, since it may compromise subsequent tracheal repair (slide tracheoplasty, in particular).

As soon as ‘stable’ ventilation is achieved the child should be transferred to a specialist unit. Such a unit must be experienced in pediatric airway management and have access to ENT, cardiothoracic surgery, and interventional radiology services. Our practice has been to take a multidisciplinary approach at the outset with a dedicated tracheal team having representation from cardiothoracic surgery, interventional radiology, ENT, respiratory medicine, physiotherapy, nursing, and intensive care. Such a team has been shown to improve outcomes and reduce costs [19]. Transfer can be extremely hazardous and, in our view, should only be undertaken by an experienced retrieval team.

43.6 Investigation

Once the patient is in an appropriate environment, careful assessment and investigation are mandatory. We perform fiber-optic bronchoscopy, fluoroscopic bronchography, and transthoracic echocardiography in all patients. More than half of our patients with tracheal stenosis have associated cardiovascular anomalies, most often a pulmonary artery sling. Computed tomographic angiography (CT) is helpful to assess vascular anatomy, especially if there is doubt on echocardiography. Many patients referred to us have had MRI scans, which have so far proved to be the least useful investigations to plan airway surgery. We suspect this may change as techniques improve.

In our experience, bronchography with the patient breathing spontaneously is a simple, cheap procedure easily combined with bronchoscopy. Bronchography is particularly good at demonstrating dynamic variation at different airway pressures and at distinguishing malacia from stenosis [20]. It also provides an excellent baseline for morphologic classification and subsequent comparative examinations, and is a crucial component of strategies for ballooning and stent placement. Microlaryngobronchoscopy with a rigid endoscope may be needed to assess the larynx and the segment of the trachea above the stenosis if there is any question of obstruction at more than one level. Angiography is now rarely indicated for the assessment of vascular anomalies associated with tracheal stenosis but is occasionally used in the assessment of more complex heart disease, especially pulmonary atresia, ventricular septal defect, and major collaterals.

After completion of investigations, detailed discussion should take place between the clinical team and the family. All treatment options must be presented and emphasis placed upon the uncertainty of long-term outcome, the frequent ups and downs of postoperative care, the invasive and regular surveillance and the limited data available on which to base advice. Long hospital stays are common and may be far from the patient's family home. It will be a very stressful time for these families.

43.7 Surgical management

The management strategy is usually based on the severity and extent of the stenosis and the nature of associated malformations. Our practice is to repair associated lesions concurrently with the trachea whenever possible.

43.8 Short segment stenosis

Classically, primary resection and end-to-end anastomosis is the treatment of choice (see Fig. 43.2). In the last 6 years, we have done six such repairs, with good outcomes except in one boy who had persistent localized malacia requiring medium term, but temporary, tracheostomy support. More recently, balloon dilatation +/- laser division has become a realistic alternative and early results are encouraging [21–23], but need to be confirmed by more centers and longer term follow up. Various stenting techniques have been employed, but few indications for their use in this setting can be seen, where good surgical repair or intermittent ballooning both permit future tracheal growth, which may be inhibited by stenting.

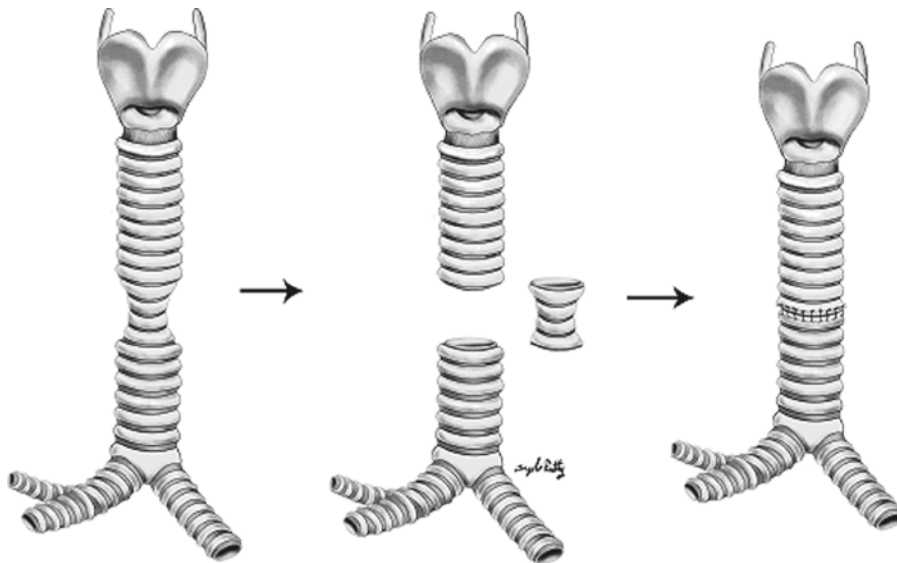


Fig. 43.2 Tracheal Resection with end-to-end anastomosis.

43.9 Medium and long length stenosis

The choice of therapy for these situations depends on the presence or absence of complete tracheal rings. If such rings are absent, then primary resection and end-to-end repair is probably best, and we have established that it is possible to resect the entire trachea with a good long term result [24], although involving second stage reconstruction later in life. If complete tracheal rings are present, slide tracheoplasty (STP) has become the treatment of choice [25]. In this operation, the stenotic segment is transected at its midpoint, the upper and lower segments are incised longitudinally (anteriorly in the upper segment, posteriorly in the lower), the

corners of the segments are trimmed to spatulate them, and the two ends are slid together and sutured using a combination of interrupted and continuous absorbable monofilament sutures (see Fig. 43.3). As a consequence, the circumference of the trachea is doubled, the cross-sectional area quadrupled and the length halved. Since, only native tissue is used normally, ciliated tracheal epithelium is immediately present and subsequent tracheal growth is satisfactory [25–27].

In children, mobilization of the trachea is usually remarkably easy with the consequence that this technique is suitable for surprisingly extensive stenoses, including extension onto the bronchus. The blood supply to the trachea is obviously severely disturbed

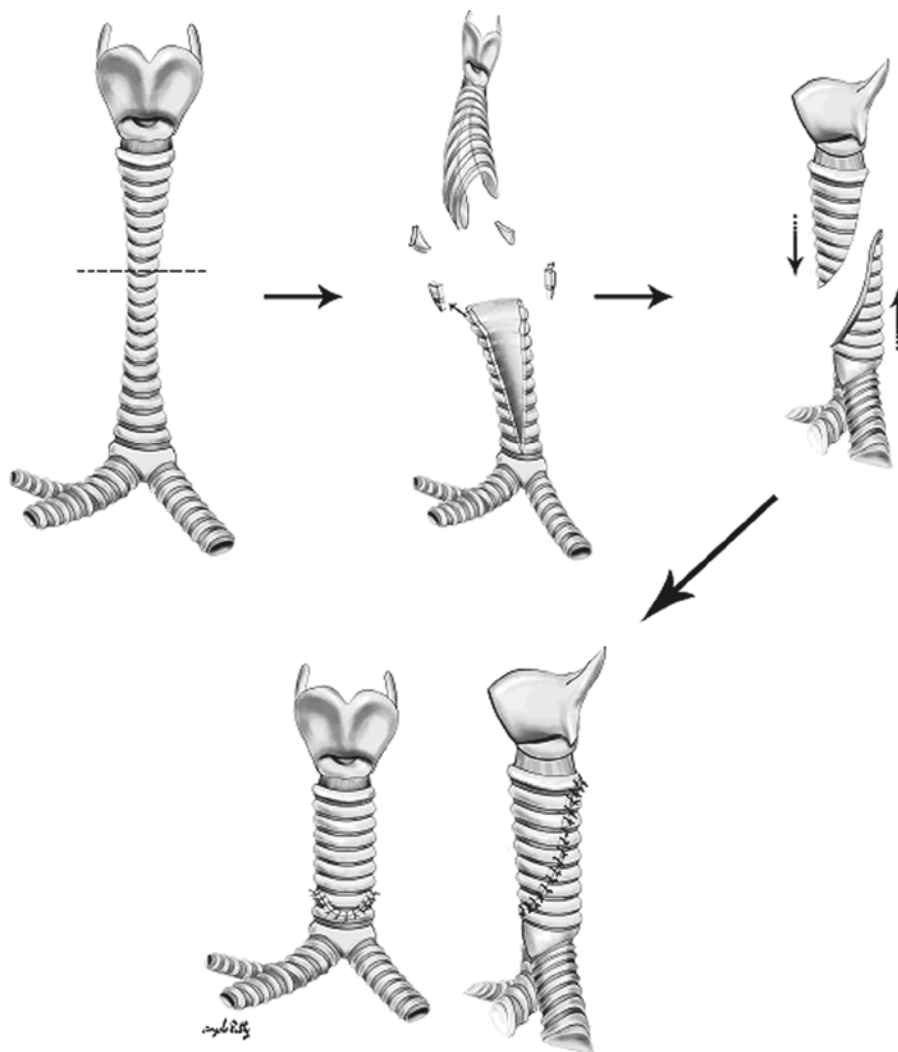


Fig. 43.3 Sliding Tracheoplasty

by this procedure, and recovery and complications depend significantly on the rate of restoration of this blood supply. Animal work has indicated the potential benefit of VEGF in accelerating revascularization after surgery in rabbits and this may hold hope for future improvements in human practice [28].

In our own institution, we have performed 52 slide tracheoplasties between 1995 and 2007. Median age at operation was 7.1 months (2.3 months–12 years). The indication was long segment tracheal stenosis in 47, all with complete tracheal rings and post-intubation mid-tracheal stenosis in 5. Left pulmonary artery sling was the commonest associated congenital anomaly ($n=20$).

Clinical presentation was with stridor and dyspnoea, near death events, cardiac arrest, and diagnosis during intubation. Nineteen (37%) needed preoperative ventilation and three required ECMO. Additional preoperative interventions included cardiac procedures in eight, tracheostomy (prior to arriving at our institution) in three and balloon dilatation in four.

Slide tracheoplasty was performed urgently in the patients on ECMO and semi-electively in 41 who were either ventilated or had stridor at rest. The procedure was elective in the remaining 9.

STP was performed via median sternotomy using cardiopulmonary bypass in all cases. Nineteen concomitant cardiovascular repairs were performed (2 intracardiac, 13 extracardiac, and 4 combined intra and extracardiac). We take the view that, unless actively contra-indicated for some reason, repair of the cardiac lesion should be performed at the same sitting.

At operation the median tracheal diameter was 1.8 mm (1.4–4.5). Bronchial extension of repair was needed in all those with bronchial origin stenosis.

We have demonstrated recently [29] that slide tracheoplasty can be used in almost all forms of stenosis with subtle modifications to technique.

There were 6 deaths (12%) with 5 (10%) in-hospital (cardiac-related in 2, intractable distal malacia in 2, and distal bronchial stenosis in 1). Mortality fell dramatically with increasing experience from 3/7 (43%) between 1995 and 2000 to 2/18 (11%) between 2000 and 2005. Since 2005, in-hospital mortality has all but been eliminated 1/27 (4%). The last patient died of severe cytomegalovirus pneumonitis, and had been on pre- and postoperative ECMO. There was one late death (2%) (renal dysfunction while awaiting transplant). Ventilation times and ICU stays have also fallen, and current data suggest a median ventilation time of

13 days and ICU stay of 23 days. However, with patients of this complexity it is to be expected that there will be outliers and some patients have required prolonged ICU care and multiple interventions.

43.10 Alternatives to slide tracheoplasty

A wide variety of approaches have been tried for long segment tracheal stenoses, but none have achieved the success or wide applicability of slide tracheoplasty [12, 24, 30–48]. The simplest operations in principle have been various forms of patch tracheoplasty (see Fig. 43.4), in which the anterior trachea is incised longitudinally and a patch of some material used to augment the trachea and correct the stenosis. Several materials have been employed over the years, but the most common and have been; autologous pericardium, rib cartilage, tracheal autograft, tracheal allograft and, most recently, carotid artery. Heterograft tissue and prosthetic material do not work and must be avoided except for temporary life saving situations.

Tracheal allograft implantation [49–51] is a good fall-back option. It is essentially a variant of patch tracheoplasty, utilizing homograft tracheal tissue.

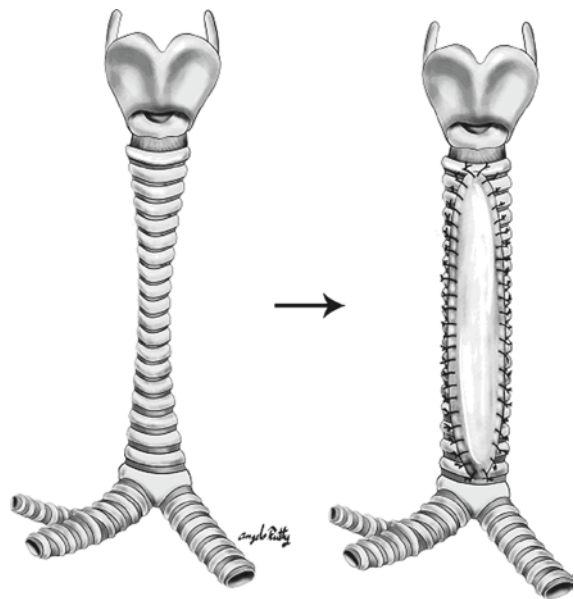


Fig. 43.4 Patch Tracheoplasty.

43.11 Postoperative management after tracheal surgery

On return from the operating room we routinely use muscle relaxation for a minimum of 24 h with appropriate sedation. It is tempting to extubate the patients immediately, but we have taken a cautious approach because of the risk of ischemia after extensive dissection. Patients should be ventilated to normal parameters but often need higher than normal PEEP (typically 10 cm water). We use continuous mediastinal irrigation with a dilute aqueous betadine solution for 48 h on the grounds of certain field contamination from the open trachea. Following this, we switch to saline irrigation checking the effluent for bacterial growth daily for the following 48 h. We use broad spectrum antibiotics for 7 days followed by long term (> 6 months) azithromycin (3 times weekly), which has proved effective in staving off the repeated URTIs to which these children are susceptible. If pseudomonas colonization occurs in the repaired trachea, nebulized colistin has proved effective.

At around 72 h postoperatively, bedside fiber-optic bronchoscopy is performed to confirm suitability for extubation. Gentle weaning of ventilation begins after cessation of muscle relaxation. If possible the PEEP should be weaned back slowly to physiological levels. Failure to tolerate this suggests residual problems (malacia or stenosis) and is an indication for further investigation, usually flexible bronchoscopy and bronchography. Weaning should continue to extubation with routine bronchoscopy and bronchography taking place thereafter at intervals of between five to seven days.

43.12 Postoperative Problems

This is a complex patient group and operations can sometimes be difficult. Postoperative problems are to be expected, and fall into distinct categories.

1. Those *related to repair of associated lesions and CPB*. Since the majority of associated lesions are cardiac, these relate to the well-described consequences of CPB or the cardiac lesion. Discussion of these is beyond the scope of this chapter.

2. *Granulation tissue formation*. Granulations occur as a part of the healing process of tracheal epithelium and are thought to be related to ischemia associated with the necessary tracheal mobilization. In animals topical VEGF has reduced the incidence [28]. There is no human experience.

Granulations result in important and even life-threatening obstruction to a relatively narrow airway and can act as ball valves causing either inflow or outflow obstruction. Clearly, their prevention and management are important issues in pediatric tracheal surgery. Attention to technical detail during repair is helpful in reducing their incidence, although there are no firm data to support this contention. Sutures (best absorbable) should be placed, if possible, deep to the tracheal mucosa in an attempt to diminish the stimuli to granulation formation.

Historically, granulations have been managed by bronchoscopic avulsion with grasping forceps or by laser. In our experience both these techniques have worsened the problem by inducing scarring and, paradoxically, greater granulation tissue formation. Our preference, in those who develop granulation tissue, is regular balloon expansion to the diameter of the repair to compress any granulation tissue development (beginning weekly and thereafter at progressively increasing intervals). This has effectively eliminated the incidence of granulation-related airway obstruction in our practice. Failure of this strategy should precipitate rigid endoscopy in an equipped operating room to allow for removal of granulations if necessary.

3. *Malacia*. As we have become more aggressive in tackling even the most severe tracheal stenoses, we have become aware that tracheal repair may unmask the underlying distal malacia or create it as a consequence of stripping the blood supply from the trachea during dissection. Absence or disorganization of distal cartilage has been an important contributor to the deaths in two of our patients. We have been able to diagnose this cartilage deficiency using optical coherence tomography. Management of malacia can be very challenging. Three strategies can be employed in the management of conventional tracheo-bronchomalacia: (a) prolonged ventilatory support with CPAP, (b) tracheostomy and “home” BiPAP support, and (c) stenting. The use of long-term

tracheostomy following tracheal reconstruction should be avoided, because of the risk of precipitating either granulation tissue formation or recurrent stenosis. We have increasingly used airway stents in these patients.

In general, we favor expandable metal stents with regular balloon dilatation, planning, in the long-term to fracture them by over dilatation to keep pace with somatic growth [52]. Such stents are not used in the presence of extrinsic vascular compression as they rarely work and may erode, particularly after pericardial patch tracheoplasty.

The management of malacia after tracheal repair remains difficult and controversial, particularly with regard to the role of stenting. The team must review the patients regularly and be prepared to be creative and flexible in strategies to optimize and make safe the airway.

4. *Infection.* While rare, infection can be catastrophic. During the initial surgery, the mediastinum is, unavoidably, exposed to the unsterile tracheal contents. If suspected, mediastinitis must be taken very seriously in this group of patients. Aggressive debridement and antiseptic irrigation should be tried first, but early muscle flap insertion may be indicated to deal with the infection and deliver new blood supply to the trachea. Early in our experience, two patients suffered serious mediastinitis. However, since we adopted the policy of elective irrigation, mediastinitis requiring secondary intervention has been eliminated.
5. *Recurrent stenosis.* Unfortunately, recurrent stenosis does occur. Abstracting the true incidence of these events from the literature is difficult, as follow up in the reported series is too short for meaningful analysis. Further, most series are published by the primary operating team and it is frequently the case that follow up is by other (often ENT) teams in the long term.

In our view, there will be an important incidence of recurrent stenosis and the more severe and extensive the primary lesion the more likely some kind of recurrence is to occur. Our management strategy is devoted to both the early detection and the prevention of progress of stenosis. Regular bronchoscopy and bronchography are performed.

Our strategies for management of recurrence are as follows:

At the first sign of significant recurrence, Radial balloon dilatation of the stenotic area is performed. Dilatation is repeated electively at frequent, but increasing, intervals until the stenosing process stabilizes. As a general rule the requirement for intervention decreases with time (see Fig. 43.5).

The decision to stent is not taken lightly and is again the result of multidisciplinary consultation. Balloon-expandable metal stents is chosen for use (for example, the Palmaz Genesis (Cordis Europa, Roden, the Netherlands)), because they can be progressively dilated over time to mimic growth [52]. They are relatively easy to insert but difficult and sometimes dangerous to remove. The risk of vascular erosion appears to be low after slide tracheoplasty because the stent is completely encased in the cartilaginous frame of the remodeled trachea. Unfortunately, this is not the case after pericardial patch tracheoplasty when the stent may directly abut the posterior aspect of the aortic arch, and/or innominate artery and erosion has occurred in these circumstances.

Extensive recurrence or failed stenting. Under these, now very rare, circumstances we would perform a tracheal homograft repair [35, 49, 51]. This represents an excellent fall back position and can be repeated, and there is a readily available pool of graft tissue. Fortunately, as the slide tracheoplasty experience has evolved, this procedure has not been performed for some years.

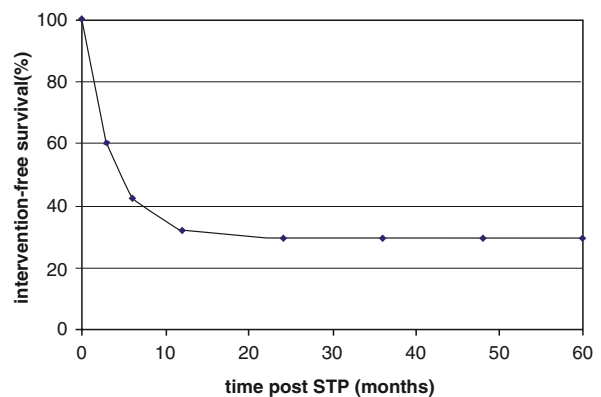


Fig. 43.5 Intervention-free survival in children following slide tracheoplasty at Great Ormond Street Hospital for Children NHS Trust, London, UK.

43.13 Long-term outlook

Few long-term data are available, largely because the first successful cases were only reported in the late 1980's. Most papers have been published in the last decade and only a few of them report long-term outcomes. It appears that if a child gets over the initial procedure (this can take months), provided that the trachea grows, late airway function can be very good. There are no long-term detailed physiological or quality of life studies. They are badly needed. What can be said is that these children are growing normally, are in mainstream mainstream schools, take part in most activities and are usually indistinguishable from their peers. Long term outcomes will be reported in due course.

43.14 The Future

There are a number of important areas of research currently underway which will impact this field. New

patch materials will be developed in the near future. As well as arterial patches, progress in tissue engineering is being rapidly developed, and groups in Europe, Japan and the USA are competing to produce usable engineered "trachea" [53–81].

Stent technology is also likely to progress. Experience with stents in the vascular bed is growing and there may be a role for drug-eluting stents within the trachea. A good absorbable stent for use in children is awaited. A great deal of research is needed in the physiological and social quality of life of these children and their families. Current data are simply inadequate.

Treatment for congenital tracheal stenosis is complex, prolonged, and expensive. It places a considerable strain on families. Dismal early results have radically improved and new sophisticated therapies are emerging. Successful strategies for recurrence exist. In our experience it is both worthwhile and cost-effective to treat this challenging patient group. Our current therapeutic algorithm is shown in Fig. 43.6.

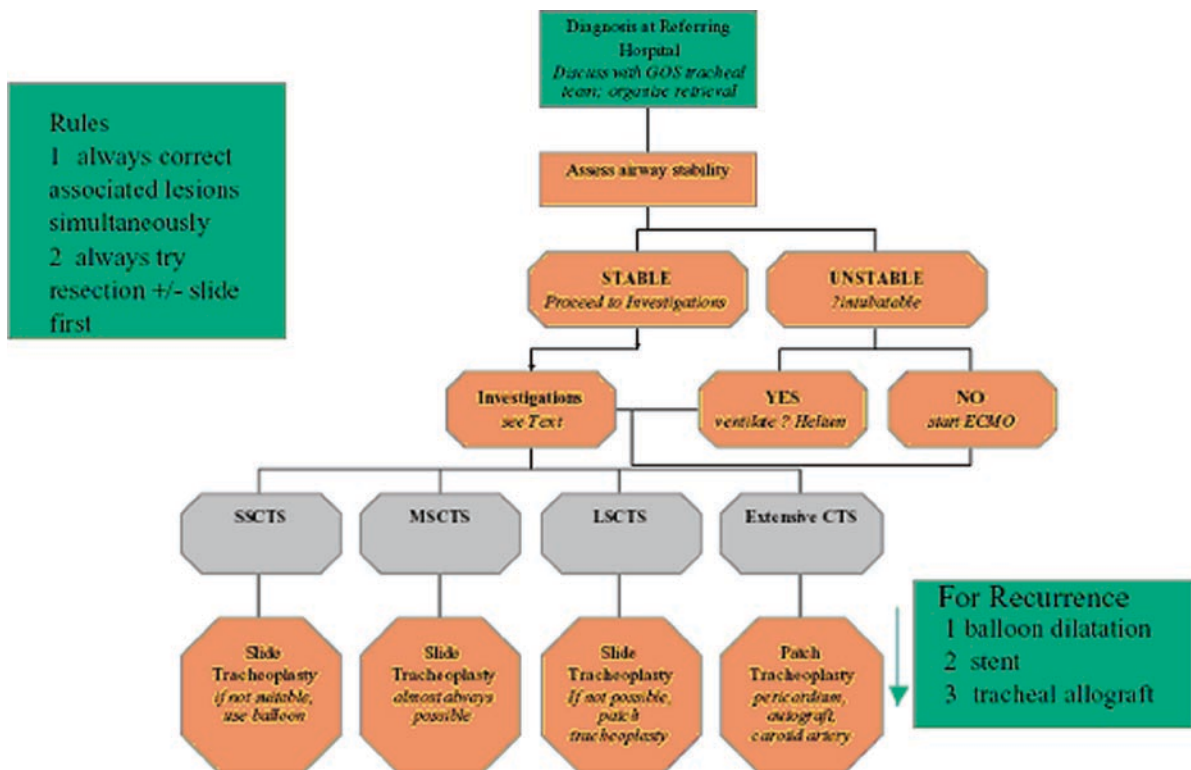


Fig. 43.6 Treatment algorithm for children with tracheal stenosis at Great Ormond Street Hospital for Children NHS Trust, London, UK. (From: [12])

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Part III

Other Topics

Chapter 44

Acute Pulmonary Hypertension

Maurice Beghetti and Eduardo M. da Cruz

44.1 Introduction

Pulmonary arterial hypertension is a hemodynamic condition defined as a pulmonary artery mean pressure higher than 25 mmHg. However, this may depend on the level of the systemic pressure. Another potential definition could be pulmonary pressure >60% systemic with signs of low cardiac output.

Pulmonary hypertension in critically-ill pediatric cardiac patient remains a clinical challenge [1–6]. Clinical practitioners still face serious problems particularly in the acute postoperative phase. This chapter provides a summary of the main aspects to be taken into account whenever managing acute pulmonary hypertensive crisis.

Firstly, it is important to describe the current knowledge regarding the pathophysiology of pre- and post-operative pulmonary hypertension in the cardiac patient.

In the preoperative phase, the increase in pulmonary pressure associated with congenital heart disease is either, in the vast majority, secondary to an increase in pulmonary blood flow (left-to-right shunts) or to increased postcapillary pressures (left heart obstruction or left ventricular dysfunction either systolic or diastolic).

Albeit, major advances in the understanding of the regulation of the pulmonary vascular bed and the pulmonary endothelial lesions leading to pulmonary vascular disease have been achieved and despite the advances in surgical repair and the discovery of

potential therapies in the pre and postoperative period, pulmonary hypertension still carries a significant mortality and morbidity rate in this population. The incidence of postoperative pulmonary hypertensive events has decreased from 31% in the 1980–1984 era to 6.8% in the 1990–1994 era, whereas mortality has decreased respectively from 5.7 to 2.4% and the survival rate continues to improve [7]. This data partly reflects the improved understanding of the pathophysiology and the rapid translation of this knowledge into therapy. However, acute pulmonary hypertension after cardiac surgery remains a major contributor to hospital length of stay and need for prolonged mechanical ventilation.

44.2 Pathophysiology

It has been recognized for many years that the endothelium is vital for the maintenance of normal vascular function by regulating flow, solutes exchanges and by inhibiting thrombosis; conversely, endothelial dysfunction plays a major role in several cardiovascular disorders.

In congenital heart disease with significantly increased pulmonary blood flow or pulmonary venous hypertension, progressive anatomic and functional abnormalities of the pulmonary vascular bed occur. This state is characterized by progressive smooth muscle hypertrophy and hyperplasia, intimal proliferation and pulmonary vasoconstriction. In addition, there are changes in the extracellular matrix and adventitia with synthesis and deposition of collagen and elastin. The role of hemodynamics in the development of pulmonary vascular disease has been clearly demonstrated. Endothelial dysfunction occurs indeed before

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the onset of pulmonary hypertension or histological evidence of smooth muscle dysfunction.

Recently, several studies have focused on the endothelial dysfunction induced by increased pulmonary blood flow, such as encountered in many congenital heart diseases cursing with increased pulmonary vascular resistance. Complex interactions between vasoactive substances produced by the vascular endothelium may partly explain the changes in pulmonary vascular tone. The cellular and molecular mechanisms underlying the pulmonary vascular remodeling in response to the mechanical stimulus of increased flow are, however, not completely understood. Shear stress has been shown to alter the production of vasoactive substances. Endothelial shear stress is directly proportional to blood flow velocity and is inversely proportional to the radius of the vessel. A high blood flow rate alters the mean shear stress and may directly damage the endothelial cell; this, in turn, may impair the balance between the vasoconstrictor/vasodilator effect, as well as promotive and antimotivic functions and lead to smooth muscle cell hypertrophy and proliferation. Cooper et al. [8] showed that in healthy adults, normal basal pulmonary vascular tone is partly related to nitric oxide production. This basal nitric oxide production may be increased in response to receptor-mediated stimulation, leading to further vasodilatation; this function can be tested with acetylcholine. Nitric oxide dependence of basal pulmonary resistance has also been described in children. Thus, impairment of nitric oxide production, secondary to an injured endothelium, may contribute to the increased pulmonary vascular resistance as observed in infants and children with congenital heart disease. As a matter of fact, Celermajer et al. [9] demonstrated that in children with congenital heart disease and abnormal pulmonary hemodynamics, endothelium-dependent pulmonary artery relaxation is impaired and that this impairment may be one of the early events in the pathogenesis of pulmonary vascular disease.

Animal and human data strongly suggest that alterations in endothelin-1 metabolism, secondary to endothelial injury, also contribute to the development of pulmonary hypertensive disorders and their associated increased vascular reactivity [10, 11]. Lamb models with increased pulmonary blood flow, secondary to experimentally created congenital heart disease also show alterations in the endothelin-1 cascade. At 4 weeks of age, these same lambs have increased plasma

and lung tissue concentrations of endothelin-1 that is secondary to an upregulation of endothelin converting enzyme. In addition, there is loss of ET_B receptor-mediated pulmonary vasodilatation and augmented ET_A receptor-mediated vasoconstriction. This is associated with increased ET_A receptor gene expression and decreased ET_B receptor expression. Recent data have also demonstrated the emergence of ET_B receptor-mediated pulmonary vasoconstriction in these lambs at 8 weeks of age, suggesting a role for both ET_A and ET_B receptor-mediated effects in the pathophysiology of pulmonary hypertension.

Several human studies demonstrate increased endothelin-1 concentrations in patients with pulmonary hypertension, including children with congenital heart disease and increased pulmonary blood flow. In addition, patients with advanced pulmonary hypertension have an increase in plasma endothelin-1 concentrations between the right ventricle and pulmonary veins and increased gene expression of endothelin-1 within pulmonary vascular endothelial cells, suggesting increased local production of endothelin-1 within the pulmonary circulation.

Prostacyclin and thromboxanes are also potential actors in the changes of pulmonary vascular tone as their balance may be impaired in patients with congenital heart disease.

However, not all patients develop fixed pulmonary vascular disease or at least not within the same timing and this may be related to a particular susceptibility to develop lesions or even the opposite, to be protected from these events. Currently, some studies are devoted to assess if there is some genetic susceptibility. The recent publication of Levy et al. [12] suggests also the role of impaired endothelial cell apoptosis and inflammatory apoptosis in the pathogenesis of pulmonary vascular lesions.

The pulmonary vascular remodeling process is reversible in the early stages of the disease but may progress, with continuous stress, to smooth muscle cell proliferation in small arteries. As described before, it provokes changes in the extracellular matrix and adventitia with synthesis and deposition of collagen and elastin; this progression renders the vessels relatively unresponsive to vasodilators and may preclude corrective surgery.

The age at which congenital heart lesions cause irreversible pulmonary vascular disease varies. The consequences of increased pulmonary blood flow are

more severe in the immature than in the mature animal. Endothelial cell morphology is modified as early as 2 months after birth in children with increased pulmonary blood flow. The development of irreversible lesions is also associated with the type of heart defect and it seems that a combination of high pressure and high flow causes a more rapid and more severe remodeling.

Thus, *surgical correction should be performed at an early age* in children with massive increase in pulmonary blood flow; before 2 years of age for ventricular septal defects and even earlier (<1 year or 6 months) for atrioventricular septal defects, transposition of the great arteries with ventricular septal defect or truncus arteriosus.

Beside the age effect, as mentioned above, individual susceptibility based on different genetic polymorphisms, plays a major role and research is currently directed at understanding why two patients with the same malformation and hemodynamic profile will not develop pulmonary vascular disease at the same time.

44.3 Classification

The Heath and Edwards describes progressive pulmonary vascular changes induced by pulmonary hypertension. Nevertheless, this classification has very poor clinical and hemodynamic correlations.

44.3.1 Heath and Edwards Classification

Grade I: Hypertrophy of the media of small muscular arteries and arterioles

Grade II: Intimal cellular proliferation in addition to medial hypertrophy

Grade III: Advanced medial thickening with hypertrophy and hyperplasia, including progressive intimal proliferation and concentric fibrosis. This results in obliteration of arterioles and small arteries

Grade IV: “Plexiform lesions” of the muscular pulmonary arteries and arterioles with a plexiform network of capillary-like channels within a dilated segment

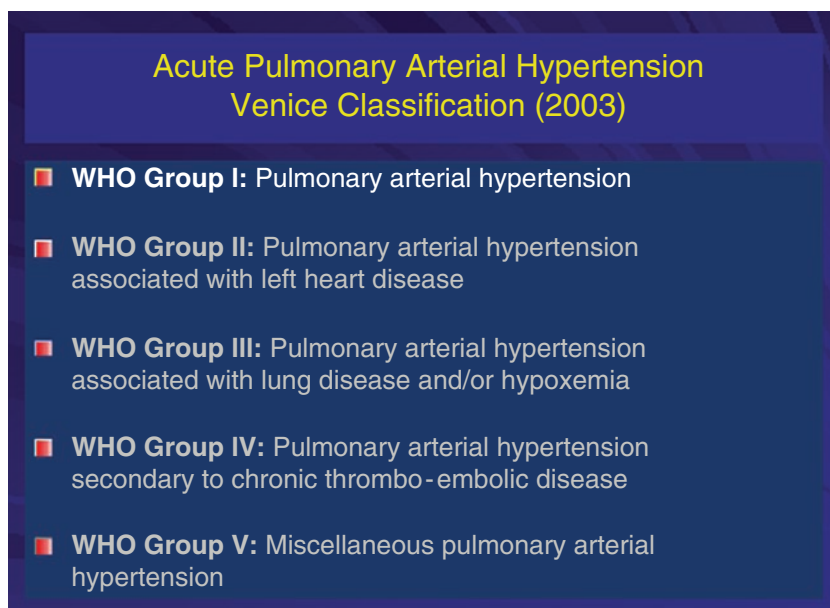
Grade V: Complex plexiform, angiomatous and cavernous lesions and hyalinization of intimal fibrosis

Grade VI: Necrotizing arteritis

The term of obstructive pulmonary vascular disease relates to pathological changes described in grades III to VI.

Currently, there is an anatomic–pathological classification [13, 14], developed in 1998 at the World Symposium of Primary Pulmonary Hypertension in Evian, France and later modified in Venice (2003). This World Health Organization (WHO) classification (Fig. 44.1) is based upon a combination of factors: pathological findings, clinical presentation, hemodynamic profile and therapeutic strategies.

Fig. 44.1 The World Health Organization (WHO) classification for pulmonary arterial hypertension



44.4 Postoperative Pulmonary Hypertension

44.4.1 Cardiopulmonary Bypass and Ischemia-Reperfusion Injury

Reperfusion of tissues exposed to ischemia can lead to a cascade of events that produce cellular dysfunction and necrosis. This phenomenon has been implicated in the pathogenesis of some complications encountered after cardiopulmonary bypass. Cardiopulmonary bypass is known to induce a generalized inflammatory response with the systemic release of proinflammatory cytokines, the activation of the complement system and endothelial dysfunction. This phenomenon is thought to be triggered by the exposure of blood to non-physiologic surfaces and the development of ischemia reperfusion injury. Endothelial cell dysfunction is common after cardiopulmonary bypass and structural and functional damage to the pulmonary vascular endothelium has been demonstrated. During cardiopulmonary bypass, lungs are hypoxic and ischemic, as the pulmonary circulation is excluded to abolish pulmonary venous return. It was long postulated that the lung was resistant to ischemia because of its dual pulmonary and bronchial blood supply and its direct source of oxygen from the alveolar space. However, bronchial flow is estimated at 0.5% of the bypass flow and indeed it has been demonstrated that pulmonary vascular endothelial cells undergo ischemia reperfusion injury. This phenomenon further aggravates the inflammatory response and subsequent lung damage as shown by a decrease in pulmonary endothelium-dependent relaxation after cardiopulmonary bypass. Lung injury following cardiopulmonary bypass is well described. Clinically, it is manifested as reduced oxygenation, reduced lung compliance, and most importantly increased pulmonary vascular resistance and augmented pulmonary vascular reactivity. Injury to the pulmonary vascular endothelium is considered to be a major factor. In fact, patients with pre-existing pulmonary vascular endothelial dysfunction are at greatest risk for developing clinically significant bypass-induced lung injury. Both animal and isolated organ models of ischemia-reperfusion confirm pulmonary vasoconstriction and increased pulmonary vascular resistance after reperfusion. Wessel et al. [15] in children and Morita et al. [16] in animal models showed that this might be related to a decrease in nitric oxide production.

A decline in the output of nitric oxide from the vascular endothelium is either due to an enhanced inactivation of nitric oxide by free radicals (superoxide breakdown) produced in post ischemic tissues, or a decrease in endogenous nitric oxide production or combination of both. It has also been suggested that nitric oxide is a physiologically relevant scavenger of free radicals and may be considered as an important cytoprotective modulator.

Thus, nitric oxide may play an important role in mitigating the extent of ischemia reperfusion injury. Moreover, its antiplatelet and leukocyte properties may be of major importance to prevent platelet aggregation and leukocyte sequestration during and after cardiopulmonary bypass. Two approaches may be adopted to overcome the decrease in nitric oxide availability: either to increase production through the administration of its precursor L-arginine or citrulline, to substitute with intravenous NO donors, or inhaled NO.

In several animal and human studies, plasma ET-1 concentrations are consistently increased during and following cardiopulmonary bypass. In a study of children with congenital heart disease, the plasma concentration of ET-1 3 h after CPB correlated with the degree of post-CPB pulmonary hypertension, suggesting a role for ET-1 in the pathophysiology of cardiopulmonary bypass-induced pulmonary hypertension. In addition, several animal studies suggest that blockade of endothelin receptors attenuate post-CPB pulmonary hypertension and its associated altered reactivity. Thus, in lambs with pre-existing pulmonary hypertension, secondary to increased pulmonary blood flow, the increase in pulmonary vascular resistance following bypass was completely blocked in lambs pretreated with either dual or ET_A receptor antagonists. In addition, the augmented pulmonary vascular reactivity following bypass, which is responsible for the potentially life-threatening acute increases in pulmonary vascular resistance, was also completely blocked in those lambs pretreated with endothelin receptor antagonists. A recent study showed that ET_A blockers might have a place in the therapeutic armamentarium.

Taking the particular situation of congenital heart surgery, where preoperative endothelial dysfunction exists in many instances, further injury to the pulmonary endothelium due to ischemia reperfusion may explain the increased pulmonary vascular resistance occurring in some patients postoperatively.

The pathophysiological events described above give a strong rationale to support the use of the therapies discussed hereafter.

44.5 Diagnosis

44.5.1 Clinical

Clinical diagnosis is facilitated by the use of indwelling catheters allowing to continuously monitor pulmonary pressures and/or left atrial pressures. As the pulmonary pressures increase, patients may display signs of increased right preload and right cardiac failure, concomitantly with signs of abruptly decreased left preload with low systemic cardiac output. This may be aggravated by compression of the left ventricle by the right ventricle, once this later develops iso- or supra-systemic pressure levels. At this point, there may also appear signs of ischemia by reduction of right coronary flow and patients may desaturate due to the appearance of right-to-left intracardiac shunts. Patients may also have arrhythmias, persistent hypoxia or metabolic acidosis; these later signs being a sign of alert, particularly in patients who do not have indwelling catheters.

44.5.2 Chest X-ray

Chest X-rays are unspecific for the diagnosis of acute pulmonary hypertensive spells although there can appear signs of hypovascularity. Yet, this technique may be useful to rule out triggering factors like volume overload and the presence of added pulmonary disease like atelectasis, pneumothorax or pleural effusions.

44.5.3 ECG

ECG may be useful in patients who develop secondary arrhythmias or ischemic changes throughout a pulmonary hypertensive crisis.

44.5.4 Echocardiography

Echocardiography undoubtedly remains the cornerstone technique to rapidly assessing pulmonary hypertension (Figs. 44.2–44.5) and its impact on cardiac function in the intensive care setting [17], mostly in patients who

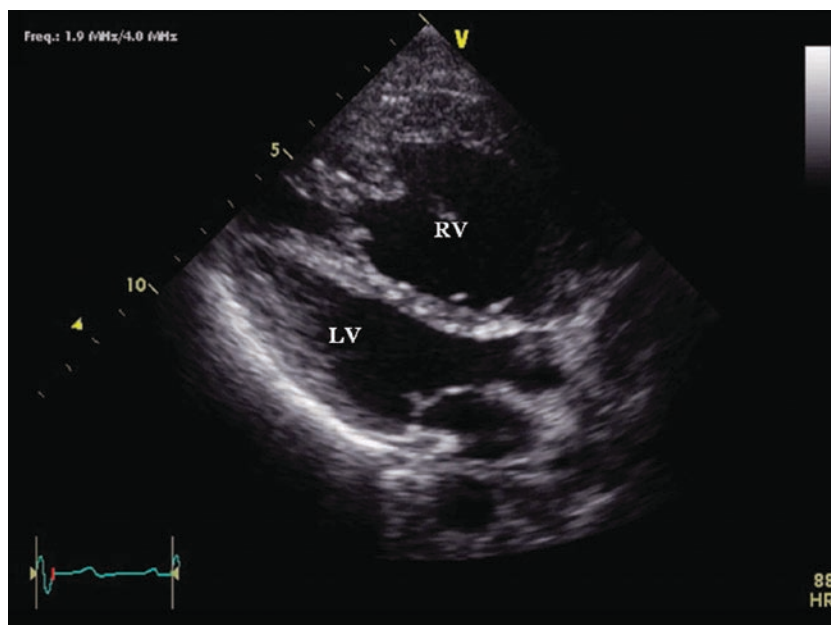


Fig. 44.2 2D echocardiography documenting severe PAH with right-to-left shift of the interventricular septum in a long-axis view (LV left ventricle; RV right ventricle)

Fig. 44.3 2D echocardiography documenting severe PAH with right-to-left shift of the interventricular septum in a short-axis view (LV left ventricle; RV right ventricle)

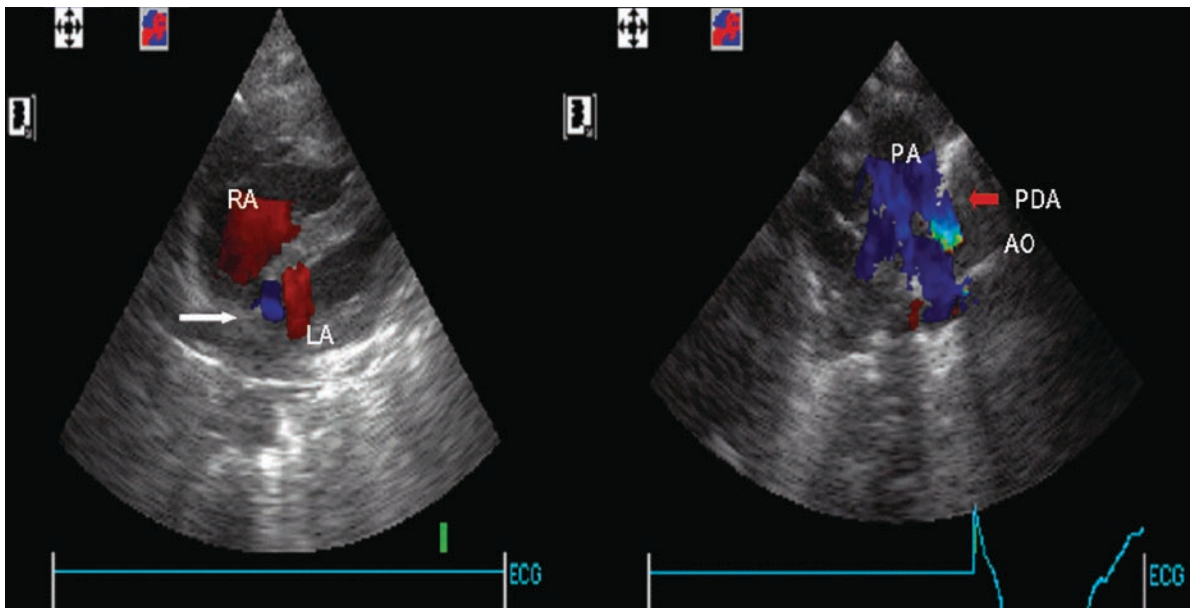
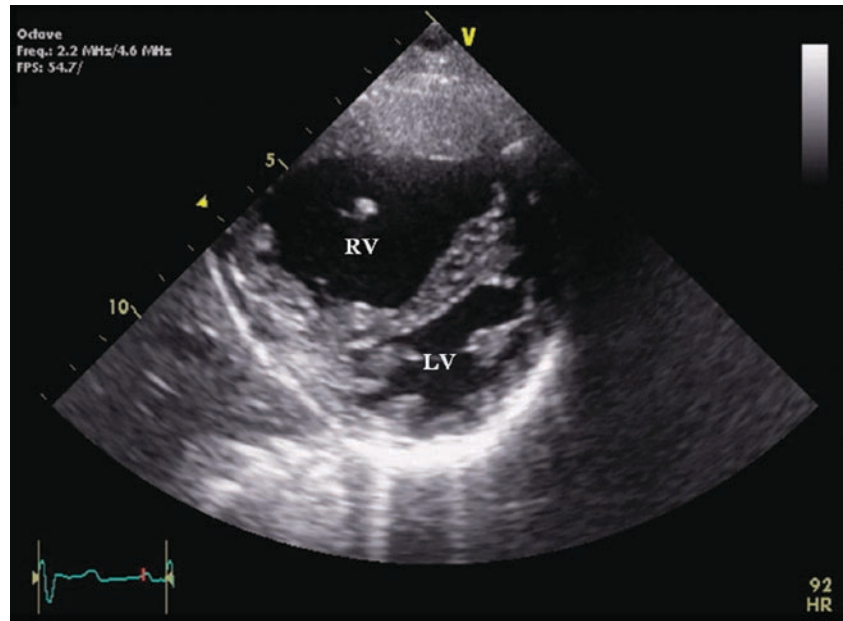


Fig. 44.4 2D and Color-doppler echocardiography showing severe pulmonary hypertension with a right-to-left shunt through the foramen ovale (white arrow) and the ductus arteriosus (red arrow)

do not have indwelling catheters. It is imperative, though, to be able to estimate right pressures by tricuspid regurgitation, although the interventricular septal geometry may be suggestive of the degree of right ventricular pressure regime, hence pulmonary hypertension, unless there is a right outflow tract obstruction. Also, the presence of pulmonary regurgitation may allow a

more comprehensive estimation of pulmonary diastolic and mean pressures. In patients with residual interventricular shunts, echocardiography may document the systolic pressure gradient between the ventricles and therefore provide a reasonable estimation of the right systolic pressures. In patients with pulmonary hypertensive spells, echocardiography is instrumental in

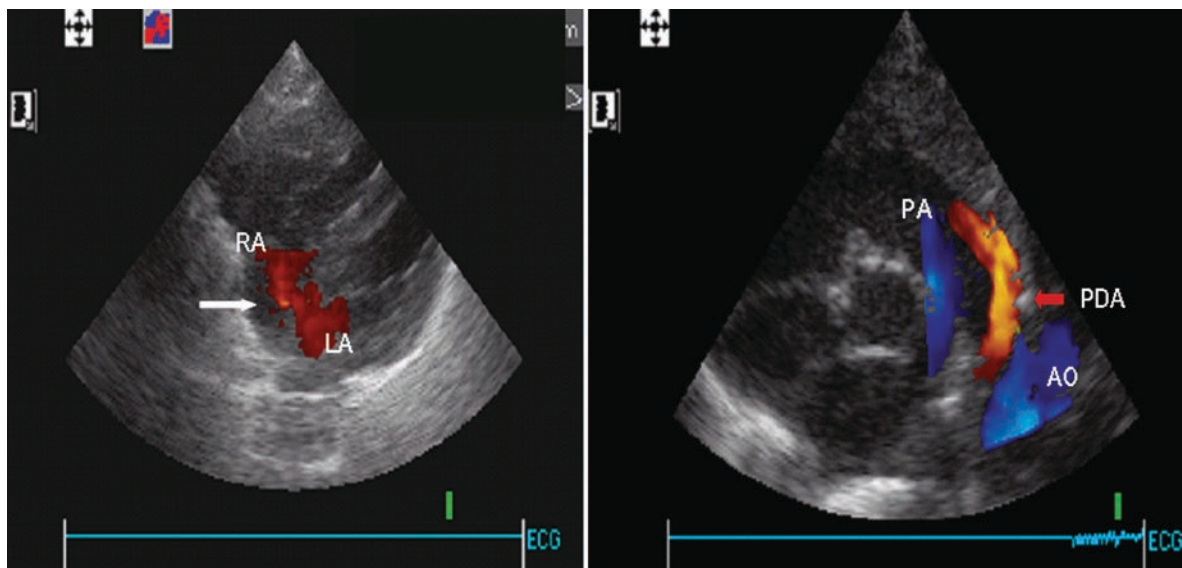


Fig. 44.5 2D and color-doppler echocardiography showing significant improvement of pulmonary hypertension after treatment, with a left-to-right shunt through the foramen ovale (white arrow) and the ductus arteriosus (red arrow)

assessing right and left ventricular function, the degree of intracardiac shunting, if any, and also the presence of residual lesions that might be at the origin of the spells. Lastly it allows follow-up of therapeutic efficiency.

44.6 Management of Pulmonary Hypertension After Cardiac Surgery

Probably the most important measures with these patients concern the *prevention* of pulmonary hypertensive crisis. Potentially malignant pulmonary hypertensive spells are usually iso- or supra-systemic and may induce low cardiac output, hypoxia, acidosis or cardiac arrhythmias.

Sudden pulmonary hypertensive crises may punctuate the postoperative course despite accurate surgery and are associated with significant mortality and morbidity. Even though it has been thought that this may become a relatively unimportant problem because of the recent progress in cardiac surgery, it seems that increased pulmonary vascular resistance after surgery remains a significant problem [18–21]. Potential therapeutic strategies for the treatment of acute pulmonary hypertension after cardiac surgery are summarized in Fig. 44.6 and in Fig. 44.7 and will be discussed hereafter.

The primary aim is to decrease pulmonary vascular resistance and pressure, and if not possible, to avoid stimulation of the pulmonary circulation and support the right ventricular function through the balance between pulmonary and systemic vascular resistances and maintenance of cardiac output. General measures to promote an anabolic status (i.e., early enteral or parenteral nutrition) should be undertaken as soon as possible after surgery.

44.7 Preventive Measures

1. Early surgical indication
2. Minimization of perioperative risks:
 - a. Adequate CPBP conditions
 - b. Surgical technique
 - c. Myocardial protection
 - d. Use of ultrafiltration
 - e. Use of systemic prophylactic steroids?
 - f. Controlled reoxygenation
 - g. Leucocyte depletion?
3. Rectify all identified “antiphysiological” conditions
4. Ensure an adequate metabolic and acid–base balance
5. Anticipate, avoid and treat the following triggers:

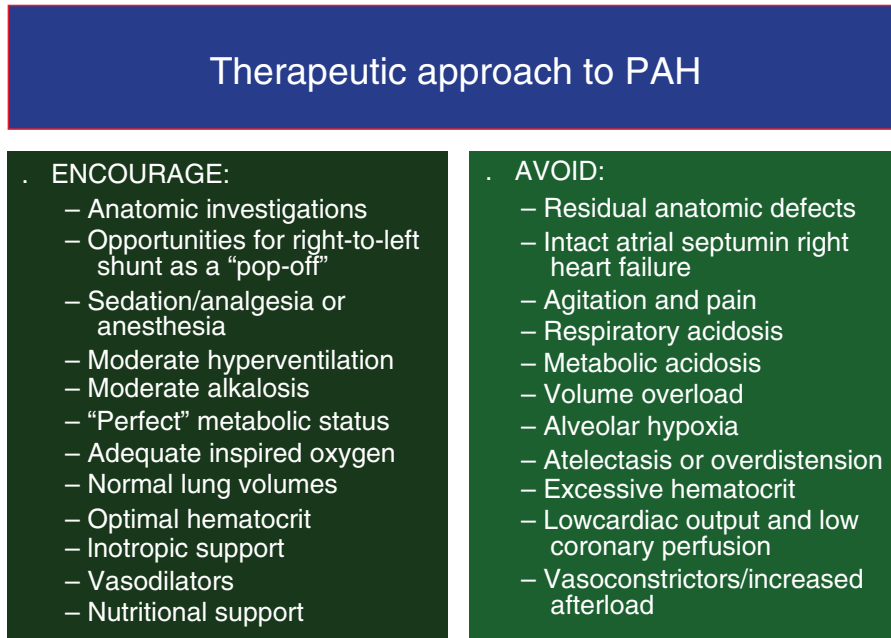


Fig. 44.6 Summary of therapeutic measures to treat acute pulmonary hypertension. (Modified from Wessel D. Postoperative treatment of pulmonary hypertension. In Beghetti M, Barst RJ,

Naeije R, Rubin LJ, eds. Pulmonary Arterial Hypertension Related to Congenital Heart Disease. Munich, Germany: Elsevier GmbH; 2006:143-175.)

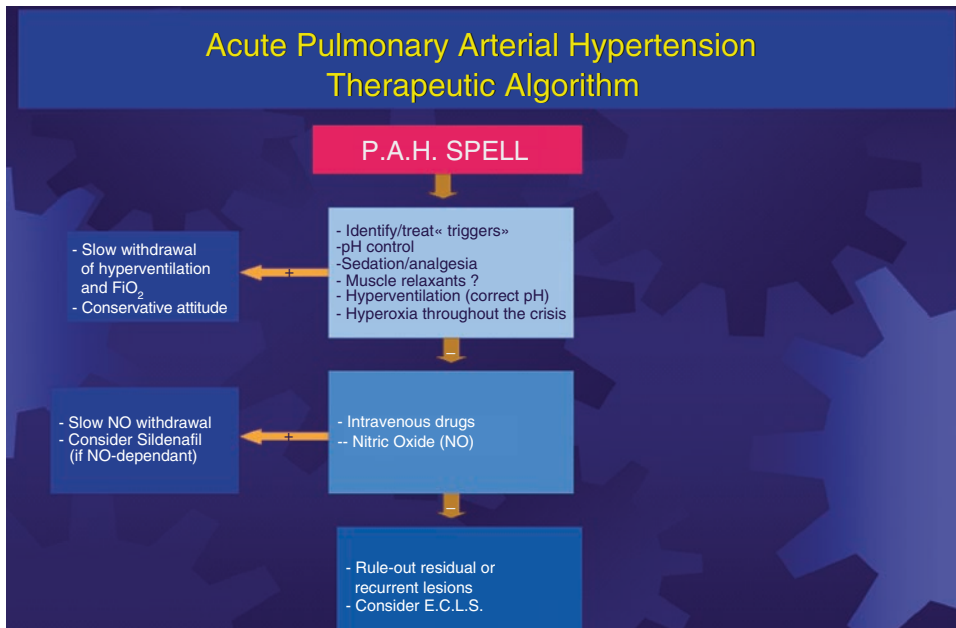


Fig. 44.7 A simple algorithm to approach acute pulmonary arterial hypertension spells

- | | |
|--|--|
| <ul style="list-style-type: none"> a. Fever b. Hypothermia c. Anemia d. Acidosis e. Dehydration | <ul style="list-style-type: none"> f. Volume overload g. Hypoxia h. Hypercapnia i. Sepsis j. Pain |
|--|--|

44.8 Therapeutic Measures

Therapy should be individualized. The main measures concern analgesia and sedation, ventilation, intravenous and inhaled drugs.

1. Anatomic considerations

First of all, residual anatomical problems should be excluded as these may be responsible for increased right ventricular pressure as in the case of residual shunts or right ventricular outflow tract obstructions. Thus, anatomic investigations should be performed such as transthoracic or transesophageal echocardiography or catheterization, particularly if a potential intervention is anticipated.

Anatomy is also important as some measures may help to maintain cardiac output through a right-to-left shunt used as a “pop off” for the right side. Preserving a calibrated atrial septal defect is a common measure, but some authors advocate the use of a valve patch when a ventricular septal defect is closed (“clap” fenestration of the VSD patch). This may be beneficial to maintain cardiac output but to the detriment of cyanosis. Oxygen delivery is maintained by increasing hemoglobin level.

Delayed chest closure may be useful to decrease the constraints on a dilated dysfunctional right ventricle.

2. Sedation and analgesia

Agitation and stress are potential triggers for pulmonary hypertensive crisis and should be avoided. Well controlled analgesia and sedation should be guaranteed whilst ensuring spontaneous breathing in stable patients who would be candidates for extubation. However, unstable patients with frequent or poorly tolerated pulmonary hypertensive spells should be kept deeply sedated and eventually on muscle relaxants as required. This is usually achieved with a combination of opioids and benzodiazepines administered as continuous infusions and titrated to effect. Fentanyl is a better indication than morphine for this specific group of patients. Other alternatives are available and depend on specific institutional protocols: dexmedetomidine, propofol, clonidine to mention some. The principle of using minimal efficient doses should be respected as much as possible.

3. Ventilation and pH

It is essential to adequately ventilate these patients and to avoid overdistention or atelectasis, known to be

potential triggers for increased pulmonary vascular resistance. It is important to remember that pulmonary vascular resistance is normal at normal functional residual capacity.

Minimal airway manipulation and suctioning is recommended.

Alkalosis induces pulmonary vasodilatation whereas acidosis induces vasoconstriction. It is known after the work of Chang et al. [22] that the triggers are mainly the pH (hydrogen ion concentration) and not the carbon dioxide levels. The current approach is to maintain a normal or slightly alkalotic pH (as to avoid aggressive ventilation) and only in rare instances to raise pH over 7.5. Morris et al. [23] showed that hyperventilation to increase pH has some deleterious effects such as an increase in systemic vascular resistance that may not be warranted in the postoperative period. Use of sodium bicarbonate or THAM may be considered in some patients in order to induce alkalosis without the potential deleterious effects of hyperventilation.

In patients considered as susceptible of developing pulmonary hypertensive spells while being de-ventilated or with significant pulmonary vascular reactivity, permissive hypercapnia leading to mild respiratory acidosis is a potentially useful test to assess feasibility of safe extubation. Well-controlled pulmonary reactivity does not preclude early extubation.

4. Oxygenation

It is well known that hyperoxia provokes pulmonary vasodilatation and that hypoxia induces pulmonary vasoconstriction. It is therefore important to maintain an adequate oxygenation (PO_2 around 80–100 mmHg) in the presence of pulmonary hypertensive crisis and with patients at risk to develop these problems. This is obtained with the administration of oxygen and again adequate ventilation ensuring a proper lung volume. However, the effect of oxygen seems not so clear in the setting of pulmonary hypertension after cardiac surgery as well as in the so-called fixed lesions. One must also remember that high levels of inspired oxygen may be deleterious and could induce lung damage.

5. Vasodilator drugs

Pulmonary hypertension may be treated with intravenous or with inhaled vasodilators.

Various intravenous vasodilators such as tolazoline, prostacyclin, phenoxybenzamine, phentolamine and nitro dilators have been used to reduce pulmonary arterial pressure. However, their lack of selectivity and

inconsistent efficacy are a limiting factor; these drugs carry a risk of systemic hypotension amongst others, which may be undesirable after cardiac surgery.

In this setting, there is a particular appeal in the therapeutic opportunities afforded by new strategies acting through a selective effect on the pulmonary vascular bed such as inhaled nitric oxide (iNO) or inhaled prostacyclin.

iNO improves right ventricular systolic function by decreasing its afterload while increasing left ventricular preload, reducing the “tamponade” effect and restoring aortic pressure and coronary perfusion [24–29]. In patients with poor left ventricular function, iNO should be used very cautiously since the preload increase may be deleterious.

Wessel et al. [27] showed that pulmonary endothelial dysfunction was present after cardiopulmonary bypass; thus the response to acetylcholine was attenuated, but the response to iNO was maintained. These authors hypothesized that a dysfunctional endothelium with reduced endogenous nitric oxide release may contribute to postoperative pulmonary hypertension. Journois and collaborators [28, 29] demonstrated that iNO was a useful therapy for pulmonary hypertensive crises refractory to conventional treatment. According to Miller et al. [30, 31], even low doses of nitric oxide (2 ppm) appear to be effective in such patients. Beghetti et al. [32, 33] showed that the effect of low-dose nitric oxide was maintained over several days at concentrations carrying little risks of toxicity. Nitric oxide has been used with success in several different congenital heart defects where increased pulmonary vascular resistance may complicate the postoperative course such as mitral valve stenosis, total anomalous pulmonary venous return, bidirectional Glenn anastomosis, and the Fontan circulation. It also appears useful after cardiac and/or lung transplant. However, a beneficial effect in patients with cavopulmonary anastomosis is not consistently reported and this despite an increase in cGMP levels [34], which is proof of effective delivery.

iNO augments right ventricular function after left ventricular assist device implantation, perhaps through an increase in pulmonary venous return and left atrial pressure, thus facilitating pump flow.

Patients who remain dependent on NO and have rebound pulmonary hypertension upon its withdrawal are candidates for therapy with sildenafil as a strategy to wean the NO [35].

Inhaled prostacyclin is increasingly used as delivered by aerosol and may overcome the necessity of a special device to deliver NO. Several series have been published with epoprostenol or iloprost [36–40] and prospective studies are underway, but one of the major problems is to define the dose to be delivered as well as the exact dose delivered when the drug is administered in ventilated patients.

When vasodilatation is not possible or is suboptimal it is appealing to try to counteract vasoconstriction and, as mentioned before, endothelin is a logical target. Animal and preliminary human studies are encouraging and several research protocols are planned or underway with selective or non-selective endothelin receptor blockers.

New strategies aiming at protection during cardiopulmonary bypass are being currently studied and may offer new therapeutic approaches in the field of prevention of endothelial lesions.

6. Inotropic and vasoactive drugs

After surgical correction of patients with preoperative pulmonary hypertension or under significant risk for postoperative pulmonary hypertensive spells, the classical drug association is milrinone [41–45] and a low dose (less than 5 µg/kg/min) of dopamine or dobutamine, eventually associated with low doses of epinephrine.

Right ventricular function may be compromised following congenital heart disease repair (Fig. 44.8) because of cardiopulmonary bypass and direct injury by the surgical procedure itself. Increased pulmonary vascular resistance further compromises right ventricular function; as a result the right ventricle becomes dilated and induces an “intrapericardial tamponade” effect of the left ventricle. This, in turn, results in secondary diastolic dysfunction of the left ventricle, which further reduces cardiac output leading to aortic hypotension and coronary hypoperfusion of the right ventricle.

The effect of the usual inotropes such as epinephrine or dobutamine on the right ventricle as well as the potential deleterious effect on the pulmonary vascular resistance is still matter of debate. It is also known that some therapies may not have the same effects on the systemic or the pulmonary circulation.

Catecholamines appear as a tempting and justified option in this setting to try to find a balance between the potential beneficial and the detrimental effects. Epinephrine can improve cardiac function but is now

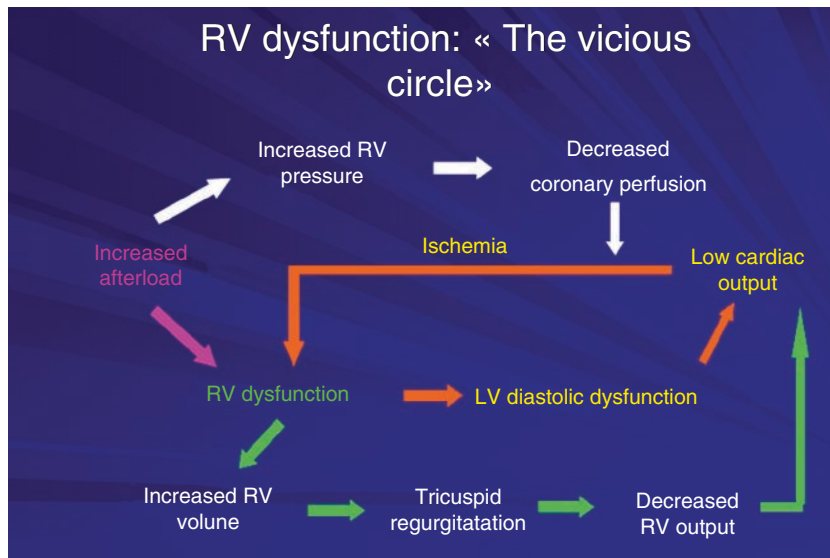


Fig. 44.8 Right ventricular dysfunction in pulmonary arterial hypertension

known to be deleterious to the myocardium if used at high doses and for a prolonged period of time. However it may still have a place at low dose.

Norepinephrine, through an increase in SVR, may improve coronary perfusion and as such improve right ventricular function. The virtues of the drug should be balanced against its side effects.

The finality is that the perfect drug should improve myocardial performance and vasodilate the pulmonary vascular bed without inducing tachycardia and oxygen consumption. Milrinone is a phosphodiesterase inhibitor that may have some of these properties and it is increasingly used in postoperative care. The role of type 5 phosphodiesterase inhibitors in the presence of pulmonary hypertension has a major interest but type 3 inhibitors such as milrinone have been by far more studied and largely used in pediatric practice.

Some new therapies are under development. Neseritide or natriuretic hormone shows some synergistic effect with nitric oxide and sildenafil, but further studies are required as available data is insufficient. The same principle applies to levosimendan, a calcium sensitizer that enhances contractility and has some vasodilatory properties without increasing myocardial oxygen consumption. It has also been shown to have some pulmonary vasodilator effects in the presence of acute pulmonary hypertension, but so far data in children is scarce and further studies are also needed.

44.9 Conclusion

Management of pulmonary hypertension in the cardiac intensive care setting should be multifactorial and multidisciplinary as it remains challenging and still carries, even if decreased compared to the previous decade, a significant mortality and morbidity. An increased knowledge of the mechanisms as well as the introduction of new therapies has led to better prognosis. Appropriate therapy requires firstly the identification of the potential cause. Beside the pharmacological approach, caregivers should consider the creation of anatomic paths to decompress the right ventricle, as the final cause of death remains ventricular failure.

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Chapter 45

Chronic Pulmonary Hypertension

Dunbar Ivy and Asrar Rashid

This chapter discusses the anatomical and physiological basis for chronic pulmonary arterial hypertension, its diagnosis and management. Pulmonary arterial hypertension (PAH) can lead to significant cardiac dysfunction and is associated with an increased risk of perioperative cardiovascular complications [1]. The selection of appropriate therapies is complex, requiring familiarity with the underlying disease process, complicated delivery systems, dosing regimens, and medication complications [2]. Recent therapeutic and surgical advances in the management of PAH have led to an improvement in prognosis.

45.1 Definition

Pulmonary hypertension is defined as a mean pulmonary artery pressure greater than 25 mmHg at rest [3]. In 1998, the World Health Organization proposed a new classification of pulmonary hypertension and this was updated in 2003 (Table 45.1), and again in 2008 at the Dana Point WHO meeting [3b].

45.2 Anatomy

PAH is a progressive disease characterized by lumen-obstructing structural alterations within the pulmonary bed [4], leading to a rise in pulmonary vascular

resistance and pulmonary arterial pressure (PAP), and eventually right ventricular failure [5, 6]. The cellular changes that may be implicated in the development of PAH are complex and some of these are detailed in Fig. 45.1 [7, 8]. The increased pulmonary vascular resistance (PVR) may be caused by both pulmonary vascular remodeling and sustained pulmonary vascular vasoconstriction [9]. The mechanisms involved in the latter include endothelial dysfunction and vascular smooth muscle hyper constriction (VSMC) [9]. It has been suggested that the muscularisation of the terminal pulmonary arterial vascular tree, caused by VSMC hyperplasia, is the earliest change [10]. In established PAH, the pulmonary arteries are characterized by intimal fibrosis, medial hypertrophy, adventitial proliferation, and obliteration of small arteries. The mechanisms and causes of development of plexiform lesions are complex and can be found in many PAH cases with multiple channels lined by cells expressing markers found on endothelial cells or smooth muscle cells (Fig. 45.2) and may represent an angiogenic response to local ischemia, hypoxia, or shear stress, and/or hyper proliferation of apoptosis resistant pulmonary artery endothelial cells [11, 12]. Other mechanisms, including activation of endogenous vascular elastase [13] and damage to the vascular endothelium play a role [14].

45.3 Pathophysiology

In the normal pulmonary circulation, pressure and resistance are 80–90% lower than in the systemic circulation. Pulmonary arteries larger than 1 mm in internal diameter are elastic and have well-developed internal and external laminae within a less distinct

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Table 45.1 Updated WHO clinical classification of pulmonary hypertension (Dana Point, 2008)

1. Pulmonary Arterial Hypertension (PAH)
 - 1.1. Idiopathic
 - 1.2. Heritable
 - 1.2.1. BMPR2
 - 1.2.2. ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)
 - 1.2.3. Unknown
 - 1.3. Drugs and toxins induced
 - 1.4. Associated with (APAH)
 - 1.4.1. Connective tissue diseases
 - 1.4.2. HIV infection
 - 1.4.3. Portal hypertension
 - 1.4.4. Congenital heart disease
 - 1.4.5. Schistosomiasis
 - 1.4.6. Chronic haemolytic anaemia
 - 1.5. Persistent pulmonary hypertension of the newborn
- 1' Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis
- 2 Pulmonary hypertension due to left heart disease
 - 2.1. Systolic dysfunction
 - 2.2. Diastolic dysfunction
 - 2.3. Valvular disease
- 3 Pulmonary hypertension due to lung diseases and/or hypoxaemia
 - 3.1. Chronic obstructive pulmonary disease
 - 3.2. Interstitial lung disease
 - 3.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
 - 3.4. Sleep-disordered breathing
 - 3.5. Alveolar hypoventilation disorders
 - 3.6. Chronic exposure to high altitude
 - 3.7. Developmental abnormalities
- 4 Chronic thromboembolic pulmonary hypertension
- 5 PH with unclear and/or multifactorial mechanisms
 - 5.1. Haematological disorders: myeloproliferative disorders, splenectomy
 - 5.2. Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis
 - 5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
 - 5.4. Others: tumoural obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

ALK-1 = activin receptor-like kinase 1 gene; APAH = associated pulmonary arterial hypertension; BMPR2 = bone morphogenetic protein receptor, type 2; HIV = human immunodeficiency virus; PAH = pulmonary arterial hypertension.

Guidelines for the diagnosis and treatment of pulmonary hypertension: The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT)

Eur Heart J. 2009 Aug 27. [Epub ahead of print]

medial layer than systemic arteries. Most pulmonary arteries run adjacent to the airways. Distal to the respiratory bronchioles, the smooth muscle layer is reduced, and the arteries are only partially muscularized or non-muscularized. Vascular tone is normally very low.

PVR is the current standard for evaluating reactivity in children with PAH. However, PVR measures only the mean component of right ventricular afterload and neglects pulsatile effects. Total right ventricular afterload can be measured as pulmonary vascular input impedance and consists of a dynamic component (compliance/stiffness) and a static component (resistance). In the normal pulmonary circulation, resistance contributes 90% of total RV afterload, whereas in significant PAH, 30% of RV afterload may be contributed by compliance and 70% by resistance. Increases in PVR and decreases in compliance of the larger pulmonary arteries will increase right ventricular afterload, and can lead to right ventricular dysfunction [15–18]. Acute PAH has a differing implication for RV dysfunction when compared to the development of chronic PAH. Acute PAH leads to an immediate increase in acute end-diastolic volume and decrease in RV ejection fraction leading to decrease in RV stroke volume. The development of chronic PAH has differing implications (see Fig. 45.3). Patients with PAH are prone to the development of the fatal complication of pulmonary hypertensive crisis, which is characterized by a rapid increase in PVR, related to pulmonary arterial vasoreactivity. PVR increases to the point where PAP exceeds systemic blood pressure, which leads to a decrease in systemic blood pressure, shift of the inter-ventricular septum leading to altered left ventricular diastolic filling, and a decrease in oxygenation. Hypercarbia, hypoxia, acidosis, and noxious stimuli such as pain and airway instrumentation can trigger a rapid increase in PVR that can lead to a pulmonary hypertensive crisis and/or right heart failure. The resulting right heart failure leads to a decrease in pulmonary blood flow, decreased cardiac output, hypoxia, and biventricular failure. Other perioperative mechanisms associated with right-sided heart failure in patients with PAH include right ventricular dilatation (leading to compression of the left ventricle), hypovolemia (inadequate preload), systemic hypotension (decreased coronary perfusion), hypoxemia, and acidosis.

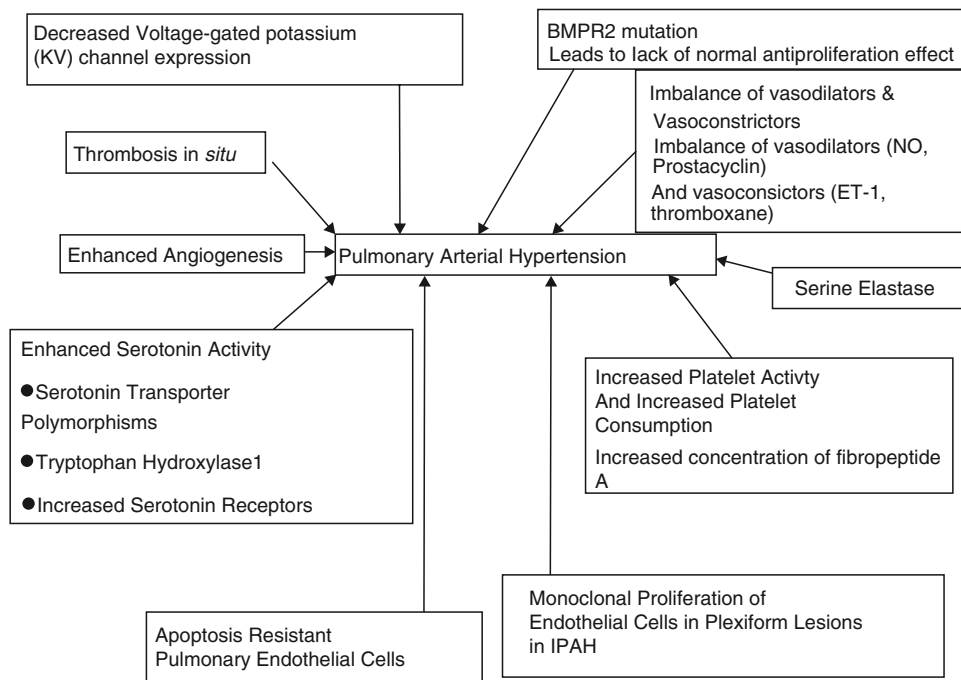


Fig. 45.1 Potential mechanisms leading to the development of PAH

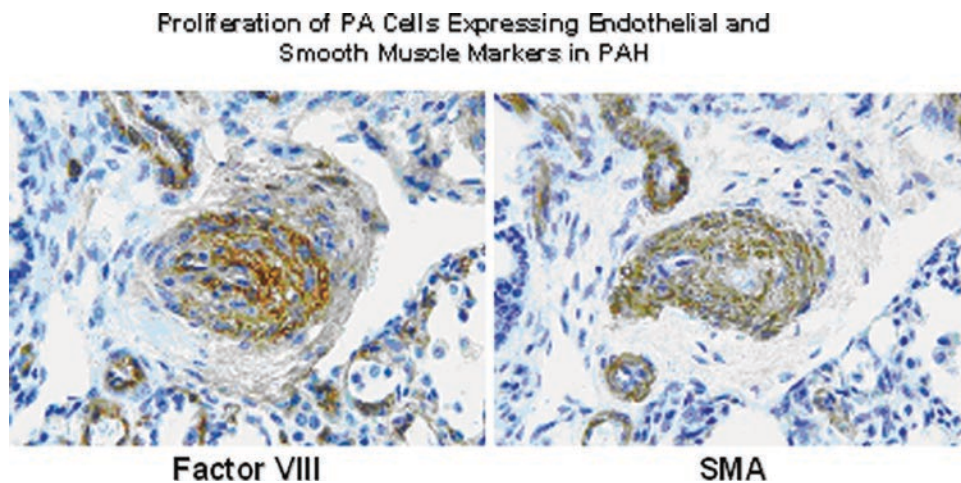


Fig. 45.2 Proliferation of PA cells expressing endothelial and smooth muscle markers in PAH

45.4 Clinical Presentation

Diagnosis of chronic PAH is often delayed due to the subtle nature of the symptoms. Nevertheless, PAH symptoms are clearly cardiorespiratory. Symptoms include exertional dyspnea and fatigue. Chest pain and

syncope are indicative of more severe limitations in cardiac output. In infants, symptoms are even less specific and may involve poor appetite, failure to thrive, lethargy, diaphoresis, tachypnea, tachycardia, and irritability [19–21].

Evaluation: See Table 45.2

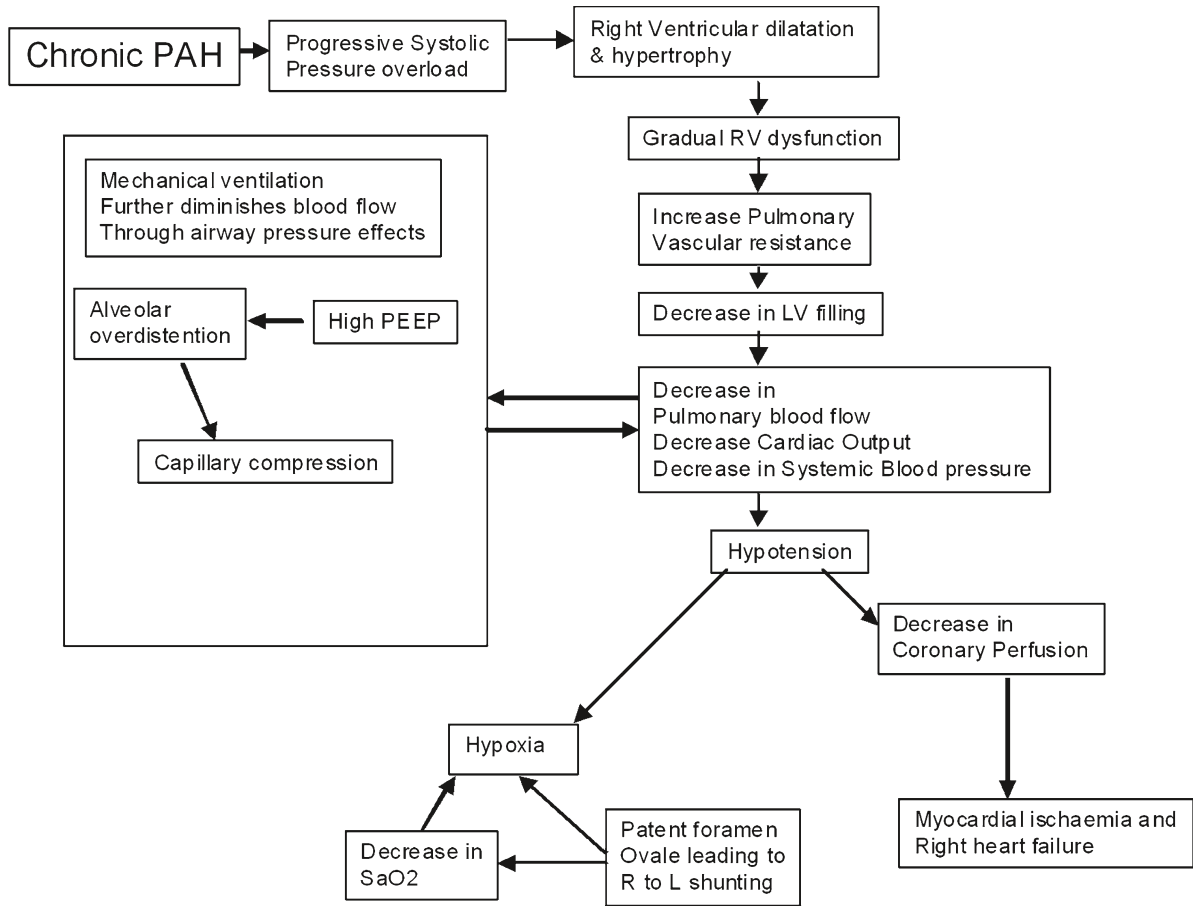


Fig. 45.3 Pathophysiology of Chronic PAH

Table 45.2 Pulmonary hypertension evaluation

PAH detection	
Chest radiography	Cardiomegaly and enlarged pulmonary arteries
Electrocardiography	Right ventricular hypertrophy
Echocardiography	Right ventricular hypertrophy, quantify right ventricular systolic pressure / function
	Exclude left heart or congenital heart disease
PAH characterization	
Cardiac catheterization with acute vasodilator testing	Evaluate pulmonary artery pressure, resistance, and degree of pulmonary reactivity
Anemia	Complete blood count with platelet count
Hypo/Hyperthyroid	Thyroid function tests
Hypercoagulable evaluation	Disseminated intravascular coagulation screen
	Antithrombin III
	Protein C
	Protein S
	Lupus anticoagulant
	Factor V Leiden
	Prothrombin gene mutation 20210
	Anti-phospholipid antibody evaluation

(continued)

Table 45.2 (continued)

Autoimmune disease evaluation	Antinuclear antibodies (DNA, Smith, ribonucleoprotein, SSA, SSB, anticentromere antibody, anti-SCL70) Rheumatoid factor Complement Erythrocyte sedimentation rate
Human Immunodeficiency Virus	HIV test
Toxicology screen	Amphetamines, cocaine, meta-amphetamines, fenfluramine, and phenylpropanolamine
Liver evaluation	Abdominal ultrasonography Liver function tests with gamma glutaryl transferase Hepatitis profile
Lung evaluation	Pulmonary function tests (to exclude obstructive/restrictive lung disease) Ventilation-perfusion (V/Q) lung scintigraphy (exclude thromboembolism) Pulmonary wedge angiography High resolution computed tomography (to evaluate for interstitial lung disease) Pulse oximetry/polysomnography (to evaluate hypoxia, diminished ventilatory drive, sleep-related breathing disorders)Lung biopsy
Exercise capacity	6-minute walk test/treadmill exercise test Cardiopulmonary exercise testing

Beghetti M, Barst RJ, Naeiji R, Rubin LJ. *Pulmonary Arterial Hypertension Related to Congenital Heart Disease*, Elsevier, 2006.

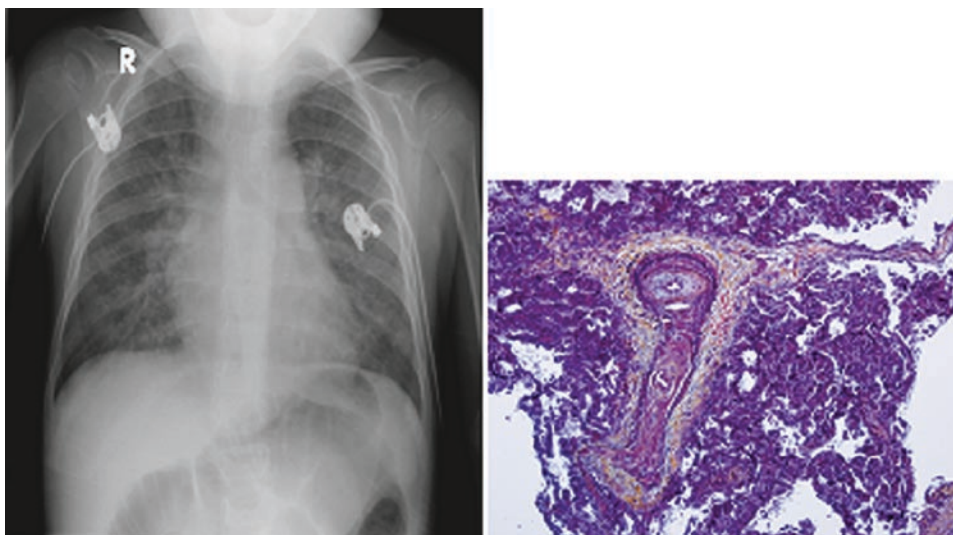


Fig. 45.4 Pulmonary veno-occlusive disease

45.4.1 Chest Radiography

The enlargement of the central pulmonary artery and or right ventricle on chest radiography suggests the presence of PAH. Prominence of the main pulmonary arteries is apparent in 90% of patients with IPAH, and peripheral pruning of the vessels occurs in approximately 50%. Yet, 6% of patients with confirmed IPAH may also present with normal radiographs [22]. The accuracy of the chest

radiography in the detection of PAH is uncertain, and no correlation has been established between the extent of the radiograph abnormalities and the severity of PAH. Chest radiography findings may be useful to uncover secondary causes of pulmonary hypertension. Pulmonary venous congestion may suggest pulmonary veno-occlusive disease (Fig. 45.4) or pulmonary capillary hemangiomatosis; hyperinflation or kyphosis are signs of restrictive lung disease; asymmetry of the enlarged central pulmonary

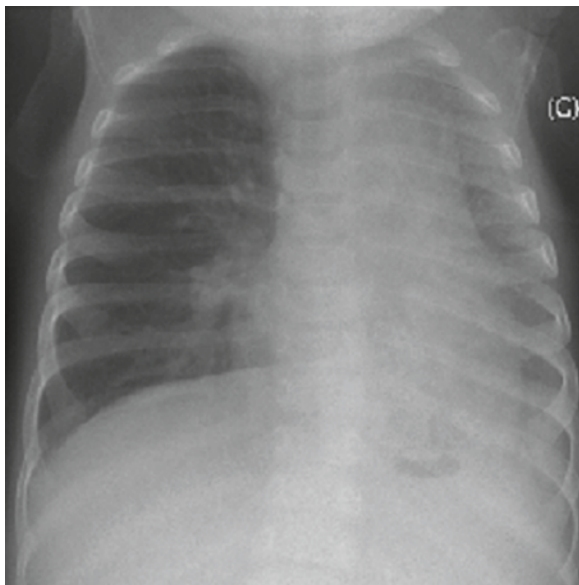


Fig. 45.5 Unilateral pulmonary vein atresia [26]

arteries may warrant investigation of chronic thromboembolic disease or porto-pulmonary hypertension [23–25]. Asymmetric lung volumes may suggest either pulmonary arterial or pulmonary venous abnormalities. For example, a unilateral small lung may be seen in unilateral “absence” of a pulmonary artery, scimitar syndrome, or congenital diaphragmatic hernia. Likewise, unilateral congenital absence of pulmonary veins may have small lung volume on X-ray [26] (Fig. 45.5).

45.4.2 Electrocardiography

Electrocardiography (ECG) is often the first test to suggest PAH by showing right ventricular hypertrophy and right atrial enlargement. Evidence of right ventricular hypertrophy on ECG is present in 87% of patients with IPAH and right axis deviation in 79%. ECG parameters reflective of physiologic and anatomic abnormalities in the right atria and right ventricle (a large P-wave amplitude $> /0.25$ mV) in lead II, QR complex in lead V1 or V3R is indicative of right ventricular hypertrophy regardless of voltage. An upright T-wave in V1 is indicative of right ventricular hypertrophy from 7 days–7 years. However, some studies have suggested that the specificity (69%) and positive predictive value (67%) of ECG is low in children with an echocardiographic diagnosis of PH [27]. However, these authors believe that that sensitivity is

much higher, especially in combination with a complete physical examination.

45.4.3 Echocardiography

Echocardiography is the most useful non-invasive screening tool to evaluate patients with a clinical suspicion of PAH [28]. The echocardiogram documents right ventricular size and function, left ventricular systolic and diastolic function, morphology and function of valves, and the presence of pericardial effusion or a patent foramen ovale. An acceleration time to ejection time ratio less than 0.3 suggests the presence, but not the degree, of pulmonary hypertension [28]. Transthoracic Doppler echocardiography can provide an estimate of the systolic pulmonary arterial pressures (sPAP). In the absence of pulmonary outflow obstruction, sPAP is equivalent to the right ventricular systolic pressure (RVSP). The systolic regurgitant tricuspid flow velocity (V) is measured and the right atrial pressure (RAP) is either a standardized value or an estimated value from the flow characteristics of the inferior vena cava or from jugular venous distention [28]. Tricuspid regurgitation of measurable quality has been reported in as many as 86% of cardiovascular patients [29, 30]. There have been reports of a correlation between Doppler echocardiography and right heart catheterization measurements of sPAP [30–32]. However, Doppler echocardiography may underestimate sPAP in patients with severe PAH [33] and overestimate sPAP in populations with mild or asymptomatic PAH [34]. When using Doppler echocardiography-estimated sPAP for detecting PAH, the sensitivity ranges from 0.63 to 1.00 and the specificity from 0.68 to 0.98 [34–36]. Despite recent advances that have improved the estimation of sPAP, Doppler echocardiography remains less accurate in most patients than invasive evaluation by right heart catheterization. Color flow Doppler imaging usually can detect intracardiac shunting [37], although contrast echocardiography may be more suited to visualize right-to-left shunting in patients with a small atrial communication [38].

The myocardial performance index (MPI) is an index of global ventricular function and correlates with hemodynamics in adults and children with PH. In children, a recent study showed that right ventricular MPI for patients with IPAH was 0.64 ± 0.30 versus 0.28 ± 0.03 in control subjects ($P < 0.01$). RV MPI had

a strong correlation with mean PA pressure ($R=0.94$; $P<0.001$), and decreased significantly in responders to bosentan therapy (range 20–44%, mean 25%) with a 5% increase in non-responders [39]. RV MPI is a non-invasive Doppler index that may be useful to follow up children with IPAH, particularly when tricuspid regurgitation data are insufficient. Measurement of the dp/dt of the tricuspid regurgitation jet may add additional information about right ventricular function.

Transesophageal echocardiography may be useful in older children for the optimal anatomic definition and may be superior to the transthoracic approach for detecting atrial septal defects [37,38,40]. Transesophageal echocardiography has also been used to detect central pulmonary artery emboli [41, 42] and may reveal the presence of chronic thromboembolism causing PAH. Differentiation between IPAH and chronic thromboembolic pulmonary hypertension (CTEPH) using normalized pulse pressures estimated from Doppler ultrasound measurements has been reported with a sensitivity of 0.95 and specificity of 1.00 [43]. Tissue Doppler imaging has recently been used to evaluate for the presence of RV or LV diastolic dysfunction.

Recent interest has grown in the area of measurement of total right ventricular afterload by measurement of input vascular impedance. Impedance incorporates the sum of total compliance and resistance of the vascular

bed [15, 44–46]. Currently, measurement of impedance requires invasive measurements in addition to measurement of Doppler flow. A recent manuscript in adults with pulmonary hypertension showed that a measure of capacitance (pulse pressure/stroke volume) was a better predictor of survival than measurement of PVR [16, 18]. In children, pulmonary vascular input impedance has recently been shown to be feasible and predict clinical outcomes better than PVR in children with PAH [46] (Fig. 45.6).

45.4.4 Other Evaluation Modalities

Cardiac MRI provides exact measurements of heart function and blood flow and is used with increasing frequency to evaluate patients with pulmonary arterial hypertension [47–50]. Cardiopulmonary exercise testing using cycle ergometry or 6 min walk testing has been shown to correlate with disease severity and prognosis, and is helpful in assessing responses to clinical treatments [47–50]. Recently published data from this center showed that children can safely undergo cardiopulmonary testing and the peak oxygen consumption is strongly correlated to disease severity [51, 52] (Table 45.2). Six-minute walk test is a sub-maximal test shown to have a strong independent association with mortality among

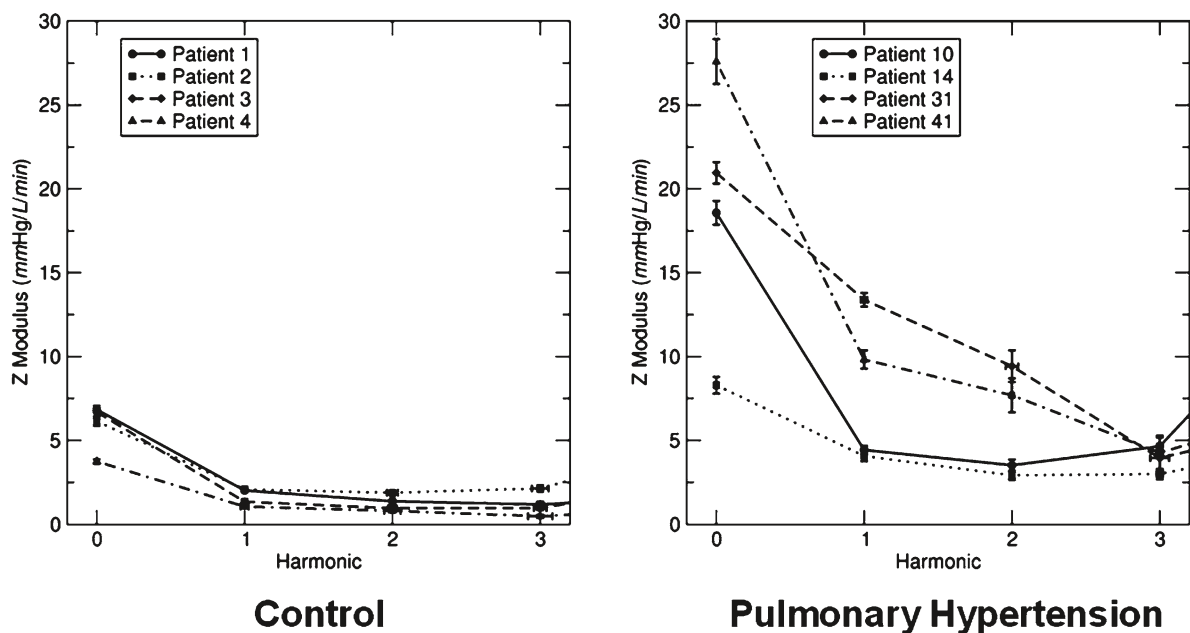
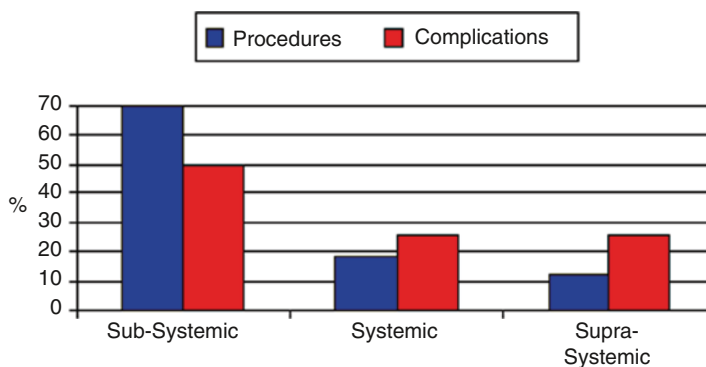


Fig. 45.6 Pulmonary vascular input impedance [46]

Fig. 45.7 Perioperative complications in children with pulmonary hypertension undergoing noncardiac surgery or cardiac catheterization [1]



patients with IPAH [53]; however, children often have less right heart failure for a given elevation of pulmonary artery pressure leading to a further distance walked.

45.5 Preoperative Management of Patients with PAH

Children with PAH may require surgical intervention, either as definitive procedure or palliation of their underlying PAH. Alternatively children with PAH may require surgical interventional not directly related to the PAH. At the preoperative stage, a full evaluation of the etiology of PAH is imperative, as well as knowledge of vasoreactivity of the pulmonary bed [4]. PAH carries a significant risk of cardiac dysfunction and thus the increased risk of perioperative cardiovascular complications (Fig. 45.7) [1].

Preoperative management is based on the following aims:

1. Ascertaining the causality of the PAH, and its reversibility, which is then related to the patient's suitability for surgical intervention.
2. Understanding whether an attempt at preoperative optimization of a patient with PAH should be undertaken. If the PAH is reversible, the clinician must understand the best form of pharmacological intervention that should be attempted, in the intervening period before surgery or catheterization.
3. If the child is already on a program of medication for PAH, this should be continued through the perioperative period. Anticoagulation should be converted from Warfarin to intravenous Heparin, if indicated.
4. Ascertaining the causality of the PAH, and its reversibility, which is then related to the patient's suitability for surgical intervention.

Table 45.3 Cardiopulmonary exercise testing in pediatric pulmonary hypertension

Variable	Adverse outcome	No adverse outcome	p
Age	11.5±0.7	11.5±3.5	NS
Peak VO ₂	14.6±3.9	26.8±7.2	<0.0001
%Peak VO ₂	33±8	60±14	<0.0001
VE/VCO ₂	55±11	39±8	<0.0001
% VE/VCO ₂	170±32	126±20	<0.0001
% O ₂ Pulse	40%	66%	0.04

Ref. [51]

Preoperative assessment in all patients with suspected PAH should include a physical examination, a recent electrocardiogram and echocardiogram as a part of an extensive evaluation (Table 45.3), and cardiac catheterization.

The aim of the initial assessment is to differentiate among known etiologies [19, 54–56]. Symptoms may include exertional dyspnea, reduced exercise tolerance, orthopnea, atypical chest pain, hemoptysis, feeding intolerance, or growth failure. Syncope in this setting may be indicative of end-stage disease.

Special situations may predispose to the development of pulmonary arterial hypertension. As an example, children living at an altitude and presenting with high-altitude pulmonary edema (HAPE) should be screened for pulmonary hypertension [57]. In addition, children with biliary atresia, cavernous transformation of the portal vein, primary sclerosing cholangitis, or cryptogenic cirrhosis, may have porto-pulmonary hypertension with an associated high mortality [58]. Some medications may predispose to the development of severe pulmonary hypertension, such as phenylpropanolamine [59].

Non-invasive testing can be useful for screening and assessing prognosis (Table 45.3). Echocardiography is important in estimating pulmonary pressures and evaluating potential structural abnormalities.

As respiratory disease is an important cause of pulmonary hypertension, radiographic and physiologic evaluation of the lung should be undertaken to exclude parenchymal lung disease.

Cardiac catheterization is important to evaluate pulmonary artery pressures and resistance as well as to determine acute reactivity of the pulmonary vasculature [56]. Right heart catheterization can confirm the diagnosis of PAH; assess the severity of the hemodynamic impairment, and target therapy. The pulmonary artery pressures and pulmonary wedge pressures are measured; shunt size and pulmonary blood flow are determined and PVR is calculated by dividing the pressure gradient across the lungs by the pulmonary blood flow. Sedation may be necessary to minimize a child's agitation. Care should be taken to avoid rebound effects of inhaled nitric oxide withdrawal acutely and within 12 h after the procedure. If right heart catheterization confirms the presence of PAH requiring treatment, a vasodilator study should be performed at the time of catheterization to determine the acute pulmonary vasoreactivity to short-acting vasodilators (discussed later in the chapter)

Various molecular markers are being assessed as to their suitability in the follow-up of patients with PAH. Such markers include Brain natriuretic peptide, Cardiac troponin T, Uric acid, Endothelin-1, products of NO metabolism and Fibrinogen metabolism products.

Possible causes of PAH are detailed below. It is critically important to identify and treat any underlying conditions associated with PAH to improve the chance of reversal of disease.

45.5.1 Idiopathic Pulmonary Arterial Hypertension

Idiopathic pulmonary arterial hypertension (IPAH) is a rare disease that occurs most frequently in young adult females [60]. IPAH is characterized by progressive and sustained elevations of pulmonary artery pressure without a defined etiology. Pediatric IPAH is well reported, and carried a dismal prognosis in the NIH cohort, with a median survival of only 10 months in individuals less than 16 years old [61]. Evaluation for IPAH in the pediatric age group is similar to that outlined for adults, but increased scrutiny for the possibility of congenital car-

diac disease is appropriate, and acute pulmonary vasoreactivity may be more common in children [62–65]. Recent study examined a previously identified cohort of 77 children diagnosed between 1982 and 1995 with idiopathic pulmonary arterial hypertension and followed up through 2002. For acute responders treated with CCB ($n=31$), survival at 1, 5, and 10 years was 97, 97, and 81%, respectively; treatment success was 84, 68, and 47%, respectively. Survival for all children treated with epoprostenol ($n=35$) at 1, 5, and 10 years was 94, 81, and 61%, respectively (Fig. 45.8); treatment success was 83, 57, and 37%, respectively [62].

45.5.2 Familial Pulmonary Artery Hypertension

Between 6 and 12% of cases of IPAH, it may be familial in origin with an autosomal dominant pattern of inheritance, and disease presents at younger ages with subsequent generations (termed genetic anticipation) [66]. The cause in childhood appears heterogeneous in nature, with genetic defects of transforming growth factor-beta receptors playing an important role [67]. BMPRII is a type 2 receptor of the transforming growth factor (TGF)- β superfamily of cytokines, members of which are essential for the cellular proliferation, differentiation, and apoptosis. Workers have postulated a different genetic background for children compared to adults, with a recessive mode of inheritance being put forward in a proportion of infantile cases [68], but this is yet to be proven. Diverse germline heterozygous mutations in the gene that encodes for the bone morphogenetic protein receptor-II (BMPRII) on chromosome 2q33 cause familial pulmonary arterial hypertension [69, 70]. These mutations appear to result in uncontrolled proliferation of vascular smooth muscle due to lack of an anti-proliferative effect of normal BMPR2 signaling [71, 72]. More than 50 disease-causing defects in the BMPRII gene have been reported, however, many have been identified in patients with no family history of pulmonary arterial hypertension, implying either a low disease penetrance or the occurrence of spontaneous mutations [69–71, 73]. BMPRII was found in 6% of a mixed cohort of adults and children with pulmonary arterial hypertension/congenital heart defects [74].

Other genetic loci may also play important roles. Studies have suggested an important role of the serotonin

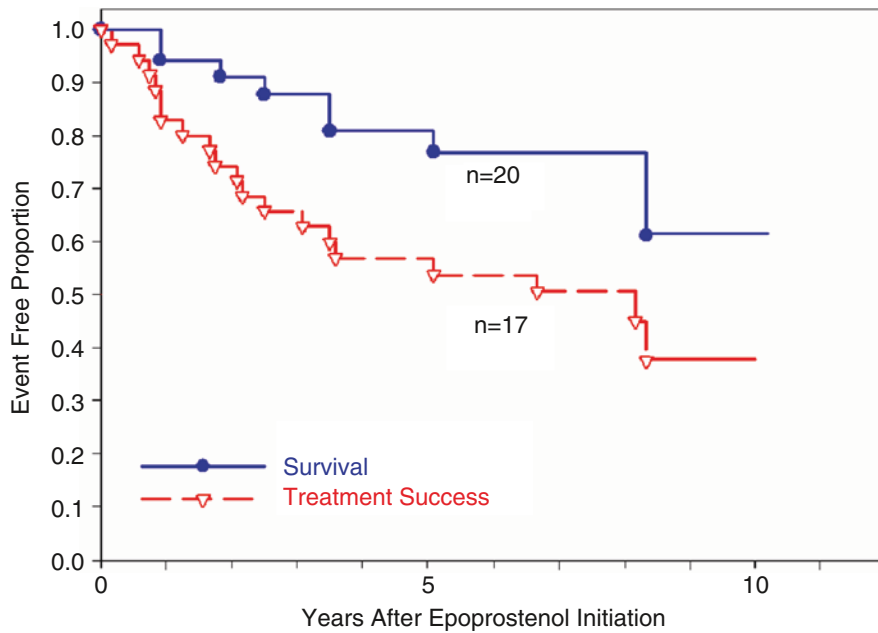


Fig. 45.8 Outcomes in children with idiopathic pulmonary arterial hypertension [62]

transporter gene in some adults with PAH [75], and a study in children found that homozygosity for the long variant of the serotonin transporter gene was highly associated with idiopathic pulmonary hypertension in children [76].

45.5.3 Congenital Heart Disease

A variety of congenital cardiac lesions can cause pulmonary hypertension [21] (Table 45.4). The age at which these lesions produce irreversible pulmonary vascular disease varies. In general, patients with a ventricular septal defect or patent ductus arteriosus do not develop irreversible pulmonary vascular changes before 2 years of age. Children with Down syndrome may have an increased risk of pulmonary hypertension, if congenital cardiac lesions are present. Similarly, infants with an atrial or ventricular septal defect with concomitant chronic lung disease are at an increased risk for the early development of severe pulmonary vascular disease. In one study of infants with bronchopulmonary dysplasia who underwent cardiac surgery for the repair of congenital heart disease, 25% of those who died had pulmonary arterial hypertension [77].

Patients with cyanotic congenital cardiac lesions such as transposition of the great arteries, truncus

arteriosus, and univentricular heart with high flow also may develop pulmonary hypertension. Palliative shunting operations for certain cardiac anomalies designed to increase pulmonary blood flow also may lead to the subsequent development of pulmonary hypertension. Hypoxia with increased shunting is believed to be a potent stimulus for the rapid development of pulmonary vascular disease.

45.5.4 Eisenmenger Syndrome

Eisenmenger syndrome describes pulmonary hypertension with a reversed central shunt [78]. In general, the term “Eisenmenger syndrome” is used mainly for shunts distal to the tricuspid valve, but some studies have included patients with a large atrial septal defect. The syndrome is characterized by elevated PVR and bi-directional or right-to-left shunting through a systemic-to-pulmonary connection, such as a ventricular septal defect, patent ductus arteriosus, univentricular heart, or aortopulmonary window. The shunt is initially left-to-right, but as the underlying condition continues to increase PVR, there is a reversal of the shunt to a right-to-left configuration, leading to cyanosis and erythrocytosis. It is not uncommon for patients that are

Table 45.4 Cardiac lesions associated with pulmonary hypertension

Left-to-right shunts	Atrial septal defect
	Ventricular septal defect
	Patent ductus arteriosus
	Atrioventricular septal (canal) defect
	Aorto-pulmonary window
Increased pulmonary venous pressure	Cardiomyopathy
	Coarctation of the aorta (left ventricular diastolic dysfunction)
	Hypoplastic left heart syndrome
	Shone complex
	Mitral stenosis
	Supravalvar mitral ring
	Cor triatriatum
	Pulmonary vein stenosis/veno-occlusive disease
	Total anomalous pulmonary venous return
	Cyanotic heart disease
Truncus arteriosus	
Tetralogy of Fallot (pulmonary atresia/VSD)	
Univentricular heart	
Anomalies of the pulmonary artery or pulmonary vein	Origin of a pulmonary artery from the aorta
	Unilateral “absence” of a pulmonary artery
	Scimitar syndrome
Palliative shunting operations	Waterston anastomosis
	Potts anastomosis
	Blalock-Taussig anastomosis

Beghetti M, Barst RJ, Naeiji R, Rubin LJ. *Pulmonary Arterial Hypertension Related to Congenital Heart Disease*, Elsevier; 2006.

detected late with Eisenmenger syndrome to not have a prior history of congestive heart failure, suggesting that PVR never fell to normal levels in the perinatal period. In general, the prognosis of patients with Eisenmenger syndrome is much better than for patients with IPAH, but syncope, right-heart failure, and severe hypoxemia are similarly associated with a poor prognosis. Phlebotomy may be utilized in Eisenmenger syndrome to provide temporary relief of hyperviscosity symptoms or to improve perioperative hemostasis, but should not routinely be performed as this leads to increased stiffness of the red blood cell [79]. Non-cardiac operations on Eisenmenger patients are associated with a high mortality rate, and should be managed by a multidisciplinary team experienced in the care of patients with this condition.

45.5.5 Hemoglobinopathies

Interest is growing in the area of pulmonary arterial hypertension associated with hemoglobinopathies, such as sickle cell disease. Studies by Gladwin and others have shown that a RVSP greater than 25 mmHg is predictive of increased mortality in adults with PAH [80]. This form of pulmonary artery hypertension may be different and associated with higher systolic rather than diastolic pressure and may be due to pulmonary vascular disease, high cardiac output, or left ventricular diastolic dysfunction. It is likely that the increased mortality in patients with SCD is multifactorial and includes diminished NO availability and the presence of diastolic dysfunction. Release of hemoglobin and arginase from lysed red cells causes scavenging of nitric oxide (NO) and catabolism of L-arginine, the obligate substrate for NO synthase (Fig. 45.9). The resulting impairment in NO bioavailability is associated with pulmonary vasoconstriction, endothelial dysfunction, thrombosis, and eventual development of plexogenic arterial lesions, the histological hallmark of all forms of PAH [81–84]. Furthermore, in addition to pulmonary hypertension, diastolic dysfunction is an independent risk factor for mortality in sickle cell disease [85].

45.5.6 Respiratory Disease

Parenchymal lung disease is an important cause of pulmonary hypertension in many patients. Complications include hypoxic pulmonary vasoconstriction, causing increased pulmonary artery pressures, and can lead to right ventricular hypertrophy and failure. Right ventricular function is usually preserved until disease is advanced. In most cases, correction of hypoxia can lead to reversal of pulmonary hypertension. However, the development of cor pulmonale carries a poorer prognosis for reversibility.

Treatment of cor pulmonale depends on the precise etiology of lung disease, as well as disease severity. Nocturnal oxygen administration may alleviate hypoxia, typically without causing hypercapnia. In patients with cystic fibrosis, calcium channel blockers have not shown proven effectiveness and may worsen oxygenation when cor pulmonale is present [86]. For patients with end-stage lung disease from cystic fibrosis,

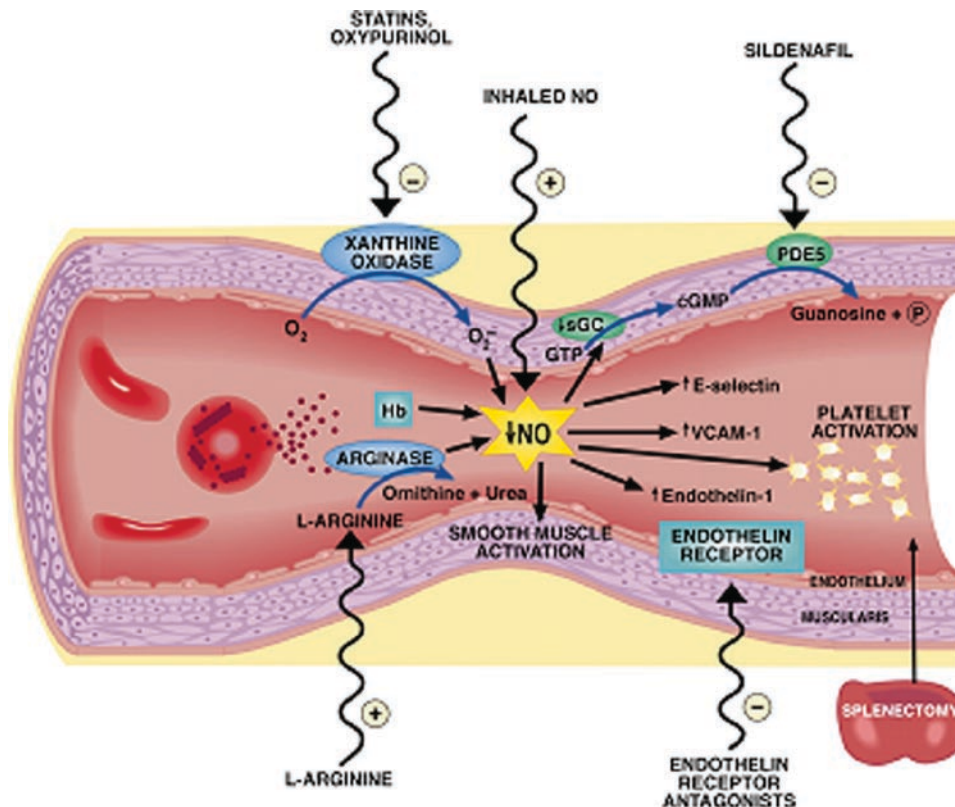


Fig. 45.9 Mechanisms of pulmonary vascular dysfunction in hemoglobinopathies [82]

lung transplantation may represent the most attractive treatment option.

Disorders of respiratory mechanics may also lead to hypoxia and the development of pulmonary hypertension, as can bronchopulmonary dysplasia [87]. More recent studies have suggested that abnormalities of the pulmonary vasculature may be a primary rather than secondary cause of abnormal alveolarization in bronchopulmonary dysplasia [88–91]. Patients with congenital diaphragmatic hernia are at risk for pulmonary hypertension, which can develop at any phases of the disease. In addition to lung hypoplasia, patients with congenital diaphragmatic hernia may develop pulmonary artery or pulmonary vein stenosis [91]. The respiratory problem causing the PAH per se may not be amenable to surgical intervention. However, if the PAH is reversible, surgical intervention may affect.

45.5.7 Thromboembolic Disease

Chronic thromboembolic disease as a cause of pulmonary hypertension in children is uncommon. However, the condition can occur rarely, and an accurate diagnosis is essential for treatment [55, 64]. Predisposing factors include anti-phospholipid antibody syndrome, collagen vascular diseases, thrombophilia, bacterial endocarditis, and ventricular-atrial shunt for the treatment of hydrocephalus and sickle cell disease. Likewise, the use of oral contraceptive agents may cause hypercoagulability, leading to pulmonary thromboembolic phenomena.

The diagnosis of CTEPH in children requires a high index of suspicion, as well as evaluation by ventilation perfusion, CT scanning, or angiography. In adults with CTEPH, surgically accessible disease

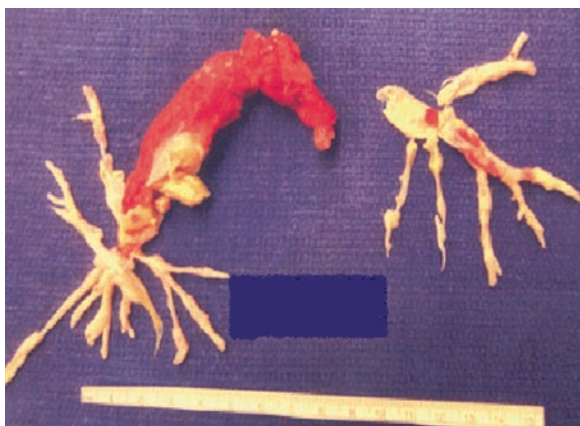


Fig. 45.10 Pulmonary thromboendarterectomy is useful in rehabilitating vascular patency in some cases of CTEPH

and no severe co morbidities, pulmonary thromboendarterectomy has been demonstrated to improve survival and quality of life in patients (Fig. 45.10) [92]. A similar approach should be considered for children who develop this condition despite the relative paucity of data on this procedure in the pediatric age group.

45.6 Pharmacological Therapy of PAH

Three classes of drugs have been extensively studied for the treatment of PAH on the basis of known mechanisms of action: prostanoids (epoprostenol, treprostinil, iloprost, beraprost), endothelin receptor antagonists (bosentan, sitaxsentan, ambrisentan), and phosphodiesterase inhibitors (sildenafil) (Table 45.4).

Without therapy, and sometimes despite appropriate surgical correction of congenital cardiac lesions, pulmonary arterial hypertension progresses at a variable rate. As vasoconstriction is an important component in the development of medial hypertrophy, vasodilators are frequently used to decrease pulmonary artery pressure, improve cardiac output, and potentially reverse some of the pulmonary vascular changes noted in the lung. Our long-term strategy for the treatment of pulmonary hypertension in children is shown (Fig. 45.11).

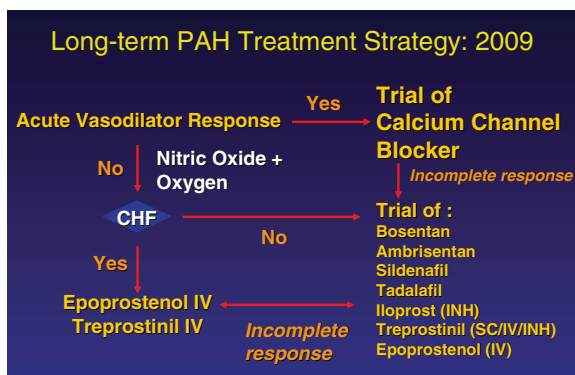


Fig. 45.11 Long-term PAH strategy. Adapted from [56]

Before commencing vasodilator therapy for chronic PAH, vasodilator responsiveness should be assessed in a controlled situation, ideally in the cardiac catheterization unit. A positive response is defined by assessing the change of cardiac and pulmonary catheter data to vasodilators [56, 93]. The younger the child at the time of testing, the greater the likelihood of acute pulmonary vasodilation in response to vasoreactivity testing [63, 94, 95]. Many oral and inhaled vasodilators have been used for testing of vasodilator responsiveness [94, 96–105].

45.6.1 Nitric Oxide

The use of newer vasodilator agents, particularly inhaled nitric oxide, has been an important advance in safely determining vasoreactivity. Inhaled nitric oxide therapy improves gas exchange and selectively lowers PVR in several clinical diseases, including idiopathic pulmonary hypertension and congenital heart disease [99, 106, 107]. Inhaled nitric oxide diffuses to the adjacent smooth muscle cell, where it activates soluble guanylate cyclase, resulting in an increase in cGMP and vasodilation. Currently, inhaled nitric oxide with oxygen is recommended by many centers as the agent of choice for evaluating pulmonary vasoreactivity.

The role of chronic inhaled nitric oxide (iNO) in the treatment of pulmonary hypertensive disorders has been studied [108, 109]. Although iNO therapy causes sustained decreases in PVR, adverse

hemodynamic effects may complicate iNO therapy after abrupt withdrawal [96, 110]. Inhibition of phosphodiesterase type 5 (see below), which degrades cGMP within vascular smooth muscle, causes vasodilation and may attenuate this rebound effect. Currently, few patients are treated with inhaled NO at home, but advancements in the use of NO in the non-intubated patient have led to greater use in the pre- and postoperative setting.

Clinically unpredictable or non-sustained responses have been noted with the iNO therapy, and its acute withdrawal can result in rapid rises in PVR [108, 111]. Alterations in endogenous endothelial activity during iNO therapy may mediate these clinical findings. ET-1 signaling pathways have been implicated in the rebound phenomena. Reactive oxygen species (ROS) may mediate these alterations and superoxide scavenging to stop the tissue increase in superoxide and peroxynitrite, preserve NOS activity, decrease eNOS nitration, and prevent the rebound phenomena [112, 113].

45.6.2 Calcium Channel Blockers

The use of calcium channel antagonists to evaluate vasoreactivity is dangerous, as these drugs can cause a decrease in cardiac output or a marked drop in systemic blood pressure [64]. Such deleterious effects may be prolonged due to the relatively long half-life of calcium channel blockers. Consequently, elevated RAP and low cardiac output are contraindications to acute or chronic calcium channel blockade. The number of patients treated with calcium channel blockers is steadily decreasing.

Our preference is to perform an acute trial of calcium channel blocker therapy only in those patients who are acutely responsive to either nitric oxide or prostacyclin. In this setting, response is defined as a fall in mean PAP of at least 10 mmHg to near normal levels and certainly less than a mean PAP of 40 mmHg. Likewise, patients who do not have an acute vasodilatory response to short acting agents and who are then placed on calcium channel blocker therapy are unlikely to benefit from this form of therapy [54]. 60 to 80% of children with severe pulmonary hypertension are non-responsive to acute vasodilator testing, and therefore require therapy other than calcium channel antagonists.

45.6.3 Prostacyclins

Adults with IPAH and children with congenital heart disease demonstrate an imbalance in the biosynthesis of thromboxane A₂ and prostacyclin. Likewise, adults and children with severe pulmonary hypertension show diminished prostacyclin synthase expression in the lung vasculature. Prostacyclin administered over the long term, utilizing intravenous epoprostenol, has shown to improve survival and quality of life in adults and children with idiopathic pulmonary arterial hypertension.

The choice of therapy for children with PAH is impacted by severity of disease, pharmacologic adverse effects, and the patient's and family's willingness to use invasive therapy. Children who demonstrate a positive response to acute vasodilator challenge in the cardiac catheterization laboratory with inhaled nitric oxide are candidates for calcium channel blocker therapy. At most, 40% of children are candidates for calcium channel blocker therapy as compared to only 10–25% of adults, which suggests an age dependent response [9]. The remaining therapies are classified by and target dysfunction in one of three major pathways: cyclic-AMP, cyclic-GMP, and endothelin. Patients with severe PAH are often treated with multi-drug therapy targeting all pathways if tolerated.

Prostacyclin and prostacyclin analogs impact the cyclic-AMP pathway to increase pulmonary vasodilation. Intravenous epoprostenol-prostacyclin was first used in the 1980s and continues to be the gold standard for treatment of severe disease (Fig. 45.8). The treatment of patients with prostacyclin is promising, however the therapy is cumbersome. The prostacyclin must be infused 24 h/day via a central venous catheter and kept cold with ice packs; the half-life of the drug is 2–5 min placing the patient at risk for an acute pulmonary hypertensive crisis if there is an accidental discontinuation of the medication. In addition, the side effects of the drug include nausea, diarrhea, jaw pain, bone pain and headaches. Epoprostenol was FDA approved in 1995 (Table 45.3).

The prostacyclin analog, treprostinil was approved by the FDA, initially for subcutaneous use (2002), and more recently for intravenous administration (2004a). While subcutaneous treprostinil allows patients to remain free of central venous catheters, it can cause severe pain at the infusion site. Recent data has shown long-term efficacy

in adults with PAH [114, 115] Treprostinil has also been given in the intravenous form. Intravenous treprostinil requires central line access and continuous infusion, but is easier for families to mix, and has a half-life of 4 h. Intravenous treprostinil has fewer side effects than intravenous epoprostenol, but there are no studies comparing efficacy [116]. Treprostinil is also being studied in an inhaled form [117].

An inhaled prostacyclin analog, iloprost, received approval for the treatment of PAH in the United States in December 2004. This medication is administered by nebulization 6–9 times a day. Iloprost requires patient cooperation with the treatment administration lasting 10–15 min, which is difficult for young children [94, 118–121]. The advantage of an inhaled prostacyclin is that it can cause selective pulmonary vasodilation without affecting systemic blood pressure. Additionally, inhaled prostacyclin analogs can improve gas exchange and intrapulmonary shunt in cases of impaired ventilation/perfusion by redistributing pulmonary blood flow from non-ventilated to ventilated, aerosol-accessible lung regions [120, 122]. In children with congenital heart disease and PAH, inhaled iloprost may be as effective in lowering pulmonary artery pressure and resistance as inhaled nitric oxide, and thus may be useful in evaluation of acute vasoreactivity [94]. One randomized controlled trial of aerosolized prostacyclin therapy in children with acute lung injury demonstrated improved oxygenation [123]. Inhaled iloprost has also been studied in combination with bosentan and sildenafil, among others [124–126].

The use of prostacyclin in patients with congenital heart disease is promising. Disadvantages of prostacyclin analogs, such as epoprostenol, include dose dependent side effects of the drug (nausea, anorexia, jaw pain, diarrhea, and musculoskeletal aches and pains) and side effects due to the method of delivery. The drug must be given through a central venous catheter and thus potential complications include clotting, hemorrhage, cellulitis, and line sepsis. Furthermore, the delivery of the drug must be uninterrupted, with abrupt cessation leading to acute deterioration, and in some cases death. In patients with residual right-to-left shunting, continuous prostacyclin occasionally may worsen shunt physiology and may result in complications such as cerebrovascular accident due to paradoxical embolism.

Beraprost is an orally active prostacyclin analog with a half-life of 35–40 min. While beneficial effects

have been noted in short-term trials, these may be attenuated with prolonged treatment [127, 128].

45.6.4 Endothelin

Another target for treatment of pulmonary hypertension is the vasoconstrictor peptide endothelin (ET) [129]. The endothelins are a family of isopeptides consisting of ET-1, ET-2, and ET-3. ET-1 is a potent vasoactive peptide produced primarily in the vascular endothelial cell, but also may be produced by smooth muscle cells. Two receptor subtypes, ET_A and ET_B, mediate the activity of ET-1. ET_A and ET_B receptors on vascular smooth muscle mediate vasoconstriction, whereas ET_B receptors on endothelial cells cause release of nitric oxide (NO) and prostacyclin (PGI₂), and act as clearance receptors for circulating ET-1. ET-1 expression is increased in the pulmonary arteries of patients with pulmonary hypertension. Bosentan, a dual ET receptor antagonist, lowers pulmonary artery pressure and resistance, and improves exercise tolerance in adults with pulmonary arterial hypertension [129]. These results can also be extrapolated to children [52, 93, 130–133]. In children with pulmonary arterial hypertension related to congenital heart disease or IPAH, bosentan lowers pulmonary pressure and resistance, and is well tolerated [93, 134]. Elevated hepatic aminotransferase levels occur in approximately 11% of adults treated with bosentan. In a 12-week study, children with IPAH or PAH related to congenital heart disease, bosentan was well tolerated and lowered the pulmonary artery pressure and resistance [93]. A more recent retrospective study of 86 children on bosentan for a median exposure of 14 months with and without concomitant therapy found that bosentan provided a sustained clinical and hemodynamic improvement, was overall well tolerated, and two-year survival estimates were 91% [132] (Fig. 45.11).

Selective ET_A receptor blockade is also possible using ambrisentan or sitaxsentan, ET receptor antagonists with high oral bioavailability and a long duration of action, and high specificity for the ET_A receptor. Selective ET_A receptor blockade may benefit patients with pulmonary arterial hypertension by blocking the vasoconstrictor effects of ET_A receptors while

maintaining the vasodilator/clearance functions of ET_B receptors. Sitaxsentan given orally for 12 weeks improved exercise capacity and cardiopulmonary hemodynamics in patients with pulmonary arterial hypertension that was idiopathic, or related to connective tissue or congenital heart disease [135–141]. Further studies using selective ET_A receptor blockade with BQ 123 in postoperative congenital heart disease [142, 143] have been reported. Ambrisentan, an endothelin receptor antagonist that is selective for the endothelin type-A (ETA) receptor was approved by the U.S. FDA in June 2007. Adults showed significant improvements in 6-min walk distance and significant delay in clinical worsening on ambrisentan. The incidence of elevated hepatic aminotransferase levels was 2.8% [144].

45.6.5 Phosphodiesterase-5 Inhibitors

Specific phosphodiesterase-5 inhibitors, such as sildenafil, [145–150] promote an increase in cGMP levels and thus promote pulmonary vasodilation and remodeling. Sildenafil is as effective a pulmonary vasodilator as inhaled NO and may be preferred because it does not increase pulmonary wedge pressure. Sildenafil may also be useful in the setting of inhaled nitric oxide therapy withdrawal [96, 110, 151] in postoperative pulmonary hypertension [152], or in the presence of pulmonary hypertension related to chronic lung disease [153]. In some settings, intravenous sildenafil may worsen oxygenation [154, 155]. Studies examining the use of oral phosphodiesterase-5 inhibitors in children are ongoing [156]. Other PDE-5 inhibitors, such as tadalafil are currently under study in adults and tadalafil received FDA approval for adults with APH in 2009.

45.6.6 Novel Therapies

Imatinib is a selective antagonist of the platelet-derived growth factor (PDGF) receptor and recently has shown promise in the treatment of severe PAH [157]. Imatinib was approved by the Food and Drug Administration for the treatment of Philadelphia

chromosome positive chronic myeloid leukemia (includes pediatric indication), relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia, myelodysplastic/ myeloproliferative disease, aggressive systemic mastocytosis, hypereosinophilic syndrome, dermatofibrosarcoma protuberans, and Kit (CD117) positive gastrointestinal stromal tumors. Platelet-derived growth factor (PDGF) has a role in vascular remodeling as PDGF participates in mitogenic signaling and smooth muscle cell recruitment. Expression of the PDGF receptor was found to be significantly increased in lung tissue from pulmonary arterial hypertension patients compared with healthy donor lung tissue [157]. Thus, imatinib as a potent antiproliferative agent may have a role in the treatment of PAH, a disease of lung vascular remodeling and proliferation. Case reports of the use of imatinib for patients with severe PAH refractory to all available treatment showed clinical and hemodynamic improvement and no toxic effects [158–160]. A controlled clinical trial for the use of imatinib in PAH is just beginning.

Statins have received growing attention in the treatment of PAH. Animal studies have shown dramatic responses in the prevention and regression of models of PAH. Inhibition of Rho-kinase expression and activity may be an important mechanism of the statin effect [161, 162]. A recent case series has suggested that this treatment requires further study [163]. A novel agent, a Rho-Kinase inhibitor, Fausidil has also been shown to reduce PVR and may show promise for the future [164].

Another promising therapy is treatment with bone-derived endothelial progenitor cells (EPCs). EPCs normally function to repair and regenerate blood vessels. The delivery of EPCs to rats with established PAH resulted in marked improvement in survival, which was greatest in the group receiving eNOS-transduced cells [165]. Therefore, the regeneration of lung vascular endothelium by injection of progenitor cells may represent a novel treatment paradigm for patients with PAH [166].

Recently, investigators in Paris and Geneva have pioneered the use of the Potts shunt to treat patients with idiopathic pulmonary arterial hypertension. By placing a Potts shunt, the right ventricle may be unloaded in systole converting the patient to an “Eisenmenger-like” physiology [167].

45.6.7 Anticoagulation

In retrospective trials in adults with IPAH and abnormal perfusion scans, the use of warfarin has been associated with improved survival. Although the use of chronic anticoagulation has not been studied widely in children, it is usually recommended. In IPAH, the aim is to maintain an INR between 1.3 and 2.0. The use of anticoagulation in patients with Eisenmenger syndrome is controversial and the potential risks and benefits of anticoagulation in this setting must be carefully weighed.

45.7 Anesthetic and Surgical Management

Inhaled nitric oxide (iNO) should be readily available for all procedures. Preferably anesthesia should be administered by a pediatric anesthesiologist experienced in cardiac anesthesia. As many anesthetics exhibit mixed hemodynamic effects, and may be unacceptable when used in full anesthetic dosage, use of a balanced anesthetic technique is suggested in which subanesthetic doses of several drugs can be combined to provide general anesthesia. Oral or IV midazolam can be administered for preanesthetic sedation. Induction can be cautiously achieved with midazolam, fentanyl, and a small dosage of propofol or low concentration of sevoflurane. Inhaled anesthesia may be maintained with isoflurane or sevoflurane; total intravenous anesthesia (TIVA) can be maintained with either infusions of propofol and or intermittent fentanyl. In general, boluses of propofol are avoided as this may decrease cardiac output. Our practice is to avoid remifentanyl as it may decrease heart rate. Rocuronium or pancuronium may be used for neuromuscular blockade as indicated. Patients may be tracheally intubated or a laryngeal mask airway may be utilized. Infiltration of surgical sites with local anesthesia may avoid the use of higher doses of general anesthetic drugs. For cardiac catheterization in older or more stable patients, the pediatric cardiologist may administer the sedation using midazolam and fentanyl and the airway is often unaided in these circumstances.

Complications have been reported in PAH patients undergoing surgical procedures, related to the anesthesia or as a complication of the underlying patient's respiratory issues requiring mechanical ventilation [1].

Major complications have also been reported as a result of a pulmonary hypertensive crisis and are probably more likely in patients with higher baseline PAH [1] and especially in patients with suprasystemic PAH, especially when undergoing cardiac catheterization [1]. This may require specific pharmacological intervention and also mechanical ventilation postoperatively in the intensive care unit [1]. The post-anesthesia period may be particularly dangerous. At this point, patients awakening from anesthesia may begin to feel pain and may be agitated. Likewise, withdrawal of inhaled nitric oxide used for vasodilator testing may predispose to pulmonary hypertensive events. It has been our practice to continue nasal cannula nitric oxide for 8–12 h after the procedure in patients with more severe disease.

Total correction of many cardiac lesions in the first months of life may prevent the late development of pulmonary hypertension. The timing of surgery in patients with congenital heart disease depends upon a number of factors including age, lesion, vasoreactivity at cardiac catheterization, findings on lung biopsy, and pulmonary wedge angiography [4, 19, 54, 55, 168].

45.7.1 Atrial Septostomy

The general indications for atrial septostomy include pulmonary hypertension, syncope and intractable heart failure refractory to chronic vasodilator treatment [168–175] and symptomatic low cardiac output states. Risks associated with this procedure include worsening of hypoxemia with resultant right ventricular ischemia, worsening right ventricular failure, increased left atrial pressure, and pulmonary edema. We favor a graded balloon dilation approach utilizing intracardiac echo and saturation monitoring to determine adequacy of shunt. We have frequently used a cutting balloon with the initial inflation followed by static balloon dilations.

45.7.2 Transplantation

For patients who do not respond to prolonged vasodilator treatment, or with certain lesions, such as pulmonary vein stenosis, lung transplantation should be considered [176–180]. Cystic fibrosis accounts for

the majority of pediatric lung transplants. IPAH as an indication for transplantation is seen in approximately 15% of patients. The data on lung vs. heart-lung transplantation for “simple” congenital heart disease associated with PAH is controversial and center-dependent. A retrospective study found similar outcomes for children with congenital heart disease undergoing repair of congenital heart lesions combined with lung transplantation as compared with combined heart-lung transplantation [181]. However, a recent report analyzed the United Network for Organ Sharing/International Society for Heart and Lung Transplantation Joint Thoracic Registry to determine predictors of survival in Eisenmenger syndrome. There was a highly significant benefit of heart-lung transplantation over lung transplantation for VSD patients ($P = 0.0001$). Survival for patients with idiopathic pulmonary hypertension undergoing lung transplantation is approximately 65% at 1 year and 45% at 5 years [182–184].

45.8 Long-Term Outlook

Pulmonary hypertension in children previously carried a very poor prognosis. In a 1965 series of 35 patients with idiopathic (primary) pulmonary arterial hypertension (IPAH), 22 patients died within one year of the onset of symptoms and none survived greater than 7 years [185]. In 1995, the prognosis was still poor, with the median survival in a series of 18 children with IPAH being 4.12 years [186]. However, recent advances in understanding the biology of the normal and hypertensive pulmonary circulations have led to a broader pharmacologic arsenal and improved prognosis of children with pulmonary hypertension. For example, in one 2004 series, children with severe IPAH and acute pulmonary vasoreactivity treated with calcium channel blockers displayed survival at 1, 5, and 10 years of 97%, 97%, and 81%, respectively [62]. Survival of children treated with epoprostenol ($n=35$) at 1, 5, and 10 years was 94, 81, and 61%, respectively [62].

Once PAH is diagnosed along with any underlying condition, the severity of the disease should be assessed to determine the appropriate therapeutic management. Useful tools to predict patient outcome include functional class, exercise capacity, pulmonary

hemodynamics, acute vasoreactivity and right ventricular function. Prognosis spans a wide range depending on the etiology. Patients with congenital heart disease may survive for several decades [187]. However, adult patients with IPAH have a median life expectancy of 2.8 years, as found in the National Institutes of Health registry, with children having a worse prognosis of 10 months without treatment [61]. Further advancements in therapy will improve long-term outcome in children.

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Chapter 46

Acute Myocarditis and Cardiomyopathies

Brian Feingold and Steven A. Webber

The definition and classification of cardiomyopathies was recently revised by an expert panel of the American Heart Association [1] following the initial classification by the World Health Organization in 1995 [2]. Cardiomyopathies are considered “a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic” [1]. Cardiomyopathies are generally considered as primary (disease solely or predominantly confined to heart muscle) or secondary, showing pathological myocardial involvement secondary to a systemic or multiorgan disease process. Both forms are commonly seen in children, although primary forms predominate.

Cardiomyopathies and myocarditis are significant contributors to end-stage heart failure in children, accounting for over 50% of all pediatric heart transplants [3]. They are also the commonest indication for ventricular assist device (VAD) support in childhood [4]. Pediatric cardiomyopathies have a reported incidence of 1.13–1.24 cases per 100,000 population in two recent large population-based studies [5, 6], though this is likely an underestimate. The true incidence of pediatric myocarditis is unknown. Many cases may be unrecognized and go on to experience clinical recovery. Some may be misdiagnosed as SIDS [7]. Others may present years later as chronic dilated cardiomyopathy with viral genome demonstrated in the myocardium but in the absence of active inflammation [8–10].

This chapter focuses on the role of the intensive care unit (ICU) in the management of the child with new-onset or established cardiomyopathy presenting with shock, heart failure or arrhythmia. Management in the ICU comprises:

1. Determination of the form of cardiomyopathy and of the most likely etiology (most commonly discerning between acute myocarditis and an acute presentation of dilated cardiomyopathy (DCM)).
2. Management of acute heart failure and / or arrhythmias.
3. Estimation of prognosis and selection of patients for mechanical circulatory support and transplantation.

46.1 Dilated Cardiomyopathy and Myocarditis

46.1.1 Anatomy

DCM is characterized by dilation of one or both ventricles (most commonly the left ventricle) often with thinning of the left ventricle free walls. Varying degrees of hypertrophy may also be seen and left ventricular mass tends to be increased, even when the ventricular walls are thin. The left ventricle often takes on a globular shape and mitral regurgitation with annular dilation is frequently seen along with left atrial dilatation (Figs. 46.1a and 46.2a). Left ventricular systolic function is usually globally depressed, though varying degrees of ventricular dyssynchrony may be observed, even in the absence of bundle branch block. In contrast, right systolic ventricular function is often only minimally decreased or normal. Right ventricular dilation, when present, may be due to myocardial

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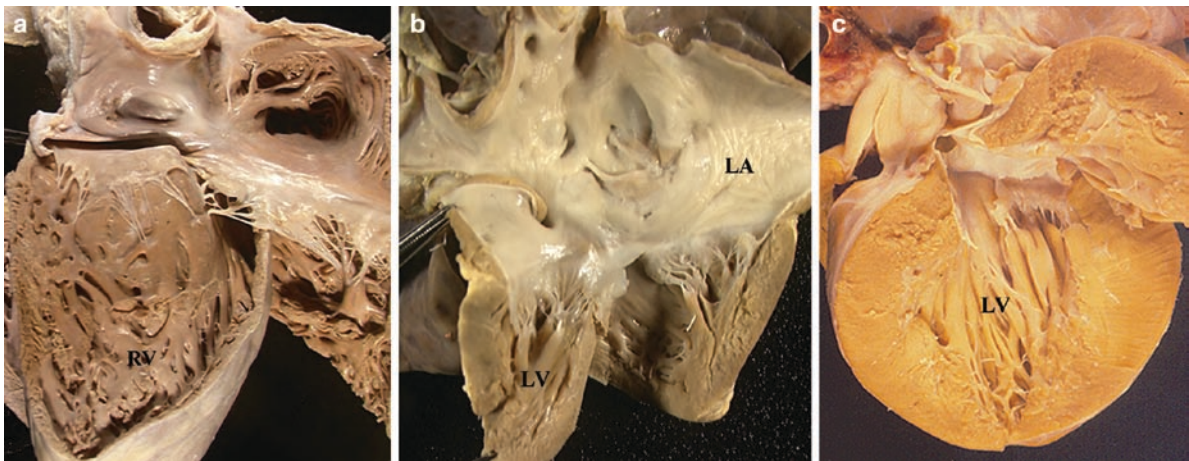


Fig. 46.1 Spectrum of pediatric cardiomyopathies. (a) Dilated cardiomyopathy (DCM) with marked ventricular dilation and wall thinning (shown from RV side). (b) Severe hypertrophic cardiomyopathy (HCM) with concentric hypertrophy, in this case secondary to Pompe's disease (glycogen storage disease

type II). (c) Restrictive cardiomyopathy (RCM) with small left ventricular cavity size and marked dilation of the left atrium. (Courtesy of William Devine, Department of Pathology, Children's Hospital of Pittsburgh). LA left atrium; LV left ventricle; RV right ventricle



Fig. 46.2 Echocardiographic findings of pediatric cardiomyopathies. (a) Parasternal long axis view demonstrates severe left ventricular dilation in a child with idiopathic DCM. (b) Asymmetric septal hypertrophy (arrows) in a child with HCM.

(c) Apical 4-chamber view demonstrates small ventricular chamber sizes and biatrial enlargement typical of RCM. LA left atrium; LV left ventricle; RA right atrium; RV right ventricle

involvement from the primary disease process or secondary to tricuspid regurgitation and pulmonary hypertension.

In contrast, patients with acute myocarditis often show only a poorly functioning left ventricle with minimal dilation with, or without, regional wall motion abnormalities. There may be ventricular thickening secondary to myocardial edema, and left atrial enlargement may not be prominent, even when mitral regurgitation is present. These findings likely reflect the short duration of the disease process.

46.1.2 Etiology and Pathophysiology

Both acute myocarditis and DCM are characterized primarily by systolic ventricular dysfunction with resultant clinical signs and symptoms of heart failure. Diastolic dysfunction may also contribute to reduced myocardial performance in both settings, but particularly in acute myocarditis. In the latter, cardiac dysfunction may result from both direct viral invasion and myocyte lysis, as well as from the effects of

myocardial inflammation. In clinical practice (beyond the neonatal period), symptoms are most often associated with (presumed) post-viral lymphocytic infiltrates and autoimmunity. Adenovirus and enteroviruses (particularly Coxsackie B) are most frequent in children [11], although many other infectious and non-infectious causes have been identified, including viral, bacterial, fungal and protozoal infections, as well as drug toxicities, and various systemic disorders. The latter include Kawasaki disease and rheumatic fever.

Pediatric DCM encompasses a final common phenotype for a wide variety of etiologies. While the causes of most pediatric DCM are unknown, it is estimated that 30–40% of DCMs are inherited [12, 13], mostly in an autosomal dominant fashion. Mutations in genes encoding myocyte cytoskeletal proteins as well as genes encoding sarcomere proteins have recently been identified as etiologies for DCMs [14]. Other genetic causes include inborn errors of metabolism (e.g., mitochondrial transport chain defects) [15] and neuromuscular syndromes (e.g., muscular dystrophies). Also, the finding of viral genome in patients with DCM suggests that at least some DCMs may result from prior myocarditis (either apparent or clinically unapparent) [9]. Other acquired forms of DCM include medication-related (e.g., anthracycline toxicity) and arrhythmia-induced (e.g., chronic, incessant supraventricular tachycardia).

46.1.3 Clinical Presentation

Heart failure in children from any cause often presents somewhat insidiously, after repeated evaluation and medical testing for other, more common conditions. Neonates and infants often present acutely unwell; yet the diagnosis of a primary cardiac disorder may not be made on initial evaluation. It is not uncommon for cardiac disease to be considered only after ancillary studies fail to corroborate the presumed diagnosis or initial resuscitative attempts fail to improve the child's condition (e.g., shock due to sepsis). While much of the diagnostic difficulty results from the relative infrequency of primary cardiac disease in children, the inability of an infant or young child to verbally convey their symptoms also contributes. Also the frequency with which young children experience nasal, respiratory, or gastrointestinal symptoms, particularly during

the winter and spring, often results in the initial symptoms of heart failure being attributed to these much more common maladies.

Infants with heart failure may present with a history of poor feeding, respiratory distress, listlessness, poor weight gain, or irritability. Common adult symptoms of paroxysmal nocturnal dyspnea and orthopnea are uncommon in pediatric patients. In older children, abdominal pain, anorexia, nausea and vomiting are often observed and are likely due to liver capsule distention from hepatomegaly and/or intestinal venous congestion.

On physical examination, the child may appear anxious and sinus tachycardia is usually present. Sweating is common in infants. Elevation of the jugular venous pulse may be present but is difficult to identify in the infant and toddler. Pallor and cool extremities may be present and are often associated with poor peripheral pulses and prolonged capillary refill. Resting tachypnea and retractions (suprasternal, intercostal, and subcostal) are common. Unlike adults, crackles are exceedingly rare in infants and young children with heart failure, even when pulmonary edema is present. Wheezes are more likely to be present. While hepatomegaly is a common finding, it is often overlooked or underappreciated by the inexperienced practitioner. Periorbital edema (infants and young children) with or without ascites (older children) are more common than peripheral edema in children. Failure to thrive may also be evident, particularly with chronic heart failure.

The clinical distinction between acute, fulminant myocarditis and acute presentation of chronic DCM is often difficult. At the time of presentation, many will have a history of an intercurrent or recent viral illness. In fact, viral syndromes are so common in early childhood that the etiologic relationship to the onset of acute heart failure is often not clear. However, the distinction between myocarditis and DCM is crucial. Many patients with fulminant myocarditis will recover completely if able to be supported, whereas children with severely decompensated heart failure from DCM often will not recover without transplantation. Thus, the expectations from mechanical support (ECMO or VAD) and consideration for cardiac transplantation are directly impacted by the underlying diagnosis.

In many cases, clinical testing may help guide the diagnosis of acute myocarditis or acute presentation of DCM. The presence of marked cardiomegaly on *chest*

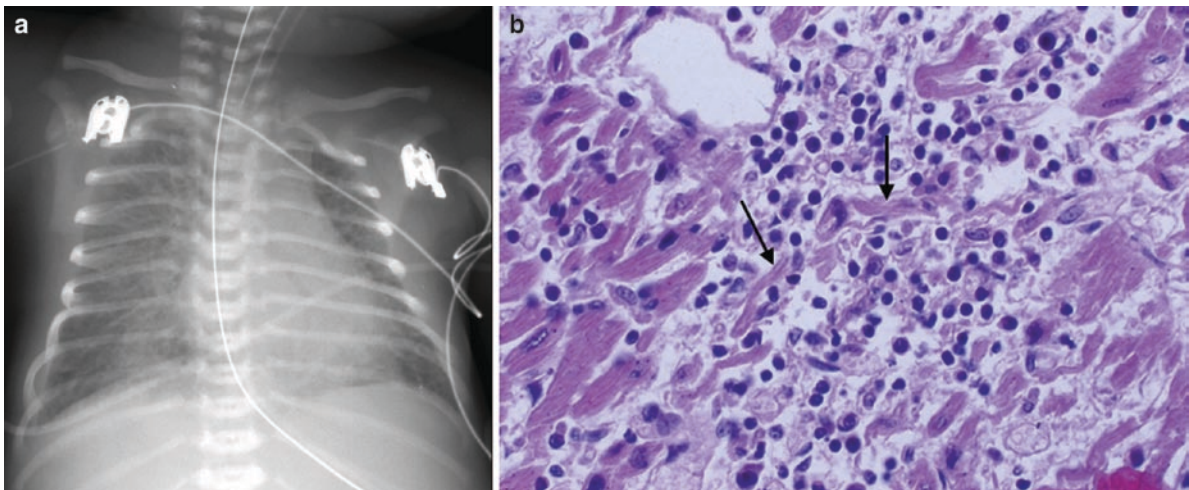


Fig. 46.3 Acute myocarditis. (a) Chest radiograph shows a small heart with pronounced pulmonary edema. (b) Endomyocardial biopsy specimen showing lymphocytic infiltrate with myocyte destruction (arrows)

radiograph and massive left-sided precordial forces on *ECG* suggest the underlying process occurred over time, favoring a diagnosis of chronic DCM over myocarditis. In contrast, absence of (or mild) cardiomegaly (Fig. 46.3a) and globally diminished voltages on electrocardiogram are more typical of acute myocarditis. Frank myocardial infarction may sometimes be observed on the 12 lead *ECG* of children with acute myocarditis. *Echocardiography* is very useful in the evaluation of infants and children suspected to have either myocarditis or cardiomyopathy and should be performed in all patients in whom these diagnoses are considered. *Endomyocardial biopsy* can generally be performed safely in children over the age of 1 year [16] and should be considered in the diagnostic evaluation, particularly when trying to distinguish between myocarditis and DCM. Biopsy samples from the right ventricle can be analyzed by routine hematoxylin and eosin staining for lymphocytic infiltrates with myocyte necrosis (Fig. 46.3b) consistent with a diagnosis of acute myocarditis [17] or for evidence of myocyte hypertrophy and/or interstitial fibrosis, favoring a diagnosis of DCM. A fresh-frozen sample should also be obtained for *PCR* analysis of common viral causes of myocarditis. *Viral cultures* of stool, urine, and respiratory secretions may contribute to the diagnosis, as may *polymerase chain reaction analysis* of blood, pericardial effusion or cerebral spinal fluid. *Viral titers* (at presentation and during convalescence) are often

performed, but are generally non-contributory to the diagnosis of childhood myocarditis.

Diagnostic evaluation for inborn errors of metabolism is generally reserved for patients presenting with dilated or hypertrophic cardiomyopathies in the first year of life. The presence of severe acidosis, hypoglycemia, elevated lactic acid, deranged liver function tests and hyperammonemia should all lead to rapid metabolic and genetic evaluation although all of these may also be observed in the setting of cardiogenic shock from non-metabolic causes. A full description of the evaluation of infants suspected of having an inborn error of metabolism is outside the scope of this text, but readers may refer to some excellent recent reviews [15, 18, 19].

46.1.4 Management

The critically ill patient, who presents on the verge of hemodynamic collapse, requires aggressive therapy to augment oxygen delivery while minimizing consumption. Intubation with mechanical ventilation and sedation (\pm paralysis) is useful to eliminate the work of breathing while improving pulmonary edema as a result of positive pressure ventilation. Placement of central venous and arterial monitoring lines is also facilitated by these maneuvers. In addition to being able to administer medications and monitoring hemodynamics, these

lines serve to limit the need for repeated phlebotomy in infants and young children, in whom fear, agitation, and site availability are complicating issues. The use of pulmonary arterial catheters is less common in the pediatric age group than in adults and rarely improves management when it is apparent that pulmonary edema is of cardiac origin.

Intravenous diuretics are used to augment diuresis and improve congestive symptoms. Continuous infusions of furosemide have been used with success in pediatric patients when intermittent dosing has failed to result in adequate diuresis. Inotropes are used to augment cardiac function and output. Therapy often consists of low to moderate doses (2–5 $\mu\text{g}/\text{kg}/\text{min}$) of dopamine for renal perfusion and blood pressure support and milrinone (0.125–1 $\mu\text{g}/\text{kg}/\text{min}$) to diminish afterload and augment cardiac output. Augmented inotropy can be achieved with dobutamine (1–10 $\mu\text{g}/\text{kg}/\text{min}$), while further afterload reduction may be achieved with sodium nitroprusside (0.3–4 $\mu\text{g}/\text{kg}/\text{min}$), if blood pressure tolerates. Rarely do patients require support with infusions of high doses of epinephrine or norepinephrine. In these cases (except when pathology is believed to be rapidly reversible), serious consideration should be given to early institution of mechanical circulatory support (see below). Caution must also be taken with regard to the arrhythmogenic potential of all inotropes, particularly with escalating doses. Appropriate monitoring is essential and care must be taken to aggressively correct all electrolyte disturbances, particularly hypo or hyperkalemia and hypomagnesemia.

Only limited data exists regarding the use of nesiritide for the treatment of acute heart failure in the pediatric population. Our experience has primarily involved its use in children who were otherwise recalcitrant to diuretics [20]. With appropriate monitoring of blood pressure and serum sodium, no complications were noted and some success was achieved in inducing diuresis. Others have reported use of nesiritide immediately after cardiac surgery, reporting no adverse hemodynamic effects or arrhythmias [21].

With stabilization and improvement in end-organ perfusion, gradual weaning of therapies is indicated. When oral medications can be safely tolerated and adequately absorbed, digoxin is often initiated, though of unproven benefit in pediatric patients. Intravenous diuretics are changed to oral forms and angiotensin converting enzyme (ACE) inhibitors are begun for afterload reduction while weaning milrinone. Beta-blockers

(other than as anti-arrhythmic agents) only play a limited role in the ICU care of the child with DCM. Indeed, during acute deterioration requiring use of intravenous inotropes, beta-blockers will generally need to be withdrawn. Institution of beta-blockers for new onset DCM is generally not performed in the ICU, since any benefits (if they exist) are long-term, and patients in the ICU are often hypotensive or being aggressively diuresed and vasodilated. Introduction of beta-blockers is part of the long-term management of chronic heart failure and is of unproven benefit (though widely performed) at this time [22]. Usually, beta-blockers are commenced after transition to oral diuretic therapy and once ACE inhibitor dosing is optimized. This generally occurs on the medical floors or in the outpatient setting.

When acute heart failure is unresponsive to aggressive medical management, institution of mechanical circulatory support must be considered. This is discussed in detail in Chapter 6. In general, ventricular assist devices are most appropriate when used as a bridge to transplantation, since prolonged periods of support may be required. Recovery from acute (including fulminant) myocarditis is often rapid, so ECMO or short-term use of VADs are more appropriate.

In acute myocarditis, therapy is primarily supportive. Only rarely is infection caused by a specific agent for which there is established antimicrobial therapy of proven efficacy. Intravenous immunoglobulin and corticosteroids have both been used [23], though there is no proof of their efficacy in randomized clinical trials. Steroids are contraindicated when there is evidence of active viral infection. More potent immunosuppressive agents, including T cell cytolytic agents and calcineurin inhibitors, have been used in some programs. There is no data to support a specific risk/benefit ratio and most programs do not use these agents.

Avoidance of dysrhythmias is a key component in the management of all patients with acute and chronic heart failure. In addition to careful attention to maintaining normal serum electrolyte concentrations, control of tachyarrhythmias (both supraventricular and ventricular) is important. Amiodarone is commonly used for treatment and prophylaxis of ventricular tachycardia, as well as for refractory atrial tachycardias.

The role of implanted cardioverter-defibrillators (ICDs) in the management of children and adolescents has not been as well defined as in adults. Evidence suggests children with DCM have a lower risk of sudden

death as compared to adults with similar degrees of ventricular dysfunction [24]. Nonetheless, in children with DCM, particularly those with evidence of ventricular tachycardia, ICDs have been utilized and are likely indicated in patients with syncope and aborted sudden death. Factors that may complicate placement of ICDs in children include greater risk of complications such as lead fracture (possibly due to growth or greater levels of activity in children as compared to adults), greater risk of inappropriate discharge due to ability to achieve higher (sinus) heart rates, and the inability to use endovascular leads in smaller children (<15 kg), necessitating epicardial lead placement [25].

46.1.5 Long-Term Outlook

Traditionally, long-term outlook in children with DCM was said to follow the “rule of thirds” with 1/3 improving, 1/3 remaining the same, and 1/3 demonstrating progressive deterioration in cardiac function. Recent population data from several groups has improved our understanding of the natural history of DCM. The National Australian Childhood Cardiomyopathy Study showed 5-year freedom from death or transplantation of 63% for children with DCM [26, 27]. The Pediatric Cardiomyopathy Registry showed a 5-year survival of 54% for DCM in North America [28, 29]. These data include outcomes for those followed with a diagnosis of DCM that may never have required intensive care. It is, therefore, of interest to note a recent important publication that focused on epidemiology and outcomes for new-onset heart failure from myocardial (non-structural) disease. In a population-based study for the United Kingdom and Ireland, 82% of children presenting with new-onset heart failure (most due to DCM) were in NYHA (or Ross) class III or IV and 41% required mechanical ventilation during first admission. One-year transplant-free survival was only 66% [30]. This is far worse than outcomes for new-onset heart failure in adults. Predictors of survival for DCM vary considerably between series. In a recent systematic review [31], it was noted that the most consistent findings associated with improved outcome were younger age at diagnosis, better fractional shortening and ejection fraction at diagnosis, and presence of myocarditis.

In general, the outcomes of acute myocarditis in children are good. A number of studies have shown

survival rates of between 75 and 100% for acute myocarditis in childhood [23], including fulminant cases that may require mechanical circulatory support. This emphasizes the benefit of knowing the diagnosis of myocarditis, since acute transplantation should be avoided even if mechanical support is required. This will provide the opportunity for cardiac recovery, as well as minimize the risks of transplantation during recent or active viral infection

46.2 Hypertrophic Cardiomyopathy

46.2.1 Anatomy

In hypertrophic cardiomyopathy (HCM), it is most common for patients to show asymmetric hypertrophy of the interventricular septum, with varying degrees of obstruction to left ventricular outflow due to prominence of the subaortic septum and/or systolic motion of the anterior leaflet of the mitral valve (Fig. 46.2b). Less commonly, children with HCM may demonstrate concentric left ventricular hypertrophy (Fig. 46.1b). In infant presentation, involvement of both the left and right ventricles is common, and biventricular obstruction may occasionally be observed. As ventricular hypertrophy may not be apparent until puberty, children with a family history of HCM in whom no genetic diagnosis/marker has been established should undergo serial evaluation with electro and echocardiography before, during, and after puberty to assess for development of abnormal cardiogram and ventricular hypertrophy.

46.2.2 Etiology and Pathophysiology

HCM is most commonly an inherited disorder (autosomal dominant) with marked variability in clinical expression. Nearly all mutations identified to date are in ten genes that encode cardiac sarcomere proteins [32]. It is likely that many other disease-causing mutations have yet to be identified. When there is a known familial mutation, testing of relatives can rule out disease. However, in many families, no mutation is identified, or testing has not been performed.

It is estimated that current screening panels for sarcomeric protein mutations reveal mutations in approximately 70% of cases. Other causes of pediatric HCM include conditions associated with left ventricular hypertrophy such as glycogen or lysosomal storage diseases, mitochondrial defects, and Noonan, LEOPARD, and Beckwith–Wiedemann syndromes.

Patients with HCM generally have thickened left ventricle walls with normal or decreased cavity size and preserved or hyperdynamic systolic function. A subgroup with pronounced restrictive physiology and atrial dilatation has been reported [33]. In some cases, there appears to be overlap of phenotype with restrictive cardiomyopathy (RCM). Cases of classical HCM and RCM have been observed in different members of the same family due to cardiac Troponin I mutations [34].

Heart failure symptoms are very rare in children and adolescents with HCM, and are most commonly a result of diastolic dysfunction. The exception is the infant with severe disease, often with biventricular hypertrophy with or without outflow obstruction. These infants commonly present with heart failure. Metabolic and genetic work-up is warranted in these cases.

Syncope and aborted sudden death may be observed in patients with HCM. The pathophysiology is often hard to define. Tachycardia and hypovolemia (for example due to dehydration and fever) maybe poorly tolerated and impaired myocardial perfusion, severe obstruction, inappropriate peripheral vasomotor tone and atrial and ventricular arrhythmias may all contribute to syncope and mortality in HCM.

46.2.3 Clinical Presentation

Patients with HCM may present in the absence of symptoms (e.g., for evaluation of a murmur) or due to a family history. Progressive activity intolerance or syncope are also common presenting complaints; however, it should be noted that in clinical practice, most children with these symptoms do not have cardiomyopathy. Affected infants may show tachypnea, hepatomegaly, and/or failure to thrive. In older children, chest pain may also be a symptom and suggests myocardial ischemia [32]. Unfortunately, it is not uncommon for sudden death (or aborted sudden death) to be the initial presentation of HCM in adolescents and young adults [35].

Undiagnosed HCM is a leading cause of sudden death in young, healthy individuals and athletes.

46.2.4 Management

Most children with HCM are asymptomatic and thus are not often encountered in the ICU. While progression to end-stage heart failure occurs, the diagnosis is relatively rare in children, accounting for only 2.5% of pediatric heart transplant listings in a recent analysis of over 3,000 pediatric transplant candidates from a large, multicenter database [36]. With advancing symptoms of heart failure, patients may be admitted to the hospital for treatment. Although so-called “burned-out” HCM occurs in children in which there is progressive systolic dysfunction and left ventricular dilation, heart failure from HCM results predominantly from diastolic dysfunction. Thus, many of the therapies employed in the treatment of heart failure from DCM are not useful or are only of limited benefit.

An ideal agent for management of heart failure due to HCM would possess positive lusitropic effects, enabling relaxation of the ventricular myocardium and thus achieving improved stroke volume at lower filling pressures. Unfortunately, this agent does not yet exist and therapies directed primarily at management of diastolic ventricular dysfunction are scant. Most common is the use of negative inotropic agents, such as non-dihydropyridine calcium channel blockers (e.g., verapamil) or beta-blockers (e.g., propranolol, atenolol). In the ICU setting, esmolol may be preferred due to its short half-life. Due to the exquisite sensitivity/dependence of the neonatal and infant heart to serum calcium levels, use of intravenous calcium channel blockers in infants less than 1 year of age is usually contraindicated. Milrinone, a phosphodiesterase III inhibitor, possesses some positive lusitropic effect [37] and thus may be of theoretical benefit in select patients with HCM and advanced heart failure symptoms in the absence of significant subaortic obstruction. As milrinone can be arrhythmogenic, careful consideration must be given to balance any potential benefits against the risks of induced tachyarrhythmias. Furthermore, vasodilatation may exacerbate any left ventricular outflow obstruction. Diuretics are often used in the outpatient setting for patients with congestive symptoms. These agents must also be used with caution in

the setting of diastolic dysfunction as cardiac output and myocardial perfusion can be compromised with insufficient preload and again outflow obstruction may be increased.

The role of ICDs in the management of children with HCM is unclear. Data from a multicenter registry of pediatric and congenital heart disease patients showed HCM was the second most common diagnosis for which subjects received an ICD [38]. In patients with HCM who experience syncope or aborted sudden death, implantation of an ICD is likely indicated. Use of ICDs for primary prevention in patients with HCM is not established.

46.2.5 Long-Term Outlook

Although the natural history of HCM in adults is quite variable [32], survival tends to be worse the younger a patient presents. In particular, infants who present with heart failure have a poor prognosis. Patients who present older than 1 year of age are unlikely to die of progressive heart failure from HCM, but may succumb to sudden death [39]. Sudden death predominates in adolescents and young adults with HCM and is thought to be more likely in those with a family history of sudden death or personal history of recurrent syncope, ventricular tachycardia, or massive left ventricular hypertrophy [35].

Hypertrophy often progresses (or may first become apparent) during periods of rapid growth (i.e., puberty) and thus patients with HCM should be monitored closely during adolescence. In a small percentage of patients, there may be a regression of hypertrophy, with ultimate development of left ventricular dilation and poor systolic function. This so-called end-stage or “burned-out” HCM typically requires treatment for systolic heart failure much like DCM and may necessitate transplantation [40]. It is rare in childhood.

Our knowledge of outcome in pediatric HCM has recently been greatly advanced through analyses from the two large multicenter registries. In the National Australian Childhood Cardiomyopathy Study [27, 41], less than 10% presented with heart failure, most presenting with a murmur for family screening. A third were syndromic (mostly Noonan syndrome). Freedom from death or transplant was 83% at 5 years and 76% at 10 years. Presentation by 1 year of age was an

important predictor of mortality. Annual mortality for patients presenting beyond this age was only 1.5%. In the Pediatric Cardiomyopathy Registry [29, 42], survival for idiopathic HCM ($n=634$) was 82% at 5 and 10 years for infantile presentation, and 94 and 86% at the same time intervals for presentation beyond infancy.

46.3 Restrictive Cardiomyopathy

46.3.1 Anatomy

Restrictive Cardiomyopathy (RCM) is a very rare form of cardiomyopathy characterized by normal or decreased volume of both ventricles associated with atrial enlargement (often massive) and with normal LV wall thickness (Figs. 46.1c and 46.2c). As mentioned earlier, there is some phenotypic overlap seen with HCM, and mild left ventricular hypertrophy is sometimes observed. Systolic function is generally normal [1].

46.3.2 Etiology and Pathophysiology

Overall, RCM is a rare diagnosis, accounting for approximately 5% of pediatric cardiomyopathies [5, 6]. The underlying cause(s) are generally unknown [43–45]. This is in contrast to adult patients with RCM, in whom infiltrative diseases such as amyloidosis and sarcoidosis are sometimes identified. While some children may present with familial forms, most cases are sporadic. Cardiac troponin I mutations have been reported as a cause of restrictive (and hypertrophic) cardiomyopathy [34]. The severe restrictive physiology leads to decreased cardiac output, elevated filling pressures, and atrial stretch that may lead to arrhythmias. Some patients demonstrate presumptive evidence of ischemia based on ST segment depression, especially during tachycardia. Elevation of pulmonary vascular resistance is frequently seen (even at presentation) and may contribute to right heart failure. Loss of systolic function is rare, although it is occasionally seen in advanced disease.

46.3.3 Clinical Presentation

Exercise intolerance, exertional angina, syncope, tachyarrhythmias, or sudden death may all occur. Atrial tachycardias are not uncommon and likely result from severe atrial dilation due to poor ventricular compliance. These are poorly tolerated in the setting of diastolic compromise.

Much like those with HCM, children and adolescents with RCM often present incidentally for evaluation of a murmur or for follow up of an atypical cardiac silhouette on chest radiography obtained for unrelated reasons. Patients may also present with symptoms of heart failure, angina, palpitations or syncope. Syncope may be precipitated by atrial or ventricular tachycardia, both of which are poorly tolerated in the setting of limited ventricular compliance. Similar to HCM, sudden death is also not an uncommon presentation of RCM [44].

46.3.4 Management

Therapeutic options for pediatric RCM are very limited. Many of the same physiologic considerations (and thus limitations in management) discussed for patients with HCM are also pertinent for those with RCM. Gentle diuresis is indicated if there is pulmonary venous congestion or pulmonary edema, but excessive diuresis may lead to reduction in cardiac output. Vasodilators may lead to hypotension, since augmented cardiac output may not occur when stroke volume is fixed. The role of beta-blockers is unclear. Slowing of the heart rate will prolong diastolic filling time but since stroke volume is relatively fixed, increasing heart rate may be an important mechanism for augmenting cardiac output.

As short-term survival is poor after a diagnosis of RCM, many centers recommend early evaluation for cardiac transplantation. Cardiac catheterization should be performed during the evaluation process because of the high likelihood of increased pulmonary vascular resistance. Hemodynamic assessment may also help with the distinction from constrictive pericarditis. Computed tomography is indicated if pericardial disease is suspected. Although secondary causes of RCM, such as amyloidosis and sarcoidosis, are exceedingly

rare in children, biopsy should be considered in older children presenting with RCM to assess for these systemic diseases.

For patients managed out of hospital, implantation of an ICD in combination with anti-arrhythmic agents may be considered, especially if prior near-syncope, syncope, or tachyarrhythmia has occurred.

46.3.5 Long-Term Outlook

Children with RCM have very poor prognosis in the absence of heart transplantation. Survival at 5 and 10 years after diagnosis was 39% and 20%, respectively at our center [43] and others have reported similar outcomes [46]. A minority of patients has been reported to survive upwards of 8–12 years [45, 47–49]; however, strong, independent predictors of prolonged survival remain to be identified. The presence of symptoms at diagnosis did not correlate with survival in our cohort. Since excessive elevation in pulmonary vascular resistance may necessitate heart–lung transplantation, progressive elevation in pulmonary resistance should also lead to consideration of early transplantation.

46.4 Noncompaction Cardiomyopathy

46.4.1 Anatomy

In left ventricular noncompaction (LVNC) cardiomyopathy, the left ventricle shows prominent trabeculations and deep intertrabecular recesses (Figs. 46.4a and 46.4b). These findings are most commonly observed at the apex of the left ventricle but can be seen in an isolated fashion along the lateral wall. There is often dilation of the left ventricle with associated depressed systolic function. There may also be coincident ventricular hypertrophy, or at least lack of expected ventricular wall thinning for the degree of chamber dilation. Noncompaction can also occur in the setting of congenital heart disease, particularly hypoplastic left heart syndrome, ventricular septal defects, and pulmonary stenosis [50].

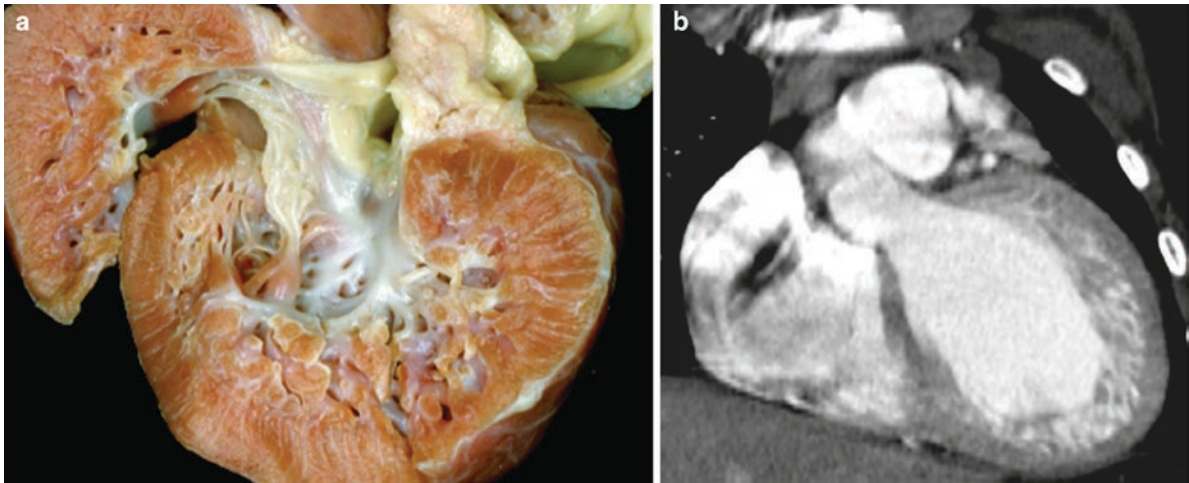


Fig. 46.4 Left ventricular noncompaction (LVNC) cardiomyopathy. (a) Pathologic specimen showing typical “spongiform” myocardium of left ventricle. (Courtesy of William Devine, Department of Pathology, Children’s Hospital of Pittsburgh).

(b) Intertrabecular recesses and dilation of the left ventricle in a teenager with noncompaction cardiomyopathy as shown by computed tomography

46.4.2 Etiology and Pathophysiology

LVNC has been increasingly diagnosed over the last 10 years. Previously, cases of LVNC may have been classified as HCM or DCM in part because of a lack of awareness of the diagnosis, limited resolution of earlier generations of echocardiography machines, and lack of standardized diagnostic criteria. LVNC may account for up to 9% of pediatric cardiomyopathies [6]. It can occur in isolation or with other congenital cardiac disease and both sporadic and familial forms have been described [51]. When LVNC is inherited, X-linked inheritance appears to be most common, but autosomal dominant, recessive, and mitochondrial inheritance may also occur. Mutations in the G4.5 gene at Xq28 (that encodes tafazzin) are responsible for X-linked LVNC [52] and also some other infantile DCMs, including Barth syndrome, which is characterized by cardiomyopathy (often with LVNC), intermittent neutropenia, peripheral myopathy, and growth delay [53, 54]. LVNC has been postulated to result from an arrest in early embryonic endomyocardial morphogenesis, resulting in a spongy meshwork of fibers and myocardial sinusoids [55]. Patients often have features most consistent with DCM, including symptomatic heart failure and arrhythmias; although some are found to have only asymptomatic LV dysfunction. Waxing and waning of ventricular function has also been described. Some

series also report relative high prevalence of ventricular thrombosis and/or systemic embolic events, particularly in adults [56–58].

46.4.3 Clinical Presentation

Approximately half of children with LVNC who present for evaluation have signs and symptoms of heart failure. Others may come to evaluation incidentally for cardiomegaly on chest X-ray, abnormal ECG findings, or for assessment of a murmur. Patients may also present with arrhythmias. Most series show a tendency to progression in heart failure symptoms over time [58, 59], although a waxing and waning course is not rare. Presentation in infancy with heart failure due to severe systolic ventricular dysfunction is not unusual and some of these cases show marked improvement over time, though this may be transient.

46.4.4 Management

Discerning LVNC from the broader category of DCM can require a high index of suspicion. Echocardiographic diagnostic criteria have been described

[60] and recently called into question [61]. Adjunctive imaging modalities such as CT or MRI may provide better diagnostic information [62] but are less readily accessible and may be impractical during the initial diagnostic evaluation of a critically ill child with heart failure. Genetic testing for mutations in the G4.5 gene may help lead to a specific diagnosis, especially when the family history suggests X-linked inheritance.

Patients who manifest primarily with heart failure due to depressed systolic ventricular function are treated in a fashion similar to those with DCM. Therapy with diuretics and ACE inhibitors, with or without beta-blockers, are often employed during long-term follow up. Although systemic embolism and arrhythmias (atrial fibrillation and ventricular tachycardia) are relatively common in the adult LVNC population, these are relatively rare in pediatric series. Ventricular ectopy may also be observed. Systemic anticoagulation is indicated when there is severe systolic ventricular dysfunction.

46.4.5 Long-Term Outlook

The relative infrequency of LVNC does not allow for proper characterization of the the clinical course of children with this diagnosis, as in patients with DCM. Ichida and colleagues [59] report the longest follow-up in their series of patients with childhood LVNC (median 6 years, range 0–17 years) and described the development of ventricular dysfunction or death in 75% of those followed for ≥ 10 years. In another series, transplant-free survival in infants with LVNC and no congenital heart defect was 52% at 3 years [50]. This was almost identical to transplant-free survival of 53% among 29 subjects with LVNC in the National Australian Cardiomyopathy Study [27]. Although these studies of LVNC in childhood report median ages at presentation of between 3 months and 7 years [50, 58, 59], there are various reports in adults that describe initial diagnosis as late as 70–75 years [56, 57] with absence of depressed cardiac function in some cases. This suggests that LVNC may be more common than has been observed, with some having only the morphologic findings (deep trabeculations) without overt ventricular dysfunction until much later in life.

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Chapter 47

Pericardial Diseases

Cécile Tissot, Christina M. Phelps, Eduardo M. da Cruz, and Shelley D. Miyamoto

47.1 Introduction

Pericardial diseases are defined as structural or functional abnormalities of the visceral or parietal pericardium that may or may not have an impact on cardiac function. Diseases of the pericardium include a spectrum of acquired and congenital problems consisting of infectious and inflammatory processes, neoplastic lesions, as well as congenital structural defects.

47.2 Anatomy of the Pericardium

The pericardium is a sac-like structure surrounding the heart, consisting of two layers: a thin inner visceral layer made up of mesothelial cells and a thick outer layer made up of collagen and elastic fibers, separated by a virtual space containing a small amount of fluid (about 20 ml) which serves as lubricant [1]. The pericardial fluid is produced by the visceral pericardium and is essentially an ultrafiltrate of plasma. The pericardial fluid normally drains through the right lymphatic duct via the right pleural space and by the thoracic duct via the parietal pericardium [2]. The arterial supply of the pericardium is via a branch of the internal thoracic artery and the venous drainage is through tributaries of the brachiocephalic veins.

The pericardium envelops the heart and great vessels, but is not attached to them. Instead, it reflects

around the great vessels forming the pericardial recesses and sinuses. The pericardium is anchored to the diaphragm by the pericardio-phrenic ligament and to the sternum by the sterno-pericardial ligament, providing support for the heart within the thoracic cage. It has been speculated that the presence of the parietal pericardium helps maintain a functionally optimal cardiac shape, since the heart tends to be more spherical after pericardiectomy.

47.3 Physiology and Pathophysiology

Although, an intact pericardium is not critical to the cardiovascular function, it assumes some minor functions including:

- Limitation of intrathoracic cardiac motion.
- Preservation of diastolic and systolic interactions between the right and left ventricles, balancing right and left ventricular output.
- Limitation of acute cardiac dilatation.
- Lubricant effect that minimizes friction between cardiac chambers and surrounding structures.
- Lymphatic and immunological functions, acting as anatomic barriers that help prevent spread of infection from contiguous structures, especially the lungs.

The normal pericardium limits cardiac distention, thereby coupling the ventricles and enhancing their interactions [3, 4]. Pressure or volume overload of one ventricle influences the compliance and filling of the contralateral ventricle via septal mediated diastolic interactions, called interventricular coupling. By influencing the effects of diastolic pressure and dimensions between the ventricles, the pericardium facilitates a balance between the right and left ventricular output.

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The normal intrapericardial pressure is subatmospheric, nearly equal to intrapleural pressure and varies with pleural pressure. The inspiratory decrease in pleural pressure slightly reduces pericardial, right atrial, right ventricular, pulmonary capillary wedge, and systemic arterial pressures. Under physiologic conditions, respiratory variations influence cardiac filling and hemodynamics. However, the effects on the right and the left heart are different, secondary to the differences in the anatomic relationship of the systemic and pulmonary venous return to the intrapleural space [5]. The systemic venous system is extrapleural as opposed to the pulmonary venous system which is intrapleural. As a consequence, decreases in intrathoracic pressure during inspiration have a different effect on the systemic and pulmonary venous return. The systemic venous return is augmented by about 50%, which increases right heart filling and output. Since pleural pressure changes are evenly distributed to the left heart chambers and pulmonary veins, there is minimal change in the pressure gradient between the pulmonary veins and the left ventricle. Therefore, left heart filling is essentially unchanged throughout the respiratory cycle [6].

Intrapericardial pressure increases when cardiac volume is greater and decreases when intracardiac volume decreases. Under physiological conditions, venous return to both atria is biphasic, with a systolic peak determined by atrial relaxation (corresponding to the “X” descent of the atrial or jugular venous pressure waveform) and a diastolic peak determined by atrio-ventricular valve resistance and ventricular compliance (corresponding to the “Y” descent of the atrial or jugular venous pressure waveform).

Abnormal pericardial fluid production is usually secondary to injury or inflammation (postoperative pericardial effusion, acute pericarditis, post-pericardiotomy syndrome). Transudative fluid results from obstruction of fluid drainage, while exudative fluid is secondary to inflammatory, infectious, malignant, or autoimmune processes. The normal pericardium has a small capacitance volume (about 150 ml) limited by the relative noncompliance of the parietal pericardial layer. When reserve capacitance has been reached, further increases in intrapericardial volume will result in a steep increment of intrapericardial pressure. The hemodynamic repercussion of pericardial fluid accumulation is highly dependent upon the rate of accumulation of fluid in the pericardial sac. Rapid accumulation of pericardial fluid

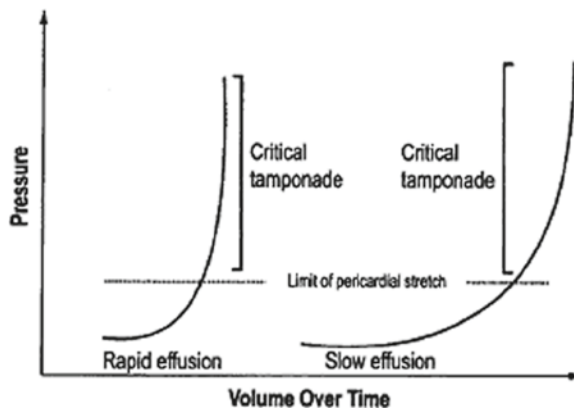


Fig. 47.1 Pericardial pressure-volume curve showing rapid and slow increase of pericardial volume over time (From [7])

causes a sudden increase in intrapericardial pressure with hemodynamic compromise. Slow accumulation of pericardial fluid can be asymptomatic even when large fluid volumes are present (Fig. 47.1) [7].

Cardiac tamponade is a consequence of markedly diminished diastolic filling that occurs when transmural distending pressures are insufficient to overcome the increased intrapericardial pressure. In tamponade, inspiration augments inflow to the right ventricle, causing an abrupt expansion of the right ventricle during diastole at the expense of the left ventricle (Fig. 47.2) [8]. Conversely, during expiration left ventricular expansion causes right ventricular and atrial diastolic collapse. This reciprocating behavior of the ventricles during respiration is responsible for a paradoxical pulse [9].

The pericardium also serves as a protective barrier from the spread of infection or inflammation from adjacent structures. Pericardial inflammation manifests as a fibrinous reaction with an exudative effusion. This can lead to fibrosis, thickening, calcification, and obliteration of the space between the visceral and parietal layers, adhesions can occur between the pericardium and myocardium leading to decreased pericardial compliance and constrictive pericarditis. This results in diminished ventricular distensibility, inability to maintain adequate preload and biventricular diastolic dysfunction. As opposed to a pericardial effusion, early ventricular filling is not altered in constrictive pericarditis. However, as the ventricles fill, they meet the inelastic resistance of the stiff pericardium, at which time filling pressure rises rapidly to an elevated plateau. This late diastolic phenomena is due

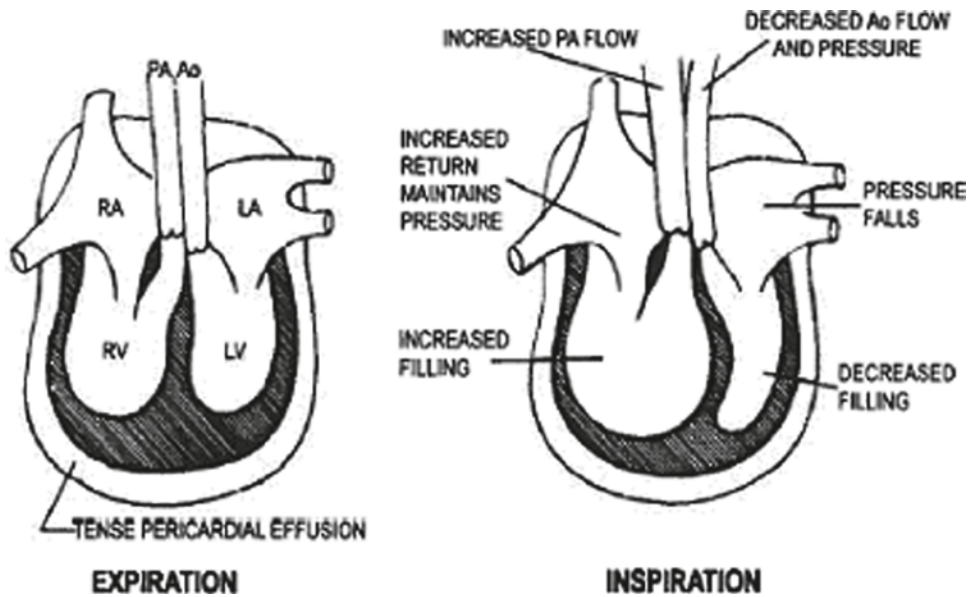


Fig. 47.2 Ventricular interdependence and mechanism of pulsus paradoxus. (From [6])

to a change in the volume-elasticity curve, a small increase in volume resulting in a considerable increase in end-diastolic pressure. Atrial filling pressures are elevated, reflecting both ventricular noncompliance and atrial constraint from the thick pericardium. Because of the isolated encasement of the pericardium and not the systemic veins or lungs, there is dissociation between intrathoracic and intracardiac pressures with marked respiratory variation and discordance in right and left heart filling [10, 11].

Through analysis of the atrial waveforms, improved understanding of the physiology of the venous circulations, the dynamic effect of intrapericardial and intrathoracic pressures and respiratory variations during the cardiac cycle is possible [12]. The atrial waveforms are constituted by two positive deflections, the A and V waves, and two negative waves, the x and y descents (Fig. 47.3). The atrial A wave is generated by atrial systole following the P wave of the electrocardiogram. The strength of atrial contraction is reflected in the rapidity of the A wave upstroke and peak amplitude. The x descent follows the A wave and is a function of atrial relaxation, which is influenced by pericardial compliance. The V wave reflects venous return resulting in atrial filling and increased atrial pressure during ventricular systole. The height of the V wave correlates with atrial compliance. The subsequent diastolic y descent represents atrial emptying.

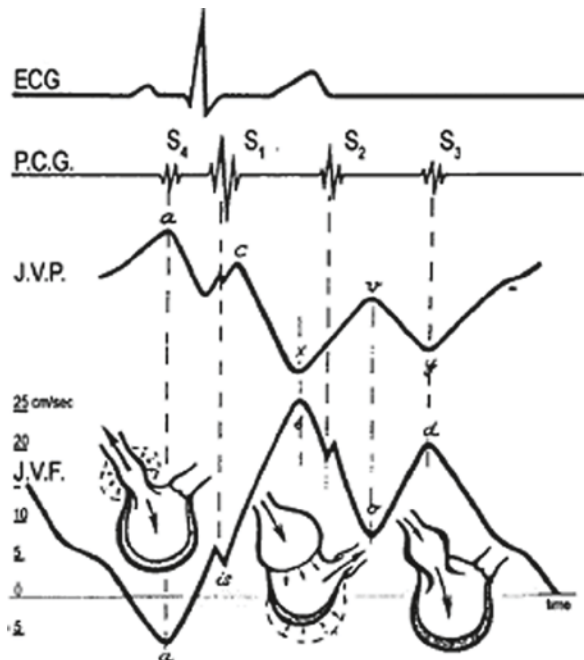


Fig. 47.3 Mechanics of atrial wave form (from [12])

The steepness of the y descent is influenced by the volume and pressure in the atrium just prior to atrioventricular valve opening and by the resistance to atrial emptying (atrioventricular valve narrowing, ventricular compliance, and pericardial compliance).

47.4 Epidemiology and Etiology

Pericardial effusions can be associated with pericarditis or be secondary to cardiac surgery (Table 47.1) [13]. Common causes of pericardial effusions in children include prior cardiac surgery, bacterial pericarditis, malignancy, and connective tissue disorders. In a significant number of children, however, despite extensive investigation, it is not possible to identify a clear etiology. A viral cause is often considered, though rarely confirmed [14].

Postoperative pericardial effusions can occur in isolation or be secondary to post-pericardiotomy syndrome. In the postoperative period, even small

Table 47.1 Causes of pericardial effusion

Causes of pericardial effusion:	
Idiopathic	
Viral	Coxsackie virus A and B Hepatitis HIV
Pyogenic	Pneumococci Streptococci Staphylococci Neisseria species Legionella species
Tuberculous	Mycobacterium tuberculosis
Fungal	Histoplasmosis Coccidioidomycosis Candidosis
Other infections	Syphilitic Protozoal Parasitic
Uremia	
Hypothyroidism	
Neoplasia	Metastases Leukemia Lymphoma
Post-cardiac surgery (post-pericardiotomy syndrome)	
Acute myocardial infarction	
Post-radiation	
Rheumatic fever	
Collagen vascular disease	Rheumatoid arthritis Systemic lupus erythematosus
Trauma (hemopericardium)	
Hypercholesterolemia	
Chylopericardium	
Sarcoidosis,	
Whipple disease	
Drug-induced	

Table 47.2 Infectious causes of pericarditis

Infectious causes of pericarditis:	
Viral	Coxsackie virus A and B Adenovirus Cytomegalovirus Ebstein-Barr virus Varicella-Zoster virus Mumps virus Influenza virus Hepatitis virus Human Immunodeficiency virus Variola and vaccinia viruses
Pyogenic	Streptococcus pneumoniae Streptococcus pyogenes Staphylococci aureus Haemophilus influenzae Neisseria meningitidis Neisseria gonorrhoeae Pseudomonas aeruginosa Francisella tularensis Bartonella henselae Cardiobacterium hominis Salmonella spp Actinomyces spp Nocardia spp Coxiella burnetii Legionella spp
Tuberculous	Mycobacterium tuberculosis
Fungal	Histoplasmosis Coccidioidomycosis Candidosis Aspergillosis Blastomycosis Echinococcosis Amebiasis
Parasites	Entamoeba histolytica Echinococcus spp
Miscellaneous	Mycoplasma Chlamydia Rickettsiae Spirochetes

amount of loculated pericardial fluid, particularly when localized along the free wall of the right atrium or ventricle, can have significant hemodynamic repercussion [15]. In developing countries, tuberculosis is responsible for approximately 70% of cases of large pericardial effusions and most cases of constrictive pericarditis. However, in industrialized countries, tuberculosis accounts for only 4% of cases of pericardial effusion and an even smaller proportion of constrictive pericarditis [16].

Post-pericardiotomy syndrome is more common in older children and can occur in any patient in whom the pericardial sac has been opened. Patients usually present within 1–6 weeks of a surgery involving a pericardiotomy. An auto-immune etiology has been postulated.

Acute pericarditis is most commonly secondary to viral infections, particularly enteroviruses and Coxsackie virus B (Table 47.2) [17]. Effusive-constrictive pericarditis is usually secondary to infections creating a thick exudate, such as pyogenic bacteria or tuberculosis. Purulent pericarditis is a medical and surgical emergency and requires prompt antibiotic treatment and pericardial drainage, to prevent adhesions and eventual constriction. The incidence of tuberculous pericarditis is increasing in underdeveloped countries, particularly in Africa, as a result of the human immunodeficiency virus (HIV) epidemic [18].

Constrictive pericarditis is rare in children in developed countries, but as mentioned above, the incidence in underdeveloped countries is much higher due to higher rates of tuberculosis. Clinical presentation depends on etiology and the rate of onset and severity of disease (Table 47.3) [19, 20].

Pericardial cyst is a rare mediastinal abnormality which is usually congenital but may also be acquired after cardiothoracic surgery. Cysts are typically located at the right cardiophrenic angle (50–70%) or at the left cardiophrenic angle (28–38%). A rare complication is associated with pericardial tamponade.

Congenital absence of the pericardium can be complete or partial and can be isolated or associated with other congenital anomalies in one-third of the cases, such as patent ductus arteriosus, mitral stenosis

or Tetralogy of Fallot. Life-threatening complications include herniation of a cardiac chamber through the defect, most commonly the left atrial appendage.

Hemopericardium should be suspected in any patient who complains of severe chest pain following traumatic injury.

Chylopericardium is a pericardial effusion comprised of chyle, the normal content of the thoracic duct. Chylopericardium may be primary (idiopathic) or secondary to injury of the thoracic duct and associated with chylothorax (post-surgery). Complications include cardiac tamponade, acute pericarditis or chronic constriction.

47.5 Clinical Presentation

The clinical presentation of pericardial diseases differs according to their etiology and will be discussed separately.

- Pericardial effusion and tamponade

Chest pain or discomfort relieved by sitting up and leaning forward and intensified by lying supine is typical. Respiratory symptoms of cough and dyspnea can dominate the clinical picture. The physical exam reveals a pericardial friction rub, heard most frequently during expiration with the patient upright and leaning forward [21]. The friction rub may not be heard in patients with large effusions. Tachypnea, tachycardia, widened pulse pressure, and hepato-jugular reflux are the signs of impending hemodynamic compromise.

Table 47.3 Causes of constrictive pericarditis

Causes of constrictive pericarditis:

Idiopathic

Post acute pericarditis

Tuberculosis

Infectious

Virus

Bacteria:

Staphylococci, Streptococci

Fungi:

Histoplasmosis

Rheumatoid disease

Sarcoidosis

Mediastinal radiation (Hodgkin's lymphoma)

Trauma (hemopericardium)

Status post-cardiac surgery (post-pericardiotomy syndrome)

Uremia

Neoplasia with pericardial infiltration

Metabolic and genetic disorders

The Classic Beck triad of pericardial tamponade includes hypotension, muffled heart sounds, and jugular venous distension [22]. Pulsus paradoxus, defined as a decrease in systolic blood pressure of more than 10 mmHg with inspiration, is a sign of falling cardiac output. Late findings are cyanosis and decreased level of consciousness.

- Post-pericardiotomy syndrome

Post-pericardiotomy syndrome typically occurs 1–6 weeks after cardiac surgery and is usually mild. The patient can suffer from fatigue and low grade fever. Anterior precordial chest pain that increases on deep inspiration is common. The typical clinical finding is that of a pericardial friction rub. When a pericardial effusion is associated, the friction rub can disappear, the heart sounds are attenuated and tamponade is a possibility.

- Acute pericarditis

With bacterial pericarditis, the patient is febrile and appears toxic. In the setting of viral or autoimmune pericarditis, fever and evidence of toxicity are generally milder. Chest pain is common, usually retrosternal or precordial. The pain usually is described as sharp or stabbing, and is made worse with inspiration or movement. Pain may be of sudden or gradual onset and may radiate to the back, neck, or left shoulder. Associated signs and symptoms include low-grade intermittent fever, dyspnea, tachypnea, cough, and dysphagia. Acute abdominal pain is not uncommon in children. The most common and important physical finding is a pericardial friction rub, which is best heard at the lower left sternal border or apex when the patient is sitting forward, and may be transient.

- Constrictive pericarditis

The history reveals symptoms of congestive heart failure, such as dyspnea, orthopnea, paroxysmal nocturnal dyspnea, diaphoresis, easy fatigability, and tachycardia. Precordial pain is unusual in chronic constrictive pericarditis, as opposed to acute pericarditis. The hallmarks of physical diagnosis include absence of a drop in jugular venous pulsations during inspiration (Kussmaul's sign) and elevated jugular pressure with prominent y descent (Friedreich's sign). Unlike other forms of pericardial disease, such as acute pericarditis, a friction rub is usually not audible. A protodiastolic knock, usually heard along the left

sternal border, corresponds to the abrupt cessation of ventricular filling during diastole. As the systemic venous pressure becomes elevated, signs of right-sided heart failure develop, such as neck vein distention, hepatomegaly, ascites, hepato-jugular reflux, and peripheral edema [23, 24]. Signs of diminished cardiac output include diminished pulse pressure, pulsus paradoxus, and a prominent third heart sound.

- Pericardial cyst

Although most pericardial cysts are asymptomatic, patients may present with atypical chest pain, dyspnea, or persistent cough [25].

- Absence of the pericardium

Complete congenital absence of the pericardium is often an incidental finding with chest imaging demonstrating deviation of the heart into the left chest. In those with symptoms, paroxysmal stabbing chest pain, largely non exertional and mimicking coronary artery disease, and dyspnea can be associated [26]. Displacement of the left ventricular impulse on clinical exam is the most common feature.

47.6 Preoperative Management

47.6.1 Pericardial Effusion and Tamponade

- Laboratory

Blood work should be directed towards identifying the etiology (Tables 47.1 and 47.2). Diagnostic studies can be performed on the pericardial fluid including cell count and differential, protein, lactate dehydrogenase, glucose, gram stain, bacterial and fungal cultures, viral PCR, mycobacterial acid fast stain, and tumor cytology. When connective tissue disease is suspected, rheumatoid factor, antinuclear antibodies, and complement levels can be measured.

- Chest X-ray

An increased cardiac silhouette that is globular (water bottle-shaped heart) can be seen with excessive pericardial fluid accumulation (Fig. 47.4) [27]. Another finding is visualization of the pericardial fat



Fig. 47.4 Chest X-ray in pericardial effusion: water bottle shaped heart.

stripe within the cardiac silhouette. The lung fields are usually oligemic and a pleural effusion is often associated.

- Electrocardiogram

Low voltage QRS with diffuse non-specific ST segment changes are present with large effusions (Fig. 47.5). Electrical alternans is pathognomonic of cardiac tamponade and is characterized by alternating P wave, QRS complex and T wave voltages attributable to swinging motion of the heart [28, 29].

- Echocardiography

Pericardial effusion appears as an “echo-free” space between the visceral and parietal pericardium on M-mode-echocardiography (Fig. 47.6) [30]. Effusions tend to accumulate posterior and inferior to the left ventricle initially. However, on echocardiographic imaging fluid visualized above the right atrium in the four chamber view is the most sensitive indication as

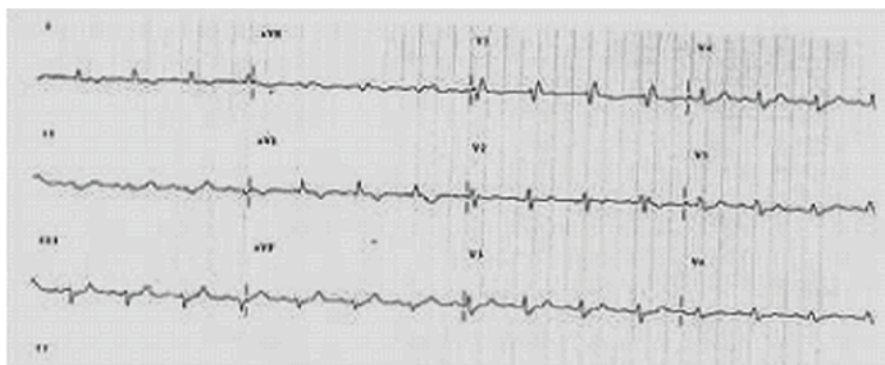


Fig. 47.5 Electrocardiogram in pericardial effusion: low voltage QRS with non specific ST segment changes

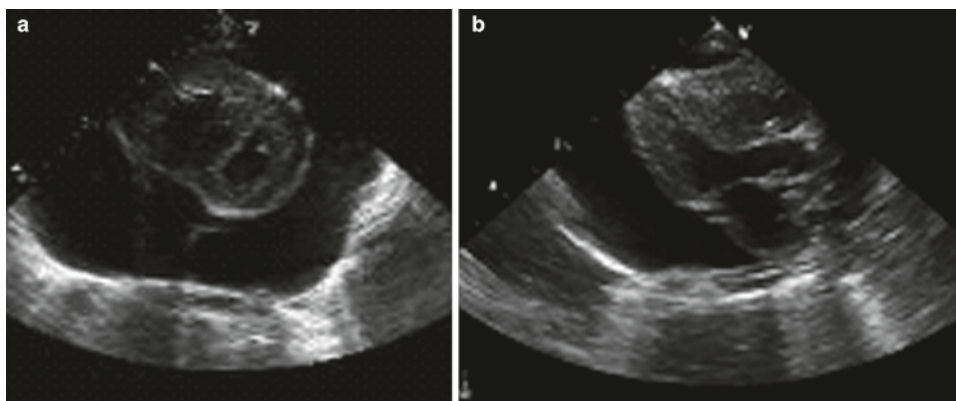


Fig. 47.6 (a) Parasternal 2D short-axis echocardiography showing a large pericardial effusion circumsccribing the heart. (b) Parasternal 2D long-axis echocardiography showing a large pericardial effusion circumsccribing the heart

this is the first place where a pericardial effusion is seen. Moderate effusions (10–20 mm in size) extend toward the apex of the heart, and large effusions (more than 20 mm) circumscribe the heart (Fig. 47.7) (Table 47.4).

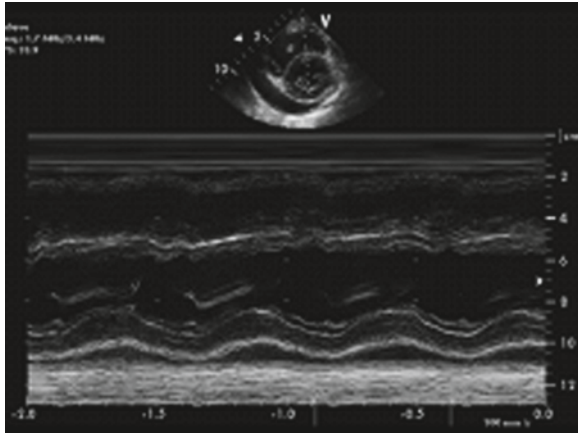


Fig. 47.7 M-mode echocardiography of a patient with a large pericardial effusion: echo-free space (arrow) between the visceral and parietal pericardium

The rapidity of fluid accumulation and the compliance of the pericardium influence the hemodynamic significance for a given fluid volume. As pericardial fluid accumulates, intrapericardial pressure increases until it exceeds normal filling pressure of the heart, leading to tamponade. The first sign of hemodynamic compromise is expiratory right ventricular free wall collapse early in diastole, reflecting the brief period when intrapericardial pressure is greater than the right ventricular transmural distending pressure (Table 47.5) [31, 32]. The right ventricle is the first to collapse due to its lower intracardiac pressure compared to the left ventricle. Although right ventricular collapse is generally a specific indicator of tamponade, the sensitivity can be reduced in conditions with increased right ventricular pressure [33].

Expiratory right atrial collapse occurs in late diastole (Fig. 47.8), and is seen as an indentation of the normally rounded anterosuperior right atrial wall. The sensitivity of expiratory right atrial collapse for diagnosing tamponade is low (55%), but the specificity is high (90%). Extension of collapse greater than

Table 47.4 Echocardiographic findings in pericardial tamponade and constrictive pericarditis (Adapted from Otto CM. *Textbook of Clinical Echocardiography*. 3rd ed. Philadelphia, PA: Elsevier; 2004; Tam JW, Shaikh N, Sutherland E. Echocardiographic assessment of patients with hypertrophic and restrictive cardiomyopathy: imaging and echocardiography. *Curr Opin Cardiol*. 2002;17:470-477)

Parameters	Tamponade	Constrictive pericarditis
RAP	↑	↑
RV and LV filling pressure	↑RV = LV	↑RV = LV
PAP	Normal	Mild ↑ RVSP <40 mmHg
RV diastolic pressure plateau		>1/3 peak RV pressure
2D echo	Pericardial effusion	Pericardial thickening, Septal shudder Interventricular dependence: IVS diastolic shift toward LV during inspiration and toward RV during expiration
M-mode		Septal notch
Doppler MV and TV	Reciprocal respiratory changes in RV and LV filling ↑ TV E during inspiration ↑ MV E during expiration LV inflow: E>A	Respiratory variation (>10%) in RV and LV filling, ↑ MV E during expiration Respiratory variation in IVRT
Doppler Pv		LV inflow: E>A ↑ TR peak velocity, VTI and duration during inspiration Respiratory variation in Pv flow ↑ D during expiration Pv flow: ↑ AR ↓ S S/D >0.65 during inspiration
TDI		Em >8 cm/s E/Em <15
Color M-mode		Vp >100 cm/s

1/3 of the cardiac cycle increases the sensitivity of this finding to more than 90% [34, 35]. Absence of expiratory right atrial collapse virtually excludes tamponade. Another sensitive marker of tamponade by

Table 47.5 Assessment of hemodynamic compromise in cardiac tamponade (Adapted from [6])

Effusion	Clinical and echo signs
Insignificant effusion	Flat neck veins Normal BP, HR, RR, good perfusion Effusion on echo, no chamber compression
Significant, compensated	Increased JVP No hypotension, tachycardia Mild pulsus paradoxus Good perfusion Effusion on echo with mild RV collapse
Severe, compensated	Increased JVP Prominent pulsus paradoxus Tachycardia, no hypotension Good perfusion Chamber collapse on echo
Severe, decompensated	Increased JVP Tachycardia, tachypnea Hypotension, pulsus paradoxus Chamber collapse, swinging heart on echo

echocardiogram is absence of inspiratory collapse (plethora) of the inferior vena cava, defined by less than 5 mm decrease in diameter during inspiration [36]. The sensitivity of inferior vena cava plethora is high (97%), but the specificity is low (66%). Diastolic collapse of the left atrium and rarely the left ventricle occurs during inspiration, related to the increased right heart inflow and abrupt expansion of the right ventricle.

Doppler echocardiography shows large swinging amplitudes of the mitral and tricuspid inflow, the aortic and pulmonary outflow and the hepatic veins. Normally, there is no more than 10% variation in the amplitude of inflow and outflow signals with respiration, but this exceeds 30% in tamponade (Fig. 47.9).

The classic Doppler patterns of cardiac tamponade include (Fig. 47.10) [37, 38]:

- Mitral inflow: During inspiration, E wave velocity decreases by more than 30% compared with expiration.
- Pulmonary veins: During inspiration, D wave velocity decreases.
- Tricuspid inflow. During inspiration, E wave velocity increases by more than 50% compared with expiration.

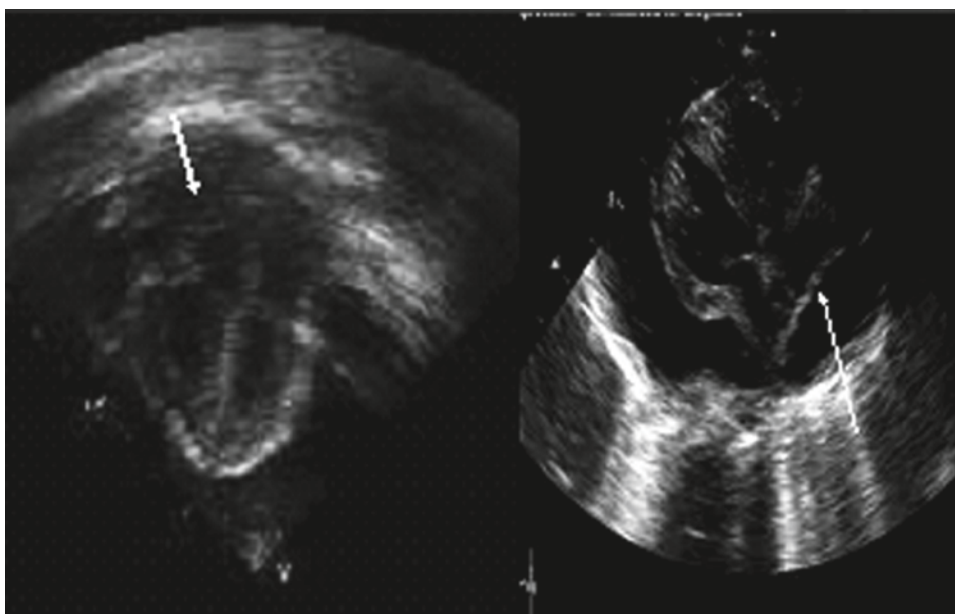


Fig. 47.8 Apical four-chamber and subcostal 2D-echocardiography views in pericardial effusion: right atrial collapse (arrow)

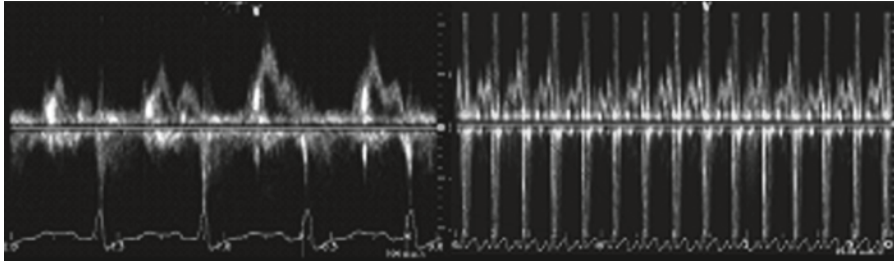


Fig. 47.9 Respiratory variation in mitral inflow by 2D-echocardiography in cardiac tamponade

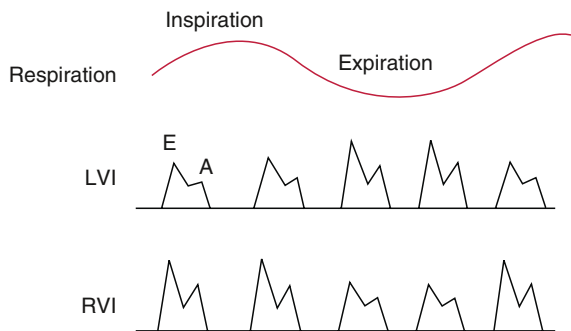


Fig. 47.10 Respiratory variations in mitral and tricuspid inflow in cardiac tamponade

– Hepatic veins: During inspiration, S is greater than D. During expiration, there is a very limited or absent D wave with prominent reversal.

- Cardiac CT and MRI

CT can potentially determine composition of fluid and may detect as little as 50 ml of fluid.

MRI can detect as little as 30 ml of pericardial fluid, and may be able to distinguish hemorrhagic and non-hemorrhagic effusions. Both MRI and CT scan may be superior to echocardiography in detecting loculated pericardial effusions and pericardial thickening.

47.6.2 Post-Pericardiotomy Syndrome

- Laboratory

Elevated white blood cell count with a left shift and elevated erythrocyte sedimentation rate (ESR) are usual.

- Chest X-ray

Radiographic evidence of pleural effusions and cardiac enlargement secondary to a pericardial effusion are common.

- Electrocardiogram

Nonspecific abnormalities of the T waves (flattening in leads I and lateral chest) and decrease in voltage with a large pericardial effusions are common findings.

- Echocardiography

Pericardial effusion is documented and its hemodynamic repercussion evaluated as described above.

47.6.3 Acute Pericarditis

- Laboratory

Inflammatory markers are usually elevated (C-reactive protein, ESR). Cardiac Troponin I rise has been described as detectable in acute pericarditis in about 30% of patients and is associated with ST segment elevation and presence of a pericardial effusion [39].

- Chest X-ray

The chest X-ray is unremarkable in the absence of a pericardial effusion.

- Electrocardiogram

The ECG can be diagnostic in acute pericarditis. It evolves four stages. The first stage is characterized by ST-segment elevation and concave upward ST segments, noted in all leads except V_1 (Fig. 47.11).

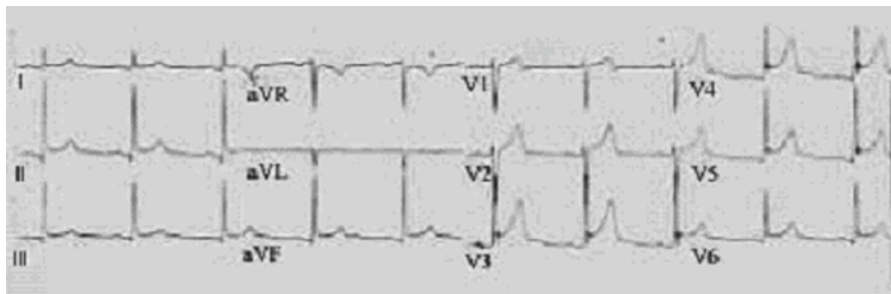


Fig. 47.11 ECG in acute pericarditis: diffuse concave upward ST-segment elevation

In the second stage, normal ST segments with T-wave flattening are noted. T-wave inversion without Q-wave formation is noticed in third stage. The fourth stage is characterized by ECG normalization. Another important ECG finding is PR-segment depression.

- Echocardiography

The echocardiogram is often normal, unless acute pericarditis is associated with a pericardial effusion. While the finding of a pericardial effusion supports the diagnosis of acute pericarditis, its absence does not exclude it. In pericarditis, the pericardium may have a normal appearance.

- Cardiac CT scan and MRI

The normal thickness of the pericardium as measured by CT scanning is less than 2 mm and 4 mm by MRI. The limitation of CT scan is the difficulty in differentiating fluid from thickened pericardium.

47.6.4 Constrictive Pericarditis

- Laboratory

Brain natriuretic peptide (BNP) is usually normal or just above normal in patients with constrictive pericarditis as opposed to elevated (>600 pg/ml) in patients with restrictive cardiomyopathy, helping differentiate between these two conditions [40]. No data on BNP levels in this setting are available in children.

- Chest X-ray

The chest X-ray is usually unremarkable. Pericardial calcifications are present in 40–50% of patients, giving an egg-shell appearance to the cardiac silhouette [41] (Fig. 47.12). The right superior mediastinum may be enlarged owing to dilation of the superior vena cava. Pleural effusions may be present, reflecting chronic elevation of right heart filling pressures. Pulmonary infiltrates are uncommon.

- Electrocardiogram

ECG is non-specific but usually demonstrates diffuse low voltage and nonspecific ST-T wave changes. Atrial dysrhythmias are common.

- Cardiac catheterization

The hallmark finding in constrictive pericarditis is the elevation and near equalization of end-diastolic pressures in the right atrium, right ventricle, pulmonary capillary wedge, and left ventricle. The right atrial pulse waveform is characterized by a prominent A wave, reflecting rapid early diastolic filling of the ventricle, a sharp x descent, due to accelerated atrial relaxation and a sharp y descent reflecting the early resistance free right ventricular filling. The mean jugular venous and right atrial pressures are elevated.

The right ventricular waveform is distinctive, with a “dip and plateau” or “square root sign” pattern (Fig. 47.13), reflecting the rapid relaxation, followed by a sharp increase in filling pressure as the expanding ventricle meets the constraints of the pericardium [42].



Fig. 47.12 Chest X-ray in constrictive pericarditis: Egg-shell appearance of the cardiac silhouette

The left ventricular pressure tracing is usually similar. Other hemodynamic findings include a right ventricular diastolic pressure exceeding one-third of the right ventricular systolic pressure, and a pulmonary artery pressure of less than 50 mmHg [43].

Another hallmark of constriction is increased ventricular interdependence. Because pericardial constraint limits total cardiac volume, there is a reciprocal relation between left and right heart filling due to

enhanced septal interaction. There is opposite directional changes in ventricular systolic pressure and reciprocal changes with respiration, with inspiration inducing an increase in right ventricular but a decrease in left ventricular pressure, a phenomenon called ventricular discordance. The opposite changes occur during expiration, with increased left heart filling and reduced right heart filling (Fig. 47.14). This may be the most reliable hemodynamic indicator of constriction [44].

When hemodynamic studies are equivocal, a bolus fluid can be administered and reveals striking elevation of the filling pressures in the case of constrictive pericarditis [45, 46].

- Echocardiography

Echocardiography remains the best tool in the initial assessment of constrictive pericarditis [47]. A thickened pericardium with some degree of pericardial effusion may be observed by 2D-echocardiography [48]. Transthoracic echocardiography is insensitive, as mildly increased pericardial thickening can be missed and false positives can be obtained if the gain is set too high. Pericardial calcifications with localized tethering of atrial or ventricular cavities may be noted, while separation of the entire pericardium by a small fixed space is known as the “halo sign.” The systemic veins are usually dilated, with the inferior vena cava showing absent collapse with inspiration (plethora). Septal “bounce” is typical, defined as abrupt posterior movement of the interventricular septum in early diastole during inspiration, and is caused by under-filling of the left ventricle and redistribution of

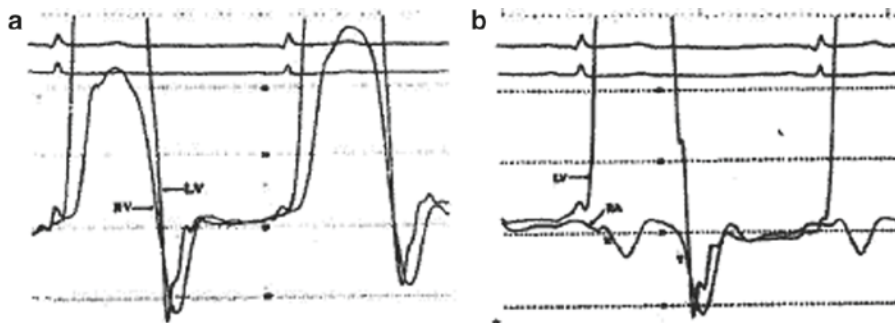


Fig. 47.13 (a) Simultaneous right and left ventricular pressure showing equalization of diastolic pressures and characteristic “dip and plateau” contour in constrictive pericarditis.

(b) Simultaneous right atrial and left ventricular pressure recordings demonstrating equalization during diastole with prominent x and y descent of the atrial tracing (from [6])

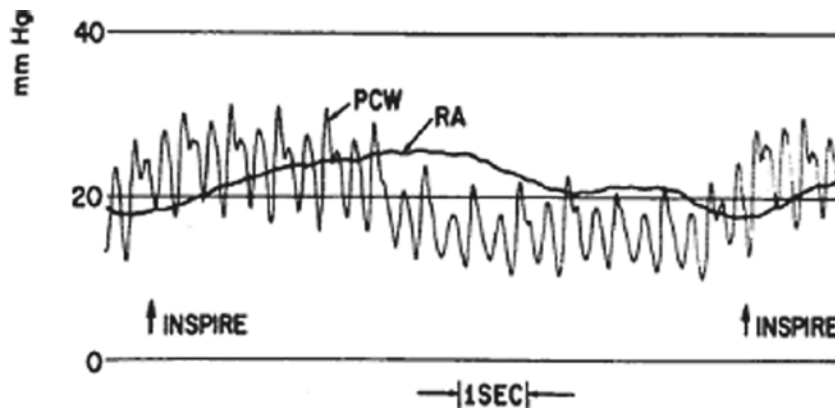


Fig. 47.14 Differential changes in the hemodynamic tracing of mean right atrial (RA) and pulmonary capillary wedge pressure (PCWP) during respiration in constrictive pericarditis. Mean RA pressure increases during inspiration (Kussmaul sign) and

PCWP decreases (from Grossman W. Profiles of constrictive pericarditis, restrictive cardiomyopathy and cardiac tamponade. Cardiac Catheterization, Angiography and Interventions 1991; Chapter 35:637)

blood from the left to the right ventricle. This “bounce” represents the first and best clue for the presence of constriction [49].

The right and left ventricular size is decreased, and both atria are mildly enlarged, related to the compliance abnormality of the ventricles. The ventricles have an elongated appearance giving the heart a tubular shape. The biventricular systolic function is usually normal. Interventricular septal motion may be paradoxical or flat as a sign of ventricular interdependence. A characteristic septal notch has been described in early diastole, corresponding to the septal bounce seen by 2D-echocardiography [50, 51]. Extensive areas of adhesions seen posteriorly by M-mode provide evidence for generalized pericardial thickening and constriction.

The hallmark of Doppler examination is reciprocal respiratory variation of right and left heart flows caused by interventricular dependence. The classical Doppler pattern consists of the following (Fig. 47.15) [52–54]:

- Mitral inflow: During inspiration, E wave to A wave ratio ($E>A$) is lower, while during expiration, there is larger E wave to A wave ($E>A$) ratio. E wave is typically increased more than 25% with expiration and the IVRT increased more than 25% with inspiration.
- Pulmonary veins: During inspiration, S and D waves are near equal in size. During expiration, larger S and D waves are noted.

- Tricuspid inflow: Shows the same pattern with reciprocal changes compared to the mitral inflow. During expiration, smaller E wave to A wave ($E>A$) ratio is noted, while during inspiration, there is larger E wave to A wave ($E>A$) ratio. E wave is typically increased more than 40% with inspiration.
- Hepatic veins: During inspiration, S wave is greater than D wave, with a small A wave reversal. During expiration, S wave is greater than D wave, with small or absent D wave and larger A wave reversal.

Also described in constrictive pericarditis is an inspiratory increase in the tricuspid regurgitant jet velocity and duration of the signal [44]. As opposed to restrictive cardiomyopathy, respiratory variation in the filling phase is more pronounced in constrictive pericarditis. Tissue Doppler echocardiography shows a normal or high early mitral annular velocity (Em wave) in constrictive pericarditis, as opposed to restrictive cardiomyopathy where it is reduced [55]. The usually positive linear relation between mitral Doppler E and tissue Doppler Em (E/Em), is useful to assess left atrial pressure and is found to be reversed in constrictive pericarditis [56]. The propagation velocity (v_p) of early diastolic transmitral flow on color M-mode is normal or increased in constrictive pericarditis [57].

- Cardiac MRI and CT

Both CT and MRI can detect a thickened pericardium (≥ 4 mm), but this is an insensitive finding. An advantage of CT is the ability to detect calcification, indica-

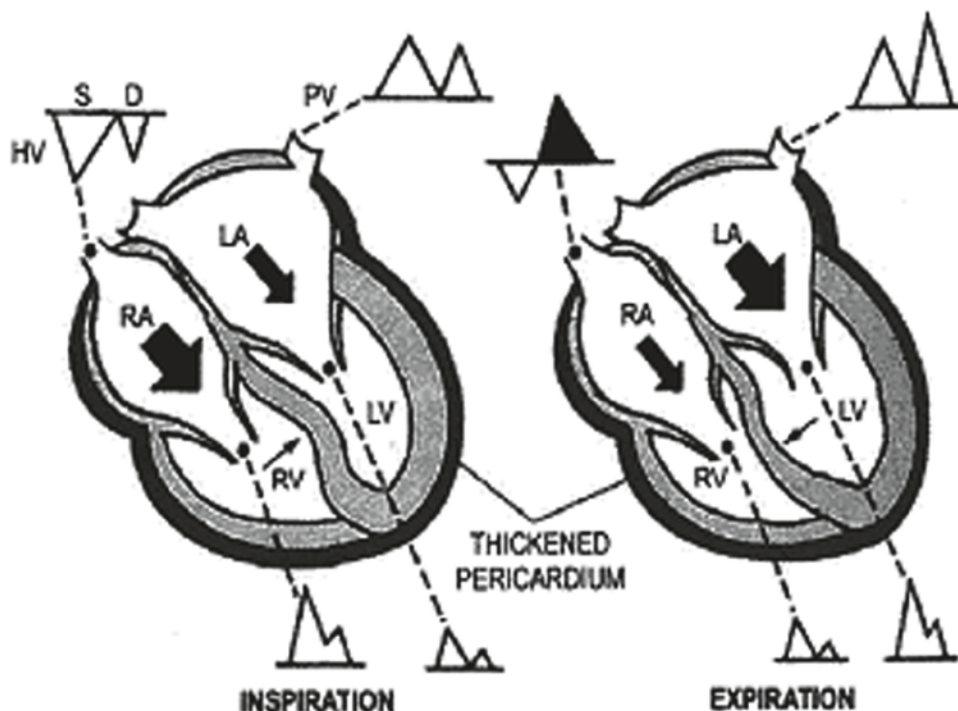


Fig. 47.15 Respiratory variation in transvalvular and central venous flow velocities in constrictive pericarditis. With inspiration, the driving pressure gradient from the pulmonary bed to the left cardiac chambers decreases, resulting in a decrease in mitral inflow and diastolic pulmonary venous velocities. Decreased left ventricular filling results in ventricular septal

shift to the left, allowing increased flow to the right-sided cardiac chambers, resulting in increased tricuspid inflow and diastolic hepatic venous velocities. The opposite changes occur during expiration (from Oh JK, Diagnostic role of echocardiography in constrictive pericarditis. *J Am Coll Cardiol.* 1994;23:154-162)

tive of constrictive pericarditis [58, 59]. However, CT may have difficulty in differentiating pericardial fluid from thickened pericardium. The absence of pericardial thickening does not rule out hemodynamically significant restrictive pericarditis.

47.6.5 Pericardial Cyst

- Chest X-ray

A pericardial cyst is typically suspected after an abnormal chest X-ray consisting of a round, discrete mass in the right cardiophrenic angle, which is the most common location of these cysts [60].

- Echocardiography

Pericardial cysts are difficult to detect with transthoracic echocardiography. They present as an echo-free space

which is more localized and spherical than a pericardial effusion [61].

- Cardiac CT and MRI

CT and MRI are the preferred methods to confirm a suspected diagnosis of pericardial cyst [25, 62]. On CT scan, pericardial cysts are thin-walled, sharply defined, oval homogeneous masses. Their attenuation is slightly higher than water density, 30–40 HU, and the cyst fails to enhance with intravenous contrast [63].

47.6.6 Absence of the Pericardium

- Chest X-ray

The chest X-ray reveals levoposition of the heart with loss of the right heart border hidden by the spine [26].

Prominence of the main pulmonary artery, interposition of a tongue of lung tissue between the pulmonary artery and the aorta (opacification of the aortopulmonary window) or between the inferior border of the heart and the left hemi-diaphragm are other findings.

- Electrocardiogram

Right bundle branch block is common. Right axis deviation with leftward displacement of the transition zone in the precordial leads can be seen.

- Echocardiography

Complete absence of the pericardium leads to enlargement of the right ventricle, excessive motion of the posterior left ventricular wall, paradoxical motion of the interventricular septum, and a shift of the heart to the left resulting in more of the right ventricle being seen on the left parasternal long axis view. All of these findings mimic right ventricular volume overload and thus this diagnosis should be excluded [64]. Partial absence of the pericardium sometimes results in herniation of a chamber through the defect, with the false appearance of wall motion abnormality. The biventricular function is usually normal. True wall motion abnormality is seen if a coronary artery is compressed.

- Cardiac MRI

The most reliable finding is interposition of lung tissue between the main pulmonary artery and the aorta. The heart can be completely displaced in the left hemithorax and its apex elevated. The main pulmonary artery and the left atrial appendage can be seen extending far beyond the mediastinal margins.

47.7 Medical Management

47.7.1 Post-pericardiotomy Syndrome

Post-pericardiotomy syndrome is usually self-limited but relapses can occur. Medical treatment includes bed rest and anti-inflammatory drugs:

- Acetylsalicylic acid (Aspirin 100 mg/kg/day or 800 mg every 6 h in adults) is thought to reduce inflammation and fever and is administered for 10 days, then gradually tapered down over 3 weeks.

High dose Aspirin should be associated with a gastro-duodenal prophylaxis (proton pump inhibitor).

- Non steroidal anti-inflammatory drugs (NSAIDs), Ibuprofen (10 mg/kg/day) is an alternative to aspirin therapy.
- Corticosteroids (Prednisone 1–2 mg/kg/day) are preferably avoided but can be used in severe or recurrent cases during 2–4 weeks followed by gradual tapering off.
- High doses intravenous immunoglobulins (IVIg) have been described in the treatment of recurrent post-pericardiotomy syndrome [65].

47.7.2 Pericarditis and Pericardial Effusion

If an infectious cause of pericarditis or a pericardial effusion is identified, obviously appropriate antimicrobial therapy should be started. In the case of a small pericardial effusion in the postoperative period, an increase in the diuretic regimen can be attempted. NSAIDs or acetylsalicylic acid are usually used to decrease the inflammatory reaction. Aspirin (100 mg/kg/day) during 7–10 days, tapered down over 3–4 weeks, is usually the first line treatment. Steroids are reserved for severe and recurrent cases, as cases of corticoid-dependant pericardial effusion has been described. It is uncertain whether adjunctive corticosteroids are effective in reducing mortality or pericardial constriction in tuberculous pericarditis, and their safety in HIV-infected patients has not been conclusively established.

47.7.3 Constrictive Pericarditis

The treatment is essentially symptomatic, with diuretics to reduce right heart failure and pulmonary edema. The only curative treatment is pericardiectomy.

47.7.4 Recurrent Pericarditis

Colchicine has been shown to be safe and effective in the treatment and prevention of recurrent pericarditis after failure of conventional treatment, especially in idiopathic

cases [66]. The dose for adults is 1.0–2.0 mg for the first day, followed by a maintenance dose of 0.5–1.0 mg daily for 3 months. No data are available in children.

47.8 Procedures

- Echocardiography-guided pericardiocentesis

The approach is to assess the size, distribution, and ideal needle entry site and trajectory to safely evacuate the pericardial fluid. The echocardiographic transducer is placed approximately 3–5 cm from the parasternal border and the area of maximal pericardial fluid accumulation is identified. The needle trajectory is established by the angle of the transducer [67–69]. The precordium is entered in the angle formed between the xyphoid process and the left costal cartilages using an 18-mm gauge needle directed at an approximate 15° posterior angle towards the shoulder. The needle is advanced with the tip bent downwards while continuous suction is performed with a syringe until fluid is obtained. Adequate drainage of the pericardial fluid is assessed by echocardiography. Echocardiography-guided pericardiocentesis is simple, safe, and effective for primary treatment of clinically significant pericardial effusion,

even in the postoperative period [70]. Complications include transient arrhythmia and hemopericardium.

- Percutaneous pericardial drainage

Frequently, pericardiocentesis is accompanied by insertion of a drainage catheter to reduce the rate of recurrence that may complicate simple needle drainage. The precordium is entered from the standard subxiphoid approach using an 18-mm gauge needle until fluid is obtained. To assess the position of the needle in the pericardial sac, saline solution can be injected and monitored via echocardiography [71]. A 0.035" guide wire is advanced into the pericardial space, under echoguidance. The needle is subsequently removed and the tract is dilated with a 7F or 8F dilator. A 7F or 8F pigtail catheter is then inserted over the guide wire, positioned in the posterior pericardial space at the level of the left atrioventricular groove (Fig. 47.16).

- Percutaneous balloon pericardiotomy

The initial part of the procedure is similar to percutaneous pericardial drainage but is performed in the catheterization laboratory under fluoroscopic guidance. The parietal pericardium is dilated using a 10F dilator. Further dilation is performed using either a single balloon (20 mm wide, 3 cm long) or trefoil (triple) balloons. The balloon is filled with a mixture of contrast

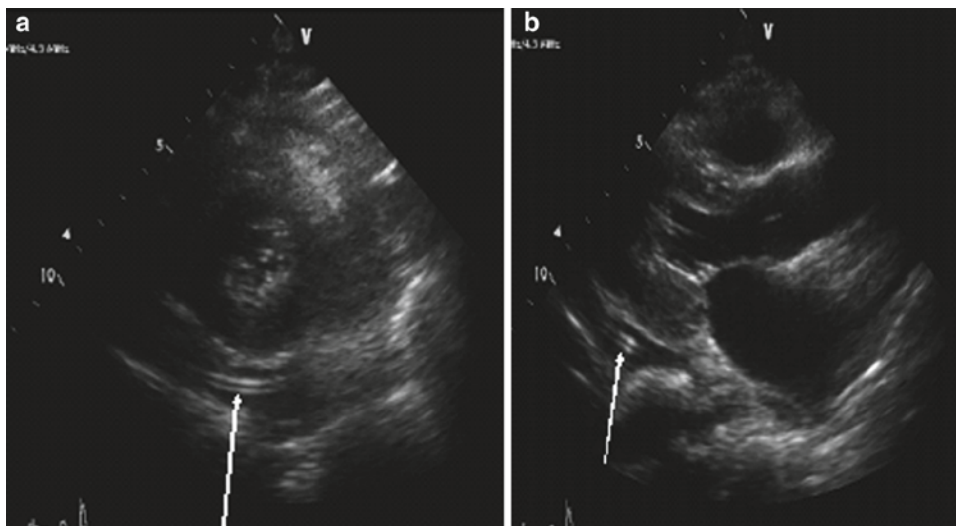


Fig. 47.16 (a) 2D-echocardiography in parasternal short-axis view showing a pericardial drain in the posterior pericardium (arrow). (b) 2D-echocardiography in parasternal long-axis view showing a pericardial drain in the posterior pericardium (arrow).

and saline, and is manually inflated to a maximum pressure of 3.5 atm until the balloon “waist” disappears. Three inflations of 15 s each are recommended. At the end of the procedure, a pigtail catheter is exchanged over the wire and left in place to allow complete drainage of the effusion [72]. Complications include fever, pneumothorax, pleural effusion, and severe chest pain. The success rate of this procedure is very high [73].

- Pericardial sclerosing therapy

When significant pericardial effusion recurs, a more definitive intervention is needed. Pericardiocentesis with instillation of sclerosing agents has been shown to be successful for malignant pericardial effusions, with a low recurrence rate. Most commonly used is tetracycline or bleomycin, instilled through a pigtail catheter [74, 75]. Common side effects include transient pyrexia, severe retrosternal chest pain and transient atrial arrhythmia. Few data are available in children [76].

47.9 Surgical Management

47.9.1 Pericardial Effusion

- Subxyphoid pericardial drainage

Subxyphoid pericardiectomy is often preferred to percutaneous pericardiocentesis in critically ill patients, or when echo-guided pericardiocentesis fails. It is performed via a midline incision from the xyphosternal junction to 6–8 cm below the tip of the xyphoid. The xyphosternal junction is split and the xyphoid process removed to expose the diaphragm. The sternum is lifted so the pericardium can be reached. The pericardium is incised allowing the fluid to drain freely and a pericardial drain is left in place [71]. Minor complications include wound dehiscence and transient pneumothorax.

- Pleuro-pericardial window

Limited pericardiectomy is performed via a left thoracotomy. No attempt is made to excise all pericardial tissue, the main objective is to provide drainage of the pericardial sac into the left pleural space. This procedure can also be performed under direct thoracoscopic vision with excellent visualization of the pericardium and pleura.

47.9.2 Constrictive Pericarditis

- Pericardiectomy

Pericardiectomy is the treatment of choice for symptomatic patients with typical constrictive hemodynamics. Limited pericardiectomy is usually performed via a left thoracotomy, but does not allow access to the right atrium and vena cava. Total pericardiectomy is defined as a wide excision of the pericardium from around the both ventricles, the great vessels, the vena cava, and the right atrium. It is usually performed via a median sternotomy or bilateral transsternal anterior thoracotomy. A median sternotomy with cardiopulmonary bypass stand-by is usually the preferred approach as it offers better exposure to the right side of the heart [77].

Poor results with persistent elevation of ventricular filling pressures have been attributed to inadequate decortication and remodeling of the ventricles after pericardiectomy. Complications include excessive bleeding and low cardiac output syndrome, thought to be secondary to fibrosis and atrophy of the myocardial fibers. Reoperation for recurrent constrictive pericarditis after partial pericardiectomy is common [78]. Improvement of symptoms and normalization of the intracardiac pressures occurs more quickly after extensive pericardiectomy [79].

47.9.3 Congenital Absence of the Pericardium

Surgical procedures employed for patients with absence of the pericardium include left atrial appendectomy, division of adhesions, pericardiectomy, or pericardioplasty. The latter is usually reserved for symptomatic patients, as the symptoms are thought to be secondary to excessive cardiac motion. It is controversial as to whether asymptomatic patients with moderate-sized pericardial defects should undergo prophylactic operation to reduce the risk of death from cardiac structure herniation or incarceration [80].

- Pericardioplasty

Surgical reconstruction of the pericardium can be performed with Gore-Tex material or xenograft pericardium. The lateral and anterior surfaces of the newly reconstructed pericardium are then sutured to

the lateral and medial aspect of the diaphragmatic surface, to avoid excessive cardiac motion. Careful attention must be paid to the left phrenic nerve [26].

47.9.4 Pericardial Cyst

Surgical excision is recommended only in symptomatic patients while asymptomatic patients can be managed conservatively [81]. Minimally invasive thoracoscopic resection of the cyst is a good alternative, as it minimizes postoperative pain and has a better cosmetic outcome [82].

47.10 Postoperative Management

Among the pericardial disease processes a common postoperative strategy may be employed. In large part, postoperative care is supportive with additional treatment directed at the underlying etiology of the disease. Management of the patient in ICU consists of fluid balance monitoring, sedation and analgesia, respiratory management, inotropic and vasodilator therapy, and recognition of anticipated complications.

In many patients, the duration of the pericardial disease process will impact their postoperative course.

- Monitoring

Continuous cardiorespiratory monitoring remains standard for these patients. Attention should be paid to alterations in heart rate, blood pressure, and respiratory rate. Most patients should be maintained in the physiologic range after returning to the intensive care unit.

- Fluid management

The fluid status of a patient with pericardial disease returning to the ICU environment should be monitored carefully. Many postoperative patients may have been on very high doses of diuretics prior to surgery and a few may be diuretic dependent. Maintenance intravenous fluid therapy should be initiated on patients unless contraindicated by concurrent illness. Most will not need the aggressive fluid management of other postoperative cardiac patients. The exceptions are those patients with restrictive physiology in whom

fluid balance will become important as their disease process progresses.

- Sedation and analgesia

Most patients should be extubated in the operating room or upon return to the ICU. Sedation should not be a significant issue in the postoperative period. Pain control can be achieved with continuous narcotic infusion or boluses. Pain from thoracotomy should not be underestimated, especially in the older patients, as atelectasis secondary to shallow breathing can be a serious complication. The transition to oral pain management should occur when the patient is capable of tolerating an oral diet. In the older child or adolescent, intermittent oral or intravenous benzodiazepines may be used for anxiolysis. Additionally, intravenous ketorolac or NSAIDs may be useful in patients with an inflammatory component to their pericardial disease.

- Respiratory management

Most patients are extubated in the operating room or immediately upon return to the intensive care unit. Adequate pain control avoids one of the most common complications after thoracotomy or sternotomy – atelectasis.

- Inotropic and vasodilator therapy

A low cardiac output state may be treated with volume resuscitation, inotropic support, and afterload reduction. Additionally, vasoactive medications may be used depending upon the clinical state of the patient.

- Anticipated complications

In-hospital mortality after pericardiectomy for constrictive pericarditis is not negligible, reported around 15%. Complications after surgery include low cardiac output syndrome and hemorrhage. Patients should be monitored for persistent effusion or restrictive physiology after surgical intervention.

47.11 Long-Term Outcome

Pericardiectomy improves symptoms in the majority of patients during late follow up. A subgroup of patients do not experience an amelioration in clinical symptoms, probably because myocardial function does not completely recover [83]. This is particularly true for

patients with long-standing constriction, especially in the setting of tuberculosis. Right ventricular dysfunction has been associated with myocardial involvement and absence of clinical improvement after pericardiectomy [84]. Recurrence is the most troublesome complication of pericarditis, occurs in 15–50% of patients and is probably an autoimmune process (e.g., Dressler's syndrome). The overall prognosis in idiopathic recurrent pericarditis is excellent and complications are uncommon. Even after numerous recurrences of pericarditis, constrictive pericarditis as a complication is extremely rare. The risk of evolution to constrictive pericarditis in idiopathic acute pericarditis is estimated to be around 1% [85]. The risk of progression to constriction is higher in tuberculous, neoplastic or purulent pericarditis.

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Chapter 48

Infective Endocarditis

Nilanjana Misra and Eric S. Quivers

Infective endocarditis (IE) is defined as a microbial infection of the endocardial surface of the heart. Native and prosthetic valves are the most frequently involved sites. Other sites can be involved, including septal defects, prosthetic materials such as intracardiac patches, surgically created shunts or a naturally occurring shunt such as an arteriovenous shunt. Central venous and pacing catheters and other sites including the great vessels, intracavitary walls, and aneurysms can also be involved.

The infecting organism may be bacterial, fungal, chlamydial, rickettsial, or viral [1]. Despite its recognition in the early 1500s by French Renaissance physician, Jean Francois Fernel, IE continues to be a diagnostic dilemma, even in the face of significant medical advances in prevention of predisposing factors, diagnostic imaging, and the areas of treatment of cardiovascular disease [2].

48.1 Epidemiology

Several parallels exist between the pediatric and adult experience with IE. The incidence of IE has remained constant over the past two decades in adult series at approximately 1.7–6.2 cases/100,000 patient years and may be increasing as reported in some recent studies. Incidence in developing countries is significantly higher due to lack of prevention, incidence of valvular disease secondary to rheumatic fever and also to associated factors like malnutrition. IE has evolved in its presentation, predisposing factors, sequelae, and microbiology [3, 4].

In developed countries, sequelae of chronic rheumatic heart disease is no longer the leading predisposing factor in IE, whereas the degenerative valve disease of the elderly is the leading cause in the adult population now [5]. There has been a change in the etiology in pediatric population over 2 years of age, as well. Chronic rheumatic valvular disease, which before the 1970s accounted for 30–50% of IE cases, has now been supplanted by congenital heart disease as the predominant underlying condition in children with IE in the USA. This includes children with a previous corrective or palliative surgery for CHD without prosthetic material or valve replacement. The most common underlying CHDs include ventricular septal defects, patent ductus arteriosus, aortic valve abnormalities, and Tetralogy of Fallot [6]. The incidence of IE as reported in large pediatric series appears to be increasing. From 1963 to 1972 the reported incidence of IE at Boston Children's Hospital was 1 of 1,800 admissions, whereas during the period of 1933–1963 it was 1 in 4,500 admissions. Other recent reviews support this increase and indicate that IE accounts for approximately 1 in 1,280 pediatric admissions a year. In both pediatric and adult populations, the mean ages have been increasing. The increase is thought to be due to better medical and surgical management of congenital heart defect and longer survival in both groups. In the pediatric group, the mean age has increased from 5 years of age between 1930 and 1950 to between 8.5 and 13.0 years during the period of 1960–1980 [7].

Children in whom IE occurs without CHD, often occurs in association with indwelling intravenous catheters, accounting for about 8–10% of cases. It usually involves the aortic or mitral valves. IE in newborns is associated with a very high mortality with the incidence increased with increased use of invasive therapies to manage extremely ill neonates with multiple medical problems [6].

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48.2 Pathogenesis

The intact endocardium is a poor surface as a stimulant for platelet aggregation and bacterial adhesion. However, injured cardiac endothelium is very conducive to thrombogenesis and thus, the possible bacterial seeding during bacteremia resulting in septic vegetation. The process includes deposition of sterile clumps of platelets, fibrin, and occasionally red blood cells giving rise to a site of nonbacterial thrombotic endocarditis (NBTE). The site can be the result from injury to the endothelium by shear forces caused by a high-velocity jet stream of blood, or the site can be caused by mechanical injury from indwelling catheters to the endocardial surface. IE may develop at the NBTE site during bacteremia if the bacteria are able to colonize the site. Once colonized, more platelets and fibrin are deposited over the multiplying bacteria, protecting them from the immunologic defenses of the body, leading to further growth of the vegetation. The infected NBTE is a source of constant bacteremia and reseeding of the vegetation. Three zones have been described in vegetations: a basal necrotic endocardium; a broad zone of bacteria, pyknotic nuclear debris, and fibrin; and a thin surface coat of fibrin and leukocytes. It is in the middle zone that the bacterial proliferation goes unchecked as the host defenses and antimicrobial therapy are unable to penetrate effectively.

Vegetations may be single or multiple, ranging in size from less than 1 mm to several centimeters. Large lesions may appear to be tumors and may cause obstruction depending on location. *Candida* spp., *Haemophilus* spp., and *S. aureus*, may produce friable lesions that can result in embolization. Ulceration of valvar tissue may result in perforation, valvar insufficiency, and sudden onset of congestive heart failure. Other cardiac complications include rupture of chordae tendineae, annular abscesses, aneurysms of the sinus of Valsalva or ventricle, myocardial infarction, fistula formation, and the development of pericardial empyema and tamponade.

Other organs are affected by IE through embolization and immune responses. A necropsy review of IE cases in pediatric patients showed that the lung is the most common site of embolic complications. Cerebral emboli with subsequent infarction have been found in 30% of adults and children who had IE resulting in abscess, mycotic aneurysm, subarachnoid hemorrhage, and acute hemiplegia. Strokes are usually associated with emboli to the middle cerebral artery. A confused

mental state may result from microemboli to the cerebral circulation. The kidney is the most common organ affected with IE on the systemic side of the heart. Also, the kidney may be affected by the deposition of circulating immune complexes resulting in focal or diffuse glomerulonephritis. Circulating immune complexes are found more often in patients with longstanding disease, right-sided disease, hypocomplementemic states, and extravascular manifestations. Autoimmune antibodies found in the course of IE include antiendocardial, anti-sarcolemmal, antimyolemmal, and antinuclear.

The CHD lesions that involve high-velocity jets and/or foreign material have the highest risk of the development of IE. CHD patients who have undergone palliative surgery with shunt or conduit placement have been recognized as the largest group at risk. High-velocity jet streams are not required to initiate IE; the presence of turbulent flow is the common prerequisite. In the nonsurgical group of children who develop IE, aortic valve disease is a common diagnosis (Figs. 48.1 and 48.2).

Neonatal endocarditis is frequently right-sided involving the indwelling catheter, tricuspid valve, or both (Figs. 48.3, 48.4 and 48.5). Sources of bacteremia include injury to the skin or mucous membranes, vigorous endotracheal suctioning, parenteral hyperalimentation, and the placement of umbilical vessel catheters.

48.3 Diagnosis

IE is a syndrome diagnosis that is dependent on the basis of the presence of multiple findings as opposed to one single definitive result. Diagnosis involves the compilation of clinical, laboratory, and echocardiographic data. The diagnosis of IE may be obvious in the patient, who has bacteremia with a predisposing cardiac condition. The more common case is that of the patient in whom it is difficult to establish the diagnosis, especially when features of IE are masked by other coexisting diseases or even in an atypical presentation. The cost of misdiagnosis may be high as it could lead to increased morbidity and mortality. The *Duke criteria* were formulated in 1994 to assist in the diagnosis of IE. The criteria have been validated by numerous studies in both adults and children. The spectrum included the elderly, prosthetic valve recipients, injection drug users,

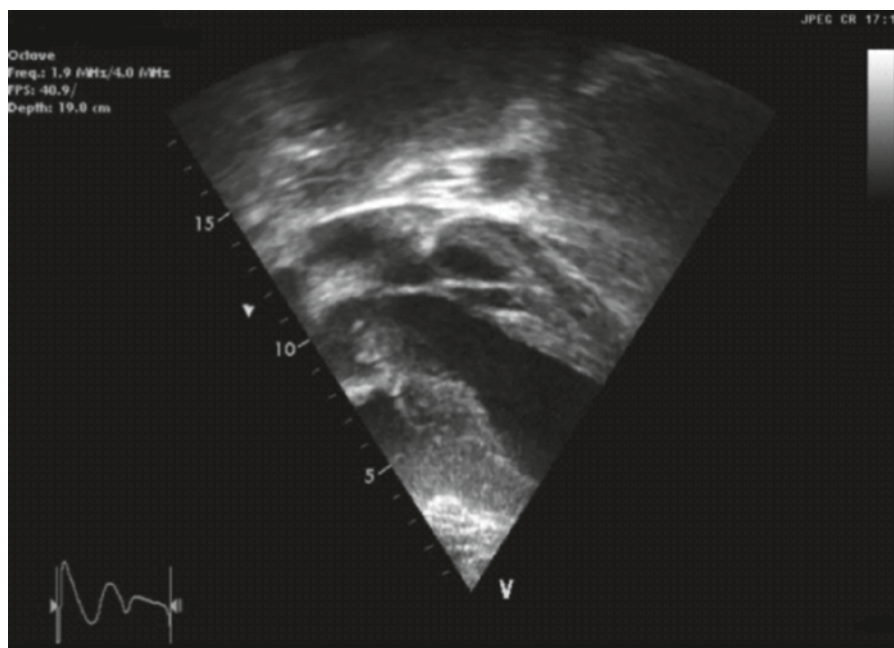


Fig. 48.1 Transthoracic echocardiography (TTE) image – apical four chamber view of aortic valve vegetation

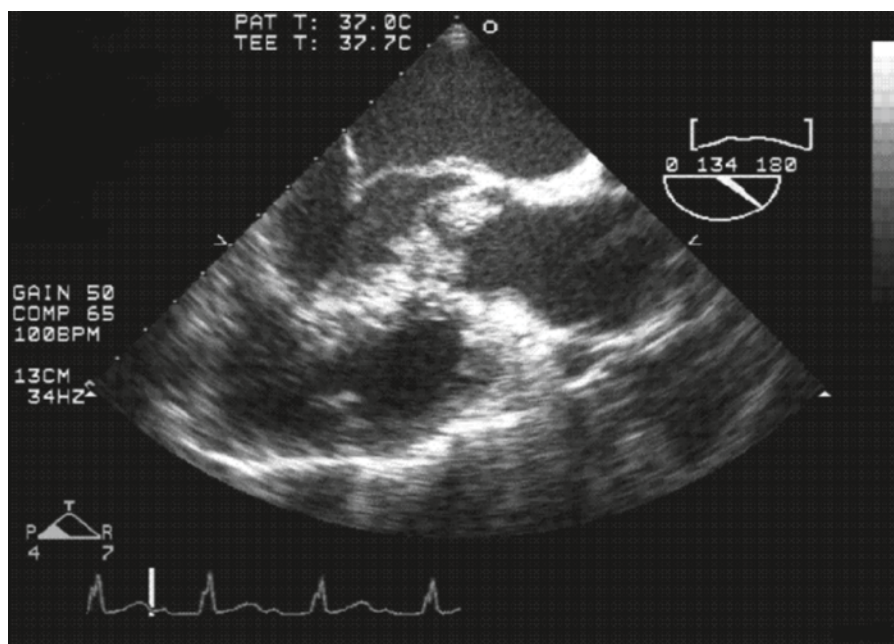


Fig. 48.2 Transesophageal echocardiography (TEE) image – mid esophageal long axis view of aortic valve vegetation

patient in various hospital settings worldwide. The presence of *two major criteria* or *one major and three minor criteria* or *five minor criteria* are required for diagnosis of IE. The Duke criteria have a high sensitivity

of >80%, and high specificity and negative predictive value which have been confirmed by several studies. However, with the changing face of IE, modifications to the criteria have been proposed to address the

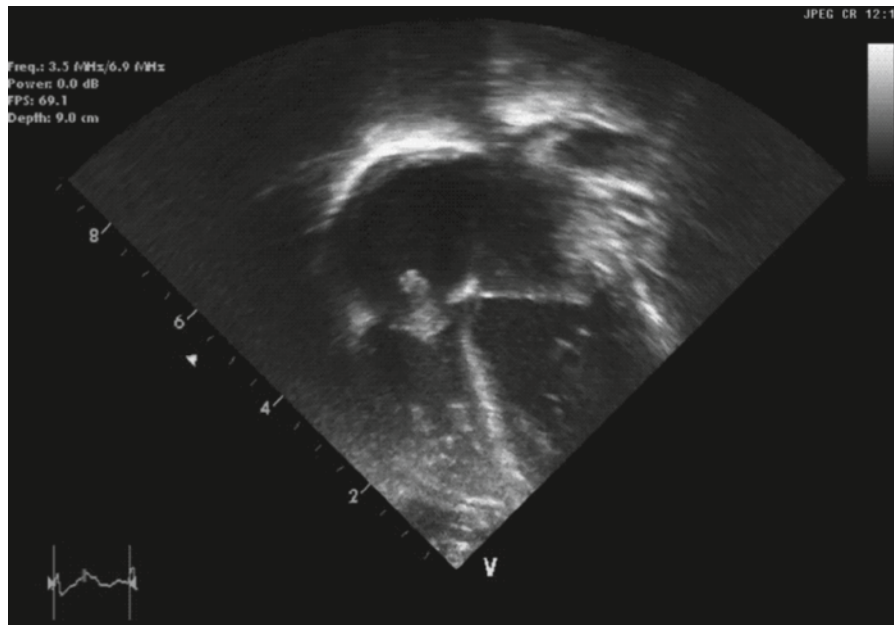


Fig. 48.3 TTE image – apical four chamber view of tricuspid valve vegetation

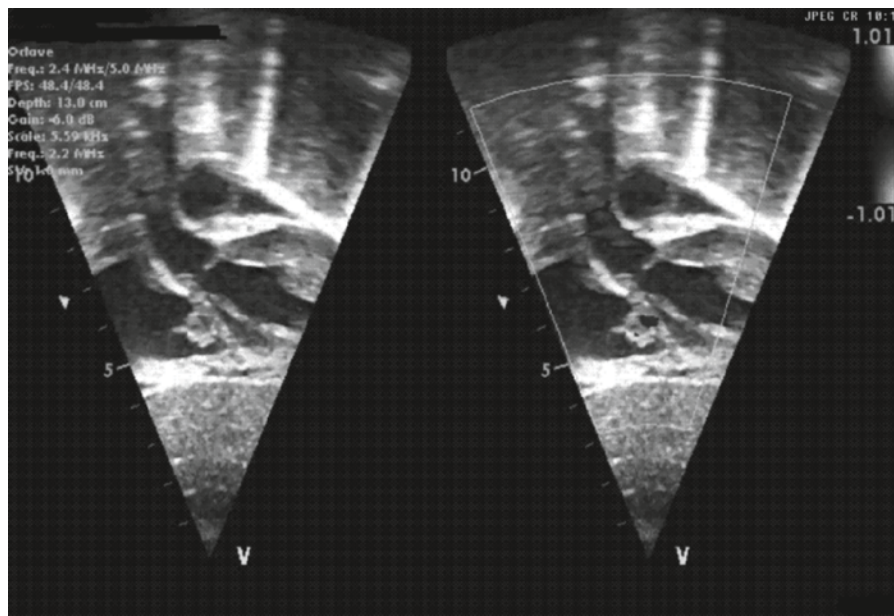


Fig. 48.4 TTE image – subcostal view of tricuspid valve vegetation

appearance of Q fever as frequent cause of IE in France and the increasing prevalence of staphylococcal infection, and the increased use of transesophageal echocardiography (TEE). In 2000, Li et al. proposed further modifications to the Duke criteria. It was recommended that the category “possible IE” be defined as having one

major criterion and one minor criterion or three minor criteria. The minor criterion addressing an echocardiographic finding consistent with IE but not meeting major criterion be eliminated, in recognition of the widespread use of TEE. Also, the bacteremia due to *S. aureus* should be considered a major criterion regardless

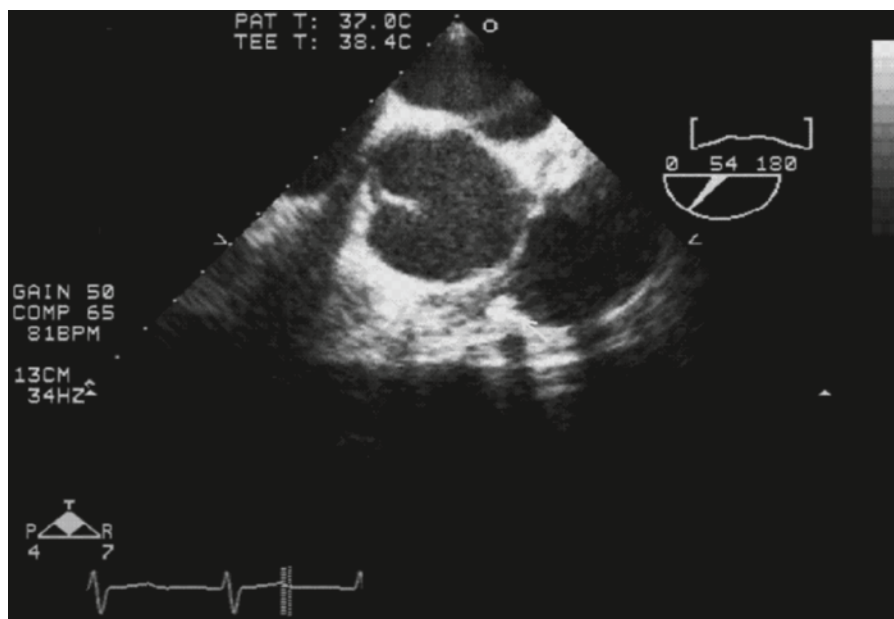


Fig. 48.5 TEE image – mid esophageal view of pulmonary valve vegetation

of whether the source is nosocomial or associated with a removable source of infection. Positive Q fever serology should be changed to a major criterion, as well (Tables 48.1 and 48.2) [8].

48.4 Clinical Findings

The presentation of IE in children is usually that of a prolonged low-grade fever, a variety of complaints, including fatigue, weakness, arthralgias, myalgias, weight loss, rigors, and diaphoresis; all of which are nonspecific, but as a group of symptoms should prompt strong consideration for IE, particular in a patient with underlying heart disease. Fig. 48.12 lists the major clinical manifestations of IE in children.

Physical findings are influenced by the presence of bacteremia (or fungemia), valvulitis, immunologic responses, and emboli. The extracardiac findings of petechiae, hemorrhages, Roth's spots, Janeway lesions, Osler nodes, or splenomegaly are significantly less common in children than in adults.

Glomerulonephritis and focal infarctions of the kidney result from embolic or immune complex-mediated processes. Emboli to other organs, such as the abdominal viscera, brain, and heart may result in symptoms associated with ischemia, hemorrhage, or

Table 48.1 Definition of infective endocarditis based on modifications to modified Duke's criteria

Definite infective endocarditis

- Pathologic criteria
 - Microorganisms demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or
 - Pathologic lesions: vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis
- Clinical criteria
 - Two major criteria; or
 - One major criterion and three minor criteria; or
 - Five minor criteria

Possible infective endocarditis

- Major criterion and one minor criterion; or
- Three minor criteria

Rejected

- Firm alternate diagnosis explaining evidence of infective endocarditis; or
- Resolution of infective endocarditis syndrome with antibiotic therapy for ≤ 4 days; or
- No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for ≤ 4 days; or
- Does not meet criteria for possible infective endocarditis, as above

both. Children with right-sided IE may present with pulmonary emboli and signs and symptoms associated with septic emboli to the lungs.

Table 48.2 Proposed changes to the modified Duke's criteria*Major criteria*

Blood culture positive for IE

- Typical microorganisms consistent with IF from two separate blood cultures:

Viridans streptococci, *Streptococcus boris*, HACEK group, *Staphylococcus aureus*; or

Community-acquired enterococci, in the absence of a primary focus; or

- Microorganisms consistent with IE from persistently positive blood cultures, defined as follows:

At least two positive cultures of blood samples drawn >12 h apart; or

All of three or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

- Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1:800

Evidence of endocardial involvement

Echocardiogram positive for IE (TEE recommended in patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE [paravalvular abscess]; TTE as first test in other patients), defined as follows:

- Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or
- Abscess; or
- New partial dehiscence of prosthetic valve

New valvular regurgitation (worsening or changing of pre-existing murmur not sufficient)

Minor criteria

Predisposition, predisposing heart condition or injection drug use

Fever temperature $>38^{\circ}\text{C}$

Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions

Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor

Microbiological evidence: positive blood culture but does not meet a major criterion as noted above^a or serological evidence of active infection with organism consistent with IE

Echocardiographic minor criteria eliminated

TEE transesophageal echocardiography; TTE transthoracic echocardiography

^aExcludes single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis

The cardiac examination of a child with IE is highly variable, dependent on the type of underlying heart disease present and site of the infection. The physical finding of a changing murmur in a child with underlying CHD is a key finding. Valvar lesions tend to produce regurgitant murmurs due to leaflet destruction. Children with cyanotic CHD palliated by systemic-pulmonary artery shunting, may not present with a change in their

murmur, but rather a decrease in their systemic saturation secondary to obstruction to flow due to the infection.

In an unusual presentation, the child may be in extremis due a fulminant course, with rapidly changing symptoms and high spiking fevers. These children are ill and require immediate stabilization and treatment.

48.5 Laboratory Assessment

For all patients with fever of unexplained origin, a pathological heart murmur, a history of heart disease, or a history of previous IE, blood cultures are required as part of the evaluation. Bacteremia in IE is continuous. Therefore, the timing of their acquisition is not crucial. It is important to obtain adequate volumes of blood to culture, 1–3 ml in infants and young children and 5–7 ml in older children. As it is rare for IE to be caused by anaerobic organisms, aerobic cultures are essential. It is recommended to obtain three blood cultures; the first day by separate venipuncture and if there is no growth in the 2 days of incubation, two more can be obtained [6]. There is usually no value in obtaining more than five blood cultures over 2 days, unless the patient has received antibiotic therapy. In patients who are stable, not acutely ill, and whose cultures are negative may have antibiotics withheld for 48 h or so, while more cultures are obtained. Acutely ill patients should receive empiric antibiotic therapy immediately after the three blood cultures are obtained. It should be strongly emphasized to the microbial laboratory that IE is suspected, to allow cultures to be processed appropriately.

48.5.1 Etiologic Agents Isolated from Blood Culture

Most organisms that cause IE in children are Gram-positive cocci. The most common organisms include the viridians group of streptococci (*S. sanguis*, *S. mitis* group, *S. mutans*), isolated between 30 and 50% of the time in numerous studies and *S. aureus* which accounts for 25–30% of isolated organisms. Coagulase negative staphylococci (CoNS) and enterococci round out the most common organisms [9]. In children older than 1 year of age, the viridans streptococcal group is the

most frequent causative agent. *S. aureus* is the second most common agent isolated in IE, but it is the most common organism associated with acute bacterial endocarditis.

The HACEK group consists of *Hemophilus parainfluenza*, *H. aphrophilus*, *H. paraphrophilus*, *Actinobacillus* (*Haemophilus*) *actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella* species, and *Kingella kingae* is a rare but important group of organisms causing IE in children.

S. aureus or CoNS are the most frequent organisms associated with IE in the presence of prosthetic material or valves, and indwelling intravascular catheters. The organisms are usually seeded at the time of cardiac surgery and IE occurs within 60 days. An infection due to CoNS may occur as late as a year after surgery. IE caused by Gram-negative bacilli is rare probably due to the poor adhesion of these organisms to the cardiac valves.

In newborns, *S. aureus*, CoNS, and *Candida* species are the most common causes of IE. With the introduction of central venous catheters and the use of hyperalimentation and high glucose concentration fluids, *Candida* infections of the mural or valvar endocardium have been well recognized. Fungal vegetations tend to be more friable and emboli from these can cause serious complications.

The special case of culture-negative endocarditis is recognized when a patient has clinical and/or echocardiographic evidence of IE but persistently negative blood cultures. Recent antibiotic therapy or a fastidious organism that grows poorly in vitro is the most common cause of this phenomenon. The prevalence in the US is between 5 and 7%. Organisms associated with culture-negative endocarditis include filamentous fungi, *Coxiella burnetii*, *Brucella*, *Legionella*, *Bartonella* (*Rochalimaea*), and *Chlamydia*.

48.5.2 Other Laboratory Tests

Although not specific in the diagnosis of Infective endocarditis, there are a variety of other laboratory tests that support and help in the management and follow up of the patients. Elevated acute phase reactants (e.g., erythrocyte sedimentation rate and C-reactive protein) and hypergammaglobulinemia are often present. Leukocytosis may be present in bacterial endocarditis

but is rarely seen in fungal endocarditis. Anemia is common and is usually secondary to long standing infection or from hemolysis. Microscopic or macroscopic hematuria may occur in renal embolization or if associated with red blood cell casts or proteinuria may represent glomerulonephritis.

48.5.3 Other Tests

The presence of conduction disturbances on the electrocardiogram should raise the suspicion of the infection extending to the valvular annulus or adjacent myocardium. Emboli to the coronary circulation may be seen as ischemic changes on the electrocardiogram.

Chest X-rays may show areas of focal infiltrates that are consistent with septic emboli to the lungs as sequelae of the right-sided lesions.

Computed tomography of the brain, abdomen can show areas of infarcts from septic emboli from the left-sided lesions and of chest for embolization to the lungs.

48.6 Echocardiography

Two-dimensional echocardiography has become a major diagnostic modality for detection of endocardial involvement. Echocardiographic findings are one of the major criteria in Duke's criteria. The guidelines recommend echocardiography in patients suspected of having IE for detection of vegetations on valves, valvular abnormalities, shunts, abscesses, and assessment of hemodynamics. It should be performed if there is a moderate suspicion of IE (Fig. 48.6). Transthoracic echocardiography (TTE) has a reported sensitivity of approximately 80% in detection of vegetations in pediatric population as compared to adults [10, 11]. TEE is considered a better mode than TTE, where there is poor ultrasound penetrance as in the obese or very muscular adolescent, in post cardiac surgery patients or in presence of respiratory compromise. TEE has been shown to be superior to TTE in detecting vegetations in adult studies but similar studies have not been done in pediatrics [12, 13]. TEE should also be considered in patients with aortic valve involvement or changing aortic dimensions seen in TTE and for perivalvular leakage and valve dehiscence in prosthetic valves.

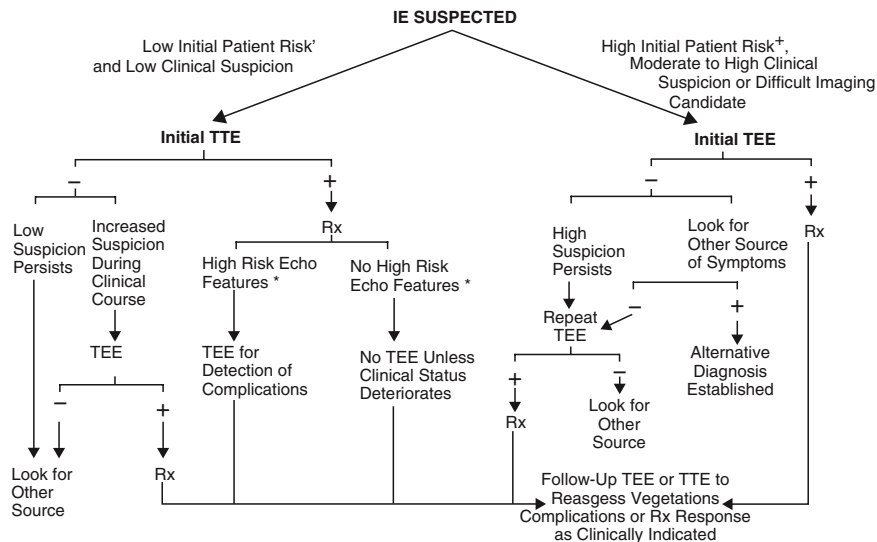


Fig. 48.6 Diagnostic approach to IE by echocardiography

Echocardiography has its limitations. An echogenic mass can represent a sterile thrombus or prosthetic material instead of an infected vegetation. The absence of vegetations on echocardiography does not rule out IE in itself. Both TEE and TTE have low diagnostic yield in patients with a low clinical probability of the disease [14, 15].

48.7 Clinical Complications of IE

Infective endocarditis remains to be one of the most frequent causes of life-threatening infectious illnesses in the United States, ranking fourth [16]. It continues to carry a high rate of mortality despite the advances in diagnosis and treatment with rates quoted of 20–35% [2]. One review of IE in children cites a mortality rate of 11%. The study included children with complex cyanotic heart disease, unrepaired VSDs, normal anatomy, and premature infants with central venous catheters [17].

Factors that affect survival and are of predicted value have been reported in the adult literature and include female gender, diabetes mellitus, *S. aureus* organism, APACHE II score at the time of admission, and the occurrence of embolic events. All of these were found to be independent variables associated with in-hospital deaths [16].

Patients with IE can present in various states of stability. Some require ICU admission and cardiopulmonary support due to severe congestive heart failure or respiratory compromise. In addition to the picture of septic shock, a patient may develop acute valvar insufficiency or heart block with involvement of the conduction system. These patients in septic shock or acute valvar insufficiency will require fluid resuscitation, inotropic therapy, ventilation therapy, and at times mechanical support. Pacemaker therapy is required for those in complete heart block or high grade second degree heart block.

The most common complication in patients with IE is cardiac in nature accounting for at least 30–50% of cases. Heart failure usually from valvular regurgitation is the most common cause of death and the most common cause for surgery. The incidence of perivalvular abscess at surgery or autopsy is reported as 30–40% with aortic valve (41%) being more commonly involved than mitral valve (6%) [15]. Perivalvular abscess affecting the conduction system is often seen in aortic valve endocarditis when involving the area between the right and noncoronary cusps (Fig. 48.7). There is a much higher rate of systemic embolization and fatal outcome in patients with perivalvular abscess. Clinical parameters for the diagnosis of perivalvular extension is difficult but persistent bacteremia or fever, recurrent emboli, heart block, CHF, or a new pathological murmur in patient with IE on appropriate therapy should raise

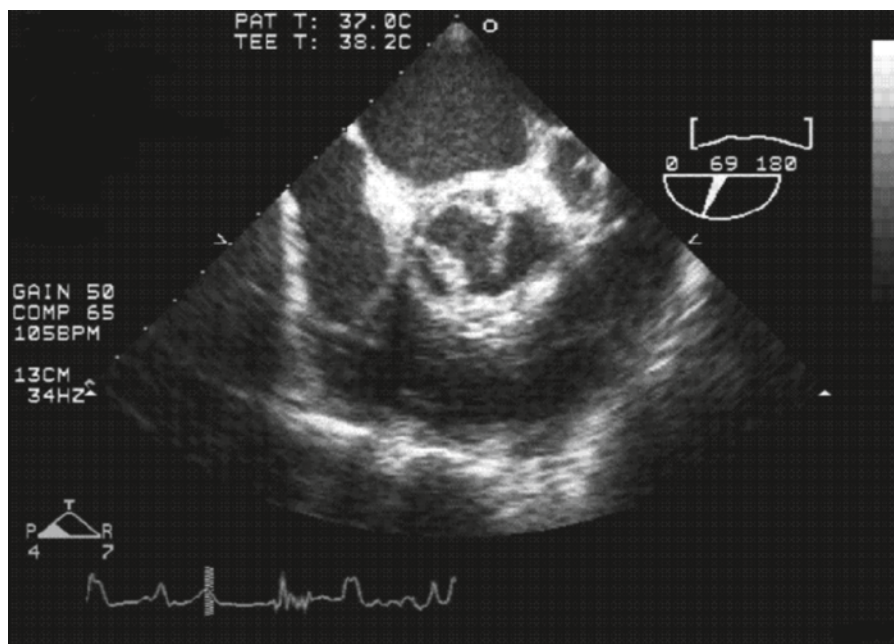


Fig. 48.7 TEE image – mid esophageal short axis view of aortic valve vegetation with perivalvular abscess

the suspicion of extension. New AV block on ECG has a positive predictive value of 88% for abscess formation but low sensitivity of 45% [18]. Pericarditis, fistula formation between aorta and atrium or ventricle, and aortic dissection are other rare cardiac complications.

Neurological complications account for 33% of cases making them the second most common complication of IE. These include stroke, brain abscess, encephalopathy, meningitis, cerebral hemorrhage, and stroke [15, 19]. The presence of neurologic complication does not contraindicate valve replacement with the exception of diffuse encephalopathy that has a higher mortality than focal involvements [20]. Fungal IE has a higher incidence of systemic embolization with the brain and femoral artery being the most common sites.

Other complications include renal infarction from embolization, renal abscess, glomerulonephritis from deposition of immune complexes and antibiotic induced interstitial nephritis. Vertebral osteomyelitis is a rare complication of *S. aureus* endocarditis. Occasionally septic arthritis of two or more joints may occur. Metastatic abscess of liver, kidney, spleen, or brain can also occur. Abdominal CT and MRI have

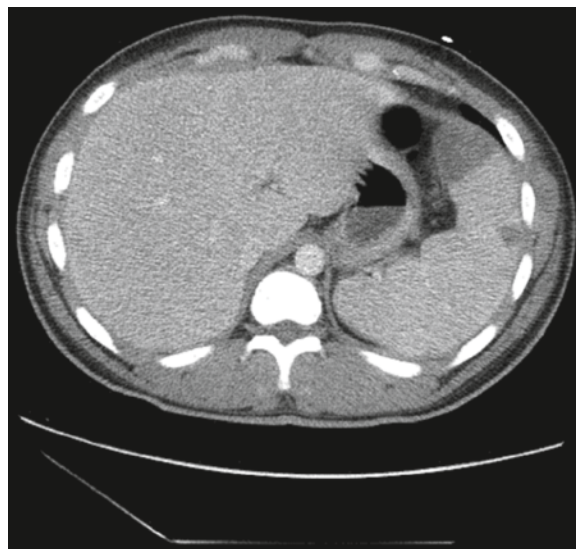


Fig. 48.8 CT abdomen – splenic infarcts

sensitivities of 90–95% in diagnosing splenic abscess (Figs. 48.8 and 48.9). Lung is the most common site of embolization in the case of right-sided lesions (Figs. 48.10 and 48.11).

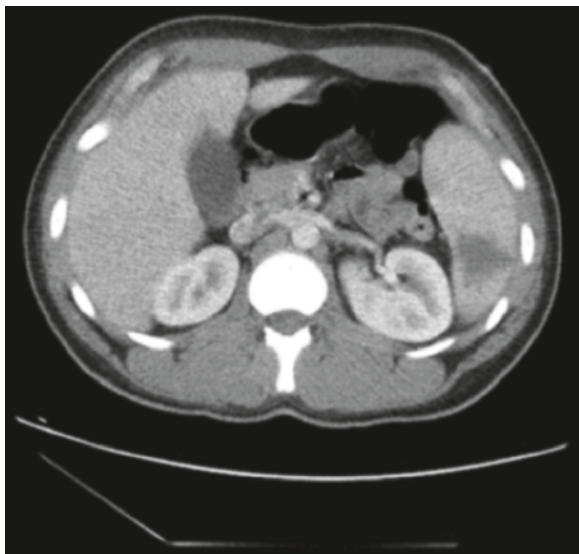


Fig. 48.9 CT abdomen – splenic infarcts

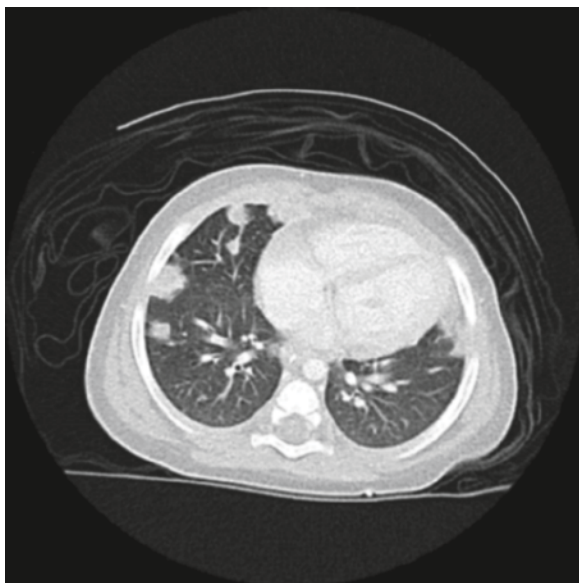


Fig. 48.10 CT thorax without contrast – septic emboli to lungs

48.8 Treatment

The general principles of treatment in pediatric patient are modeled on the treatment of the adult patient. Antimicrobial treatment via the intravenous route is the preferred route of administration because of the desirability to obtain high blood levels of these agents.

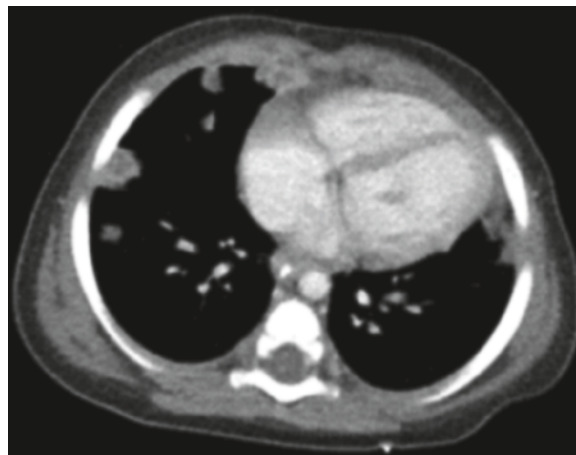


Fig. 48.11 CT thorax with contrast – septic emboli to lungs

Oral administration can have poor and erratic absorption leading to treatment failure and relapse. Bactericidal agents are preferred as there are treatment failures and relapses seen with the use of bacteriostatic agents.

The preferred duration of treatment is 4–6 weeks with the antimicrobial agent tailored to the organism isolated. The AHA statement on IE in 2005 states that *the counting of days for the recommended duration of therapy should begin on the 1 day of the first negative blood culture in cases in which blood cultures were initially positive*. At least two sets of blood cultures are required every 24–48 h of infection until the blood stream is cleared.

Secondly, for patients with native valve endocarditis who undergo valve resection with prosthetic valve replacement, the postoperative treatment regimen should be one that is meant for prosthetic valve instead of native valve endocarditis. Therefore, if the resected tissue is culture positive, an entire course of therapy is recommended after valve replacement. However, if the resected valve is culture negative, the duration of treatment for the prosthetic valve should be less the number of days for the treatment given for native valve infection before the replacement of the valve.

Thirdly, in regimens that require combination antimicrobial therapy, the agents should be administered together or close together for maximum synergistic effect on the infecting pathogen [21].

Documentation of cessation of bacteremia should be obtained early in therapy to measure the adequacy of treatment. If potentially toxic antibiotics such as aminoglycosides are used, then serum peak and trough

levels should be monitored to ensure that levels are not in toxic range. Close follow up is essential. Blood cultures should be obtained occasionally during the first 8 weeks after therapy is stopped as most relapses occur during this period.

The role of cardiac surgery in therapy of IE is determined by the site of infection, the clinical course, and the hemodynamic status of the patient.

48.9 Antimicrobial Therapy

The AHA/infectious diseases task force has given a detailed set of guidelines for the treatment of IE in 2005 [19].

48.9.1 Streptococcal Endocarditis

Patients with highly penicillin-susceptible Viridans group streptococci and *S. bovis* with minimum inhibitory concentrations ($MIC \leq 0.12 \mu\text{g}$) have bacteriologic cure rates of $\geq 98\%$ with 4 weeks of therapy with parental penicillin or ceftriaxone. Ampicillin can be used as an alternative to penicillin. In selected patients, treatment for 2 weeks with either penicillin or ceftriaxone with an aminoglycoside for synergy shows cure rates that are similar in result to monotherapy with penicillin or ceftriaxone for 4 weeks. However, this therapy should be restricted to those patients with uncomplicated IE caused by highly penicillin-susceptible viridans organisms. It is not recommended in patients with extracardiac manifestations or with renal insufficiency (creatinine clearance of $<20 \text{ mL/min}$).

An effective alternative treatment for patients who are allergic or unable to tolerate penicillin or ceftriaxone is intravenous vancomycin. It should be administered $\geq 1 \text{ h}$ to avoid the risk of histamine release “red-man” syndrome.

For relative penicillin resistant strains ($MIC >0.12$ to $\leq 0.15 \mu\text{g}$), combination therapy of penicillin or ceftriaxone for 4 weeks administered with single daily dose of gentamicin for 2 weeks is the preferred treatment regimen.

For more resistant streptococci ($MIC >0.5 \mu\text{g}$), treatment for 4–6 weeks with vancomycin combined with gentamicin is recommended. These patients need to be monitored closely for ototoxicity and renal toxicity.

48.9.2 Staphylococcal Endocarditis

Since only a small percentage of *S. aureus* strains are penicillin-susceptible, the therapy includes penicillinase resistant penicillin (e.g., oxacillin) for 6 week with optional addition of gentamicin for first 3–5 days. Addition of gentamicin fails to improve cure rates but results in more rapid sterilization of blood stream. For penicillin allergic patients, ceftazidime for 6 weeks with optional addition of gentamicin for 3–5 days can be used. Most coagulase negative staphylococci and few *S. aureus* strains are resistant to penicillin and penicillinase-resistance penicillins. Methicillin resistant staphylococci should be treated with vancomycin for 6 weeks.

48.9.3 Gram-Negative Bacterial Endocarditis

The fastidious group of HACEK organisms account for approximately 5–10% of native valve endocarditis in patients who are not IDU's. Since β -lactamase producing strains of HACEK are increasing in frequency, these organisms are considered to be ampicillin resistant and ceftriaxone (or other third or fourth generation cephalosporins) or ampicillin–sulbactam for 6 weeks is recommended.

Fluoroquinolones can be considered as an alternative treatment for patients unable to tolerate β -lactam therapy.

Endocarditis caused by non HACEK Gram-negative organisms is less frequent and therapy must be individualized and guided by in vitro antimicrobial susceptibility testing. Enterobacteriaceae such as *Salmonella*, *E. coli* have an affinity for abnormal cardiac valves, usually on the left side of the heart. Morbidity and mortality is high. Cardiac surgery (valvulotomy or vegetectomy without valve replacement) in combination with a 6 week course of penicillin or cephalosporins with aminoglycosides is recommended. *Pseudomonas endocarditis* is usually seen in IDUs and commonly affects normal valves. Left-sided lesions are often associated with complications such as embolic events, neurological complications, and annular abscesses and carry high morbidity and mortality. Hence, early surgery is preferred in such patients. Right sided lesions are more amenable to medical therapy that includes high dose tobramycin, in combination with

extended spectrum penicillin (ticarcillin, piperacillin) or ceftazidime or cefepime for 6 weeks.

Gonococcal endocarditis can be treated with high dose penicillin if penicillin sensitive or penicillin resistant, with a third generation cephalosporin.

48.9.4 Culture Negative Endocarditis

Blood cultures are negative in up to 20% of patients with IE diagnosed by strict criteria [22]. Appropriate therapy is difficult in patients with culture negative endocarditis as there has to be a fine balance between the need to provide adequate empiric coverage and the need to limit the possible toxic effects of agents such as aminoglycosides. The treatment regimen should take into account epidemiological features and the clinical course of infection. In case of native valves, ampicillin–sulbactam plus gentamicin or vancomycin (in patients not able to tolerate penicillin) for 4–6 weeks is recommended. Ciprofloxacin may be required in certain cases. If presentation is acute, coverage for *S. aureus* is required. If patients have a more subacute presentation, coverage should include for *S. aureus*, viridans group streptococci, enterococci, and HACEK organisms. Patients with prosthetic valve of <1 year duration should have coverage for oxacillin resistant staphylococci (vancomycin for 6 weeks with gentamicin for 2 weeks) and if the onset of infection is within 2 months of prosthetic valve placement, then coverage with Cefepime for Gram-negative bacilli should be included. Rifampin may be added for synergy. If onset of infection is after 1 year of prosthetic valve placement, therapy should cover for oxacillin susceptible staphylococci, viridians group streptococci and enterococci as in case of native valve endocarditis plus rifampin.

There is limited data regarding infections with rare organisms such as suspected Bartonella infection. Ceftriaxone for 6 weeks plus gentamicin for 2 weeks with or without doxycyclin is then considered.

48.9.5 Fungal Endocarditis

This is seen in patients with multiple predisposing conditions such as prosthetic valves and indwelling central venous catheters. Prognosis is poor with evi-

dence of high mortality and morbidity. Treatment with antifungal agents alone is unsuccessful. In recent years therapy has evolved in two phases. The first phase includes control of infection with use of antifungal agents such as amphotericin B in conjunction with surgical replacement of the infected valve with excision of surrounding infected tissue. If the patient survives, the antifungal treatment should be for ≥ 6 weeks. Renal function and potassium levels have to be carefully monitored through the course of treatment.

Due to the high rates of relapse and the prolonged delay in relapse, in patients who respond to initial therapy, long-term (lifelong) suppressive therapy with oral azoles is recommended.

48.9.6 Prosthetic Valve Endocarditis

Antibiotic therapy is tailored as per the infecting organism. The duration of therapy is usually 6 weeks or longer. If the infection is caused by a highly penicillin-susceptible strain of viridans streptococci, treatment is with penicillin or ceftriaxone for 6 weeks with or without gentamicin for 2 weeks. If it is caused by a highly resistant strain (MIC $>0.12 \mu\text{g/mL}$) then a combination of penicillin or ceftriaxone with gentamicin should be used.

Because of high morbidity and mortality rates for *S. aureus* prosthetic valve endocarditis, combination therapy is preferred. Thus, in case of an oxacillin susceptible strain, nafcillin or oxacillin with rifampin is preferred. In oxacillin resistant strains, vancomycin and rifampin is used. Gentamicin should be administered for the initial 2 weeks in either regimen. If the strains are gentamicin resistant, then a fluoroquinolone may be used. Cardiac surgical interventions play an important role in treatment of *S. aureus* prosthetic valve endocarditis.

Studies have shown that prosthetic valve endocarditis caused by CoNS within 1 year of surgery are usually oxacillin resistant and need vancomycin and rifampin for 6 weeks with the use of gentamicin in the first 2 weeks of therapy. Fluoroquinolone may be used if the strain is resistant to aminoglycoside. Usually, CoNS prosthetic valve infections especially those involving aortic valves are frequently complicated by perivalvular abscess or valvular dysfunction and surgery is the life-saving treatment.

Table 48.3 Definition of infective endocarditis according to the proposed modified Duke criteria, with modification shown in boldface

Definite infective endocarditis
Pathologic criteria
1. Microorganisms demonstrated by culture or histologic examination of vegetation, a vegetation that has embolized, or an intracardiac abscess specimen.
2. Pathologic lesions; vegetation or intracardiac abscess confirmed by histologic examination showing active endocarditis
Clinical criteria
1. Two major criteria
2. One major criterion and three minor criteria
3. Five minor criteria
Possible infective endocarditis
1. One major criterion and one minor criterion
2. Three criteria
Rejected
1. Firm alternate diagnosis explaining evidence of infective endocarditis
2. Resolution of infective endocarditis syndrome with antibiotic therapy for ≤ 4 days
3. No pathologic evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for ≤ 4 days
4. Does not meet criteria for possible infective endocarditis (as above)

Treatment of prosthetic valve endocarditis by HACEK organisms and culture negative prosthetic valve endocarditis are covered earlier under their respective treatment options.

48.10 Indications for Surgery

The proportion of patients undergoing surgery has undergone very little change in the past three decades, in spite of improvements in surgical techniques. The identification of patients requiring cardiac surgery and the optimal timing of repairs is a difficult management decision. The ACC/AHA task force published recommendations for surgery in IE patients with native valve endocarditis and prosthetic valve endocarditis in 2006 (Fig. 48.12). Surgery is definitely indicated in patients with life-threatening CHF or cardiogenic shock due to surgically corrected lesions with or without proven endocarditis, if the patient had reasonable prospect of recovery with satisfactory quality of life. However, if the possibility of recovery is remote due to the presence of complications or comorbid conditions, surgery is deferred.

The risks for surgery are higher in patient with PVE than NVE, but the recommendations for surgery are same for both types of endocarditis.

Despite a higher mortality rate in patients with CHF than without CHF, patients with IE and CHF who have undergone valve surgery have a reduced mortality rate than those treated with medical therapy alone which is as high as 51%. The incidence of reinfection of newly implanted valves in patients with IE is around 2–3%. Surgical approach to IE patients with CHF must take into account the distortion of the valve and its surrounding structures.

Surgical interventions should also be considered in patients with fungal IE, infection with aggressive antibiotic resistant organism, left-sided IE caused by Gram-negative bacteria such as *Pseudomonas* species and *S. marcescens*, persistent infection with positive blood cultures 1 week after the initiation of antibiotic therapy or one or more embolic events during the first 2 weeks of treatment.

Other indications of surgical intervention are echocardiographic evidence of valve dehiscence, perforation, rupture or fistula, or a large perivalvular abscess. Anterior mitral leaflet vegetation >10 mm in size, persistent vegetation after systemic embolization and an increase in vegetation size despite appropriate antimicrobial therapy indicate a possible need for surgery.

If a patient with IE is on long-term course of oral anticoagulation, then oral coumadin should be discontinued and patient should be started on heparin therapy immediately after the diagnosis of IE is established in the event that surgical therapy is required.

48.11 Management After Completion of Therapy

Before completing the antimicrobial therapy, patients should receive TTE to serve as a baseline for follow up. They should be educated about the signs of IE with instructions to get evaluated immediately if there is any concern. Thorough dental evaluation should be done and any cause for oral infection should be dealt with. All catheters should be removed after the completion of therapy.

In the immediate short term, relapse is a great concern. Patients should be monitored closely for any sign of relapse, such as new onset of fever, chills or other evidence of systemic toxicity. They should be instructed

to attain immediate evaluation including ≥ 3 sets of blood cultures from different sites. Patients who are more than 1 month from the completion of antimicrobial therapy need a complete examination.

Developing or worsening CHF should also be kept in mind during the initial short term follow up. Such patients should be evaluated for cardiac surgery.

Antibiotic toxicity such as ototoxicity and nephrotoxicity are also of great concern, as these may manifest as delayed toxicity of aminoglycoside use. Diarrhea or colitis from *Clostridium difficile* can occur as late as 4 weeks after the last dose of treatment.

On a long-term basis, patients need ongoing observation, thorough examination and education regarding recurrent infection, and delayed or worsening valvular function. Importance of daily dental hygiene should be stressed and they should get regular evaluations by a dentist.

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Chapter 49

Cardiac Failure

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49.1 Definition

Heart failure is defined as the inability of the heart's output to meet the metabolic demands of the body; or the heart is able to meet these demands only in the setting of an abnormally elevated filling pressure. The clinical appearance of a patient with heart failure can vary from a well compensated state, which can be associated with minimal signs or symptoms, to fulminant cardiogenic shock. Heart failure is often a result of myocardial failure, but may also occur in the presence of near-normal cardiac function under conditions of extremely high demand. Irrespective of etiology, the end result of heart failure is circulatory failure.

49.2 Pathophysiology

Inadequate adaptation of the cardiac myocytes to increased wall stress in order to maintain adequate cardiac output is the inciting event in cardiac failure. The most important adaptations are outlined below:

- Frank–Starling mechanism is the ability of the heart to alter its contractility based on the degree of venous return. In the failing heart, increasing preload can increase stroke volume to maintain cardiac output [1–5].
- Activation of neurohumoral systems including increased activity of the [1] sympathetic nervous

system [6] and [2] renin–angiotensin system along with increased release of [3] vasopressin and [4] natriuretic peptides, act to maintain blood pressure and end-organ perfusion [7–9].

- Myocardial remodeling results in augmentation of contractile tissue (ventricular hypertrophy) [10, 11].

49.2.1 Frank–Starling Mechanism

The Frank–Starling mechanism allows augmentation of cardiac output by the failing myocardium at the expense of elevated end-diastolic volume. As heart failure worsens, elevations in end-diastolic volume are associated with an increase in end-diastolic pressure resulting in pulmonary edema. Circulatory failure as a result of heart failure occurs when further increases in end-diastolic volume no longer result in increased ventricular performance and end-organ perfusion is inadequate.

49.2.2 Neurohumoral Activation

49.2.2.1 Sympathetic Nervous System

Activation of the sympathetic nervous system results in increased release and decreased uptake of norepinephrine (NE) and to a lesser degree epinephrine results in vasoconstriction, so arterial pressure is maintained and end-organ perfusion is preserved. This sympathetic stimulation also increases afterload and myocardial cytosolic calcium entry [6]. The increased calcium entry into the myocytes augments myocardial contractility (inotropy) while impairing myocardial relaxation (lusitropy).

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The combination of an increase in afterload and inotropy and impairment of myocardial lusitropy leads to an increase in myocardial energy expenditure and oxygen demand. Additionally, elevations in plasma norepinephrine are responsible for downregulation of β_1 -adrenergic receptors [12]. In children with a left-to-right shunt, the increase in afterload (systemic vascular resistance) worsens the left-to-right shunt, leading to an increase in the pulmonary to systemic flow ratio ($Q_p:Q_s$) and worsening symptoms of pulmonary overcirculation.

49.2.2.2 Renin–Angiotensin System

The activation of the renin–angiotensin–aldosterone system (RAAS) leads to increased circulating levels of renin, angiotensin II, and aldosterone. Release of these RAAS mediators occurs secondary to decreased perfusion and sympathetic stimulation of the kidney. Renin is responsible for cleaving angiotensinogen to form angiotensin I, which is converted into angiotensin II with the action of angiotensin-converting enzyme (ACE). Angiotensin II is a potent vasoconstrictor, which enhances NE release and is associated with myocyte hypertrophy and cell death [13]. Aldosterone causes salt and water retention, resulting in increased preload, which further increases in myocardial energy expenditure and peripheral edema [7–9].

49.2.2.3 Vasopressin

Vasopressin is a pituitary hormone that is essential for the maintenance of normal plasma osmolality. Vasopressin levels are increased in heart failure and probably contribute to poor free water clearance (V_2 receptors) and systemic vasoconstriction via the V_1 receptors [14].

49.2.2.4 Natriuretic Peptides

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are released in response to changes in atrial and ventricular wall tension, respectively, as a result of volume/pressure expansion. Both peptides promote vasodilation and natriuresis, owing to reductions in cardiac preload and afterload. BNP produces afferent arteriolar vasodilation and inhibits sodium

reabsorption in the proximal convoluted tubule. BNP also inhibits renin and aldosterone release, is an important diagnostic tool, and has therapeutic implications discussed later in this chapter [15–17].

49.2.3 Myocardial Remodeling

Chronic neurohumoral activation eventually leads to increased myocardial volume and mass. This myocardial remodeling process is responsible for early adaptive mechanisms such as augmentation of stroke volume (Starling mechanism) and decreased wall stress (Laplace mechanism). However, persistent activation of neurohumoral systems is eventually harmful as maladaptive mechanisms such as increased myocardial oxygen demand, myocardial ischemia, impaired contractility, and arrhythmogenesis result. At the cellular level, chronic stimulation of the sympathetic nervous system results in myocyte hypertrophy, myocyte cell death, and eventually cardiac norepinephrine depletion [18]. For these reasons the neurohumoral system is an important target of therapy resulting in improved long-term heart failure outcomes.

49.3 Etiology

The causes of cardiac failure in the intensive care unit are varied, but are best classified by the time course of onset (acute or chronic) and mechanism of failure – systolic, diastolic, or a combination (Table 49.1).

49.3.1 Acute Heart Failure

One of the most common causes of acute cardiac failure in the pediatric population is myocarditis. Myocarditis is usually viral in origin and patients with fulminant myocarditis present in shock with rapid onset of hemodynamic deterioration. Endocarditis, rheumatic heart disease, and rarely trauma can result in severe valve injury which can present acutely in the intensive care unit.

Table 49.1 Causes of cardiac failure in pediatrics

	Systolic heart failure		Diastolic heart failure
Arrhythmias	Intrinsic heart disease	High output failure	
Supraventricular tachycardia	Myocarditis (infectious, autoimmune)	Anemia	Infiltrative cardiomyopathy (amyloidosis, hemochromatosis, eosinophilic cardiomyopathy)
Bradycardia (complete heart block)	Ischemic heart disease (ALCAPA, Kawasaki's, transplant vasculopathy)	Thyrotoxicosis	Hypertrophic cardiomyopathy
Ventricular tachycardia (arrhythmogenic right ventricular dysplasia – ARVD)	Rheumatic heart disease	Arteriovenous malformations	Restrictive cardiomyopathy
	Valvular heart disease (endocarditis)	Sepsis	Systemic hypertension?
	Toxin-induced (anthracyclines, carbon monoxide)		Heart transplant rejection
	Dilated cardiomyopathy (idiopathic, metabolic, post-infectious, genetic)		Sarcoidosis
	Congenital heart disease (right- or left-sided obstruction, chronic valvar insufficiency)		Endomyocardial fibrosis
	Myocardial noncompaction		
	Heart transplant rejection		

49.3.2 Chronic

Patients with chronic heart failure can decompensate and present with signs and symptoms requiring intensive care management. Although it is not always possible to determine the cause, decompensated heart failure can be preceded by an acute infection, noncompliance with medical therapy, or onset of arrhythmias.

49.3.3 Systolic Heart Failure

Most forms of cardiac failure consist of a combination of systolic and diastolic failure. Systolic heart failure is defined by inadequate ventricular inotropy to meet the body's physiologic needs. Systolic heart failure occurs in the setting of myocarditis, dilated cardiomyopathy, ischemia (congenital coronary artery anomalies, Kawasaki's disease, post-transplant coronary vasculopathy, coronary injury after cardiac surgery), excessive pressure (left-sided obstructive lesions) or volume overload (long-standing valve insufficiency, intracardiac shunts). Inadequate perfusion of vital end organs results in presenting signs and symptoms such as mental status changes, poor end-organ function (kidney and liver), and vomiting or feeding intolerance.

49.3.4 Diastolic Heart Failure

Diastolic heart failure is defined by inadequate lusitropy, or abnormalities of ventricular relaxation. Isolated diastolic heart failure is rare and as mentioned above usually occurs in combination with systolic heart failure. Restrictive and hypertrophic cardiomyopathies are common causes of diastolic heart failure while systolic function is initially preserved. Presentation of diastolic heart failure is related to the extent of elevation in atrial pressure as a result of ventricular stiffness. Elevated right atrial pressure results in jugular venous distention, hepatic congestion, and lower extremity edema. Elevated left atrial pressure is associated with pulmonary edema and orthopnea; exercise intolerance and dyspnea are common. Diastolic heart failure should not be confused with other causes of impaired ventricular filling such as constrictive or restrictive pericarditis, large pericardial effusions, mitral or tricuspid stenosis, or obstruction of systemic or pulmonary venous return. Despite their similar presentation to true diastolic heart failure, ventricular relaxation is usually normal in these settings.

49.4 Staging

The New York Heart Association (NYHA) classification is based on the relation between symptoms

Table 49.2 The New York Heart Association (NYHA) classification of cardiac failure

NYHA classification:	
Class I	No limitations. Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitations
Class II	Slight limitation of physical activity, comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnea
Class III	Marked limitation of physical activity. Although comfortable at rest, less than ordinary activity leads to fatigue, dyspnea, palpitations
Class IV	Symptomatic at rest. Discomfort increases with any physical activity

and the amount of effort required to provoke them (Table 49.2).

Because of the inability to use this classification in small children, R.D. Ross has proposed to grade the severity of heart failure in infants based on feeding, respiratory pattern, and clinical parameters [19]:

- Congestive heart failure (CHF) is present with a history of less than 105 ml/feed, respiratory rate greater than 50/min, an abnormal respiratory pattern, diastolic filling sounds, and hepatomegaly.
- Moderate to severe CHF is present when patients take less than 90 ml/feed or greater than 40 min/feed, have an abnormal respiratory pattern with a resting respiratory rate greater than 60/min, and have a diastolic filling sound and moderate hepatomegaly.
- Severe CHF is accompanied by a heart rate greater than 170/min, decreased perfusion, and severe hepatomegaly.

49.5 Clinical Features

In the infant, clinical history can reveal failure to thrive, poor feeding associated with diaphoresis, vomiting, increased work of breathing and irritability. The older child can present with dyspnea, orthopnea, paroxysmal nocturnal dyspnea, poor appetite and growth, fatigue or weakness.

Although some of the physical signs of heart failure described in this section can be seen in the compensated patient, the focus here will be on the expected features of a patient with decompensated or severe acute heart failure as would be seen in the ICU setting.

- General appearance
 - Central cyanosis.
 - Diminished pulse pressure, dusky discoloration of the skin with delayed capillary refill time due to poor peripheral perfusion.
- Reduced systolic arterial pressure, weak, rapid, and thready pulse.
 - Evidence of increased adrenergic activity manifested by tachycardia, diaphoresis, pallor, peripheral cyanosis with pallor, and coldness of the extremities.
- Tachycardia or arrhythmia.
- Tachypnea, increased work of breathing.
- Pulmonary rales over the lung bases, frequently accompanied by wheezing, especially in the infant.
- Pleural effusion, usually bilateral, and/or ascites.
- Jugular venous distention and peripheral edema, due to systemic venous hypertension – may be difficult to appreciate or absent in infants.
- Hepatojugular reflux, found in older children with right-sided heart failure.
- Hepatomegaly, most reliable sign of cardiac failure in the infant.
- Gallop rhythm, with a protodiastolic (S_3) and/or telediastolic (S_4) gallop, one of the earliest cardiac physical finding in decompensated heart failure.
- Accentuated second heart sound if associated with pulmonary hypertension.
- Cardiomegaly with a displaced apical impulse.
- Systolic murmurs
 - Mitral and tricuspid regurgitation murmurs are often present in patients with decompensated heart failure because of ventricular dilatation.
- Failure to thrive and cachexia
 - Related to increased total metabolism secondary to augmentation of myocardial oxygen consumption and excessive work of breathing.

49.6 Laboratory Studies

- Complete blood count
 - Useful to assess anemia, which may cause or aggravate heart failure. Leukocytosis may result from stress or signal an underlying infection.
- Electrolytes
 - Hyponatremia reflects an expansion of extracellular fluid volume in the setting of a normal total body sodium.

Table 49.3 Viral etiologies of myocarditis

Viral etiologies of myocarditis:

Coxsackie virus	Respiratory syncytial virus	Cytomegalovirus	Herpes virus (herpes simplex and human herpes virus 6)
Adenovirus	Mumps	Echovirus	HIV
Parvovirus B19	Rubella	Epstein–Barr virus	Parainfluenza
Influenza A virus	Varicella	Hepatitis C virus	Measles

- Hypokalemia and hypochloremia can be the result of prolonged administration of diuretics.
- Hyperkalemia can be the result of impaired renal perfusion and marked reductions in glomerular filtration rate (GFR) or from intracellular potassium release due to impaired tissue perfusion.
- Renal function tests
 - Elevated BUN and BUN/creatinine ratios are seen in decompensated heart failure.
- Liver function tests
 - Congestive hepatomegaly is often associated with impaired hepatic function, which is characterized by elevation of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactic dehydrogenase (LDH), and other liver enzymes.
 - Hyperbilirubinemia (both direct and indirect) is related to acute hepatic venous congestion and is common with severe right heart failure. Elevated alkaline phosphatase, and prolongation of the prothrombin time can be seen. In children with long-standing heart failure and poor nutritional status, hypoalbuminemia results from hepatic synthesis impairment.
- B-type natriuretic peptide
 - BNP is a natriuretic peptide released in response to ventricular volume expansion and pressure overload. In normal individuals, BNP levels are elevated immediately after birth, but fall to adult levels by 3 months of age [20]. In the setting of heart failure, BNP levels correlate closely with the NYHA Classification of Heart Failure and with ventricular filling pressures [21–24]. BNP levels of more than 80 pg/ml have a good specificity and sensitivity in diagnosing heart failure [17].
- *CPK-MB, troponin I and T* can be useful if the clinical scenario is suggestive of an ischemic process.
- Lactate
 - Elevated lactate is seen in patients with decompensated heart failure as a result of decreased tissue perfusion and/or decreased metabolism due to secondary liver dysfunction and can be a useful serologic marker for monitoring response to therapeutic interventions. Abrupt elevations on lactate levels may occur early in the process of decompensation and should motivate caregivers to aggressively treat patients, trying to reverse or to compensate the acute changes leading to the cardiac failure.
- Infectious serologies
 - Viral infections (Table 49.3) are the most common cause of infectious myocarditis, but bacterial, rickettsial (e.g., Q fever), fungal, spirochetal (e.g., Lyme disease), and protozoal (e.g., Chagas, malaria) infections are other possibilities.
- Metabolic work-up
 - Metabolic evaluation of a patient presenting to the intensive care unit with cardiac failure should be dictated based on patient age, history, and clinical suspicion.
 - Total carnitine level and an acylcarnitine profile can demonstrate carnitine transporter defects.
 - Urine organic and amino acids. Specifically, quantitative 3-methylglutaconic aciduria should be obtained in boys with clinical suspicion for Barth syndrome. This X-linked disorder is associated with dilated cardiomyopathy, failure to thrive, neutropenia, and muscle weakness.
 - Thiamine deficiency is a rare problem in developed countries, but when found usually occurs in association with lactic acidosis and anemia.
- Inflammatory markers
 - C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and TNF- α are nonspecific, but can be supportive evidence of an acute inflammatory process and indicative of ongoing cardiac injury.
 - The presence of autoantibodies (e.g., antimyosin) is a negative Prognostic finding [25].
 - Endocrine work-up
 - Thyroid function tests – both profound hyper or hypothyroidism can cause heart failure.
- Arterial blood gas

- ABGs usually reveal mild hypoxemia in patients who have mild-to-moderate heart failure. Severe heart failure often leads to severe hypoxemia, or even hypoxia. Hypocapnia occurs in the early stages of pulmonary edema because of ventilation/perfusion (V/Q) mismatch, progressing to hypercapnia and respiratory acidosis, related to decreased vital capacity and poor ventilation.

49.7 Diagnostic Studies and Imaging

49.7.1 Chest Radiography

- Cardiomegaly and alveolar edema with pleural effusions and bilateral infiltrates in a butterfly pattern are the classic findings on chest radiography in the setting of heart failure (Fig. 49.1).
- Other signs are haziness of hilar shadows, vascular redistribution and thickening of interlobular septa (Kerley B lines).

49.7.2 Electrocardiogram (ECG)

- Sinus tachycardia is a common and nearly universal finding in acute and decompensated heart failure.



Fig. 49.1 Chest X-Ray in cardiac failure: cardiomegaly with increased vascular markings suggestive of pulmonary oedema

Heart rhythm can be abnormal secondary to cardiac dysfunction or electrolyte abnormalities. However, because an underlying primary arrhythmia (e.g., supraventricular tachycardia) may be the cause of heart failure, the heart rhythm at the time of presentations should be closely scrutinized.

- Conduction abnormalities
 - Heart block can occur as a result of the inciting event (e.g., in association with infectious myocarditis) or in association with medical therapies (e.g., digoxin, verapamil – 1° or higher levels of heart block; amiodarone – prolonged QTc).
 - Congenital complete heart block is associated with eventual development of dilated cardiomyopathy and heart failure. The reported incidence of heart failure in this patient population has been variable, and ranges from 6 to 23% [26–28].
- Prolonged QTc and abnormal QT dispersion are commonly associated with cardiomyopathies due to repolarization abnormalities and both have been noted to be markers for poor outcome [29, 30].
- Chamber enlargement/hypertrophy
 - Left atrial enlargement and LV hypertrophy is sensitive for chronic LV dysfunction. In the setting of acute LV dysfunction, with the exception of sinus tachycardia, the ECG may be normal.
 - In acute myocarditis, the classic ECG findings are low QRS voltages with T wave flattening or inversion.
- Prominent Q waves and ST segment abnormalities suggest myocardial ischemia (e.g., anomalous coronary artery, Fig. 49.2).

49.7.3 Echocardiography

Transthoracic echocardiography can thoroughly assess both systolic and diastolic ventricular function. The presence and extent of valvular heart disease, structural congenital heart disease, LV wall thickness, chamber sizes, pericardial disease, regional wall motion abnormalities, proximal coronary artery distribution and size can all be accurately determined in most children with echocardiography (Fig. 49.3). Shortening fraction (SF) by m-mode and ejection fraction (EF) by M-mode or Simpson's biplane can be obtained (Fig. 49.4). Mitral inflow Doppler, pulmonary venous Doppler, and tissue

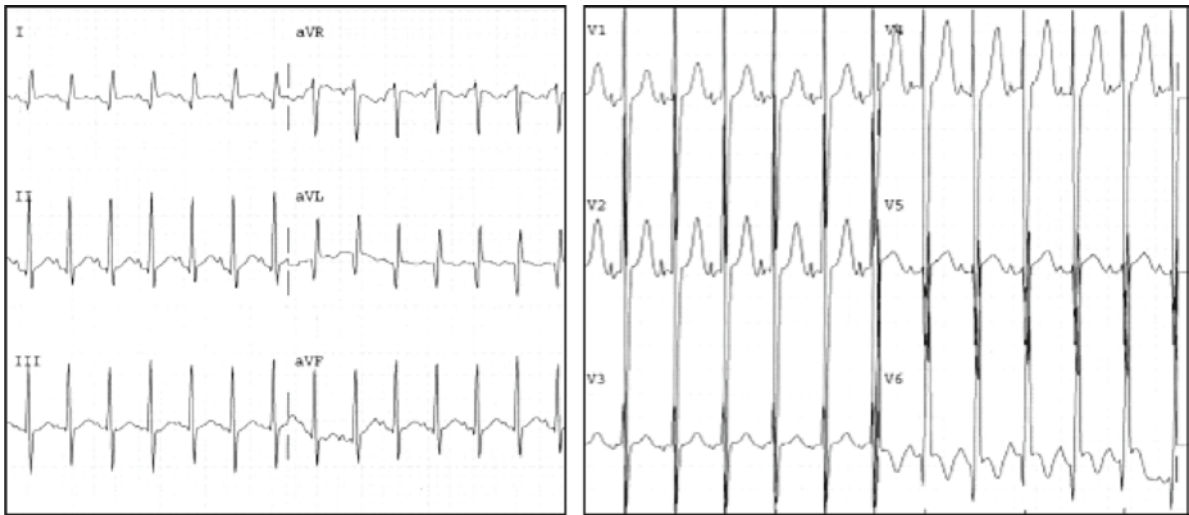


Fig. 49.2 Typical electrocardiogram in anomalous left coronary artery arising from the pulmonary artery (ALCAPA) syndrome: Q waves in I and aVL with prominent Q waves in V6

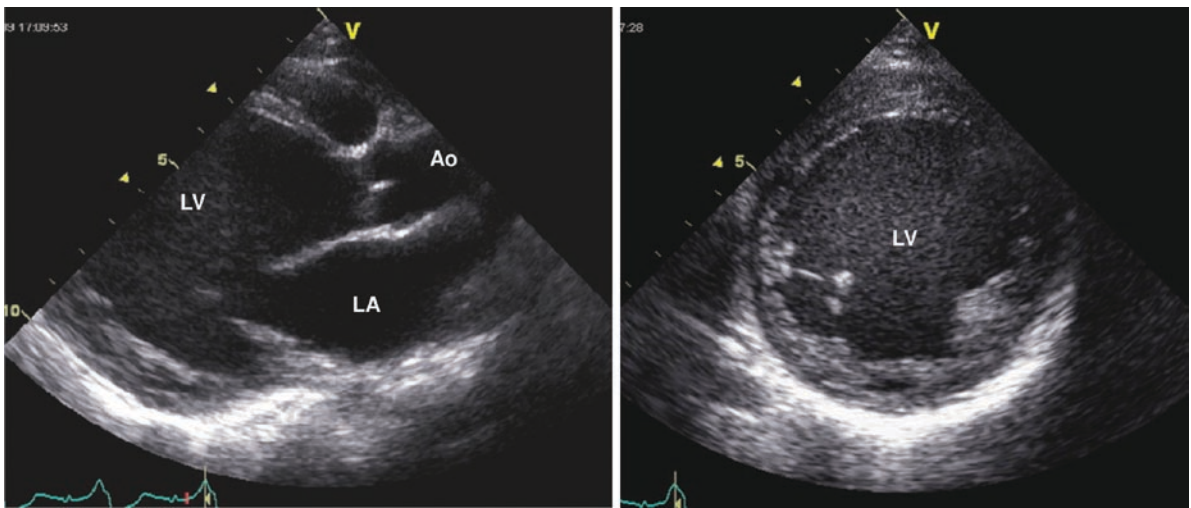


Fig. 49.3 Echocardiogram: Parasternal long-axis and short-axis view in a patient with dilated cardiomyopathy showing a very dilated and globular left ventricle

Doppler techniques can be used to assess left ventricular diastolic function.

Transesophageal echocardiography (TEE) is seldom necessary in pediatric patients as good quality conventional transthoracic echocardiography is usually obtained. TEE imaging can be helpful when endocarditis is suspected, especially when there is concern about aortic root involvement.

49.7.4 Cardiac Catheterization

Cardiac catheterization is often a necessary adjunct in the diagnostic approach to a patient with heart failure. Direct hemodynamic data in combination with angiograms clarifying structural anatomy can be essential in diagnosing and in some cases treating structural causes of heart failure. Despite advances in imaging

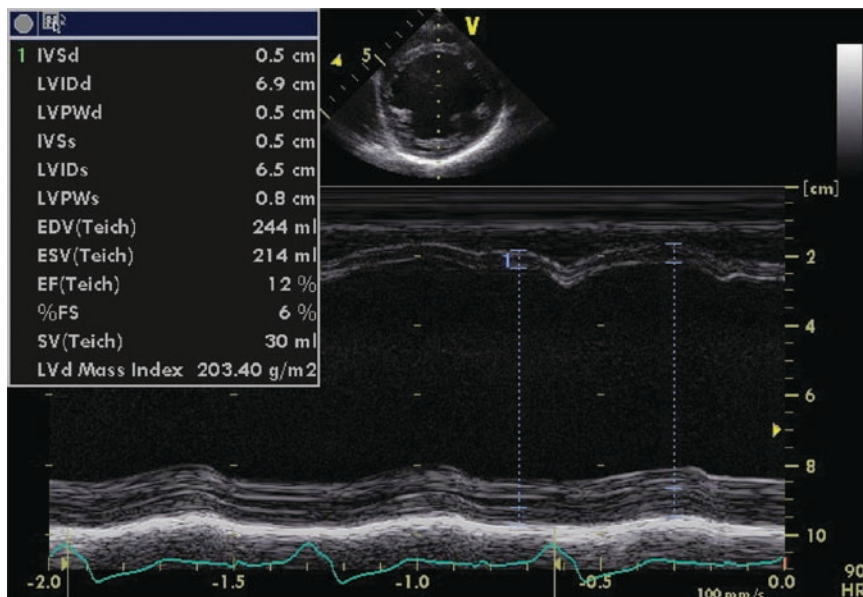


Fig. 49.4 M-mode echocardiography in a patient with dilated cardiomyopathy demonstrating severely depressed left ventricular systolic function (decreased SF and EF)

technology, anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) remains an elusive diagnosis by echocardiography in some situations and can be definitively identified in the catheterization laboratory.

In idiopathic causes of cardiomyopathy a myocardial biopsy can result in a definitive diagnosis. Viral myocarditis, metabolic storage diseases, infiltrative cardiomyopathies, and mitochondrial disorders among others can be diagnosed by biopsy. However, unfortunately nonspecific findings such as myocyte hypertrophy, abnormal nuclei and fibrosis are common [31]. Endomyocardial biopsies are not without risk. Injury to the tricuspid valve, heart block, arrhythmias, cardiac perforation and death although rare, can occur.

49.7.5 Cardiac Magnetic Resonance Imaging (MRI)

Although not often necessary in the evaluation of heart failure, cardiac MRI can be a useful noninvasive adjunct in select cases. Myocardial function including wall motion abnormalities as well as myocardial perfusion and viability can be determined with MRI [32, 33]. Identification of myocardial noncompaction,

arrhythmogenic right ventricular dysplasia, and constrictive pericarditis can be difficult diagnoses to make with echocardiography, but can be well-defined by MRI.

49.8 Monitoring

Of course the care of all critically ill patients starts with stabilization of the airway and circulation. Once these goals are obtained further management of the heart failure patient is optimized with the use of invasive hemodynamic monitoring devices.

- Central venous pressure monitoring is necessary to accurately assess fluid status and to evaluate for alterations in the degree of restrictive physiology present. Patients in decompensated heart failure are highly dependent on adequate preload to maintain cardiac output. However, excessive fluid is counterproductive at some point and induction of diuresis may become necessary.
- Swan Ganz catheters allow measurement of right atrial pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, and mixed venous oxygen saturation. Use of these catheters is often

not realistic in young infants, but transducing any central venous line that could be used to trend the filling pressure of the right heart.

- Arterial pressure monitoring is necessary in patients with marked hemodynamic deterioration requiring intravenous support. Continuous arterial pressure readings allow titration of therapy to ensure adequate end-organ perfusion pressure.
- All patients with heart failure should be on constant telemetry in the intensive care unit. Heart rhythm abnormalities and alterations in heart rate must be rapidly assessed and treated.
- In patients who are critically ill and sedated, a Foley catheter can serve as a necessary means of obtaining precise measurements of urine output as a surrogate for renal perfusion.

- Near infrared spectrometry (NIRS) is an emerging technology that may be a useful noninvasive tool for assessing tissue oxygenation and perfusion in the intensive care unit. A study of abdominal site NIRS readings in infants and children requiring an intervention for congenital heart disease demonstrated good correlation with serum lactate and systemic mixed venous saturation [34].

49.9 Medical Treatment

Medical therapy of heart failure (Table 49.4) focuses on three main goals:

Table 49.4 Medical therapy for cardiac failure

Medication	Dosage (iv)	Dosage (po)
Amrinone	Loading 1–4 mg/kg (optional) then 3–15 mcg/kg/min	
Atenolol		1–2 mg/kg q 12–24 h
Captopril		Initial 0.05 mg/kg, then 0.1–2 mg/kg q 8 h
Carvedilol		0.08–0.7 mg/kg q day 12–24 h
Chlorothiazide	5–10 mg/kg q 12 h	10–20 mg/kg q 12 h
Digoxin		Age dependent dosage: Loading 8–20 µg/kg, then 5–10 µg/kg q day
Dobutamine	5–20 µg/kg/min	
Dopamine	Dopa 3–5 µg/kg/min, beta-1 5–15 µg/kg/min, alpha 15–20 µg/kg/min	
Enalapril		Initial 0.05 mg/kg, then 0.1–0.5 mg/kg q 12 h
Epinephrine	0.01–1 µg/kg/min	
Esmolol	Loading 100–500 µg/kg, then 50–300 µg/kg/min	
Furosemide	0.05–0.4 mg/kg/h, 1–2 mg/kg q 6–24 h	1–2 mg/kg q 6–24 h
Hydrochlorothiazide		1–2 mg/kg q 12–24 h
Labetalol	0.25–4 mg/kg/h, 0.2–1 mg/kg q 6–12 h	1–2 mg/kg q 6–12 h
Levosimendan	Loading 12 µg/kg over 1 h, then 0.1–0.2 µg/kg/min for 24–48 h	
Lisinopril		0.1–0.4 mg/kg q day
Losartan		0.5–1.5 mg/kg q day
Metoprolol	0.1 mg/kg then 1–5 mcg/kg/min	0.1–2 mg/kg q day
Milrinone	Loading 50 µg/kg (optional), then 0.25–0.75 µg/kg/min	
Morphine	0.05–0.4 mg/kg/h, ventilated up to 1.2 mg/kg/h, 0.1–0.2 mg/kg q 1 h	
Nesiritide	Loading 1 µg/kg, then 0.005–0.02 µg/kg/min	
Nitroglycerin	0.5–10 µg/kg/min	
Nitroprusside	0.3–12 µg/kg/min	
Norepinephrine	0.05–0.5 µg/kg/min	
Phenoxybenzamine	Loading 1 mg/kg, then 0.5 mg/kg q 8–12 h	0.2–0.5 mg/kg q 8–12 h
Phenylephrine	Loading 5–10 mcg/kg, then 1–5 mcg/kg/min	
Propranolol		Initial 0.5 mg/kg, then 1–4 mg/kg q 8 h
Spirinolactone		1–3 mg/kg q 12–24 h

1. Preload reduction results in decreased pulmonary capillary hydrostatic pressure and reduction of fluid transudation into the pulmonary interstitium and alveoli.
2. Afterload reduction obtained by decreasing systemic vascular resistance results in increased cardiac output and improved end-organ perfusion.
3. Inhibition of both RAAS and vasoconstrictor neurohumoral factors results in vasodilation, thereby increasing cardiac output and reducing myocardial oxygen demand.

49.9.1 Diuretics

- Loop diuretics
 - Diuretic therapy is the cornerstone of heart failure treatment.
 - Loop diuretics inhibit the $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ cotransport system in the loop of Henle. The result is increased excretion of sodium, potassium, chloride, hydrogen, and water. Loop diuretics reduce preload through diuresis and by increasing venous capacitance.
 - Furosemide is the most commonly used, but bumetanide has a higher bioavailability and may be more effective [35].
 - In patients with diastolic heart failure or restrictive physiology who are minimally fluid overloaded, aggressive diuretic use may be associated with hypotension and adverse outcomes, so careful titration based on cardiac output and central venous monitoring is essential.
- Thiazides
 - Thiazides inhibit the Na^+/Cl^- cotransporter in the distal convoluted tubule resulting in increased sodium and chloride excretion.
 - Hydrochlorothiazide, chlorothiazide, and metolazone are particularly useful in combination with loop diuretics in patients suffering from heart failure.
- Potassium sparing diuretics
 - The mechanism of action of spironolactone is to block aldosterone effect in the distal tubule and collecting duct. The association of a loop diuretic and spironolactone is useful to maintain serum potassium levels and avoid the need for potassium supplements.
- The RALES (Randomized Aldactone Evaluation Study) trial in adults demonstrated improved NYHA class and decreased mortality and hospitalization rate in patients with advanced heart failure treated with spironolactone [36]. Whether these findings would translate to the pediatric population is unknown.

49.9.2 Vasodilators

- ACE inhibitors
 - ACE inhibitors block the adverse effects resulting from the chronic activation of the renin-angiotensin system that occurs in heart failure. Prevention of the formation of angiotensin II and its subsequent vasoconstrictive effects and promotion of vasodilation via bradykinin results in reduced afterload and preload, improved stroke volume and cardiac output.
 - Left ventricular remodeling is diminished by ACE inhibitor therapy. Prevention of the formation of angiotensin II results in limitation of myocyte hypertrophy, fibrosis, and myocyte apoptosis that would otherwise occur [37].
 - Captopril rather than enalapril is preferred in neonates because of the delayed capacity of neonates to biotransform enalapril to enalaprilat [38].
 - Studies consistently demonstrate that ACE inhibitors prolong survival and reduce morbidity in heart failure [39–41].
 - In children with a left-to-right shunt, ACE inhibitors reduce the $Q_p:Q_s$ by decreasing systemic vascular resistance, but is less effective in those with elevated pulmonary pressures [42, 43]. ACE inhibitors have also been demonstrated to be efficacious for valvular regurgitation in children [44].
- Angiotensin receptor blockers (ARBs)
 - ARBs inhibit angiotensin II and are especially useful in patients with heart failure who are otherwise intolerant to ACE inhibitors [44]. Few data are available in children so far.
- Sodium Nitroprusside
 - Results in simultaneous preload and afterload reduction with a greater effect on afterload reduction through direct smooth muscle relaxation.
 - Potency and rapidity of onset make it an ideal medication in critical situations and dose should be

titrated based on reduction in filling pressures and improvement in symptoms. Because it may induce precipitous falls in blood pressure, intraarterial blood pressure monitoring is often recommended.

- Byproducts of nitroprusside include nitric oxide and cyanide. Prolonged use and use in those with hepatic dysfunction should be avoided due to increased risk of thiocyanate toxicity.
- Nitroglycerin
 - Intravenous nitroglycerin provides rapid and titratable preload reduction by increasing venous capacitance. Its arterial vasodilatory effects result in afterload reduction as well. It is widely used in the adult population for patients with ischemic heart disease given its coronary vasodilatory properties, and more sporadically used in pediatrics.
 - Nitroglycerin may be useful in children who have had coronary reimplantation as a result of the arterial switch operation or ALCAPA repair, as it provides afterload reduction while decreasing myocardial oxygen consumption and providing coronary vasodilation and decreasing transmural tension. Nitroglycerin may reverse the coronary vasoconstrictive effects of endothelin-1 post-bypass in children undergoing cardiac surgery [46].
- α -adrenergic blockers
 - Phenoxybenzamine, phentolamine, and nicergoline are potent vasodilators that have been used for the treatment of severe left ventricular failure. Although not widely used for heart failure, these drugs decrease peripheral vascular resistance, resulting in an increase in cardiac output and stroke volume.
 - Combined use of phenoxybenzamine and dopamine has been shown to be beneficial in children with low cardiac output syndrome who are difficult to wean from cardiopulmonary bypass, by preventing the α -adrenergic action of dopamine and encouraging its β -adrenergic action [47].

49.9.3 Intravenous Inotropes

Inotropic support must be used judiciously and with caution in the setting of patients with heart failure. Although increased inotropy results in improved cardiac output and blood pressure, it comes at the expense of increased myocardial oxygen consumption and demand. The failing myocardium has a limited

reserve and complete hemodynamic collapse can occur as a result of high-dose inotropic support in this setting. For this reason, early and elective use of mechanical circulatory support should be considered in all patients with severe myocardial dysfunction that is refractory to medical therapy including low-dose inotropic support. Mechanical support is covered in detail elsewhere and will not be discussed in this chapter.

- Dopamine
 - Effects are dose-dependent. As with other inotropic agents, moderate and high dosages are arrhythmogenic and may be counterproductive as a result of increased myocardial oxygen demand.
 - Low dosages (0.5–3 $\mu\text{g}/\text{kg}/\text{min}$) cause stimulation of dopaminergic receptors within the renal and splanchnic vascular beds, causing vasodilation and increased diuresis.
 - Moderate dosages (3–10 $\mu\text{g}/\text{kg}/\text{min}$) cause stimulation of β -receptors in the myocardium, resulting in increased cardiac contractility (inotropy), blood pressure, and heart rate.
 - High dosages (10–20 $\mu\text{g}/\text{kg}/\text{min}$) cause stimulation of α -receptors, resulting in peripheral and pulmonary vasoconstriction and therefore increased SVR and PVR.
- Dobutamine
 - A β_1 -receptor agonist, with some β_2 -receptor and minimal α -receptor activity.
 - Intravenous dobutamine induces significant positive inotropic effects with mild chronotropic effects. It also induces mild peripheral vasodilation, decreasing SVR and PVR.
 - The combined effect of increased inotropy with decreased afterload results in a significant increase in cardiac output.
- Epinephrine
 - A β_1 -, β_2 -, and α -receptor agonist that primarily exerts β effects at low doses (0.01–0.02 $\mu\text{g}/\text{kg}/\text{min}$) with α and β effects at higher doses. Vasodilation via β_2 -receptor effect is seen in low doses, while at higher doses, positive inotropic effects, tachycardia, and mild increased blood pressure secondary to vasoconstriction result.
- Norepinephrine
 - An α - and β_1 -receptor agonist, resulting in vasoconstriction and significant increases in afterload with subsequent increase in myocardial oxygen demand and reduced cardiac output.

- Isoproterenol
 - β_1 - and β_2 -receptor agonist, induces increased inotropy and increased heart rate, but is potentially arrhythmogenic.

49.9.4 Phosphodiesterase Inhibitors (PDEIs)

- Milrinone and amrinone
 - PDEIs increase intracellular cyclic AMP (cAMP) by inhibiting phosphodiesterase III. Increased cAMP results in kinase activation and phosphorylation of phospholamban resulting in improved calcium metabolism by the sarcoplasmic reticulum.
 - The hemodynamic results of increased cAMP are positive inotropic effect, peripheral vasodilation (activation of protein kinase G), and improved myocardial relaxation (lusitropy). PDEIs do not cause tachycardia and therefore myocardial oxygen demand is not increased as with other inotropic agents. However, ventricular arrhythmias remain a side effect.
 - Milrinone has been demonstrated to be useful in children with low cardiac output syndrome following cardiac surgery [48, 49].
 - As PDEIs are not dependent on adrenoreceptor activity, they are less likely to induce tolerance. Alternatively, tolerance to catecholamine-based inotropes can develop rapidly through downregulation of adrenoreceptors.
 - In adult studies oral milrinone therapy for heart failure was associated with worse outcome and increased mortality [50].

49.9.5 Oral Heart Failure Agents

- β -adrenergic blocking agents (metoprolol, carvedilol)
 - Ratio of β_1 : β_2 -receptors in the non-failing myocardium is approximately 3:1. Downregulation of β_1 -receptors in the failing heart results in a ratio of 1:1.
 - The beneficial effect of β -blockade is mediated primarily through inhibition of sympathetic system activation that occurs in heart failure, but also reversal of adverse remodeling and upregulation of myocardial β -receptors.
 - β -blockers improve symptoms, exercise tolerance, cardiac hemodynamics, LV ejection fraction,

decrease mortality and decrease myocardial oxygen consumption [51–53]. β -blockers are recommended for use in adults with stable heart failure resulting from left ventricular dysfunction. Data in children is less clear with the results of a multicenter, placebo controlled trial expected soon [54].

- β -blocker effectiveness for heart failure depends on the type of β -receptor activity present as well as α -blocking properties. Carvedilol specifically is a β_1 and β_2 antagonist, is an α -blocker and has antioxidant effects and is thus thought to have advantages over agents such as metoprolol – a pure β_1 -blocker [55].
- In children with left-to-right shunts and overcirculation, β -blocker therapy improves feeding, weight gain, and symptoms [56].
- When initiating therapy, β -blockers should be started at a very low dosage and gradually increased to maximum therapeutic dosage with close monitoring according to heart rate and blood pressure [57].
- Digoxin
 - Acts by inhibiting the Na^+/K^+ -ATPase transport pump and inhibits sodium and potassium transport across cell membranes. This increases the velocity and shortening of cardiac muscle, resulting in a shift upward and to the left of the ventricular function (Frank–Starling) curve. The positive inotropic effect is due to an increase in the availability of cytosolic calcium during systole, thus increasing the velocity and extent of myocardial sarcomere shortening [58, 59].
 - Routine use of digoxin for pediatric heart failure is controversial. Adult studies demonstrate no mortality benefit, but improved symptoms and decreased hospitalizations [60].
 - Digoxin toxicity can affect the gastrointestinal (nausea, vomiting), neurologic (headache, visual disturbances) and cardiac (heart block and arrhythmias) systems. Particular attention should be paid when digoxin is used in association with loop diuretics, as hypokalemia enhances digoxin intoxication.
- Nesiritide
 - A recombinant B-type natriuretic peptide.
 - Nesiritide is used for symptomatic relief of acute decompensated heart failure in adults.
 - In children with primary heart failure or low cardiac output after heart surgery, nesiritide has been associated with improved diuresis [61]. In children awaiting cardiac transplantation, nesir-

itide has been related to increased urine output without significant blood pressure change [62]. Pediatric data is still scarce.

- Levosimendan
 - A new calcium-sensitizing agent with inodilator properties.
 - In children with low cardiac output post-cardiopulmonary bypass, levosimendan demonstrates trends toward improved hemodynamics with heart rate reduction, increase in mean arterial blood pressure, improvement of systolic and diastolic function, reduction in lactate, and reduced conventional inotropic requirement [63].
 - Levosimendan does not increase myocardial oxygen consumption and has also resulted in objective improvement in myocardial performance in children with end-stage or acute heart failure who are dependent on intravenous inotropic support [64].

49.9.6 Anticoagulation

Intracardiac thrombus and embolic events are a complication of heart failure in children. The protective effect of anticoagulation to prevent thromboembolic events is unclear with ongoing studies aimed at determining optimal therapy [65]. Risk factors to consider include severe left ventricular dysfunction and dilation, history of thromboembolism, and atrial fibrillation.

49.10 Nutrition

Growth failure is common in infants and children with significant heart failure due to increased metabolic demands. Infants suffering from heart failure require a higher caloric intake, about 140–160 kcal/kg of body weight, to ensure adequate weight gain [66]. In order to avoid volume overload, the concentration of the formula is increased (20–24 kcal/30 ml) providing no osmotic diarrhea occurs.

If the child is too sick to eat by mouth, gavage feeding should be instituted. In infants with severe heart failure or ductus arteriosus dependent circulation, enteric feeding should be carefully monitored as mesenteric ischemia can lead to necrotizing enterocolitis. In this situation, parenteral nutrition is an alternative.

49.11 Outcome

The outcome of pediatric heart failure depends on the underlying diagnosis and the availability of appropriate medical and surgical treatment. Dilated cardiomyopathy is the most common form of heart muscle disease in children. The survival rate for this disease in children is highly variable, ranging from 40 to 80% at 5 years [67–70]. Myocarditis has generally had a better prognosis than idiopathic dilated cardiomyopathy even if mechanical circulatory support is necessary. Fifty to eighty percent of patients with viral myocarditis have been reported to have complete resolution of their cardiomyopathy within 2 years of their diagnosis [71–73].

Children with failed palliation of congenital heart defects present another group of patients that require management for heart failure. Systemic right ventricular failure, single ventricle failure, or post-cardiopulmonary bypass failure all present unique management challenges in the cardiac intensive care unit. New modalities of therapy have improved outcomes and survival in pediatric patients with heart failure. Mechanical circulatory support and heart transplantation are viable options in patients with end-stage heart disease or complex cardiac defects. These subjects are discussed in detail elsewhere in this text and therefore will not be addressed here, but nevertheless are important and vital adjuncts when medical therapy fails.

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Chapter 50

Shock in the Cardiac Patient: A Brief Overview

Eduardo M. da Cruz and Jonathan Kaufman

50.1 Definition

Shock is a situation of circulatory failure characterized by a generalized and severe decrease of tissue oxygen and nutrient delivery. Shock, whatever the etiology, induces reversible and later irreversible cell lesions.

The immediate effect of this imbalance of supply and demand, is that cells cannot sustain their normal aerobic oxygen production and have to develop anaerobic pathways to generate energy. The activation of these anaerobic pathways results in the production, excretion, and accumulation of lactic acid. Nevertheless, this resource is limited and cells develop membrane ionic pump lesions with accumulation of intracellular sodium, efflux of potassium, and accumulation of cytosolic acid with subsequent membrane breakdown and cell death.

Shock can damage all tissues and systems and rapidly progress toward multiorgan failure. It must can be identified as early as possible, and aggressively treated, in order to reverse the metabolic derangements.

It is therefore fundamental to:

- Identify the type of circulatory failure
- Identify predisposing and triggering factors
- Define etiological and pathophysiological patterns that will conduce to a therapeutic plan

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50.2 Brief Pathophysiological Summary

Circulatory function depends on complex interactions between, the heart, central, and peripheral circulation and the neurohormonal axis. All of these components constantly change in order to adapt to tissue oxygen demands. The final product of these interactions is an adequate tissue perfusion and oxygen delivery that depends on the following factors:

- Cardiac output (CO)
- Systemic vascular resistances (SVR)
- Oxygen transport and delivery
- Oxygen extraction and consumption

Disruption of one or multiple of these aspects may result in shock.

50.3 The Cardiac Output

Cardiac output (CO) depends essentially on four factors: preload, afterload, heart rate (HR), and contractility (Fig. 50.1).

Preload:

Preload represents the initial ventricular volume before ejection. It depends on the following factors:

- Total circulating volume
- Distribution of intra and extrathoracic volume:

Intrathoracic pressure (cardiopulmonary interactions are essential)

Intrapericardial pressure

Body position

Myocardial “pump” effect

Venous tonus

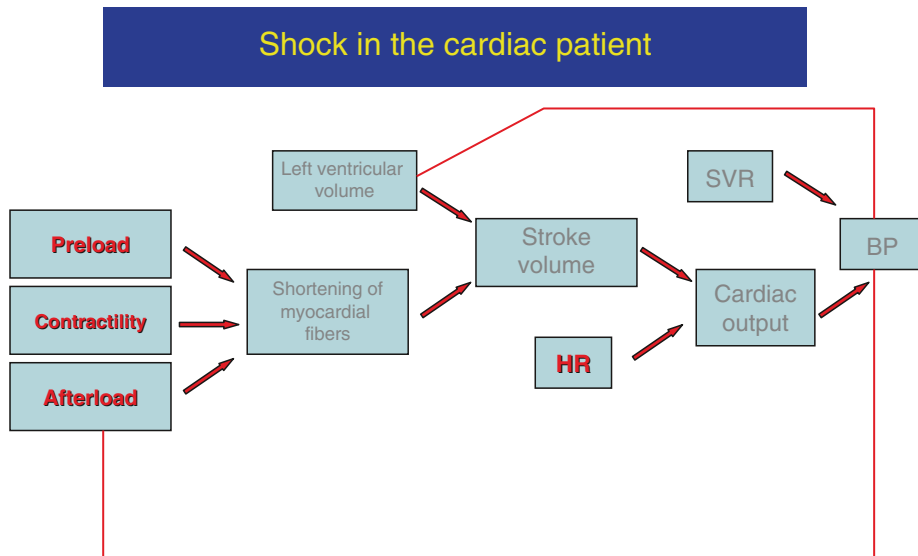


Fig. 50.1 Factors involved in cardiac output

- Atrial contraction

Afterload:

The afterload represents the addition of resistances against which the ventricle ejects blood into the vessels, added to central vascular impedance and to vascular bed resistances. Afterload depends on the following factors:

- Blood pressure (BP)

SVR

Arterial stiffness

Stroke volume

- Ventricular volume and thickness

Heart rate (HR):

Heart rate is particularly important in the neonate and the young infant as this is the most important means by which they increase cardiac output. Heart rate depends on a large variety of factors.

Contractility:

Contractility is the intrinsic capacity of the myocyte to contract, thus representing the inotropic status. It is modified by a number of metabolic and hormonal demands that can ultimately impact the systolic function:

- Endogenous adrenergic activity
- Circulating catecholamines

- Force–velocity ratio
- Exogenous inotropic agents
- Physiological depressors
- Pharmacological depressors
- Loss of ventricular mass
- Intrinsic myocardial depression

50.4 Factors that Influence Both the Cardiac Output and the SVR

- Diastolic function and compliance
- Release of local vasodilators (i.e., adenosine)
- Release of endothelial vasodilators (i.e., EDRF-NO)
- Release of endothelial vasoconstrictors (i.e., EDCF)
- Smooth muscle activity
- Autonomic nervous system (ANS) activity (sympathetic/parasympathetic balance)
- Modulation of the ANS by baroreceptors and central vasomotor control
- Catecholamine effect (“stress-response”)
- Renin–angiotensin–aldosterone activity
- Vasopressin levels
- Levels of endogenous vasodilators (i.e., quinines-PG)

50.5 Oxygen Delivery, Transport, and Extraction

The capacity to ensure an adequate transport of oxygen and nutrients and to eliminate metabolic waste is determined by the following factors:

- Adequate ventilation
- Adequate oxygen transport by a normal hemoglobin (may be affected, i.e., by methemoglobin)
- Adequate oxygen extraction and consumption (may be affected, i.e., by CO intoxication or factors altering the hemoglobin dissociation curve)

Alteration of hemoglobin dissociation curve (Fig. 50.2):

- Right shift:

Increase of: H^+ , pCO_2 , T° , 2–3 DPG

- Left shift:

Decrease of: H^+ , pCO_2 , T° , 2–3 DPG, methemoglobin, fetal hemoglobin

- Other important factors to consider:

Cardiopulmonary interactions

Interventricular interactions

Interventricular and atrioventricular synchrony

50.6 Diagnosis

Five types of cardiocirculatory failure may be defined as follows (Figs. 50.3 and 50.4).

Hypovolemic shock is secondary to a deficiency of intravascular volume. This accounts for the most frequent causes of shock in pediatrics. Rapid reduction of intravascular volume causes an abrupt reduction of cardiac preload and therefore of stroke volume and cardiac output.

Hypovolemic shock may also be caused by hemorrhage. In this case, hemoglobin transport is also affected.

Hypovolemic status may also be identified in patients with cardiac dysfunction, after CPBP, who have developed a significant capillary leak. Although these patients appear total body fluid positive, their intravascular space may be severely depleted.

Cardiogenic shock is due to a primary “pump” dysfunction, such as the case of severe and persistent arrhythmias, myocardial ischemia, cardiomyopathy, or in the context of postoperative low cardiac output syndrome (LCOS).

The *obstructive (extracardiac) shock* is due to obstructions that produce a massive increase in afterload or that reduce the filling capacity of the heart.

The hemoglobin oxygen dissociation curve

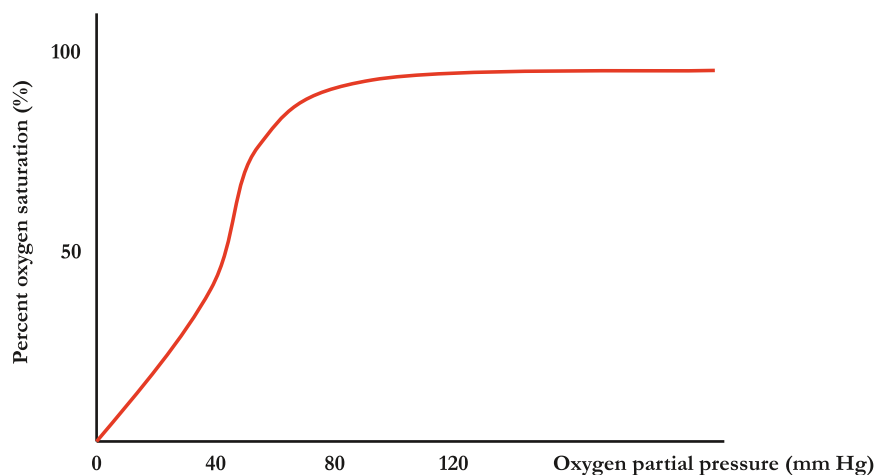


Fig. 50.2 The hemoglobin dissociation curve

Shock in the cardiac patient Diagnosis

Cardiogenic	Obstructive (extra-cardiac)	Hypovolemic	Distributive or Vasoplegic	Dissociative
“Pump” dysfunction	Restriction to flow	Inadequate volume	Vascular bed anomaly	Decreased capacity to deliver O ₂
Infarct/ischemia	Tamponade	Hemorrhage	Sepsis	Severe anemia
Dilated cardiomyopathy	Constrictive pericarditis	Dehydration	Toxic	Metahemoglobin
Dysfunction/sepsis	PTE		Anaphylactic	Co intoxication
Mitral regurgitation	Severe hypertension		Neurogenic	
Left obstruction	Aortic coarctation/ interrupted aortic arch		Endocrinologic	
Arrhythmia	Tension pneumothorax		Inflammatory	
L.C.O.S.				

Fig. 50.3 Types of shock in pediatric cardiac patients

Shock in the cardiac patient Diagnosis

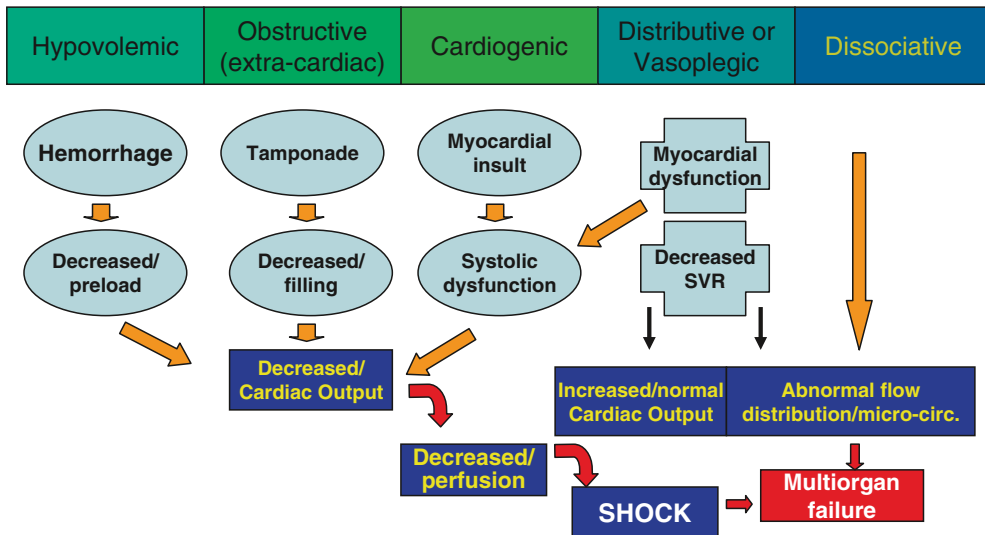


Fig. 50.4 Brief pathophysiology of the different types of shock affecting pediatric cardiac patients

This may happen with anatomic anomalies, such as left side anatomic obstructive lesions that significantly increase left afterload: aortic stenosis, aortic coarctation or interrupted aortic arch, or with functional

anomalies like systemic hypertension (left-sided functional obstruction that increases the afterload), pulmonary hypertension (right-sided functional obstruction that increases the afterload). It may also be secondary

to situations that affect cardiac filling like cardiac tamponade or a tension pneumothorax.

Distributive or vasoplegic shock appears in patients who may have normal or hyperdynamic cardiac function but in whom the vascular tone is severely decreased, as in the case of sepsis, anaphylaxis, systemic inflammatory disorders, and spinal cord injuries. These patients have a relative hypovolemia due to an increased vascular capacitance but do not adequately respond to massive volume administration alone.

Dissociative shock happens in the context where the capacity to transport (i.e., severe anemia or abnormal hemoglobin) or to extract (i.e., CO intoxication) oxygen is severely depressed.

Diagnosis of shock involves the clinical recognition of symptoms and signs, although these may be very non-specific and appear clinically late in presentation. This sometimes makes the identification of shock rather difficult, particularly in small infants and in those patients in whom the circulatory failure is still partially compensated. Thus, clinical diagnosis often occurs late and identification of early markers is crucial not only for diagnosis but also for follow up.

It is important to keep in mind that different types of shock may coexist in the same patient.

50.6.1 Clinical History

Clinical background is essential to make diagnosis particularly in patients known to have cardiac disease. However, a crucial concept to keep in mind is that *a cardiac patient in shock is not necessarily in cardiogenic shock*.

A history of increased volume losses (diarrhea, vomiting, bleeding, trauma) may steer the caregiver toward the diagnosis of hypovolemic shock.

Fever, background of immunosuppression (i.e., transplanted patients), young age may suggest sepsis.

Neonates with tachypnea on feeding or feeding refusal who present with cardiac murmurs, cyanosis, or anomalous peripheral pulses may have a cardiogenic shock.

50.6.2 Clinical Examination

A full clinical examination remains an important diagnostic tool although it may not always be a specific one. Crucial aspects to keep in mind are:

- General condition, presence of irritability, weakness, asthenia, lethargy, neurologic status, peripheral perfusion and pulses, quality of peripheral pulses, presence or modification of cardiac murmurs, presence of organomegaly
- Vital signs: blood pressure (upper and lower limbs), central venous pressure (CVP), heart rate, respiratory rate, T^o, O₂ saturation

Tachycardia is a common sign of shock, particularly in neonates who compensate cardiac output by increasing cardiac rate. In some circumstances, this physiological response is blunted by autonomic or pharmacologic changes. Patients in shock tend to be tachycardic whether they are compensated or not.

Blood pressure may be within the adequate range for the age in patients in early shock in whom compensatory mechanisms (i.e., increased peripheral resistances) are activated.

Skin perfusion may be instrumental in orienting therapy. As shock progresses, the microcirculation tends to promote perfusion of target organs by inducing vasoconstriction. However, there are two main exceptions to this scenario. First, patients in septic, anaphylactic, or inflammatory shock who present in “warm” vasoplegia, may have very well-perfused skin. Second, patients with severe vasoplegia may have very low peripheral resistances in major vessels, and yet, their microcirculation promotes vasoconstriction. In other words, these patients look clinically peripherally vasoconstricted and still may require vasopressors rather than vasodilators. This situation may be difficult to assess in small infants.

- Other unspecific markers that may be affected by shock:

Increase of central to peripheral T^o gradient:

Normal <3°C

Decrease of diuresis:

Normal >1 ml/kg/h

50.6.3 Complementary Tests

- Arterial blood gases

Modifications in blood gases may be poorly specific or sensitive and may not be identified early enough. Usually, patients in shock have metabolic acidosis and

eventually hyperlactatemia or lactic acidosis, depending on the degree of cellular injury.

- Chest X-ray

Chest X-ray may be useful in assessing the cardiac silhouette for cardiomegaly, lung fields for differential perfusion, and to evaluate for infection, noncardiogenic lung edema (ARDS-type), or other respiratory anomalies.

- ECG

ECG is very unspecific but may be useful in patients with cardiac anomalies and to rule-out arrhythmias and conductive disorders.

- Biologic and metabolic status, cultures

CBC, inflammatory markers (CRP, ESR) and cultures are essential to rule-out sepsis. Procalcitonin levels may become an important marker of infection, particularly in patients who have undergone recent cardiac surgery on CPBP.

- Echocardiography

Echocardiography is important in the diagnosis of cardiogenic shock as well as other types that may induce cardiac dysfunction. Regardless of the etiology of shock, an assessment of cardiac function may be vital in steering the medical therapy and to assess efficacy of treatment.

- Cardiac catheterization, CT scan, and MRI

Cardiac catheterization, CT scan, and MRI may also be useful tools to assess residual cardiac lesions and function in patients with severe cardiac dysfunction in whom echocardiography or invasive measurements do not provide clear data.

- More specific evaluation of cardiac output

This may be difficult in neonates and young infants:

- Fick's method
- Thermodilution techniques/PiCCO®/Flo-Trac®/Swan-Ganz®

These techniques allow estimation of cardiac output and index (Swan–Ganz, PiCCO, Flo-Trac), pulmonary and systemic peripheral resistances and pulmonary capillary wedge pressure (Swan–Ganz), and left ventricular diastolic volume (PiCCO). The Swan–Ganz technology has been fully validated for decades whereas

PiCCO and Flo-trac are under investigation in the pediatric population.

- Doppler/electric impedance
- rSO₂: near infrared spectroscopy (NIRS):

NIRS is an important tool to assess regional perfusion, mostly in the brain, in the kidneys, and in the mesentery. It may provide useful information as a trend monitor of regional perfusion and response to medical therapy.

- SvO₂:

The use of mixed venous saturations may be restricted by the need for indwelling catheters in very small patients. A blood sample must be taken from the right atrium (via a central venous catheter or via a Swan–Ganz catheter). The result may be determined by comparing the venous saturation (SvO₂) with the arterial saturation (SaO₂), measured directly by the oxygen saturation or by a peripheral arterial blood gas. In patients with normal SaO₂ (above 90%), the normal SvO₂ should be around 70%.

This technique is limited in patients with univentricular physiology in whom the mandatory intracardiac mixing does not allow interpretation of a given result, although trends may be useful to assess response to therapy.

If the oxygen extraction difference increases, the SvO₂ will drop (below 65%). This may suggest that the perfusion to peripheral tissues is inadequate as it happens in low cardiac output conditions (cardiogenic shock).

If the oxygen extraction difference decreases, the SvO₂ increase (above 80%) suggesting an inappropriate distribution of flow in the microcirculation as it happens in distributive and vasoplegic shock.

- Blood lactates:

The importance of blood lactates has been well recognized:

- a) Early marker, reliable, quite specific and sensitive
- b) Easily available
- c) Correlation with mortality/complications
- d) Normal <1.5 mmol/l; alert if >4 mmol/l
- e) Value trend is crucial
- f) Hyperlactatemia versus lactic acidosis: isolated increase in blood lactates is considered as hyperlactatemia and may be an indicator of a starting

cellular injury or of lack of lactate elimination (mostly in the liver). Lactic acidosis is a more severe process in which cellular injury is ongoing and reflects the elimination of cellular lactates and H^+ ions into the blood stream.

g) Combination Lactate/SvO₂

50.6.4 Multiorgan Assessment

Assessment of multiorgan compromise is vital in patients admitted in shock. Exhaustive clinical and complimentary tests should be run to appraise the function of kidneys, liver, pancreas, brain, lungs, gut, and adrenocortical glands, in addition to the cardiovascular evaluation.

50.7 Management of Shock

Management of shock in the pediatric patient shares common aspects regardless of the etiology and must be started while waiting for complementary diagnostic data. The main initial objective is to preserve life and secondarily to preserve multiorgan function. No workup or imaging studies should delay medical measures to stabilize the patient.

There are therefore *three lines of management*:

- Resuscitation following the “A-B-C” principles
- Multiorgan support
- Specific therapy oriented by etiological suspicion

Patency of patient’s airways must be ensured as well as adequate oxygenation and gas exchange. If the patient has respiratory distress, caregivers should consider intubation and mechanical ventilation sooner than later. A word of caution must be said though, with regard to the induction of anesthesia or sedation, particularly in cardiac patients. Rapid sequence protocols should be strongly considered in such cases. Etomidate is to be avoided if there is concern for infection or adrenocortical dysfunction.

The next step should be to ensure that the effective circulating volume is optimized. For this purpose, the assessment of the type of venous lines is essential. Patients who stay relatively stable may be managed with peripheral lines at the beginning, monitoring for

rapid improvement. However, patients who present critically ill or in whom peripheral access is deemed difficult to obtain should have an indwelling central line inserted as soon as possible. Intraosseous lines remain a good palliation until further stabilization allowing the insertion of safer lines. The same principles apply to the insertion of a peripheral arterial line. An arterial line allows for continuous blood pressure monitoring and is a means to obtain serial blood gases in a less traumatic manner.

Circulatory improvement is usually achieved by the following measures, determined by the etiological orientation:

- *Administration of volume expanders*: the choice of the fluid to administer ought to be individualized (i.e., blood and fresh frozen plasma if the patient is bleeding, isotonic crystalloid infusions like 0.9% sodium chloride or Ringer’s solution in dehydrated patients, colloid such as albumin in other circumstances).

Patients who receive aggressive and early fluid resuscitation have the best chance of surviving severe septic or hypovolemic shock. Nevertheless, volume must be very cautiously administered in cardiogenic shock states and particular attention must be paid to the diastolic function.

Patients who do not improve in spite of adequate and aggressive volume administration should have a cardiovascular workup, including an echocardiogram, to rule-out associated cardiac dysfunction.

- *Inotropic agents, vasodilators, or vasopressors*: the choice of drugs to use depends on the etiological suspicion. All inotropic and vasoconstrictor agents should be carefully used, taking into account their potential for adverse effects, including increased myocardial oxygen consumption and arrhythmias.

Dopamine is the main drug used as a first choice in patients with unspecified shock, either alone or combined with other inotropic agents. It remains the recommended first choice for fluid-refractory septic shock (American College of Critical Care Medicine Task Force, 2002). At doses between 2 and 5 $\mu\text{g}/\text{kg}/\text{min}$, it promotes renal and splanchnic perfusion, between 5 and 10 $\mu\text{g}/\text{kg}/\text{min}$, it adds a beta-1 agonist effect that improves myocardial contractility, cardiac output, and enhances conduction and between 10 and 20 $\mu\text{g}/\text{kg}/\text{min}$,

it induces peripheral vasoconstriction by an added alpha-agonist effect.

Dobutamine, a primary beta-1 agonist, also offers the advantage of a more marked beta-2 mediated vasodilatory effect in patients requiring peripheral vasodilation. In some circumstances a very appropriate choice for a patient with cardiogenic shock, helping to increase myocardial contractility and improving tissue perfusion. Therapeutic dose varies between 5 and 20 µg/kg/min.

Patients with cardiogenic shock may also benefit of *milrinone* (0.3–1 µg/kg/min) and may require further peripheral vasodilation (i.e., with *sodium nitroprusside*, between 0.5 and 10 µg/kg/min). For patients with primary cardiac anomalies, congenital or acquired, milrinone is the first line inotrope. It improves myocardial contractility while inducing peripheral systemic vasodilation and provides some degree of nonselective pulmonary vasodilation.

When cardiac function is significantly depressed, regardless of the etiology, an *epinephrine* (adrenaline) drip should be promptly started. Epinephrine stimulates alpha and beta receptors increasing myocardial contractility, but peripheral vasoconstriction may occur. Myocardial oxygen consumption increases and ventricular dysrhythmias may be triggered. Epinephrine may be titrated between 0.05 and 0.3 µg/kg/min in severe shock.

Patients with vasoplegic shock require the use of peripheral vasopressors, as selective for the peripheral receptors as possible, like *phenylephrine* (0.5–5 µg/kg/min), *vasopressin* (0.0001–0.005 units/kg/min), or eventually *norepinephrine* or noradrenaline (0.05–0.5 µg/kg/min). These vasopressors may be associated with inotropic agents if the cardiac function is affected.

- *Calcium:*

Calcium therapy (10–20 mg/kg/h using 10% calcium chloride) may be useful when treating shock in patients with documented hypocalcemia, in patients having required blood transfusion, and also for treating shock caused by arrhythmias precipitated by hyperkalemia, hypermagnesemia, or calcium blockers intoxication. Some reports in literature have raised concerns with regard to rapid and supratherapeutic levels of calcium and potential myocardial toxicity.

- *Antibiotics and steroids:* Recommended as an initial coverage in patients with suspected septic shock.

- The use of corticosteroids although controversial is currently recommended, particularly in patients with purpura fulminans or suspicion of Waterhouse–Friderichsen syndrome. Administration of hydrocortisone hemisuccinate at 50–100 mg/m²/day may be beneficial and lifesaving. A cortisol level may be drawn prior to the administration of the first dose, in order to decide the need to pursue steroid administration if baseline levels are less than 20 µg/dl.
- *Sodium bicarbonate:* the use of sodium bicarbonate in the treatment of shock is controversial.

Patients with depressed myocardial function who develop severe acidosis may not optimally respond to catecholamines.

However:

- Studies in patients with cardiac arrest have not demonstrated improved survival rates associated with the use of bicarbonate
- Use of bicarbonate has not demonstrated to improve the ability to defibrillate or to enhance oxygen debt
- Treatment with bicarbonate may theoretically worsen intracellular acidosis while correcting serum levels. This is due to the fact that bicarbonate combines with acid (H⁺) in serum resulting in the production of carbon dioxide and water (Henderson–Hasselbach equation). Then, it readily enters the cells and triggers the opposite reaction increasing intracellular acidosis.
- Treatment with bicarbonate may induce a paradoxical cerebral acidosis (for the same reason as above)

Therefore, patients in shock who develop severe acidosis should be corrected with a judicious use of inotropic drugs and volume and with optimal ventilation.

Nevertheless, with patients in refractory shock, who do not respond to catecholamines or whenever there is an ongoing bicarbonate loss, careful and slow use of bicarbonate may be indicated.

There are two ways to estimate the amount of bicarbonate to administer:

- To administer 0.5–2 mEq/kg/dose infused over 2 min IV
- To calculate the dose of bicarbonate based upon the base deficit as estimated in the arterial blood gases, with the following formula:

$$\text{HCO}_3^- (\text{mEq}) = \text{Base deficit} \times \text{weight (kg)} \times 0.3$$

Half of the estimated amount of bicarbonate may be administered over 20 min and the other half over 4 h, if a new arterial blood gas reveals the persistent need for it.

- *Prostaglandin E₁* (PGE₁): neonates who present in shock of unknown etiology or with cardiac murmurs, cyanosis, asymmetrical peripheral pulses, absent femoral pulses, or any other signs suggesting obstructive left cardiac malformations, must be immediately started on a continuous infusion of PGE₁ between 0.05 and 0.1 µg/kg/min. This may be a lifesaving measure as it reestablishes patency of the ductus arteriosus.

Figures 50.5–50.9 describe simple management *algorithms* for patients in shock.

50.8 Specific Therapies

Some patients in cardiogenic shock of specific etiology or refractory to medical therapy may require more specific management, namely:

- Treatment of pulmonary arterial hypertension
- Treatment of arrhythmias

- Surgery (i.e., creation of an intracardiac “pop-off”...)
- Refractory cases:
 - a) Sternum opening (after cardiac surgery)
 - b) Total exanguino-transfusion or plasmapheresis
 - c) Anti-endotoxins
 - d) Continuous veno-venous hemodiafiltration (CVVHD)
 - e) Hypothermia
 - f) Atrioventricular and interventricular resynchronization
 - g) Extracorporeal life support (ECLS)

50.9 Conclusions

Shock in the pediatric patients may be difficult to identify in its early phase. Medical therapy ought to be started with general lifesaving measures while gathering information that will be helpful in identifying a specific etiology. Therapy goals should be oriented by the etiological suspicion.

Pediatric cardiac patient who present in shock are not necessarily in cardiogenic shock and may still require a full workup.

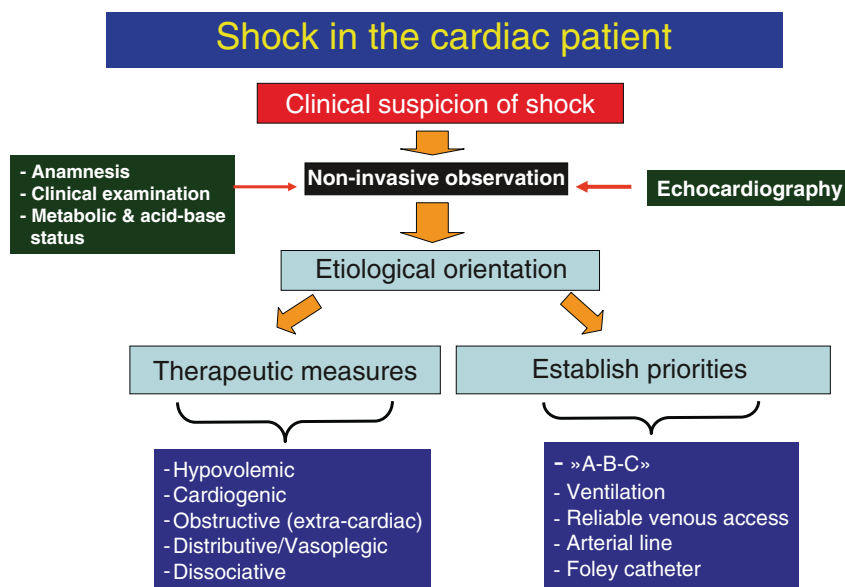


Fig. 50.5 General algorithm for medical management of patients in shock

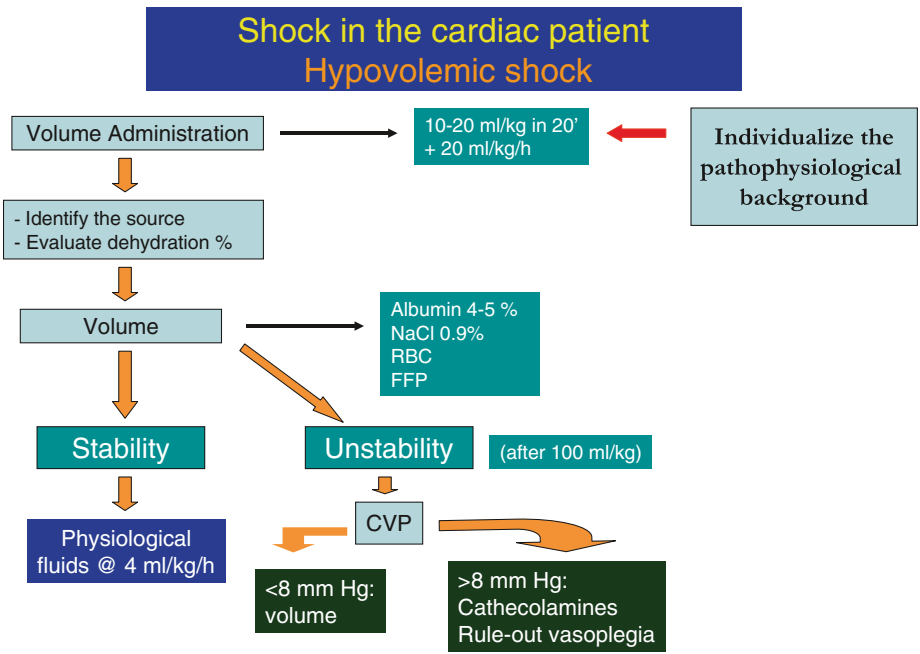


Fig. 50.6 Therapeutic algorithm for patients in hypovolemic shock

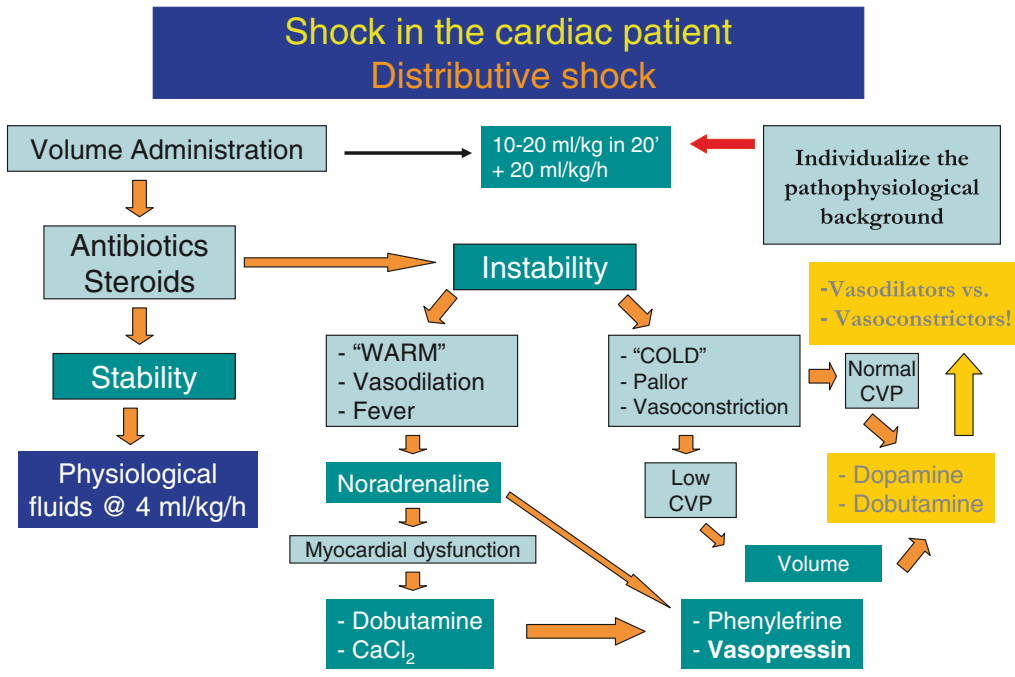


Fig. 50.7 Therapeutic algorithm for patients in distributive shock

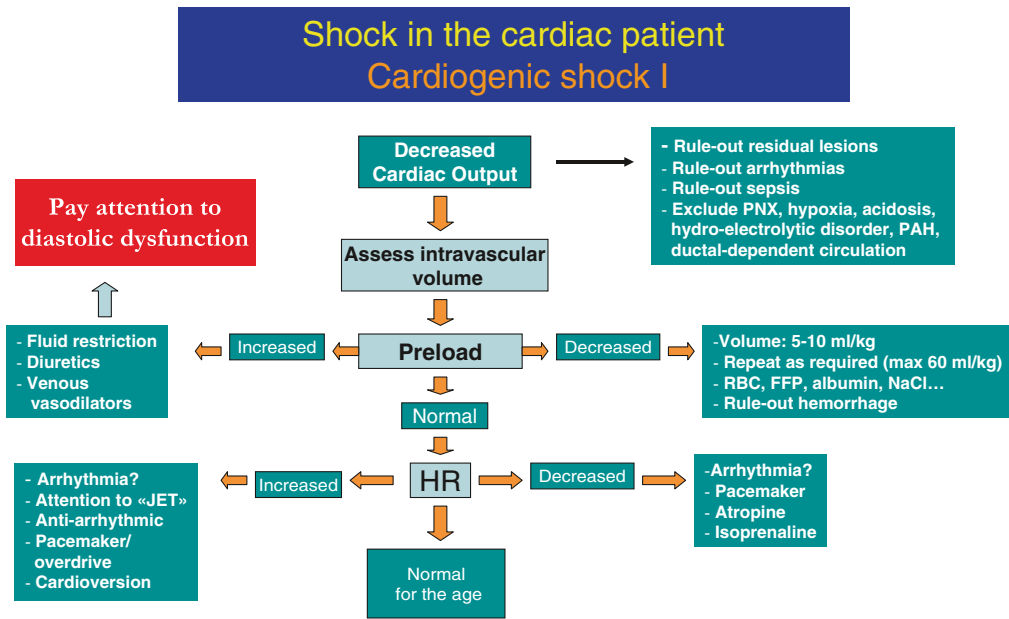


Fig. 50.8 Therapeutic algorithm for patients in cardiogenic shock I

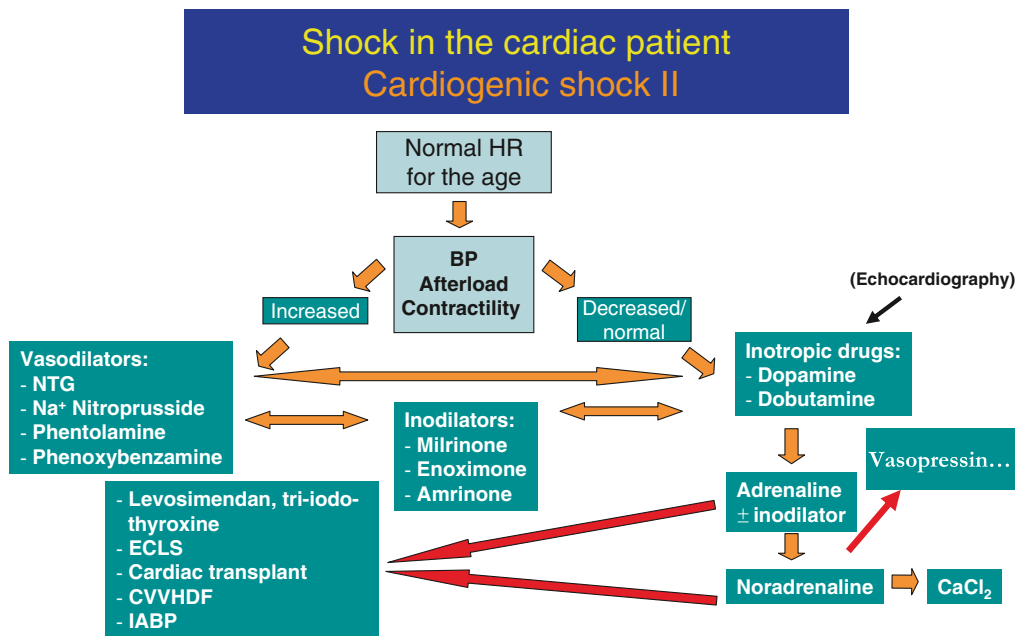


Fig. 50.9 Therapeutic algorithm for patients in cardiogenic shock II

Also, “miscellaneous” shock exists and patients who do not respond to therapy may be further investigated following the differential diagnosis algorithms.

Last but not least, multidisciplinary management of shock improves patients’ outcome.

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Chapter 51

Mechanical Circulatory Support in Pediatric Cardiac Surgery

Peter D. Wearden, Ana Maria Manrique, and Kent Kelly

Extracorporeal membrane oxygenation (ECMO) or extracorporeal life support (ECLS) is the implementation of the cardiopulmonary bypass machine for prolonged periods of time to sustain systemic perfusion and gas exchange. The support is preferred for patients with potentially treatable pulmonary or cardiac disease. Currently, it is the most common method of mechanical circulatory support for pediatric patients. The development and improvement of this technology has allowed ECMO to progress from a salvage therapy to a commonly used treatment allowing time for cardiopulmonary recovery. Many centers have continually available rapidly deployed ECMO teams for the rapid resuscitation of patients. Some of the advantages of ECMO include rapid setup, provides both respiratory and cardiac support, reliable support with known outcomes, and a now vast clinical experience.

reported a case series of 13 patients carrying a cardiac diagnosis with a 48% of survival. Today, the yearly number of cardiac cases supported with ECMO has increased from 30 in 1986 to 682 in 2007.

Other important events in the development of ECLS include:

1960–1968, Lande AJ, Bramson ML, Pierce EC, Kolobow T: Development of membrane oxygenator

1972, Hill et al.: first successful use of prolonged extracorporeal support

1973, Soeter et al.: first reported use of ECMO in a child with Tetralogy of Fallot after surgery for an extended period of time.

1976, Bartlett RH et al.: first successful clinical application for neonatal respiratory failure

1986, ECMO progresses from a clinical research project to a standard of care for neonatal respiratory failure after Bartlett's larger publication [1, 2].

51.1 Background

In 1977, Bartlett et al. published the first larger series of neonates undergoing ECMO for respiratory failure with a survival rate of 55%. Prior to this an NIH sponsored adult study had demonstrated poor outcomes and ECMO had been largely abandoned. At the time of Bartlett's paper, cardiac disease was viewed as a contraindication for mechanical support. Incidentally, some patients had been placed on ECMO prior to a cardiac diagnosis being made and these cases were reported as being successful. In 1987, Kanter et al.

51.1.1 The Development of the Extracorporeal Life Support Organization (ELSO)

In 1989, a group of centers began to pool their data regarding number of cases, etiology of cardiopulmonary failure, complications and survival by center with regard to the utilization of ECMO. This group was increased as continually more centers began to adapt this technology. In 1989, cardiac indications for ECMO were only 7% of the total of pediatric ECMO cases. This number has rapidly increased as has the survival of these patients. In July 2007, a 61% survival for pediatric cardiac ECMO was reported and a 58% survival for neonatal cardiac cases [3].

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51.2 Circuits and Equipment

The typical ECMO system is composed of the following:

1. Pump
2. Oxygenator
3. Heat Exchanger
4. Cannulae

In the typical veno-arterial ECMO (VA) system the deoxygenated blood is removed from the patient through a venous cannula, and as it moves through the circuit it passes through the bladder, the saturation probe (which continuously monitors the SVO_2), and the access ports (where blood sampling is drawn and medications are given). Blood next passes through the pump. The blood is then pumped through the oxygenator and then the heat exchanger. Finally the blood is returned to the patient through an arterial line and cannula (Fig. 51.1).

From this basic model there are many different configurations according to center preferences.

51.2.1 Pump

There are two types of pumps commonly utilized: roller pumps and centrifugal pumps.

The *Roller Pump* generates a continuous blood flow by compressing the tubing within a “raceway.” The *Centrifugal pump* forces blood flow via a spinning rotor, which is magnetically coupled to a motor. The drainage of blood from the patient depends in part upon gravity, the hydrostatic pressure as determined by the difference in the height of the right atrium of the patient and the level of the pump, and by any negative suction created by the pump itself. Pump output can be recorded as liters of flow per minute or revolutions per minute (rpm).

There are several other differences between roller and centrifugal pumps. Despite certain advantages of the centrifugal pumps, their use has become limited (in combination with silicone membrane oxygenators) because of the increased compliance and higher resistance, thus leading to increased hemolysis [4] (Table 51.1)

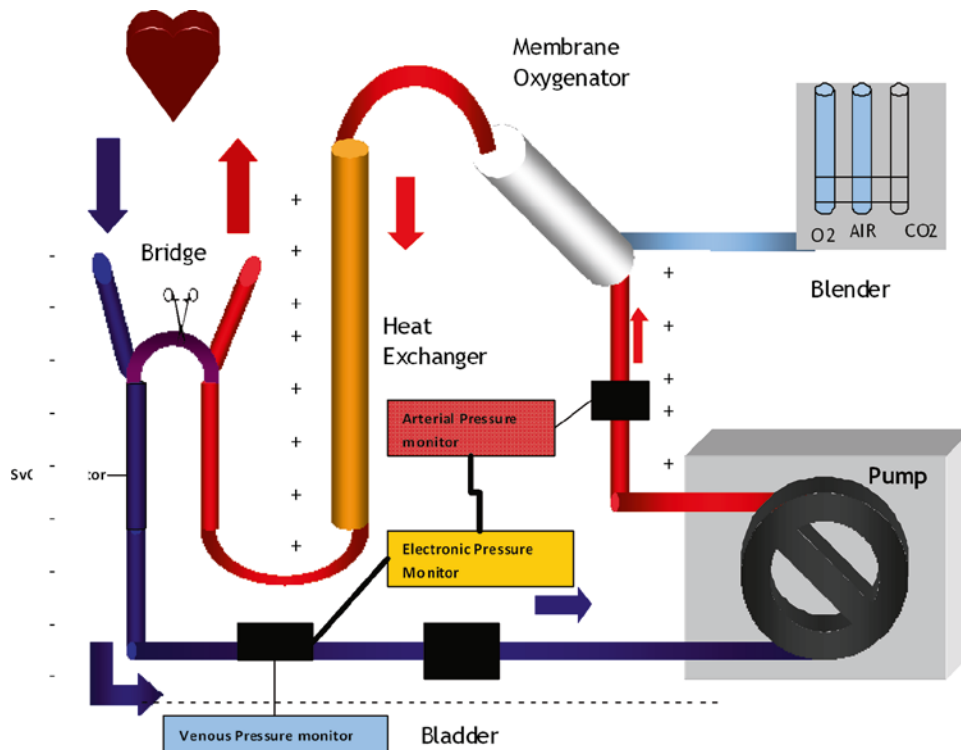


Fig. 51.1 ECMO Circuit. — Negative pressure; ++ Positive pressure

Table 51.1 Differences between roller and centrifugal Pumps

	Roller pumps	Centrifugal pumps
Blood flow	Sequential tubing compression	Spinning rotor
Venous drainage	Gravity dependent	Dependent on suction generated by rotor
Pressure control	Continuous servo-regulation	Electromagnetically
Preload dependent	++	+++
Afterload dependent	+	+++
Excessive negative pressure	+++	++
Tubing wear-rupture	+++	+
Hemolysis	+++	++
Hemolysis with low or high flow	++	+++
Length of functional life	+++	+
Embolization of air or particles from the tubing	+++	+
Platelet activation	+++	+
Complement and cytokine levels	+++	+

51.2.2 Oxygenator

The first attempt to use a pump oxygenator was made in 1951 by Clarence Dennis. At this point in time the most commonly used oxygenator was the bubble oxygenator. This type of oxygenator was used from the mid 1950s and until the late 1970s. The issues related to this type of oxygenator, particularly with foaming and massive air embolism encouraged the development of membrane oxygenators. In membrane oxygenators, as opposed to the bubble type, there is no direct interface between gas and blood. Gas exchange instead occurs across the surface of a membrane. There are two types of membrane oxygenators widely available: microporous and nonporous membranes. These oxygenators permitted indirect contact with oxygen minimizing the risk of air embolism and do not need a gas removal and defoaming system. Several materials have been used to develop these membranes including cellulose, polyethylene, silicone, and most recently polymethylpentene. In 1972, Y. Nose developed the first polymeric hollow fiber oxygenator device which increased the surface area over which gas exchange could occur.

The currently preferred membrane has a flat reinforced rubber membrane envelope wound in a spiral fashion around a polycarbonate spool. The unit is encased by a tight fitting silicone rubber sleeve. The gas compartment is formed by the inside of the envelope. Blood flows on the outside of this envelope. The gas flows through a countercurrent system across the membrane. Additionally, this system confers low flow resistance and low priming volumes.

Gas exchange is facilitated by a countercurrent system, in which the delivered gas from the circuit is regulated to the blood flow of the patient. The difference in the partial pressure of the gases between one side and the other of the membrane, the countercurrent flow, and the ongoing consumption of the O₂ and CO₂ production will determine the rate of gas exchange.

The diffusion of CO₂ through the membrane is particularly effective. CO₂ transfer rate is 6 times greater in the silicone membrane than O₂ exchange; thus, the rate of CO₂ transfer provides a sensitive measure of the loss of functioning membrane surface area. CO₂ is controlled by the rate (sweep) of the ventilating gas delivered to the membrane. Due to this great effectiveness of CO₂ exchange, paCO₂ may decrease below normal levels, requiring the addition of CO₂ to the gas mixture to prevent the suppression of the respiratory center and alterations in pH.

The coefficient of diffusion of oxygen is significantly lower than that for CO₂ and is dependent on the transit time of the oxygenated hemoglobin through the membrane. The oxygen blood saturation is restricted in each oxygenator because of their limited flow rate. There are different size and surface area oxygenators used for a given patient's body surface area.

Oxygenators may experience several mechanical complications. These include: a propensity for plasma leakage, structural defects, extravasation or accumulation of fluid and blood products and thromboses. These issues may be exacerbated by certain conditions, particularly the use of parenteral lipid nutrition.

51.2.2.1 Bladder

The bladder is the inlet portion of the circuit and provides a buffer of volume for the normal fluctuations of venous return and also serves as a location for air trapping on the venous side of the circuit. The bladder provides access to blood flowing through the circuit,

whereby pharmacologic agents, blood products, and fluid may be administered.

The pump stops when the level drops below a programmed level. Blood from the cannula drains into the bladder passively. The function of this bladder is to prevent negative pressure from pulling the vessel wall into the cannula and reducing the risk of damage to the vena cava. The bladder is connected to a servo regulator mechanism, which reduces or stops pump flow in the event of venous return decrease to unsafe levels. Some centers, in order to reduce the artificial surface contacting the blood, have replaced bladders with negative pressure sensing mechanisms.

51.2.3 Heater Exchanger

The heater maintains and regulates the corporal temperature from 25 to 40°C. The device is equipped with a water reservoir and a pump. This is a polycarbonate cylinder with stainless steel tubes inside for blood passage. Hot water circulates into the cylinder transferring heat to the stainless steel tubes, which are filled with flowing blood.

During the time that blood flow through the circuit is cooling, the heat exchanger warms the blood to body temperature before it returns to the patient. It also serves as an air trap. Heat loss is avoided with the distal placement of the heat exchanger in the circuit. The post-heat-exchanger blood temperature is monitored and the water temperature is adjusted accordingly.

Failure of this system occurs 1–2% and is due to leakage.

51.2.4 Cannulae

Cannulae are available in various shapes and sizes depending upon patient size and the site of cannulation. There are recommended guidelines regarding the appropriate size cannula based upon desired flow rates and pressure drops, the site of placement (neck vs. groin vs. chest), flow direction (venous vs. arterial), and patient weight.

Selection of the appropriate cannula size will decrease hemolysis and will increase the system

efficiency. Oversized cannula will obstruct flow especially in neonates when it is placed in the aortic position and increase rates of thrombosis.

51.2.4.1 Tubing

Tubing is an important component in the system particularly with regard to the systemic inflammatory response and anticoagulation. Several materials have been developed since 1930. The most commonly used material is polyvinyl chloride (PVC). This material has the disadvantage of releasing di-2-ethylhexylphthalate (DEHP), which has been associated with decreased fertility in animal studies; however, there are not conclusive studies of detrimental effects in neonates exposed to this material during ECMO runs. The leaching is further promoted by the action of the roller over the tube wall. This part of the tubing, or “raceway section,” is often made of thicker tubing which gives more durability and resistance to the rupture.

More recently, heparin-bonded tubing has been introduced, with which anticoagulation with heparin may be avoided for a limited period of time. This tubing is coated with a bioactive surface of covalent forces which bind heparin to the tubing. There are several experimental and clinical studies demonstrating a decrease in the release of inflammatory reactants and platelet consumption utilizing this tubing. Currently, there are not conclusive data regarding mortality. Carmeda Bioactive Surface (CBAS; Carmeda Stockholm, Sweden) is the most common heparin-coated circuit used [5, 6].

51.2.4.2 Bridge

The venous circuit may be connected to the arterial circuit through a short segment of tubing. This segment allows continuous blood flow through the system while the patient is temporally disconnected from the ECMO support; such as, during a trial of weaning. During this process the cannula are usually “flushed” or opened every 10–20 min to decrease risk of segmental blood stasis in the segment closed to blood flow. Generally bridges are placed only at the time of weaning.

51.2.4.3 Equipment System

The ECMO console includes three components: (Fig. 51.2)

1. console or base
2. The pump module
3. System control panel

Monitoring and Alarm System: There are two safety systems required; air detectors and pressure alarms.

There are several alarm systems throughout the circuit: Pressure of the returning flow is monitored before it reaches the bladder. This servo-regulated system in the roller pump permits a decrease or halt to pump flow when the volume in the bladder, or venous cannula, is under a critical pre-estimated level. The venous alarm will be activated whenever there is decreased blood return to the pump as may happen in the case of displacement, obstruction or kinking of the venous cannula, decrease in the blood volume, pneumothorax, pneumopericardium, hemothorax, or hemopericardium. The next set of pressure transducers is usually placed before and after the oxygenator and may alert the operator to thrombosis or failure of the membrane; those conditions increase the pressure and can cause rupture of the circuit.

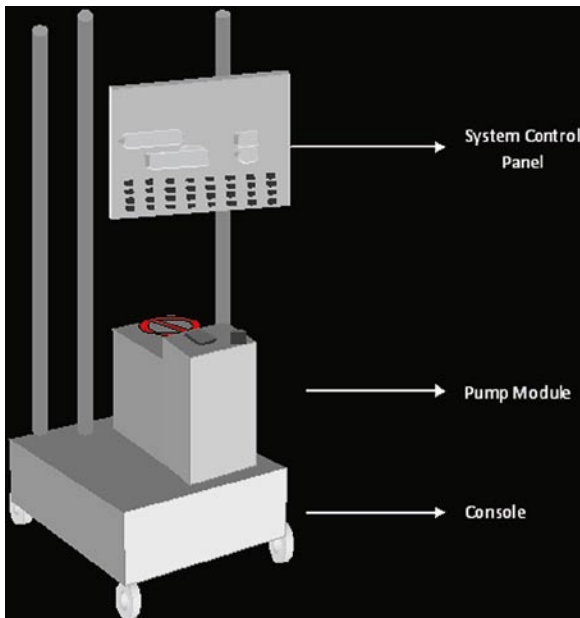


Fig. 51.2 ECMO pump system

Air trapping can occur in the bladder, the oxygenator, and the heat exchanger. Additionally, there is a bubble detector and trapping mechanism just before the circuit returns to the patient. All these systems permit the aspiration of the bubbles through the ports placed near each component.

51.2.4.4 The Gas Delivery System

Is composed of three basic components:

1. O₂ flowmeter
2. CO₂ flowmeter
3. Air/oxygen blender

51.2.4.5 Types of ECMO

1. Venous-arterial ECMO (VA)

Blood is drained from the right atrium to the pump and returned to the patient through an arterial cannula (aorta, carotid artery, or femoral artery). This is the mode which provides both cardiac and pulmonary support

2. Venous-venous ECMO (VV)

The catheter is a double lumen one placed in the right atrium which can remove and infuse blood flow at the same time. This system requires normal cardiac function and provides only respiratory support. Its function is dependent upon minimal "recirculation" of blood.

51.3 Indications for ECMO Support

Selection of appropriate patients for ECMO support is challenging, continually evolving, and institution dependent. There are several criteria which have been developed to help in this decision-making process. However, these criteria have been based on indicators of tissue perfusion and they are not applicable for all the cases.

There are several pediatric cardiac clinical scenarios in which ECMO is most frequently used:

1. Acute heart failure (AHF) in patients with congenital heart disease (CHD) and acute decompensation

2. AHF after Pediatric cardiac surgery (Ventricular dysfunction and failure to wean from cardiopulmonary bypass or low cardiac output syndrome (LCOS)
3. Severe pulmonary hypertension with CHD
4. Cardiomyopathy with acute heart decompensation as a bridge to recovery or transplantation
5. During cardiopulmonary reanimation or cardiogenic shock

Current publications from some centers have used it routinely in hypoplastic left heart syndrome repair (Stage I) for 24–48 h and some use it as a “prophylactic” tool in patients with a high risk of developing postoperative myocardial dysfunction [7].

ECMO support is used for both short and long term, depending upon the indications and the state of recovery. Despite improved outcomes in cardiac ECMO the outcomes remain inferior when compared to ECMO for respiratory indications. In this regard, careful selection of the patients is the main point to improve survival.

51.3.1 Acute Heart Failure (AHF)

Pediatric patients with AHF have a high incidence of cardiac recovery with mechanical assistance. The causes of acute heart failure can be postsurgical, or not related with cardiac surgery.

Postoperative AHF may occur in patients with previous normal myocardial function induced by prolonged cardiopulmonary bypass, complex surgery, cardiomy, and inadequate myocardial protection. Moreover, patients with previous cardiac dysfunction have an increased tendency to develop AHF after exposure to CPB.

There are two reasons to consider ECMO after surgery:

1. LCOS that usually occurs after surgery and has an etiology which is multifactorial.
2. Difficulty in weaning from CPB.

Currently, there is a tendency to initiate ECMO in the early postoperative period to maintain adequate perfusion, minimize ongoing myocardial insult, and enhance myocardial recovery.

The initiation of ECMO in these patients creates a favorable environment for myocardial recovery.

Studies have supported improved outcomes with the prompt implementation of ECMO after surgery is performed [8].

Considering AHF in a non-postoperative setting such as acute myocarditis and end-stage cardiomyopathy, ECMO is an important tool as a bridge to heart transplant or recovery. Higher mortality in this group of patients may be related to the length of time on ECMO before finding a suitable organ donor. The inevitable consequences of a prolonged ECMO run including multiorgan failure remain the limiting factor for survival [9].

Appropriate selection of patients with reversible ventricular dysfunction and avoidance of end organ failure are the essential goals of therapy. Infants with a severe coagulopathy that cannot be corrected or patients with major bleeding complications should generally not be considered for ECMO.

The contraindications to ECMO are constantly reassessed according to each center’s experience. However, there are certainly some conditions where the use of ECMO is not generally beneficial. Those include patients with incurable malignancy, extreme prematurity, and poor neurological prognosis [10, 11].

51.4 Pre-ECMO Evaluation

Several factors impact survival; these include younger age, low weight, severity of diagnosis, renal dysfunction, sepsis, and multiorgan failure. All of these should be carefully evaluated prior to surgery and an optimized management strategy will improve the outcomes.

Prior to initiating ECMO, a prepared team of surgeons, intensivists, cardiologists, perfusionists, and nurses with assigned roles should be informed, a coordinator will check and maintain the circuit, medications, and presence of the entire staff. It is recommended that each institution develop guidelines according to its experience and resources.

51.5 Timing

The decision to initiate ECMO in a patient after cardiac surgery follows the instinctive judgment of the surgical team; however, early institution of mechanical support has been related with better outcomes.

AHF produces a critical mismatch between tissue oxygen demand and delivery, both for systemic circulation and the myocardium. Medical management of myocardial dysfunction with inotropic support produces tachycardia, increased afterload, and myocardial wall tension increasing oxygen demand and consumption. These stresses increase cardiac injury and compromise the myocardial recovery. The early institution of ECMO allows for a rapid improvement in myocardial perfusion and maximizes oxygen delivery and cardiac output. Organ injury is the major contribution to morbidity and mortality in patients with cardiac dysfunction. As such, prompt optimization of systemic perfusion with mechanical support will avoid the multi-organ failure cascade.

Early mechanical circulatory support should be considered as a tool to address severe heart failure after surgery rather than as a “rescue” therapy. The early use of ECMO in that setting improves clinical outcomes and increases hospital survival [12].

51.6 Initiation of ECMO

51.6.1 Cannulation

Procedures for cannulation require preparation of the necessary equipment and medications including muscle relaxant, sedatives, heparin, and the medications required to the prime pump.

Options for veno-arterial cannulation include:

1. Transthoracic: Right atrium – Ascending aorta.
2. Peripheral:
 - a. Internal jugular vein–Common carotid artery (Right Side)
 - b. Femoral vein–Femoral artery

The selection of the cannulation site should be based on the specific conditions of the patient such as age, weight, accessibility, and indication. Transthoracic cannulation is usually indicated in the postoperative setting during emergent situations such as cardiac arrest or into the operating room.

In neonates and infants, not in the immediate postoperative period, cannulation of the neck is preferred. Larger children and adults will require femoral cannulation in order to achieve adequate drainage.

Disadvantages of the cannulation of the neck include the need of reconstruction or sacrifice of the vessels once the ECMO support is discontinued. Generally only the right neck is utilized.

In transthoracic cannulation, the aortic cannula should be placed above Sino-tubular junction. Adequate position of the cannula in all cannulations is confirmed by chest X-ray. The tip of the arterial cannula in neck cannulation should be just above the arch of the aorta at the base of the innominate artery, the venous cannula should be in the right atrium and with the patient’s neck hyperextended, proper position will be just slightly above the right hemidiaphragm. In the Femoral cannulation the arterial cannula should be advanced through the descending aorta.

The potential for left ventricular distension should be recognized. Increasing the flow through the pump will decrease the pulmonary flow and the venous return to the left heart when the pressure of the left atrium is high. An atrial septostomy, or separate left ventricular vent may be necessary to vent the left atrium. This procedure is especially necessary in patients with severe ventricular dysfunction. The decompression of the left ventricle is extremely important to decrease the risk of myocardial ischemia. Septostomy and venting is also useful to avoid pulmonary edema.

51.7 Operation of the System

Resistance: The flow through the system follows the Poiseuille’s Law; the resistance through the circuit is determined by the length and diameter of the tubing and by the viscosity of the fluids.

$$R = 8nl / \pi r^4 \text{ dyne-s/cm}^2 \text{ (R=resistance)}$$

With a longer tube the resistance is greater; resistance decreases with a larger radius. The highest resistance of the circuit is at the level of arterial cannula. Also the resistance is given by the difference between the pressures at the inlet and the outlet port. It is expressed as mmHg/LPM

The highest point of pressure (200–350 mmHg) is between the pump head and the membrane. The usual pressures in the circuit are between 80 and 250 mmHg. Pressures over 300 mmHg will cause hemolysis and could rupture the circuit. The difference in pressure

between the inlet and outlet of the circuit is close to 100–150 mmHg.

Causes of higher pressures post-membrane include: kinked tubing, clots, cannula which are tied too tightly, flow too great for the particular size of the cannula, malpositioning against the wall of the aorta or dissection of the aortic arch.

Blood flow: Depends on length and radius of the tubing, but in this case the amount of flow also depends on the diameter of the venous catheter. Large catheters maximize flow and improve oxygenation.

The “ideal” flow through the circuit should be laminar to avoid shear of the blood and clot formation which occurs at the angles and connections.

The level of pressure controls the direction of the flow. Negative pressures are necessary from the outflow catheter (venous catheter) up to the pump head. High flow makes these pressures more negative.

The flow produced by the pump is non-pulsatile.

Venous saturation is continually monitored and may decrease from the acceptable range due to anemia, blood loss, and a decrease in pump flow or an increase in oxygen consumption.

Gas Transfer: Oxygen transfer is related with the FIO_2 of the ventilating gas, hemoglobin level, bypass flow, and the oxyhemoglobin saturation.

Carbon dioxide transfer is related to the CO_2 level in the inlet blood, the rate of flow of oxygenator ventilating gas, and the CO_2 level in the oxygenator ventilating gas.

Pressure in the blood compartment should be greater than pressure in the gas compartment to avoid over-pressurization and the passage of gas into the blood resulting in air embolism.

Oxygen Delivery: The oxygen delivery will be determined by the oxygen content ($HbO_2 + O_2$ dissolved) and the blood flow. An increase in flow, Hb blender O_2 and a decrease of any right to left shunt increases the oxygenation. An adequate cannula size to maximize the venous blood drainage and the maintenance of a high hematocrit will help to provide adequate oxygen delivery.

Carbon dioxide: pCO_2 40–45 torr provides adequate respiratory drive for the brain. This can be achieved by intraining CO_2 to the ventilating gas of the membrane. CO_2 levels may also be maintained by increasing or decreasing the total sweep flow. Approximately, 0.8 m^2 of membrane surface will transfer 70 cc/min/m^2 of O_2 .

51.8 Management

51.8.1 Monitoring

End-organ perfusion:

1. SVO_2
2. Lactate
3. Thromboelastogram
4. NIRS
5. Oxygen saturation

Arterial Blood Gases (ABG) should be performed at least daily on the patient and compared with machine gases. Discrepancies may be related to the failure of the membrane

Flow Rate: Indicators of systemic perfusion will determine the adequacy of ECMO flow. Those include urinary output, body temperature, capillary refill, SVO_2 , and lactate. There are recommendations for flow rate according body surface area. Flows may be achieved at 120–150 cc/kg/min. Neonates may need-flow up to 200 cc/kg/min, where as in adults 80 cc/kg/min are adequate flow rates.

The blood flow rate is used according to the surface of the membrane, from 2.5 L/min until 13.5 L/min.

Patients with large PDA's or systemic-pulmonary shunts may require higher flow rates to maintain effective oxygen delivery.

51.8.2 Regulation of pO_2 and pCO_2

The concentration and flow of the gases will determine the gas exchange. The gas exchange occurs down a concentration gradient. The ventilatory gas flow is called “sweep flow.” The gas flow through the membrane is regulated by O_2 and CO_2 flow meters and an oxygen blender. The flow of the gas in the membrane is limited to ensure that the pressure of the gas is lower than the pressure of the blood. The FIO_2 can be manipulated by mixing O_2 with air. A larger membrane should be used to increase pO_2 when the FIO_2 is maximal (100%). The exchange of CO_2 is much more efficient than O_2 . To remove CO_2 from the system the gas flow should be increased. The percentage of CO_2 gas in the total gas flow should be below 5%.

The total gas flow should be maintained above 1 L/min to blow off the water vapor formed during the passage of cool gas over the warm blood.

To decrease the patient pCO_2 level:

1. Increase the O_2 flow
2. Decrease the CO_2 flow
3. Increase the level of ventilation by the respirator

To increase the patient pCO_2 level:

1. Decrease the O_2 flow
2. Increase the CO_2 flow
3. Decrease the level of ventilation from the respirator

To increase the patient's pO_2 :

1. Increase the rate of flow
2. Increase oxygenator FiO_2
3. Increase the FIO_2 in patient ventilator settings

To decrease the patient's pO_2 :

1. Decrease the rate of flow
2. Decrease the oxygenator FIO_2
3. Decrease the FIO_2 on the ventilator

51.8.3 Anticoagulation

The flow of the blood through the ECMO circuit produces profound effects on hemostasis. Platelets decrease in number and function due to the continuous microthrombi formation. In addition, activated platelets undergo a morphologic change and express GPIIb/IIIa receptors, increasing platelet binding with fibrinogen. The artificial material of the circuit interacts with proteins of the membrane surface and coagulation factors activating the coagulation cascade. This effect can be decreased by the administration of albumin to the circuit.

Heparin will block the clot formation by its binding and activation of Antithrombin III. Antithrombin III inactivates thrombin, factor Xa, IX, XI and XIII, and thrombin. Regular measurement of activated clotting time (ACT) is necessary to achieve equilibrium between the thrombus formation and bleeding. Heparin should be initiated with a beginning dose of 30–150 Units/Kg before cannulation to reach an ACT approximately 200 s to assure adequate systemic anticoagulation.

After initiation of ECMO a continuous infusion of Heparin of 25–50 Units/kg generally will achieve an ACT in the desired range of 180–200 s. If the ACT falls below 160 s or drops rapidly an additional bolus dose of heparin (10–20 Units/kg) may be necessary. If the ACT is greater than 300 s the heparin infusion should be continued at a lower rate.

Heparin requirements will change according to transfusions as well as renal and liver function.

During ECMO patients frequently require packed red cell transfusions to ensure adequate oxygenation. Additionally, FFP and cryoprecipitate are required when fibrinogen levels decrease below 100 mg/dl. Platelet count should be maintained over 100,000 with normal platelet function.

Anti-fibrinolytics are used to decrease fibrinogen consumption. Continuous infusions of Aminocaproic acid, Tranexamic acid, and Aprotinin have been shown to decrease the incidence of hemorrhage.

Other reported alternatives for anticoagulation include *Argatroban* and *Nafamostat mesilate*. They have in addition an anti-fibrinolytic effect. They can also be used to inhibit platelet aggregation induced by adenosine diphosphate (ADP), platelet activating factor, and arachidonic acid.

Heparin coated circuits have been developed with the goal of reducing heparin requirements. With the help of covalent or ionic forces, they are able to maintain locally the heparin within the internal surface of the circuit.

51.8.4 Fluids and Electrolytes

The non-pulsatile flow from the pump produces alterations in the metabolism of the renin and increases its production resulting in altered electrolyte balance. During ECMO, the requirements for potassium are often higher while requirements for sodium may be decreased. Loss of fluid through the oxygenator can be about 2 cc/m²/h.

Electrolytes: should be maintained at normal levels.

An adequate replacement would be:

$Na^+ = 0-2$ mEq/kg/day

$K^+ = 4-6$ mEq/kg/day

$Ca^{2+} = 30-50$ mg/kg/day

Daily fluids should range from 80–150 ml/kg/day of $D_{10}W$ to $D_{20}W$ depending on the age and other factors

such as sepsis, cerebral ischemia, etc. Electrolytes should be monitored every 8 h. The production of renin will produce a decrease in the urinary output that can be resolved with the addition of diuretics (Furosemide 1–2 mg/kg).

Blood glucose should be monitored every 4 h.

Hyperalimentation is usually maintained.

51.8.5 Pulmonary Function

Mechanical ventilation decreases atelectasis and reduces afterload and pulmonary resistance during the support period and should be maintained. Ventilation should be maintained with parameters that avoid barotrauma, pneumothorax, or collapse. Pulmonary care with periodic bagging, suctioning, and tracheal lavage should be performed. Ventilator parameters should be increased progressively during ECMO weaning.

51.8.6 Hemofiltration–Renal

During the first 24–48 h ECMO patients may experience a decrease in urine output. Hemodialysis may be needed during ECMO and can be performed via a direct connection to the ECMO circuit.

A hemofilter is connected to a port on the arterial side of the ECMO circuit and the outlet to a venous side. It is used to remove fluid from the patient during transfusions, fluid replacement, or when urine output decreases. The micropores of the hemofilter are not bigger than 5 μm and this permits constant blood flow through the hollow fibers. The system will pull out water and mineral solutes and heparin while red blood cells are retained.

51.8.7 Shunt

Due to the lower pulmonary resistance almost all infants develop a left to right or systemic to pulmonary shunt through a patent PDA during the first 2–3 days of ECMO, this can be suspected because of a persistent low paO_2 , pulmonary edema, and low urine output in the

face of high ECMO flows. These patients require a careful fluid management and consideration of surgical reduction of the degree of shunting (i.e. shunt ligation).

51.8.8 Nutrition

Early initiation of nutrition will improve recovery in these patients. Enteral nutrition has some advantages in maintaining the gut membrane integrity and the immunologic system. The risk of enterocolitis in neonates due to a decrease in splanchnic perfusion has not been demonstrated during ECMO. Parenteral nutrition increases the risk of obstruction of the membrane due to the fat emulsion (the lipid component should be administered in a different central venous line and not to the circuit if at all possible).

51.8.9 Medications and Blood Products

RBC's, albumin, IV infusion medications, antibiotics, and other medications are usually administered through the venous line. Hyperalimentation, heparin drips, and continuous infusion drips are usually administered through the arterial side after the oxygenator. Platelets, cryoprecipitates, antihypertensive agents, sedation drugs, and emergency medications should be given in the arterial line after the oxygenator and before the heat exchanger.

The volume of distribution of most medications is altered during ECMO due to changes in the total body water in addition to renal and hepatic metabolic changes, making the pharmacokinetics of most drugs unpredictable. Also some medications may bind to the circuit material decreasing their bioavailability.

51.9 Systemic Response to ECMO

When evaluating the systemic response to ECMO one should consider that there are some differences between CPB and ECMO with regard to the inflammatory response:

1. Longer duration of ECMO compared with CPB.
2. Protamine administration after CPB to reverse anticoagulation.
3. Hypothermia.
4. Presence of a cardiotomy reservoir with including cardiotomy suction and an air blood interface.
5. Ischemia and reperfusion injury during and after aortic cross-clamp.
6. Cardiorespiratory support is usually partial during ECMO support; the heart maintains the pulsatile flow preserving organ function and preventing vasoconstriction.

The activation of the inflammatory cascade is due to the exposure of the patient's circulating blood to the surface of the circuit. Inflammation triggered by ECMO can lead to organ dysfunction and derangement of the hemostatic and fibrinolytic cascades.

The neutrophils are the final effectors of cell and tissue damage. Their activation maintains and amplifies the inflammatory cascade. Clinically, the peak value of leukocytosis during ECMO is usually (36 h after initiation) and is correlated with worsening of the pulmonary dysfunction. Plasmapheresis and leukocyte filtration are techniques used to decrease the number of activated cells in the plasma. There are not conclusive studies, but these modalities are frequently used.

Activation of the immunologic system has been demonstrated by:

1. An increase of the complexes of factor XIIa-C1 esterase inhibitor
2. A decrease of kallikrein inhibitory capacity
3. An increase of thrombin–antithrombin formation
4. The generation of fibrinogen degradation products

The system activates platelets causing morphologic changes and the release of their granule content. This platelet activation produces a complex interaction with cytokines, leucocytes, complement system, and other systemic inflammatory mediators.

Medications used during ECMO are often given to decrease the inflammatory response and to modulate the platelet activation.

Use of steroids has been correlated with a reduction of pro-inflammatory cytokines and an enhanced level of anti-inflammatory IL-10, in the clinical setting its use has been correlated with shorter ECMO support duration and mechanical ventilation days. The improvement of the pulmonary microcirculation may play a major role in the beneficial effect of the steroids during ECMO.

51.10 Weaning

The decision to wean ECMO should depend on the condition of the patient, the correction of the underlying anatomical or physiologic defect, the neurological prognosis, and the family dynamics. Despite its generally limited time frame some publications have reported ECMO support for up to 6 weeks, the neurological outcomes and quality of life remain unclear. Poor survival has generally been described after 3 weeks of support in different studies [13].

Biochemical and clinical indicators of improvement include: during a decrease pump flow, adequate blood pressure is maintained with a recovery of the cardiac function by echocardiography.

Several attempts at weaning ECMO may cause reperfusion injury and can be detrimental. Thus, it is reasonable to have several positive indicators before attempting a trial. It is also important to balance this with the knowledge that patients having a shorter duration of support will have a greater chance of survival [14, 15].

51.11 Complications

Complications of ECMO include mechanical, hemorrhagic, neurologic, renal, cardiovascular, pulmonary, infectious, and metabolic.

The most common complication, excluding requirement of inotropic support, in the neonatal group is bleeding and it is also the main cause of death. Organ injury is the major contribution to morbidity, especially neurologic injury, which is the most common reason to discontinue ECMO [16].

Stroke, disseminated intravascular coagulation (DIC), and renal dysfunction or multiorgan dysfunction has been identified as the major complications causing death in ECMO after pediatric cardiac surgery.

The highest reported mechanical complication includes clots in the system.

Renal insufficiency requiring hemofiltration is also one of the most common causes and is associated with high mortality.

Complications of cannulation include misplacement of the cannulae which may cause occlusion, injury, and damage to the aortic wall or valve leaflets.

The major complications of ECMO have been related to cerebral edema and intracranial hemorrhage. Patients should be followed closely to detect any presence of seizure. Intracranial hemorrhage may be examined for with head ultrasounds. An intracranial hemorrhage greater than grade II generally requires adjustments in heparin doses and close follow up and potential discontinuation of support.

51.11.1 Failure of Circuit

Membrane failure can be evidenced by an increase in the CO₂ content and a decrease of the O₂. The failure is caused by membrane defects and exposure of the membrane to high outflow pressures or clots.

Consideration should be given to changing the circuit or its components when there is a clot in the circuit (post-membrane) or when there is a concern of the possibility of rupture.

Power failure: The pump should be hand-cranked manually until the power returns.

Air: If the air is distal to the oxygenator connection, ECMO flow should be stopped immediately. When the air is in the venous line it can be trapped in a bridge, bladder, or the oxygenator and removed.

51.12 Current Outcomes

The large surface area that ECMO circuit requires enhances the inflammatory response, with activation and consumption of the coagulation factors increased hemolysis, thrombosis, and multiorgan dysfunction. New systems of circulatory support without oxygenators permits prolonged periods of support and currently are seeing increasing acceptance and better outcomes [17]. The greatest challenges of ECMO support are related to: anticoagulation, neurological outcome, duration of support, recovery, trauma to blood elements and mechanical issues (Table 51.2)

Cardiac arrest, bleeding, renal failure, and prolonged intubation prior to ECMO have been identified as risk factors for death [16].

Table 51.2 Current ECMO outcomes for cardiac support

Author, year of publication, city,	Years of study, number of patients	ECMO indication	Hospital survival	Cause of death	Neurological injury after survival
Alsoufi et al. 2007 [21] (Toronto–Saudi Arabia)	2000–2005 80 patients	ECMO in refractory cardiac arrest	37%	Ischemic brain injury	11%
Fisher et al. ELSO registry 2007 [22] (Toronto–Michigan)	1987–2005 151 patients	For primary graft dysfunction after lung transplantation	42%	Multiple organ failure (12%)	12%
Delmo Walter EM et al. 2007 (Berlin)	1987–2005 110 patients	Perioperative circulatory failure	57%	Multiple organ failure	
Sachweh et al. 2007 [13] (Aachen)	1996–2007 24 patients	Failure to wean from cardiopulmonary bypass	50%	Multiple organ failure	4%
Pizarro C et al. 2006 [17] (Wilmington)	2004–2005 44 patients	For postoperative rescue of high-risk patients following cardiac repair:	50%	Multiple organ failure	10%
Thourani V et al. 2006 [23] Atlanta	27 patients	(VA-ECMO) in pediatric cardiac support	59%		
Ravishankar C et al. 2006 [7] Philadelphia–Pittsburgh	1998–2005 382 patients	After stage I reconstruction	38%		
Hoskote A et al. 2006 [24] Toronto	1997–2003 25 patients	After staged palliation of a functional single ventricle	44%	Multiorgan failure	

(continued)

Table 51.2 (continued)

Chow NK 2006 [24] Tapei	1987–2004 204 patients	For Perioperative Cardiac Allograft Failure	52%	
Allan C et al. 2006 [25] Boston	1996–2004 22 patients	Emergent use of ECMO during pediatric cardiac catheterization	82%	48%
Balsaim G et al. 2006 [15] Jeddah	2000–2004 26	After pediatric cardiac surgery	46%	Stroke, DIC
Chaturvedi RR et al. [18] 2004	81 patients	Postcardiotomy Cardiac Failure	Initiated in ICU : 29% Initiated in OR : 64%	
Mehta U et al. 2000 [24]	8 patients	Cardiomyopathy, myocarditis, or arrhythmia	End-stage dilated cardiomyopathy: 80% Acute myocarditis: 33%	
Morris MC et al. 2004 [18]	1997–2004 137 patients	Pediatric cardiac ICU	39%	
Del Nido P et al. 1992 [26]		After sudden cardiac arrest in the postoperative period	55%	

A multivariate analysis from Morris et al. [18] revealed that age less than 1 month and male gender significantly affected hospital survival in patients who required ECMO after cardiac surgery. They did not find any significant independent predictors in the non-surgical ECMO group. Furthermore, they did not find that failure of separation from the cardiopulmonary bypass machine or cardiac physiology alterations (single ventricle) were correlated significantly with hospital survival.

The duration of ECMO has been shown to affect survival. While some have shown that most patients who survive recover contractile function within 48–72 h. The time interval from CPR to rescue R-ECMO has been noted as a limiting factor in the effectiveness of any rescue during acute cardiac and pulmonary failure. At the Children's Hospital of Pittsburgh, survival was 100% in patients with CPR times less than 15 min, whereas survival was 55% in those who underwent CPR for more than 42 min.

51.13 Pediatric Ventricular Assist Devices

With the advent of improved technology, circulatory support without an oxygenator is available for the pediatric population. The experience published by

different institutions around the world is growing. Some studies have demonstrated improvements in survival, especially when the indication is for long-term bridge in pre-transplant patients [16, 19].

Advantages:

1. Relatively easy implantation
2. Fast set-up time
3. Low priming volume
4. Low level of anticoagulation
5. Less trauma and risk of infection
6. More mobility of the patient
7. Do not require ICU
8. Decreased requirement of anticoagulation
9. Longer term support
10. Pulsatile flow
11. Small size

The indication for circulatory support with a Ventricular Assist Devices (VAD) system is oriented to the patient disease process [19, 20].

Types and availability of VADs used in the pediatric population include:

1. *Paracorporeal:*

a. *Pneumatic pulsatile*

- i. Abiomed BVS 5000 (Abiomed Inc., Delaware, MA)
- ii. Berlin Heart EXCOR (Berlin Heart AG, Germany)

- iii. MEDOS HIA (MEDOS, Germany)
- iv. Heartmate I (Thoratec, Plasanton, CA)
- v. Toyobo (Japan)
- vi. Novacor (Baxter, Irvine CA)

2. Intracorporeal or Implantable

a. Continuous Axial or Centrifugal Flow:

- i. MicroMed DeBakey (Micromed technologies)
- ii. Jarvik 2000 (Jarvik, NY)
- iii. The INCOR VAD Berlin Heart (Germany)
- iv. Thoratec Heartmate II Duraheart (Temuro, Japan)

51.13.1 Devices Underdevelopment

1. Pediatric Ventricular Assist Device (Penn State)
2. Pediatric Jarvik 2000 (Jarvik Heart Inc. NY)
3. PediaFlow VAD (Pittsburgh)
4. PediPump (Cleveland Clinic)
5. Levitronix centrifugal Pump (Pittsburgh)
6. Pediatric Cardiopulmonary Assist System (Enson)
7. Pediatric pVAD (Cardiac Assist, Inc. Pittsburgh)
8. Toddler VAD (Pittsburgh)

51.13.1.1 Anticoagulation

Anticoagulation management for VADs reflects the post-surgical nature of VAD implantation and focuses more heavily on platelet inhibition. Unfractionated heparin should be started 24–48 h after implantation if the platelets count is higher than 20,000/ μ L and there is no clinical bleeding.

51.13.1.2 Unfractionated heparin therapy (IV)

Initial dose is 10 Units/kg/h (15 Units/Kg/h < 12 months of age), after 6 h if the patient is not bleeding, increase infusion to 20 Units/kg/h (28 Units/kg/h < 12 months of age). PTT and antifactor X_a should be obtained 6 h after the increased dose. Therapeutic range for PTT of 1.5–2.5 times (patient baseline) and antifactor X_a of 0.35–0.5 U/ml, then use PTT to follow therapy.

Tromboelastograms should be obtained in the early postoperative period and every 24 h during the first week

Heparin should be increased if R < 8.0 and decreased if R < 15

In addition, renal and hepatic functions require monitoring.

51.13.1.3 Platelet Inhibition Therapy

Initiate Dipyridamole 4 mg/kg/day (max dose 10 mg/kg/day) after 48 h if there is not bleeding, patient is hemodynamically stable, and platelet function in the TEG is normal (MA >56 mm, G > 6 and <10, araquidonic acid inhibition is <70%) and the platelet count is >40,000.

Aspirin may be started (1 mg/kg/day) at day 4 post-implantation when the MA > 72 mm and G >8.

Fresh frozen plasma (10–15 ml/kg) or platelets (1 unit/5 kg body weight) might be administered in case of decrease in clot factors or platelet dysfunction.

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Chapter 52

Heart Transplantation

Steven A. Webber and Victor O. Morell

52.1 Introduction

Cardiac transplantation offers the only hope for survival and improved quality of life for selected children with end-stage heart disease, whether due to cardiomyopathy or congenital defects. The first pediatric transplant was performed by Kantrowitz and associates in December, 1967, only a few days after Dr. Christian Barnard's pioneering operation in an adult. Interest in transplantation of the heart declined throughout the 1970s, due to the high mortality resulting primarily from lack of effective immunosuppressive medications. A resurgence of clinical activity developed in the early 1980s with the introduction of cyclosporine, the first oral immunosuppressive agent with relative specificity for inhibition of T-lymphocytes, the primary mediators of allograft rejection. This resulted in dramatic improvements in survival of all transplanted organs. Progress in the field of pediatric heart transplantation has been recently summarized [1]. With improvements in candidate and donor selection, preoperative management, surgical technique and early postoperative care, approximately 95% of heart transplant recipients should leave hospital alive and in good health after transplantation. Furthermore, pre-transplantation mortality has fallen. Thus, survival at all times after listing has also improved. This section will give an overview of the current state-of-the-art of pediatric heart transplantation, focusing on issues of key interest to those who work in the intensive care unit.

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52.2 Indications for Transplantation

Transplantation of the heart is generally considered to be indicated when expected survival is less than 2 years, and/or when there is unacceptable quality of life. Cardiomyopathy (predominantly dilated forms) and complex congenital heart defects remain the primary indications, and together account for approximately 90% of transplantations undertaken in children [2]. World-wide transplant activity has remained constant over the last decade. Diagnoses leading to transplantation are age dependent, with congenital heart disease accounting for two-thirds of transplants in the infant age group, with cardiomyopathy accounting for a similar proportion among adolescents [2].

The appropriate indications for heart transplantation in childhood were summarized in a 1999 report from the Pediatric Committee of the American Society of Transplantation [3]. More recently, a consensus group of the American Heart Association has addressed the same topic [4]. In general, there is broad consensus in the pediatric cardiology community as to when transplantation is indicated. Perhaps the most controversial indication for heart transplantation is hypoplastic left heart syndrome and related pathologies in the newborn. Survival rates in excess of 80% at 1 year may be achieved in experienced centers with either Norwood reconstruction or primary transplantation for this condition. Median waiting times for newborn heart transplant candidates are approximately 2 months in the United States (and longer in some countries), resulting in very high costs of care prior to transplantation, significant pre-transplant morbidities, and a wait list mortality as high as 25%. In light of these observations, most centers have moved away from transplantation, and toward staged reconstruction, for neonates with

HLHS. This strategy increases availability of organs for other infants with cardiac disease unsuitable for surgical palliation.

Relative and/or absolute contraindications include chronic infection with either hepatitis B or C, or human immunodeficiency virus, prior non-adherence with medical therapy, recent or current treatment of malignancy with inadequate follow up to ensure likely cure, active acute viral, fungal or bacterial infections, excessive and fixed pulmonary vascular resistance (above 10 IU), inadequate intraparenchymal pulmonary vascular bed, diffuse pulmonary vein stenosis, and major extracardiac disease felt to be nonreversible with heart transplantation (i.e., severe systemic myopathy). Inevitably, some centers consider specific contraindications absolute, whereas others may feel they are relative. Decision making is based on consensus discussion among all team members, including intensive care staff.

52.3 Evaluation of the Candidate

Currently, the majority of children undergoing heart transplantation are hospitalized in the intensive care unit at the time of transplantation. For many, the transplant will occur during the first hospital admission. Thus, the intensivists will often be involved in the transplant evaluation. The evaluation includes the assessment of expected survival without transplantation, the patients' current quality of life, the potential for alternate surgical or medical therapies, as well as the inherent risks of the transplant surgery itself. A typical evaluation protocol is shown in Table 52.1.

52.3.1 Anatomic and Hemodynamic Considerations

The most complex anatomy may be transplanted provided the lung vasculature is adequately developed and pulmonary vascular resistance is acceptable. Anatomic points of most interest to the surgeon include abnormalities of cardiac and visceral situs (especially anomalies of the systemic and pulmonary venous return), as well as the size and anatomy of the main and branch

Table 52.1 Evaluation of candidates for heart transplantation

History and physical examination
Required consultations:
– Pediatric cardiologist, congenital cardiovascular surgeon, cardiac anesthesiology, infectious disease specialist, psychiatrist or psychologist, transplant coordinator, social worker
Additional consultations (as required):
– Neonatology, genetics, neurology, dental, oncology, immunology, nephrology, nutritional services, physical/occupational therapy, developmental pediatrics, hospital financial consultant
Cardiac diagnostic studies
– Chest radiograph, electrocardiogram, echocardiogram, cardiac catheterization
– In selected patients: Exercise test, ventilation-perfusion scan, chest CT or MRI, pulmonary function tests
Blood type (ABO), anti-HLA antibody screen, complete blood count and white cell differential, platelet count, coagulation screen, blood urea nitrogen, serum creatinine, glucose, calcium, magnesium, liver function tests, lipid profile, brain natriuretic peptide.
Serological screening for antibodies to the following pathogens: cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex, human immunodeficiency, varicella, hepatitis A, B, C, D and measles; antibodies to <i>Toxoplasma gondii</i>
PPD/Mantoux placement
Update immunizations including hepatitis B, pneumococcal and influenza (in season)

pulmonary arteries, including the presence of stenoses, distortions, and non-confluence. Intracardiac anatomy is less important since the bulk of the cardiac mass will be explanted. Abnormalities in the relation of the great arteries usually pose few problems. Attention must also be given to the relationship of key structures such as right ventricular-pulmonary artery conduits or giant right atria (after Fontan procedure) to the posterior aspect of the sternum. Computed tomography and/or magnetic resonance imaging are well suited to delineating cardiac anatomy, but cardiac catheterization is usually indicated pre-transplantation to assess pulmonary vascular resistance. Excessive fixed resistance will result in acute donor right ventricular failure and an inability to wean the patient from cardiopulmonary bypass.

In general, children with indexed pulmonary vascular resistance (PVRI) ≤ 6 IU are considered low risk for acute donor right heart failure. If resistance is between 6 and 10 IU, the risks are higher, but transplantation is still generally not considered to be contraindicated. A PVRI in excess of 10 IU is usually considered as a contraindication to isolated heart transplantation unless there is a major fall (to well below 10 IU) with

pulmonary vasodilator therapy. In borderline cases, restudy of hemodynamics after several days of inotropic and vasodilator therapy may be indicated, as pronounced falls in PVRI are occasionally seen. It should be noted however, that rapid fall in pulmonary resistance can lead to acute elevation in left atrial pressure in patients with very poor left ventricular function, even precipitating pulmonary edema. The role of chronic VAD therapy as a strategy to unload the left ventricle and reduce excessive PVRI to prepare children for orthotopic transplantation is unknown at this time.

52.3.2 Laboratory Investigations

These are summarized in Table 52.1. Blood typing is necessary to assure ABO compatibility with the transplanted organ, though infants and young children with absent or low anti-A and anti-B isohemagglutinin titers may be safely transplanted across traditional ABO barriers. This strategy was introduced by West and colleagues in Toronto [5] and is based on the principle that isohemagglutinins against blood group antigens do not normally develop until the latter part of

infancy. Transplantation across blood group barriers before the development of naturally occurring anti-A and anti-B isohemagglutinins appears to result in outcomes comparable to ABO compatible transplants [5]. Furthermore, most of the transplanted infants did not form antibodies against donor blood group antigens during long-term follow up, possibly due to the development of B cell tolerance. This strategy has profound implications for ICU care, since use of blood products pre- and post-transplant must be carefully planned to avoid transfusion of blood products containing inappropriate anti-A and anti-B antibodies. Acceptable products should be summarized in collaboration with the blood bank and posted at the patient's bedside. These restrictions will apply indefinitely and information on acceptable blood products must be provided to the family prior to hospital discharge.

Evaluation for the presence of preformed anti-HLA antibodies ("sensitized") is performed using panel reactive antibody and solid phase assays. Infectious disease evaluation includes serologic testing for cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella, herpes simplex virus, *T. gondii*, human immunodeficiency virus (HIV), measles and hepatitis viruses A, B, C, and D. Serologic status for these agents may guide prophylaxis as well as the diagnostic evaluation of post-transplantation fever. Very rarely, it may lead to exclusion of candidacy of the child for transplantation. The infectious disease evaluation should also include review of immunization history. Those candidates in whom transplantation is not likely to be imminent should undergo an update of appropriate immunizations at the time of the pre-transplant evaluation.

Table 52.2 Evaluation of the cardiac donor

History

- Donor age, height, weight, and gender
- Cause of brain death
- History of cardiac arrest and length of resuscitation
- Evidence of chest trauma
- History of intravenous drug usage
- Past history of cardiovascular disease
- Distance from transplant center
- History of malignancy

Cardiovascular status

- Heart rate, blood pressure, central venous pressure
- Fluid balance
- Blood gas
- Types and doses of intravenous inotropes
- Inotropic support increasing or decreasing

Cardiovascular testing

- Electrocardiogram
- Chest radiograph
- Echocardiogram
- Cardiac enzymes

Other testing

- Infectious disease screen: CMV, EBV, *T. gondii*, HIV-1, HIV-2, HTLV-1, HTLV-2, RPR, Hepatitis B and C
- All culture results since admission to intensive care unit

52.3.3 Consultations

Each candidate is evaluated by a multidisciplinary team that includes the transplant cardiologist and surgeon, social worker, transplant coordinator, and infectious disease expert. A screening psychiatric/psychological examination of the patient and their family is also very beneficial to the transplant team and the patient and their family. The primary purpose of this evaluation is to identify patients and families at high risk for poor psychosocial outcome, while waiting for transplantation and after transplantation.

Evaluation of past history of non-adherence to medical therapy is critical. Additional consultations may be required from specialist services such as hematology–oncology (when there is past history of malignancy), child development, genetics, neurology, and feeding and nutritional specialists. Patients with Fontan circulation require evaluation of the liver for evidence of cirrhosis and may require formal hepatology consultation.

52.4 Donor Evaluation

Although the intensivist is not usually involved in the donor evaluation process, it is important for the ICU team to know about key aspects of the potential donor. Evaluation of the donor heart begins with a careful review of the history. This includes donor age and gender, body size, cause of death, presence of any chest trauma, need for cardiopulmonary resuscitation, length of resuscitation, and evaluation of the hemodynamic status of the donor (including blood pressure, heart rate, and central venous pressure, if available). The amount of inotropic support, and trends in usage over time, are also noted. A history of cardiopulmonary resuscitation is not, in itself, a contraindication to cardiac donation for pediatric recipients. It must be recognized that brain death results in dramatic physiological disturbances in the donor. These include temperature instability with hypothermia, circulatory volume changes (most commonly depletion) and neuroendocrine dysfunction. There is depletion of circulating thyroxine, cortisol, insulin, glucagon, and antidiuretic hormone (ADH).

To rule out structural abnormalities and to evaluate cardiac function, a complete echocardiogram should be performed. Most centers avoid the use of donor hearts whose systolic function is more than mildly impaired after treatment with inotropic agents or thyroid hormone (e.g., shortening fraction less than 26%, ejection fraction less than 50%). Some degree of atrioventricular valvar regurgitation is common after brain death and mild degrees do not constitute a contraindication to organ donation. Pericardial effusion may be indicative of myocardial contusion. A 12-lead electrocardiogram should be performed. Mild nonspecific ST and T wave changes are commonly present, and usually reflect central nervous system effects, electrolyte disturbances or hypothermia. These do not contraindicate organ donation. Interpretation of cardiac enzymes may be

difficult in the setting of generalized trauma. However, the elevation in cardiac troponin I levels in donor serum appears to be a useful predictor for acute graft failure after infant heart transplantation. Evaluation of adult donors for coronary artery disease by selective coronary arteriography is commonplace in adult transplantation. Use of older donors (e.g., above 35 years of age) for pediatric recipients is associated with high risk of post-transplant coronary disease and poor long-term survival [6]. Such donors are generally avoided.

Size matching is a critical issue in the selection of potential donors. Most centers avoid under-sizing the donor below 75–80% of recipient weight. Below this, cardiac output of the donor may be insufficient to meet the needs of the recipient. Use of oversized donors is common. Most candidates will have marked cardiomegaly, leaving ample room within the chest for an oversized donor heart. Use of donor: recipient weight ratios of 2.5:1 is common in pediatric practice, and ratios of 3–4:1 have been successfully used, especially in newborn and infant candidates. Marked over-sizing often results in delayed sternal closure and in infant recipients, donor : recipient weight ratios of greater than two have been associated with a more prolonged ventilator course and increased risk of primary graft failure [7]. Oversized donor hearts may also give rise to a postoperative syndrome characterized by high output state associated with systemic hypertension, raised intracranial pressure, and even mental status changes.

It has been suggested that over-sizing of donors may improve outcome when there is significant preoperative pulmonary hypertension in the recipient. Certainly, under-sizing should be avoided in the presence of recipient pulmonary hypertension, and in adults it has been shown that use of female donors is associated with higher perioperative mortality when recipient pulmonary vascular resistance is elevated.

All donors should be screened for CMV, EBV, human immunodeficiency viruses 1 and 2 (HIV-1, HIV-2), human lymphotropic viruses 1 and 2 (HTLV-1, HTLV-2), and hepatitis viruses A, B, and C. Donors are also screened for syphilis and for antibodies to *Toxoplasma gondii*. Presence of antibodies to CMV, EBV or *T. gondii* do not constitute contraindication to transplantation but helps guide post-transplantation therapy and surveillance. Evidence of donor retroviral infection (HIV or HTLV) is considered an absolute contraindication to heart transplantation. The presence

of donor hepatitis B surface antigen is also usually considered an absolute contraindication to heart donation. The usage of hepatitis C positive donors remains controversial. Evaluation of the cardiac donor is summarized in Table 52.2.

52.5 Surgical Considerations

There are several factors contributing to the complexity of cardiac transplantation in patients with congenital heart disease, including:

1. The high incidence of anatomical abnormalities
 - a. Anomalous systemic and/or pulmonary venous return
 - b. Dextrocardia with/without situs inversus
 - c. Malposition of the great arteries
2. Small size
 - a. Resulting in significant size mismatch between the donor organ and the recipient
3. Previous operations
 - a. Altered anatomy
 - b. Abnormal circulatory physiology
 - c. Increase risk of bleeding

Therefore, it is crucial to clearly delineate the patient's cardiac anatomy at the time of transplantation in order to identify special needs and adequately plan the surgical procedure.

52.5.1 Recipient Cardiectomy

The recipient cardiectomy is performed under cardiopulmonary bypass with bicaval cannulation and an LV vent, at a temperature of 28–32°C. After aortic clamping, our preference is to transect the SVC and then the IVC, leaving a small cuff of atrium attached to each cava (preserving the length). The aorta and pulmonary arteries are then divided proximally; finally the left atrium is transected, leaving a generous cuff of atrium attached to the pulmonary veins. If the biatrial technique is being utilized then a segment of the right atrium is left connected to the superior and inferior cava.

52.5.2 Implantation

At the Children's Hospital of Pittsburgh we are utilizing the bi-caval technique as our procedure of choice in all patients, irrespectively of their age and size (Fig. 52.1). This technique minimizes atrial suturelines and provides for more normal atrial geometry. When compared to the biatrial technique (Fig. 52.2), it appears to have a lower incidence of postoperative arrhythmias and thrombus formation. Also, it may be associated with improved atrio-ventricular valve function and post-transplant survival.

52.5.2.1 Anomalous Systemic Venous Return

When bilateral SVCs are present (without a connecting vein) our preference is to obtain the full length of the donor's SVC and the innominate vein in order to perform an end-to-end anastomosis between the recipient's left-sided cava and the donor's innominate vein. If the LSVC drains into the coronary sinus, then another alternative is to preserve the coronary sinus during the cardiectomy and perform a biatrial cardiac anastomosis, leaving the coronary sinus draining into the right atrium. If a connecting vein is present, the left SVC can be simply ligated.

Dextrocardia with Situs Solitus

In patients with dextrocardia and normal systemic venous return the only modification we utilize is the release of the left side of the pericardium in order to allow the apex of the heart to protrude into the left hemithorax.

Dextrocardia with Situs Inversus

For these patients our approach has been to resect the interatrial septum and reroute the SVC and IVC flow to the right side using atrial flaps as tunnels. Cardiac transplantation is then performed using the biatrial technique.

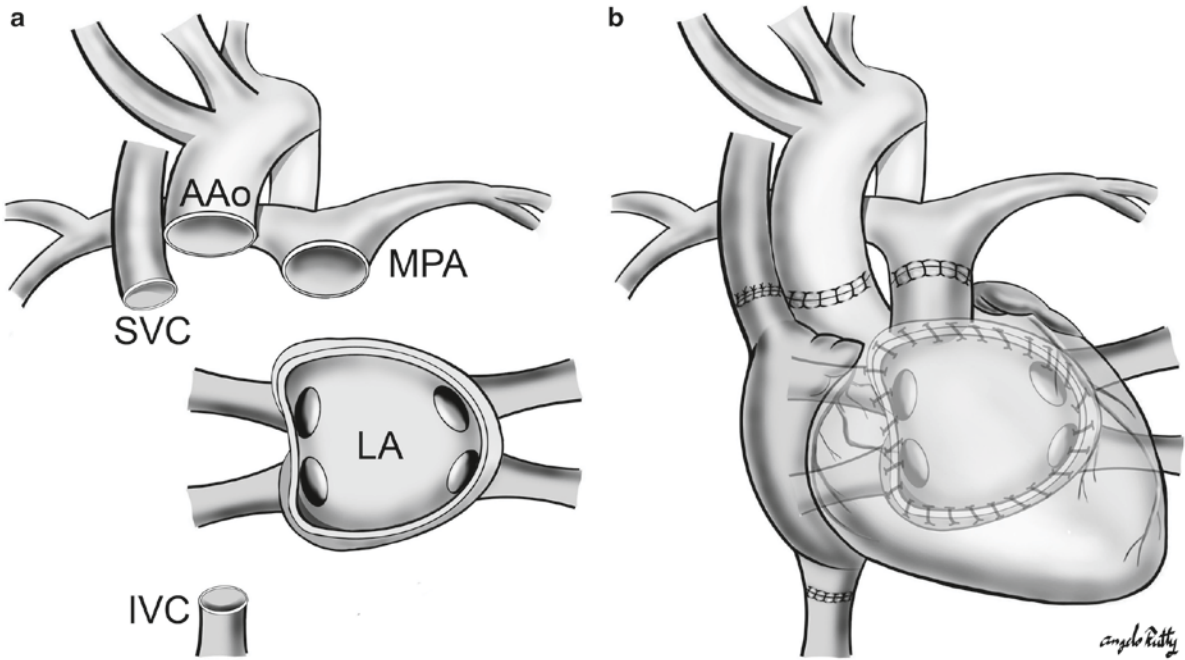


Fig. 52.1 Bicaval technique. (a) The recipient cardiectomy has been performed; note the left atrial (LA) cuff and the transected ends of the superior vena cava (SVC), inferior vena cava (IVC), ascending aorta (AAo), and main pulmonary artery (MPA). (b) The donor

organ has been sutured in place; all the anastomosis are performed with a running non-absorbable suture except for the SVC suture line in which interrupted sutures are used to prevent the development of late stenosis (especially important in neonates and infants)

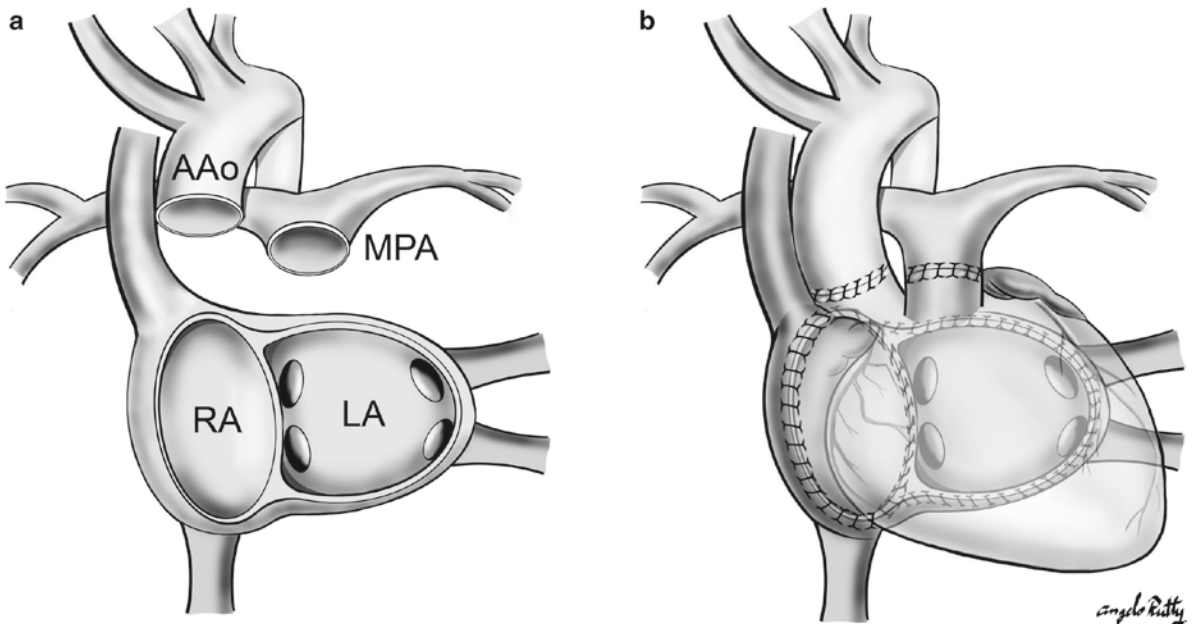


Fig. 52.2 Biatrial technique. (a) The recipient cardiectomy has been performed; note the left atrial (LA) and right atrial (RA) cuffs and the transected ends of the ascending aorta (AAo) and

main pulmonary artery (MPA). (b) The donor organ has been sutured in place; all the anastomosis are performed with a running non-absorbable suture

52.5.2.2 Anomalous Pulmonary Venous Return

In patients with total anomalous pulmonary venous return, we first proceed with a standard intracardiac repair, connecting the pulmonary venous confluence to the left atrium, followed by cardiac transplantation.

52.5.2.3 Hypoplastic Left Heart Syndrome

Cardiac transplantation in neonates and infants with hypoplastic left heart syndrome involves one extra step, the reconstruction of the hypoplastic aortic arch. Therefore, during the procurement, it is important to harvest as much of the donor aorta as possible.

52.6 Postoperative Management and Early Complications

Many of the fundamental principles of early postoperative management after heart transplantation are similar to those for pediatric patients undergoing other procedures with cardiopulmonary bypass. This section focuses on aspects of care that are specific to the transplant recipient.

52.6.1 Cardiovascular Considerations

52.6.1.1 Inotropic Agents

Abnormalities in cardiac function are inevitable due to the obligatory hypoxic – ischemic insult that the donor heart endures. Recovery of systolic function is usually rapid. Abnormalities in diastolic function, however, may persist for many weeks. Most heart transplant recipients will benefit from low dose inotropic support in the immediate postoperative period, though often this is only required for 2–3 days. The choice of inotrope will reflect both physician preference and hemodynamic factors such as heart rate, pulmonary vascular resistance, and blood pressure. Low dose dobutamine and isoproterenol are common

choices. The latter is sometimes recommended because of its combined properties of chronotropy, inotropy, and pulmonary vasodilatation. The addition of a combined vasodilator/inotropic agent such as milrinone is logical when there is low cardiac output and evidence of high systemic vascular resistance. Occasionally, particularly in infants with markedly oversized donors, the simplest way to improve cardiac function is to leave the chest open at the end of the transplant procedure. The insertion of a Swan-Ganz catheter may provide useful hemodynamic information throughout the first 48 h of postoperative course.

52.6.1.2 Systemic Hypertension

In contrast to the non-transplant cardiac surgical patient, systemic hypertension is common. Many factors contribute including vigorous function of an oversized donor organ and use of high dose corticosteroids. It is not unusual to observe quite severe systolic hypertension within 24 h of a successful transplant procedure. If good ventricular function is confirmed by echocardiogram, rapid wean of inotropic support is performed. Where systemic resistance appears high, intravenous vasodilators (i.e., sodium nitroprusside, nicardipine) are a logical choice. In the case of a vigorous oversized organ, some have advocated beta blockade.

52.6.1.3 Pulmonary Vascular Resistance

The importance of pulmonary vascular resistance as a risk factor for acute donor right ventricular failure is discussed above. If there is a concern about elevated pulmonary vascular resistance, on the basis of preoperative evaluation, additional precautions should be taken. Nitric oxide is begun in the operating room and is used to wean from cardiopulmonary bypass. Acidosis must be avoided and high levels of inspired oxygen are provided. Hyperventilation is performed and generous sedation is provided in the early postoperative period. If necessary, prostaglandin E₁ can also be used. The right heart may require significant inotropic support, and sometimes epinephrine may be required in addition to milrinone and dobutamine. If right ventricular dysfunction persists with poor cardiac output despite this level of support, then mechanical

assistance should be provided. If pulmonary vascular resistance is moderately elevated pre-transplantation, (or if there is an acute elevation in resistance following bypass in a child with previously low resistance), then 24–48 h of support will often enable the right ventricle to recover enough to support the circulation, despite elevated pulmonary pressures. If acute donor right heart failure reflects poor candidate selection (e.g., indexed pulmonary resistance greater than 10 IU after vasodilator challenge), then recovery of right heart function is unlikely.

52.6.1.4 Cardiac Rate and Rhythm

Postoperative tachy- and brady-arrhythmias have been observed in children following heart transplantation. The commonest rhythm abnormality (other than sinus tachycardia) is sinus node dysfunction leading to sinus bradycardia, with or without an atrial or junctional escape rhythm. The denervated sinus node responds appropriately to exogenous chronotropic agents and isoproterenol is useful in this respect. A simpler approach is atrial pacing, and all transplant recipients should have temporary pacing wires placed in the operating room. Sinus node dysfunction reflects ischemic and/or traumatic injury, but usually recovers in a few days. Ventricular ectopy and nonsustained ventricular tachycardia are also quite common in the first week or two after transplantation. These presumably relate to the obligatory ischemia-reperfusion injury, and rarely require treatment.

The fresh cardiac allograft has limited ability to increase stroke volume, and therefore establishing an adequate heart rate is important for maintaining cardiac output. It is our practice to maintain a heart rate that reflects slight tachycardia for age. For instance, in an infant, a heart rate of 140–150 would be maintained, and in a teenager a heart rate of around a 100 beats per minute would be acceptable. Atrial pacing is most commonly used to control the heart rate.

52.6.1.5 Primary Graft Failure

Failure to wean from cardiopulmonary bypass, or early postoperative graft failure, is a serious complication associated with high mortality. The term primary graft failure is often reserved for the finding of acute left

ventricular or biventricular failure not due to high pulmonary vascular resistance. Poor donor selection, very prolonged ischemic time, poor preservation technique and hyperacute rejection should all be considered. The latter is extremely rare with routine recipient pre-transplant screening for anti-HLA antibodies. When primary graft failure occurs (not due to hyperacute rejection), recovery is frequently possible if the circulation can be supported. This is usually achieved with extracorporeal membrane oxygenation (ECMO) [8]. Re-transplantation for early graft failure is generally associated with very poor outcomes [9], and many consider this a contraindication to re-transplantation.

52.6.2 Respiratory Support

The principals of respiratory support do not differ from those of other pediatric open heart procedures. Early extubation should be the goal. The patient who has required prolonged preoperative mechanical ventilation will usually need more prolonged ventilatory support postoperatively as retraining of respiratory muscles will be required. Infants with long-standing cardiomegaly will often have significant tracheobronchomalacia and persistent or recurrent pulmonary atelectasis is not unusual, especially of the left lower lobe.

52.6.3 Renal Function

The combination of chronic heart failure, cardiopulmonary bypass, and use of cyclosporine or tacrolimus all contribute to postoperative renal dysfunction. This is exacerbated if there is low cardiac output state postoperatively. Oliguria is common. Fortunately, acute renal failure is rare in children and dialysis is seldom required. Persisting oliguria is managed with loop diuretics and low dose dopamine (e.g., 3–5 µg/kg/min). Low output is managed with inotropic agents as discussed above. Administration of a continuous furosemide infusion (up to 6 mg/kg/day) may be helpful. These maneuvers are usually successful in stimulating an adequate urine output (>1 ml/kg/h). In some cases, particularly in neonates and infants, intravenous

prostaglandin E_1 may also provide a diuretic effect. When urine output remains low, it may be necessary to withhold calcineurin inhibitors (tacrolimus or cyclosporine) for a few days. This can be facilitated by the use of intravenous induction agents as part of the early immunosuppressive regimen (see below).

52.6.4 Gastrointestinal Considerations

Gastrointestinal complications are quite common early after pediatric heart transplantation [10]. All patients should receive intravenous, and subsequently oral, H_2 antagonists to decrease the risk of stress ulcers in the early postoperative period. These are usually continued until corticosteroids have been weaned to low doses or discontinued. The nasogastric tube is removed as soon as the patient is extubated and able to take oral feeds and medications. Attention is paid to providing optimal calories without use of excessive volumes since most patients will tend to retain fluid in the early postoperative period. Pancreatitis is not uncommon following transplantation and should be sought when there is abdominal pain or unexplained feeding intolerance. Immunosuppressive regimens that avoid the use of azathioprine and corticosteroids may reduce this complication. Symptoms of gastrointestinal perforation may be subtle in small children on immunosuppressive medications, especially if corticosteroids are being used. Many children with chronic heart failure have gastroesophageal reflux disease. This should be aggressively managed, but with knowledge that there are many drug interactions between immunosuppressant medications and drugs used for gastroesophageal reflux disease including antacids, antihistamines, and prokinetic agents.

52.6.5 Infectious Precautions

Infections are a leading cause of death and morbidity in the first year following heart transplantation. Most severe infections occur during the initial hospitalization. During the first week after transplantation, invasive lines and drains are removed as soon as possible. A short course of antibiotics (e.g., 72 h) is

given as prophylaxis against mediastinal and wound infection. Usually a first generation cephalosporin will suffice. Broader staphylococcal coverage (i.e., vancomycin) is given if the patient has had a prolonged ICU stay and has long-standing lines in place. Such lines are usually replaced in the operating room. Patients colonized with MRSA are also covered with vancomycin. Oral nystatin is started in the ICU, along with ganciclovir, if recipient or donor are seropositive for CMV. Patients at high risk for yeast infections (e.g., patients on pre-transplant ECMO) are frequently given prophylaxis with fluconazole. However, it should be noted that all “azole” antifungals have a profound effect on calcineurin inhibitor metabolism (via the cytochrome P450 system). A marked reduction in tacrolimus or cyclosporine dosing (50–90% reduction) is required during concomitant use of an azole antifungal agent. Initiation of prophylaxis against *Pneumocystis carinii* can follow nearer to the time of hospital discharge.

52.6.6 Immunosuppression and Early Acute Rejection

High dose intravenous methylprednisolone (e.g., 15–20 mg/kg) is given in the operating room. A tapering course of corticosteroids is usually given over the next 1–2 weeks, with the majority of centers discharging patients on maintenance corticosteroid therapy [2]. However, there is increasing use of steroid-free immunosuppressive regimens in pediatric practice. Cyclosporine or tacrolimus is commenced generally within 24–48 h of surgery once good urine output has been established. Both agents can be given intravenously or enterally. If anti-T cell induction therapy is used (most commonly polyclonal rabbit antithymocyte globulin; less often with an interleukin-2 receptor antagonist), then there is less urgency to introduce a calcineurin inhibitor in the immediate (first 1–2 days) post-transplant period. Cyclosporine or tacrolimus can then be commenced by the oral route rather than intravenously. Delay in commencement of these agents for several days (under coverage of induction therapy) may be particularly useful when urine output is low or renal function is deteriorating.

There are an enormous number of strategies for maintenance immunosuppression [11]. All centers currently use a calcineurin inhibitor as the primary

Table 52.3 Potential combinations of maintenance immunosuppressive drugs used in pediatric heart transplantation. All maintenance regimens may be used with, or without, induction therapy with T cell depleting antibody preparations or with interleukin-2 receptor antagonists

Number of agents	Potential combinations	Comments
Monotherapy	Tacrolimus or cyclosporine	Monotherapy rarely used with cyclosporine.
Dual therapy	Tacrolimus or cyclosporine with azathioprine or mycophenolate mofetil or sirolimus/everolimus or corticosteroids	Little experience with the mTOR (target of rapamycin) inhibitors sirolimus and everolimus in children. Steroid avoidance increasingly common in pediatric heart transplantation.
Triple therapy	Tacrolimus or cyclosporine with corticosteroids with azathioprine or mycophenolate mofetil or sirolimus/everolimus	In triple therapy regimens, mycophenolate mofetil is being used with increasing frequency in lieu of azathioprine.

immunosuppressive agent and there is approximately equal use of tacrolimus and cyclosporine at this time. Most centers also use a second, adjunctive, agent. More centers are using steroid avoidance regimens or early steroid weaning in children. The principals of maintenance therapy are summarized in Table 52.3. In general, agents of similar classes are not given together as they tend to enhance toxicities. Combination therapies use two or three agents of different classes with different mechanisms of action.

Careful daily assessment is performed for signs of rejection, though severe rejection before 7–10 days is rare (except in the sensitized patient). Rejection is generally delayed with use of induction therapy. Infants and young children experience less acute rejection than adolescents. Pallor, increasing tachycardia, abdominal pain, gallop rhythm, and oliguria all are suggestive of severe rejection. Ideally, rejection is identified by echocardiography and/or surveillance biopsy before such signs develop. The electrocardiogram may show reduced precordial voltages. The tempo of rejection can be quite abrupt in the early post-transplant period, and any deterioration in the patient's condition after initial recovery from surgery must be taken very seriously. If there is unequivocal evidence of new graft dysfunction, empiric treatment (usually consisting of bolus intravenous corticosteroids), or immediate endomyocardial biopsy, should be performed. Biopsy generally shows lymphocytic infiltrates (predominantly T cells) with varying degrees of edema and myocyte damage. Endomyocardial biopsies are graded according to an internationally agreed classification system developed by the International Society for Heart and Lung Transplantation (ISHLT) [12].

52.7 Medium-Term and Late Complications

A detailed discussion of all complications of heart transplantation beyond the immediate postoperative period is outside the scope of this text and readers are referred to other reviews [1, 13]. This section focuses on those complications that the intensive care team will be required to manage from time to time.

Immunosuppressive therapy aims to prevent or minimize the immune response of the host to donor antigens, while avoiding complications of therapeutic immunosuppression. Immunological complications of transplantation fall into two main groups - allograft rejection and graft dysfunction (both acute and chronic) reflecting inadequate or ineffective immunosuppression and manifestations of nonspecific immunosuppression, including infections and malignancy. Finally, non-immune side effects of immunosuppressive therapy (i.e., tissue and organ toxicities) are an important cause of morbidity, and occasionally mortality, after heart transplantation in children.

52.7.1 Acute Rejection

Patients remain at risk for acute rejection indefinitely. There is no evidence that heart transplant recipients become truly tolerant to their allograft. The importance of acute rejection episodes becomes evident when causes of death after heart transplant are examined. Data from the ISHLT show that acute rejection is the commonest cause of death between 30 days and 3 years

after heart transplantation, accounting for almost 30% of all deaths [2]. The peak hazard, or instantaneous risk, for first rejection is between 1 and 2 months after transplantation. By 1 year after transplantation, only 40% of pediatric heart recipients are free of acute rejection. Late acute rejection episodes (occurring beyond the 1 year after transplantation) appear to carry a particularly poor long-term prognosis [14], especially if associated with graft dysfunction. When there is any degree of systolic dysfunction with acute rejection, rapid deterioration is common, even when the patient appears well and free of heart failure at presentation. Thus, it is prudent to admit all patients with acute graft failure to the intensive care unit for initiation of therapy. If systolic failure is more than mild, intravenous milrinone should be initiated and the patient should be monitored for arrhythmias. Unless graft failure is known to be due to coronary artery disease, treatment for acute rejection/graft dysfunction should be initiated with intravenous methylprednisolone 10–15 mg/kg (maximum 1 g) daily for 3–5 days. It is optimal to obtain an endomyocardial biopsy since acute graft dysfunction may be associated with “acellular rejection.” Such cases may be due to humoral rejection secondary to circulating anti-HLA antibodies. Additional therapies may then be required, including urgent plasmapheresis. It should be emphasized that treatment of severe acute rejection should not be delayed while waiting for endomyocardial biopsy to be performed or results to be obtained.

Acute rejection with hemodynamic compromise can rapidly lead to graft failure. Unless there are specific contraindications, such patients should receive full hemodynamic support, including use of mechanical support since the condition is generally reversible in nature.

52.7.2 Chronic Rejection or Post-Transplantation Coronary Arterial Disease

The terms chronic rejection and post-transplant coronary arterial disease (CAD) are generally used synonymously. Coronary disease subsequent to transplantation is an accelerated vasculopathy that is the leading cause of death among late survivors of

pediatric heart transplantation [2]. It accounts for approximately 40% of deaths in the period 3–5 years after transplantation. The pathology differs somewhat from that of ischemic heart disease in the normal adult population. Typical allograft CAD consists of myointimal proliferation that is generally concentric and involves the entire length of the vessel, including intramyocardial branches. Eventually, luminal occlusion occurs. There is often associated inflammation. Both immune and non-immune mechanisms likely contribute to the development of graft vasculopathy, though immune mechanisms are probably of central importance in young children. Intriguing data have recently been published showing that persistence of viral genome of various viruses (especially adenovirus) detected in the myocardium of heart biopsy samples by polymerase chain reaction predicts the development of coronary disease and late graft loss in children [15]. Use of older donors, late acute rejection episodes, and older recipient age are all risk factors for the development of post-transplant CAD [6]. CMV infection may also contribute to the development of graft vascular disease [16].

Symptoms of ischemia are often absent, though some children will experience episodes of abdominal pain and/or chest pain, despite operative denervation of the heart. Syncope and sudden death are also common presentations of graft coronary disease in children. In the current era, the diagnosis is most often made during surveillance selective coronary angiography. Intravascular ultrasound has much greater sensitivity for this diagnosis, though experience in children is much more limited than adults.

Unfortunately, no curative treatment exists for established CAD. Diastolic dysfunction tends to develop early and may be observed even when there is little evidence of epicardial coronary artery narrowing [17]. This may be a reflection of diffuse small vessel disease in many patients. Once overt systolic failure ensues, survival is poor and consideration should be given to re-transplantation. Outcomes for late re-transplantation (beyond 6 months from primary transplant) are similar to those for primary transplantation [9]. These patients sometimes require admission to the intensive care unit for heart failure management. Inotropic agents should be used with great caution as for adults with ischemic myopathy. Patients with ischemic-induced syncope should receive automatic implantable cardioverter-defibrillators (AICD) if they are to be discharged from hospital. However, it may be more prudent to

keep such patients in hospital until retransplantation can be performed. Beta blockers may be given for their anti-ischemic benefits if heart failure is not advanced and beta agonists are not required.

52.7.3 Infections

An increased prevalence of all forms of infection is seen compared to the general population of children. Most infections are caused by pathogens that also cause infection in the non-immunocompromised host. Common examples include respiratory viruses, *Streptococcus pneumoniae*, and varicella virus. All infections that occur in non-immunocompromised patients can cause greater disease severity in the recipient of a transplanted heart. Of particular note in this respect are infections due to CMV and EBV, which only rarely cause severe disease in the immunocompetent host. More rarely, opportunistic infections are seen such as that due to *Pneumocystis jiroveci* (formerly *Pneumocystis carinii*). Although most infections are well tolerated, infection is second only to graft failure as the leading cause of death in the first 30 days after transplantation, and second only to acute rejection as the main cause of death during the remainder of the first post-transplant year [2]. On rare occasion, transplant recipients with severe infection require admission to the intensive care unit. The principals of treatment are broadly the same as for severe infection/septic shock in the non-immunocompromised host. Severe infection is often associated with immune paralysis, and in general, if the child is sick enough to warrant admission to the intensive care unit, maintenance immunosuppression should be temporarily withheld. However, corticosteroids should not be discontinued if they are being used chronically, and stress dosing may be indicated.

Broad spectrum antibiotic coverage is required in any septic transplant recipient until an organism has been identified. *Streptococcus pneumoniae* infections occur with increased frequency and choice of antibiotics must include coverage of this agent. When there is clinical and radiographic evidence of pneumonia and deteriorating clinical status, there should be a low threshold for performing bronchoalveolar lavage in order to obtain deep cultures for viruses, fungi and bacteria. *Pneumocystis jiroveci* should be ruled out

when there is hypoxia and characteristic chest X-ray changes. Respiratory viral pathogens (e.g., RSV, influenza, parainfluenza, adenovirus) should be sought when there is evidence of severe respiratory infection in a heart transplant recipient. While viral respiratory disorders tend to be well tolerated in older children and later out from transplantation, acquisition of one of these respiratory viruses in the first few weeks after transplant can occasionally cause devastating disease, especially in infants.

Primary CMV infection is less problematic in heart transplant patients than in lung transplant recipients. In the former, pneumonitis is rare, whereas it is a common site of disease in lung and heart–lung recipients who develop primary infection post-transplantation. In heart recipients, gastroenteritis, hepatitis, and bone marrow suppression are relatively common findings. Diagnosis is facilitated by evaluation of peripheral blood by PCR or antigenemia (pp65) testing. Diagnosis of CMV disease remains a tissue diagnosis. When the diagnosis is made early, treatment with intravenous ganciclovir and/or oral valganciclovir is usually very effective.

EBV infection in the immunocompromised host can be asymptomatic, or may cause a nonspecific viral syndrome, mononucleosis, fulminant “viral sepsis,” or a post-transplant lymphoproliferative disorder (PTLD). The strongest risk factor for the development of PTLD is the development of primary EBV infection post-transplantation, though children who are seropositive for EBV at the time of transplant are not completely protected from this complication. A recent analysis of the Pediatric Heart Transplant Study database (PHTS) provides the most comprehensive analysis of PTLD in the pediatric heart population. This study identified 56 cases among 1,184 primary transplants (4.7%) at 19 North American centers [18]. Almost nine-tenths were driven by EBV and all but one were of B cell origin. Most patients were treated with reduced immunosuppression and this resulted in complete remission in 75% of cases. However, relapse occurred in 19% and the probability of survival was only 75, 68, and 67% at 1, 3, and 5 years after diagnosis. Therapeutic strategies include reduction or temporary cessation of immunosuppression, antiviral agents (invariably used though of unproven benefit), monoclonal antibodies directed against B cell antigens (e.g., rituximab, a human/mouse chimeric monoclonal antibody directed against the CD20 antigen carried

on almost all B cells), chemotherapy, and rarely, cellular (adoptive) immunotherapy. In the latter, patients are given infusions of autologous cytotoxic T-lymphocytes (cultured *ex vivo*) directed against EBV-specific antigens. This experimental approach is under investigation in children in a small number of centers. Children with fulminant EBV sepsis, and some with severe PTLD, require admission to the intensive care unit. The major role of the intensivist is general supportive care, recognition and treatment of co-morbid infections, and monitoring of graft function which may be compromised at presentation, or following therapeutic reduction in immunosuppression. Coordination of care among multiple specialists is an important aspect of the management of these sick patients in the ICU.

52.7.4 Non-immune Complications

In addition to the consequences of over or under-immunosuppression, transplant recipients experience a wide array of non-immune toxicities of immunosuppressive therapies. These include systemic hypertension, hyperlipidemia, glucose intolerance, decreased bone mineral density, and bone marrow suppression, among others. Toxicities of immunosuppressive agents in children have been recently reviewed [13]. It is important that intensive care team members who look after transplant patients be familiar with these adverse effects, as well as with dosing regimens and drug interactions [11]. One complication worthy of particular attention is that of progressive renal dysfunction due to calcineurin inhibitor renal toxicity. This is becoming increasingly problematic as larger numbers of children survive long-term after heart transplantation. Some have already developed end-stage renal failure requiring renal transplantation [19]. It is important to carefully monitor renal function in all transplant recipients admitted to the ICU and to make appropriate dose adjustments to relevant medications based on estimates of creatinine clearance. It should be noted that estimates, and direct measures, of creatinine clearance overestimate glomerular filtration rate in this population and that the severity of renal disease is generally greater than perceived [19]. Use of nephrotoxic drugs should be minimized as far as possible.

52.8 Survival After Listing for Transplantation and After Transplantation

Parents and patients are interested in the chances of survival once a decision has been made to proceed with listing for transplantation. Despite this, emphasis is rarely given to pre-transplant mortality and the optimal timing of transplantation. Premature transplantation results in exposure of the recipient to the hazards of transplantation and long-term immunosuppression. Excessive delay may result in death without transplantation or the development of co-morbidities that may increase operative risk. These co-morbidities include progressive end-organ dysfunction (especially renal), malnutrition associated with advanced heart failure, and progressive rise in pulmonary vascular resistance. These observations emphasize the importance of studying outcomes after listing for transplantation, and not just after transplantation.

Data from the United States Scientific Registry of Transplant Recipients reveal that children in all age groups have substantially shorter waiting times for heart transplants than do adults, but they have a greater risk of death while waiting (www.ustransplant.org). The highest death rate is among infants less than 1 year of age. The use of ABO incompatible heart transplants may decrease wait-list mortality in infant heart transplant candidates [20]. Several analyzes of the PHTS have focused on understanding risk factors for survival after listing for transplantation and for defining the optimal timing of transplantation. It has recently been shown that children awaiting transplant at the lowest urgency status (UNOS status 2 in the United States) have a very low risk of sudden death while waiting if the underlying etiology is dilated cardiomyopathy. This contrasts with the high risk of sudden death in adults with ischemic etiology on the transplant waiting list. These data suggest that routine use of AICD in all children awaiting transplant is not indicated, though certain subpopulations may benefit.

Data from the registries of the ISHLT, the United States Scientific Registry of Transplant Recipients and the Pediatric Heart Transplant Study all demonstrate important trends in post-transplant survival over the last decade. Importantly, there have been significant improvements in outcome in recent years; the improved survival being most evident in the infant age group and

in smaller volume centers. Most of the improvement appears to be due to reduction in early mortality. One year survival is now approximately 90% in many centers, with only a relatively small drop over the next 3–4 years. The PHTS and the ISHLT databases continue to show a slightly higher perioperative and early mortality for infant recipients, but interestingly, these youngest recipients have the greatest conditional graft half life based on analysis of 1 year survivors [2]. It is likely that this reflects a lower incidence of post-transplant coronary artery disease in these very young recipients and a degree of immune privilege. The results of transplantation for congenital heart disease still lag slightly behind those of transplantation for cardiomyopathy; this difference is due to slightly higher perioperative mortality. Importantly, there is evidence of reduced survival among black pediatric recipients compared to other racial groups. Data from the U.S. United Network for Organ Sharing from 1987 to 2004 shows that the median graft survival for black recipients was only approximately half that for other recipients (5.3 vs. 11.0 years).

52.9 Conclusions and Future Directions

During the last two decades, several advances have resulted in marked improvement in medium-term survival for infants and children undergoing heart transplantation. The improved outcomes appear to be limited to the early postoperative period, and this improvement is most apparent among infants and those with congenital heart disease. Pre-transplant wait-list mortality also appears to have improved and likely reflects better medical care for critically sick candidates. There is also evidence for improved success rates for VAD support as a bridge to transplantation. Despite these advances, heart transplantation remains palliative and all transplant recipients are at risk for the adverse effects of nonspecific immunosuppression, including infections, lymphoproliferative disorders and non-lymphoid malignancies. In addition, current immunosuppressive agents have narrow therapeutic windows and exhibit a wide array of organ toxicities. This poses special challenges for the young patient who must endure life-long immunosuppression. New immunosuppressive regimens have lowered the rates of acute rejection but appear to have had relatively little impact

on the incidence of chronic rejection, the principal cause of late graft loss. The ultimate goal is to induce a state of donor-specific tolerance, wherein the recipient will accept the allograft indefinitely without the need for long-term immunosuppression. This quest is currently being realized in animal models of solid organ transplantation, and offers great hope for future children undergoing heart transplantation.

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Chapter 53

Arrhythmias in the Intensive Care Unit

Lee Beerman, Gaurav Arora, and Sang C Park

Recognition and management of disorders of cardiac rate and rhythm are key aspects of the care that must be provided to pediatric patients in the intensive care setting. In this chapter we will discuss the use of the 12 lead ECG, rhythm strip, cardiac bedside monitor, and atrial electrograms in the general approach to the diagnosis of arrhythmias. Management of specific arrhythmias will then be reviewed.

Arrhythmias may present a major threat to hemodynamic stability in a critical ill or postoperative cardiac patient. Cardiac output is compromised by extremes in rate and the loss of AV synchrony which prevents atrial augmentation of atrioventricular filling and output. Numerous factors in the cardiac surgical patient predispose to the development of arrhythmias, including myocardial dysfunction or ischemia, electrolyte abnormalities, hypoxia, a hyperadrenergic state with excess catecholamines (endogenous or therapeutic), recent or old scars in the myocardium, sutures, residual hemodynamic abnormalities following cardiac repair, pain, and anxiety [1, 2].

53.1 Electrocardiogram

A full description of the 12 lead ECG is beyond the scope or purpose of this chapter, but certain features are important to stress as they may be helpful in identifying arrhythmias [3]. It is essential that any

patient undergoing cardiac surgery have a preoperative electrocardiogram available to serve as a baseline. An early postoperative ECG is mandatory for early recognition of ischemia, infarction, or new conduction abnormalities.

53.1.1 P Waves

The morphology of the P wave should be assessed to determine whether or not the origin is sinus. Sinus P waves will have a frontal plane axis of 0–90 degrees and should be positive in leads I, II, and AVF. An abnormal P wave axis would indicate an ectopic focus, participation of the atria in a re-entrant arrhythmia, cardiac malposition with dextro- or mesocardia or heterotaxy syndromes with atrial isomerism.

53.1.2 Q Waves

Pediatric patients often have prominent Q waves in the inferior and lateral precordial leads due to the normal initial septal depolarization. As long as these Q waves are less than 0.04 s in duration they may be normal, even with an amplitude up to 7–8 mm. Underlying cardiac conditions, which result in abnormal size or location of Q waves, include congenitally corrected transposition of the great arteries, Wolff Parkinson White syndrome, myocardial infarction, and left ventricular hypertrophy, particularly in the setting of hypertrophic cardiomyopathy. New onset Q waves that are wider than 0.04 s may suggest an evolving myocardial infarction.

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53.1.3 QRS Morphology

The QRS complex in a postoperative patient should be compared to the preoperative sinus QRS morphology. If it is the same, the rhythm has to be supraventricular in origin; if it is wider or different from the sinus QRS, it is either ventricular in origin or supraventricular with aberrant conduction. The aberrant conduction may be related to abnormal conduction over the right or left bundle branches, or anterograde conduction over an accessory pathway. The QRS should be evaluated for axis deviation, hypertrophy, abnormal precordial R wave progression, or conduction abnormalities such as

a bundle branch block pattern or preexcitation. A *right bundle branch block* (Fig. 53.1a) is frequently seen in patients who have had surgical repair for Tetralogy of Fallot and, less commonly, AV septal defect or ventricular septal defect. A *left anterior hemiblock* resulting in left axis deviation may be associated with a right bundle branch block in 25% of postoperative patients with Tetralogy of Fallot [3]. Left axis deviation is seen pre-operatively in certain congenital defects, most notably AV septal defect and tricuspid atresia. A *left bundle branch block* (Fig. 53.1b) pattern may be noted after surgery on the left ventricular outflow tract in patients with discrete or muscular subaortic stenosis.

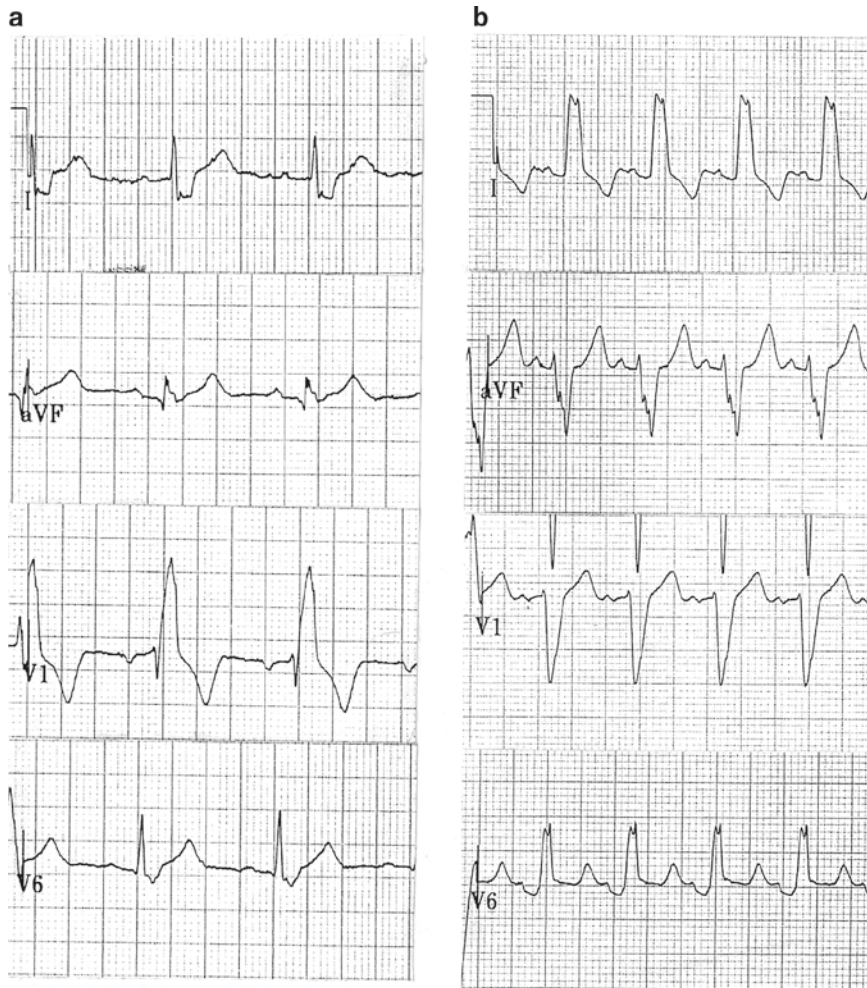


Fig. 53.1 (a, b) Right and left bundle branch block patterns. (a) Right Bundle Branch Block (RBBB) pattern and in a patient status postrepair of Tetralogy of Fallot. Note the slurred R' in V1 and S wave in V6, (b) left bundle branch

block pattern in a patient status postsurgical resection of subaortic stenosis. Note the slurred positive RR' wave in I and V6. There is also a left axis deviation manifested by the negative QRS in aVF

The example of left bundle branch block shown in Fig. 53.1b also shows the usual accompanying left axis deviation.

53.1.4 ST-T Waves

Nonspecific ST-T wave changes are commonly seen in any patient who has had open heart surgery with the exposure of the epicardial surface to mechanical trauma, blood, fluid, or air. These changes may simply reflect transient pericardial or epimyocardial injury. Worrisome changes possibly indicating myocardial ischemia include focal ST elevations, particular convex upward, or depressions, either horizontal or down sloping. A higher index of suspicion is required following surgical procedures which result in the manipulation of the coronary arteries such as arterial switch operation, Ross procedure, or aortic valve or root replacement. However, any open heart procedure involving bypass has some intrinsic risk for air or particulate emboli into the coronary arteries.

53.2 Rhythm Strip

The rhythm strip, particularly one with multiple leads, used in conjunction with the 12 lead ECG is the essential tool utilized for the diagnosis of arrhythmias. The most important aspect of arrhythmia analysis is to identify the P waves, QRS complexes, and note the rate and morphology of each as well as the relationship of the P wave and QRS activity. P wave morphology is analyzed to determine whether it is sinus or ectopic in origin. The QRS should be defined as narrow (or identical to the QRS noted in baseline sinus rhythm) or wide. A narrow QRS indicates a supraventricular, above the His bundle, origin of the impulse. On the other hand, a wide QRS has a broader differential diagnosis and may be due to a ventricular origin, a supraventricular beat that is conducted aberrantly through one of the bundle branches or anterograde conduction over an accessory pathway. The relationship of P and QRS waves will either be 1:1 association, intermittent association or complete dissociation between atrial and ventricular activity.

Recognition of P waves presents the biggest challenge because of their relatively low amplitude and they may be “hidden” within the QRS complex or ST-T waves. P wave detection can be enhanced by the use of the 12 lead ECG, a multi-lead rhythm strip, atrial electrograms, and by the administration of Adenosine. Multiple lead analysis will often allow recognition of a P wave not seen in a standard single lead rhythm strip. An atrial electrogram can be obtained by using intraoperatively placed epicardial wires or by a transesophageal pacing lead (Fig. 53.2). Adenosine is extremely helpful unmasking an atrial tachyarrhythmia obscured by a rapid ventricular response by providing transient AV block (Fig. 53.3).

53.3 Atrial Electrograms

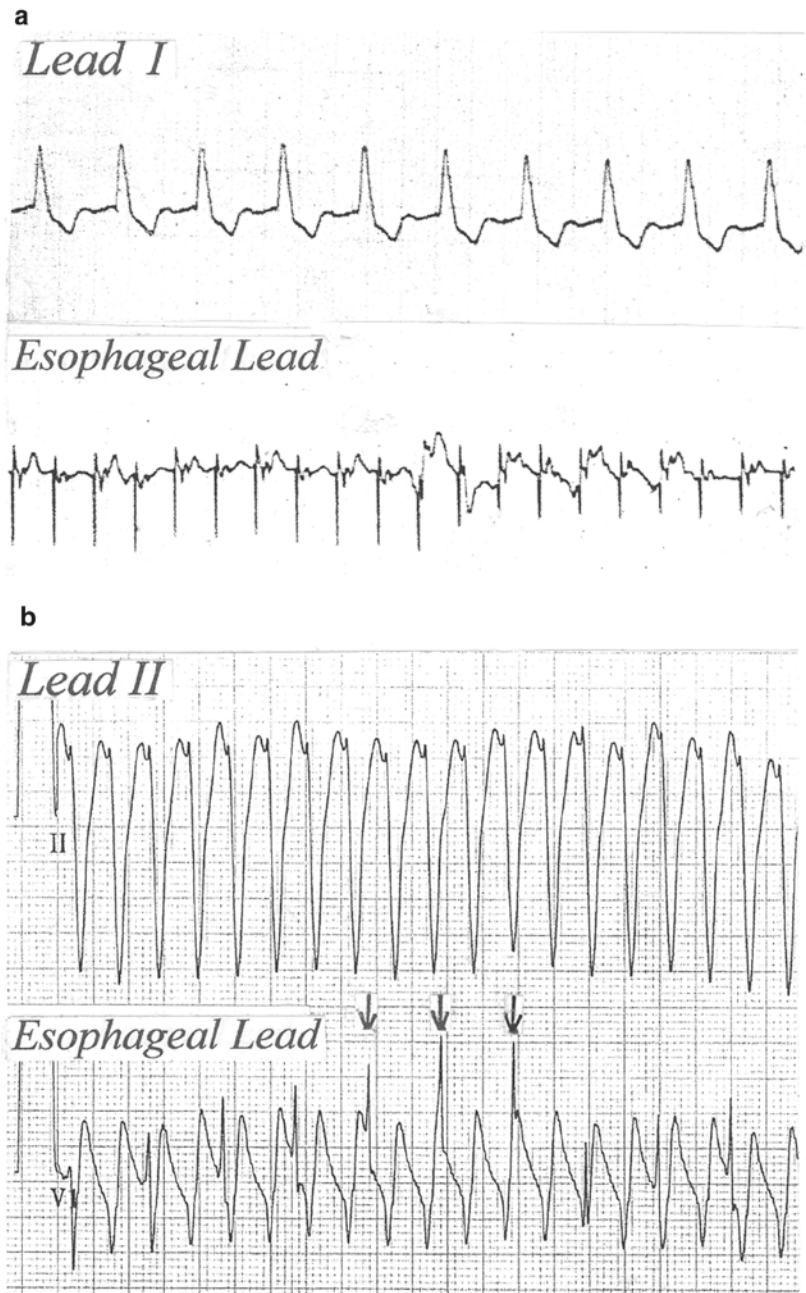
The proper use and understanding of atrial electrograms is extremely valuable in the care of critically ill patients with arrhythmias. Recognition of the relationship between atrial and ventricular activity allows for rapid and accurate diagnosis of almost all disturbances of rhythm and conduction.

Atrial electrograms can be obtained with an esophageal electrode or surgically placed wires, and can be either unipolar or bipolar recordings. Unipolar recordings have smaller atrial deflections, but allow for simultaneous display of surface leads, which is advantageous. Bipolar electrograms, on the other hand, have larger atrial deflections, but do not allow simultaneous display of a pure surface lead, which sometimes makes distinguishing atrial from ventricular activity difficult.

The esophagus sits directly posterior to the left atrium, so a specifically designed esophageal lead may be placed through the nose or mouth into the esophagus to record atrial activity [4]. Alternately, surgically placed atrial wires may be used. If two atrial wires are placed, either unipolar or bipolar electrograms can be recorded [5].

We recommend recording a 3 lead rhythm strip with Leads I, II, and V1. The atrial wire may be connected to either V1 or the left arm lead, which will allow recording a unipolar atrial recording simultaneously with a pure surface Lead II (Fig. 53.4a). A bipolar atrial recording may be obtained by connecting one atrial wire to the right arm lead, and the other atrial wire to the left arm ECG lead. Lead I will then record

Fig. 53.2 (a, b) Use of esophageal atrial recording. (a) Surface lead I shows a tachycardia without evident P waves; the esophageal lead clearly shows the underlying rhythm is atrial tachycardia with 2:1 AV block, (b) surface lead II shows a wide QRS tachycardia without evident P waves; esophageal lead shows atrial activity (arrows) with VA dissociation indicative of ventricular tachycardia



a bipolar atrial electrogram, with leads II and V1 demonstrating unipolar tracings (Fig. 53.4b). As mentioned above, with bipolar electrograms there is no pure surface lead displayed. For that reason, we predominantly record unipolar atrial electrograms, or obtain both unipolar and bipolar tracings, in our clinical practice.

53.4 Mechanism of Arrhythmias

Almost all arrhythmias are due to one of two mechanisms, re-entry or abnormal automaticity (sometimes referred to as ectopic) [6, 7]. Other mechanisms, such as triggered automaticity are less common,

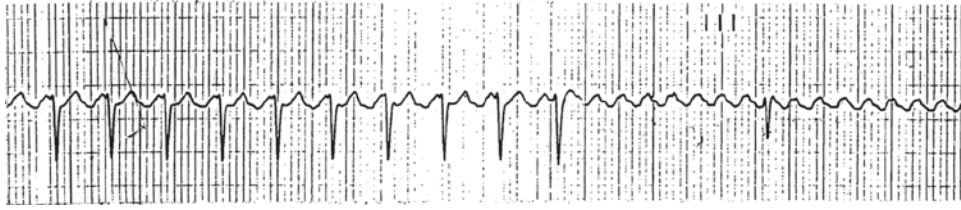


Fig. 53.3 Diagnostic use of adenosine. Adenosine given during a rapid supraventricular rhythm unmasks the underlying atrial flutter not evident before the adenosine induced AV block

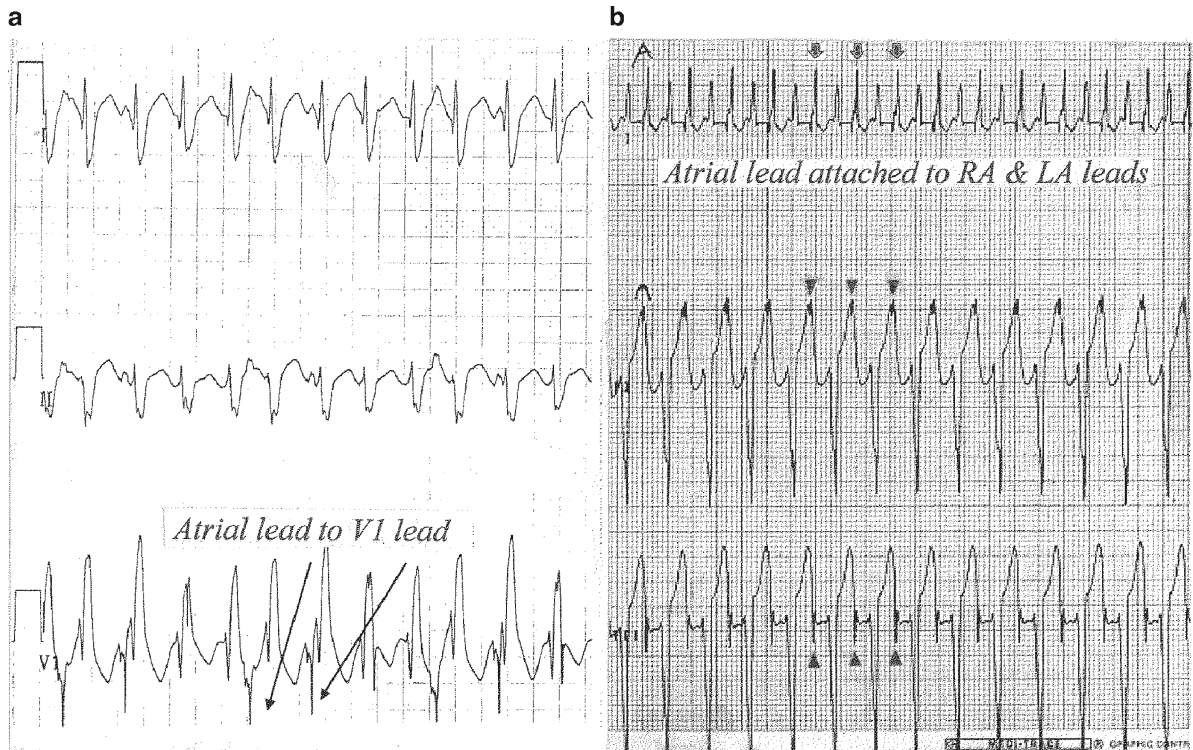


Fig. 53.4 (a, b) Atrial electrograms. (a) Unipolar atrial electrograms are obtained by connecting one atrial lead to V1 ECG cable in a patient with JET. Arrows show atrial activity confirming AV dissociation, (b) bipolar atrial electrograms are obtained by connecting one atrial lead to the right arm ECG cable and the

other atrial lead to the left arm ECG cable. Lead I (top) shows bipolar atrial electrograms (double arrows) indicating rhythm is likely sinus tachycardia. Leads II and III below show unipolar atrial electrograms (triangles)

but may play a role in digitalis toxicity associated arrhythmias or channelopathy related ventricular arrhythmias. The characteristics of re-entry and automatic arrhythmias are noted in Table 53.1. Re-entrant arrhythmias typically have a paroxysmal occurrence, sudden onset and offset, and a relatively constant rate. They are effectively treated by overdrive pacing, cardioversion and respond dramatically to Adenosine if the re-entrant loop involves the AV node.

Conversely, automatic tachycardias tend to be incessant, demonstrate warm up and slow down and have variable rates related to changes in autonomic tone. They are suppressed but not terminated by overdrive pacing or cardioversion. Some ectopic foci are adenosine sensitive, but most ectopic rhythms are not directly affected by this drug. Review of the heart rate trend display on the bedside monitor is often valuable in determining the mechanism of an arrhythmia.

Table 53.1 Characteristics of arrhythmias*Re-entry mechanism*

1. Paroxysmal
2. Abrupt onset/offset
3. Constant rate
4. Pacing – induce/terminate
5. Cardioversion – very effective

Automatic mechanism

1. Warm up/cool down
2. Variable rate
3. May be incessant
4. Pacing – not effective
5. Cardioversion – not effective

A re-entrant arrhythmia will display a box or rectangular type pattern with an abrupt onset, steady rate, and abrupt offset as opposed to automatic tachycardias that have a more gradual upward and downward heart rate slope.

53.5 Classification and Management of Arrhythmias (Table 53.2)

53.5.1 Tachyarrhythmias

53.5.1.1 Supraventricular Arrhythmias

Atrial arrhythmias

All of the rhythm disturbances in this category depend only on atrial tissue and are independent of AV node conduction.

Premature atrial complexes: These are relatively common in the newborn and the young infant. They are frequently associated with aberrant conduction and can be differentiated from premature ventricular beats by identifying a preceding P wave (Fig. 53.5a, b). Intermittent pauses may be due to premature contractions that occur so early they are not conducted through the AV node, resulting in an apparent pause. If these non-conducted premature atrial beats occur in a bigeminal fashion, the rhythm can be difficult to distinguish from sinus bradycardia, but the diagnosis should be made by noting P waves on the ST-T wave segment.

Treatment: Premature atrial complexes do not require treatment as long as they do not precipitate runs of sustained tachycardia.

Table 53.2 Classification of arrhythmias*Tachyarrhythmias*

1. Supraventricular
 - a. Atrial (independent of AV node)
 - i. Premature atrial complexes
 - ii. Atrial ectopic tachycardia
 - iii. Atrial muscle re-entry: classic atrial flutter, atrial fibrillation, intra-atrial muscle re-entry
 - b. Junctional (involving AV nodal tissue)
 - i. Paroxysmal supraventricular tachycardia
 - ii. Junctional ectopic tachycardia
2. Ventricular
 - a. Ventricular ectopics
 - b. Ventricular tachycardia
 - c. Ventricular flutter and fibrillation

Bradyarrhythmias

1. Sinus node dysfunction
2. AV block

Atrial Ectopic Tachycardia (AET): This arrhythmia may present with incessant tachycardia leading to a cardiomyopathy. It may also occur as a transient post-operative phenomenon within the first several days of surgery. The hallmark of the diagnosis is an abnormal P wave morphology, unless the ectopic focus arises from the high right atrium near the sinus node. The tachycardia displays a gradual warm up and slow down pattern (Fig. 53.6), and the rate varies with autonomic tone, stress, and exogenous catecholamines. A form of AET with multiple P wave morphologies and short nonsustained bursts of tachycardia is called chaotic atrial rhythm, or multifocal atrial tachycardia. This arrhythmia is most commonly seen in the newborn period or first few months of life.

Treatment: AET is often difficult to treat as it responds only transiently to overdrive pacing and cardioversion. In the immediate postoperative period, it usually requires anti-arrhythmic therapy with intravenous amiodarone or procainamide. Temporizing measures with AV nodal blocking agents (i.e., digoxin, beta blockers or calcium channel blockers) may slow the ventricular rate to a level that is better tolerated from a hemodynamic standpoint.

Atrial muscle re-entry: There are numerous types of tachycardia related to re-entry within the atrial myocardium.

1. **Classic atrial flutter:** This involves a macro re-entry circuit through the right atrium and is rare in pediatrics outside of the newborn period. The rate varies from 280 to 500 bpm, generally 300 bpm,

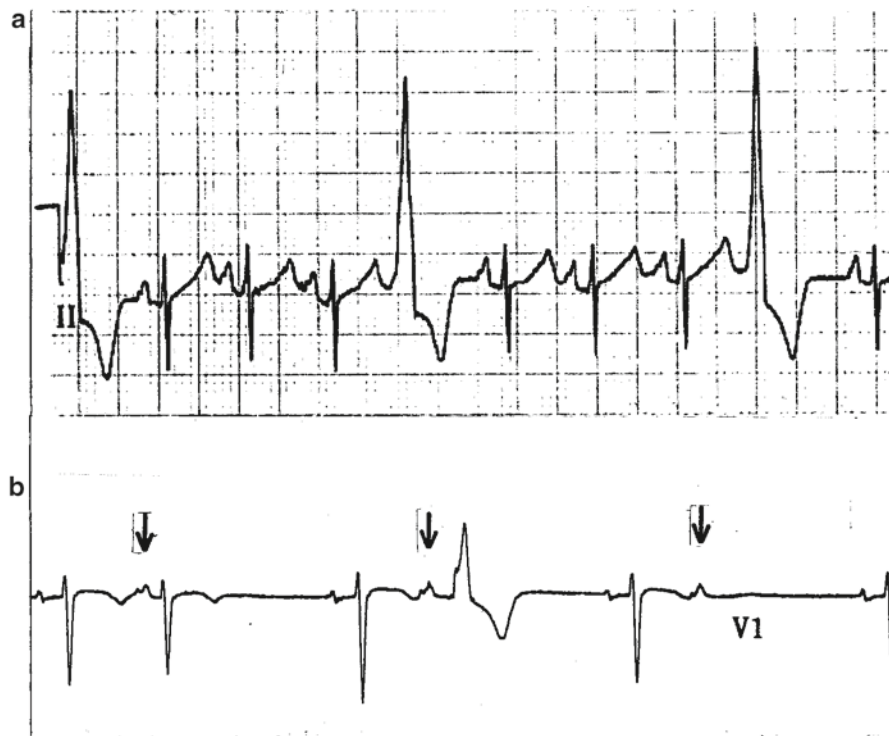


Fig. 53.5 (a, b) Premature ventricular and atrial beats. (a) Premature ventricular complexes demonstrating a wide QRS, abnormal T wave and no preceding P wave, (b) Premature Atrial Complexes (PAC) (arrows) showing three different ventricular responses: first arrow shows normal QRS, second arrow shows aberrant QRS with RBBB pattern, third arrow shows nonconducted PAC resulting in a brief apparent sinus pause. *RBBB* right bundle branch block



Fig 53.6 Atrial ectopic tachycardia. Note P wave before every QRS and gradual “warm up” and “slow down” of tachycardia rate.

and is associated with the classic “saw tooth” flutter waves (Fig. 53.7). Conduction to the ventricular is may vary from 1:1 to 3:1 or more, but most often there is a 2:1 block which may make recognition of the flutter waves difficult. Adenosine is extremely helpful in unmasking the saw tooth wave pattern

during the transient AV block that occurs seconds after the administration of this drug (Fig. 53.3).

Treatment of atrial flutter is either atrial overdrive pacing or synchronized cardioversion. AV nodal blocking agents are used if immediate rate control is required. Anticoagulation issues are important with atrial flutter,

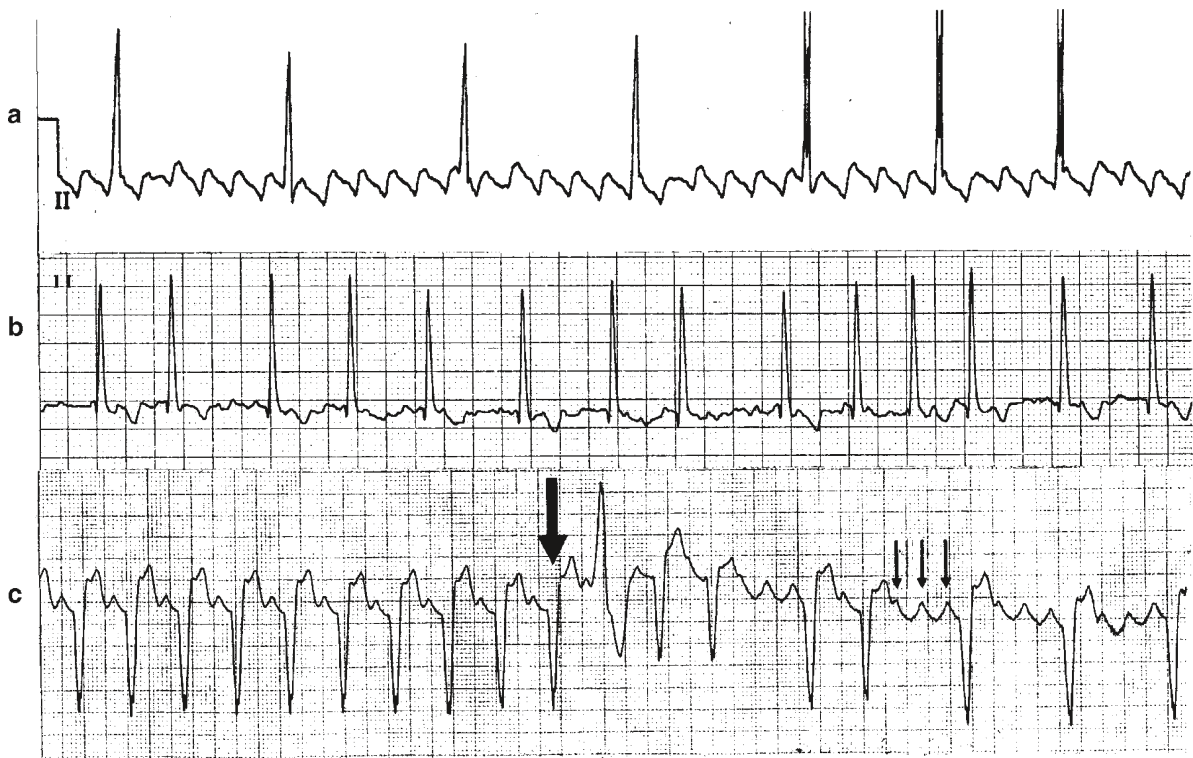


Fig. 53.7 (a–c) Atrial muscle re-entry. (a) Atrial flutter with typical saw tooth pattern of atrial activity with variable AV block, (b) atrial fibrillation with irregularly irregular RR intervals and a coarse baseline, (c) intra-atrial re-entry

tachycardia in a patient with Fontan procedure. Atrial rate not evident until onset of adenosine effect (*large arrow*), which increases AV block and reveals atrial rate of 250 bpm (*small arrows*)

as they are with all sustained atrial arrhythmias [8] and are discussed below.

2. *Atrial fibrillation*: This is the most common arrhythmia seen in the adult intensive care setting, but is extremely uncommon in the pediatric ICU. The characteristics include an irregular rhythm without a set pattern and a coarse baseline without consistent or well-formed P waves (Fig. 53.7b). It may occur in adolescents or adults with congenital heart disease and cardiac lesions resulting in long standing atrial dilation or elevated atrial pressure. Hyperthyroidism should be considered in a patient with new onset atrial fibrillation and no underlying structural heart disease.

Treatment initially consists of rate control with digoxin, beta blockers, or calcium channel blockers. The calcium channel blocking agent diltiazem has become the drug of choice for rate control, as intravenous administration allows titration of the AV block. Thromboembolic complications are a risk if a rapid atrial arrhythmia

persists for more than 24–36 h and anticoagulation with heparin should be considered. Conversion to sinus rhythm may occur with intravenous amiodarone, procainamide or ibutilide (a medication with a relatively high risk of torsade de pointes within the first several hours after administration). Synchronized DC cardioversion is generally effective, but the arrhythmia may be recurrent requiring suppressive therapy with amiodarone or procainamide.

3. *Intra-atrial Re-entry Tachycardia (IART)*: This rhythm disorder, characterized by a re-entry circuit within atrial myocardium circulating around natural barriers or scar tissue, is being seen with increasing frequency in adolescents and adults with repaired congenital heart disease. The rapidly enlarging population of patients who have had Fontan procedures or atrial repairs for Transposition of the Great Arteries (i.e., Mustard or Senning operations) is at the greatest risk for IART to develop years after the initial repair. However, this rhythm

disturbance may be seen in any anyone who has had a previous atriotomy, even an uncomplicated ASD repair. IART is distinguished from classic atrial flutter because the rates are slower, ranging anywhere from 100 to 250 bpm, and P waves are discrete with abnormal morphology. As with atrial flutter, AV block is variable and 2:1 block may make the diagnosis difficult. Adenosine is useful in providing transient AV block allowing easy recognition of the atrial tachycardia (Fig. 53.7c).

Treatment initially consists of rate control, usually with diltiazem. If the duration of the arrhythmia is greater than 36 h or unknown, there is a risk of systemic emboli and stroke, particularly with conversion to sinus rhythm. In this situation, anticoagulation is necessary and cardioversion, electrical or pharmacologic, should be preceded by transesophageal echocardiography to rule out a thrombus within the heart. Alternatively, it may be reasonable to maintain therapeutic anticoagulation with Coumadin for 4 weeks before an attempt at conversion. Overdrive pacing and electrical synchronized DC cardioversion are very effective in acutely terminating the rhythm, but there is a strong tendency for recurrence and long-term anti-arrhythmic therapy and or an attempt at ablation of the arrhythmia circuit is generally necessary [9].

For recalcitrant IART, a surgical MAZE procedure may need to be considered [10].

The *management of sustained atrial arrhythmias* is summarized in Table 53.3.

Junctional Arrhythmias

These arrhythmias involve AV nodal tissue or portions of the His bundle.

Paroxysmal Supraventricular Tachycardia (SVT): Paroxysmal SVT (Fig. 53.8) is due to re-entry and is the most common arrhythmia requiring treatment in the pediatric population with no underlying structural

Table 53.3 Management of Atrial Arrhythmias

1. Control ventricular rate by AV block
a. Intravenous: digoxin, beta blockers [esmolol], calcium channel blockers [diltiazem]
2. Risk of thromboembolism
a. Duration <36 h low risk
b. If high risk: transesophageal echocardiogram versus 4 weeks of anticoagulation
3. Conversion to sinus rhythm
a. Pharmacologic – intravenous amiodarone, procainamide, ibutilide
b. Electrical DC conversion – 1 J/kg

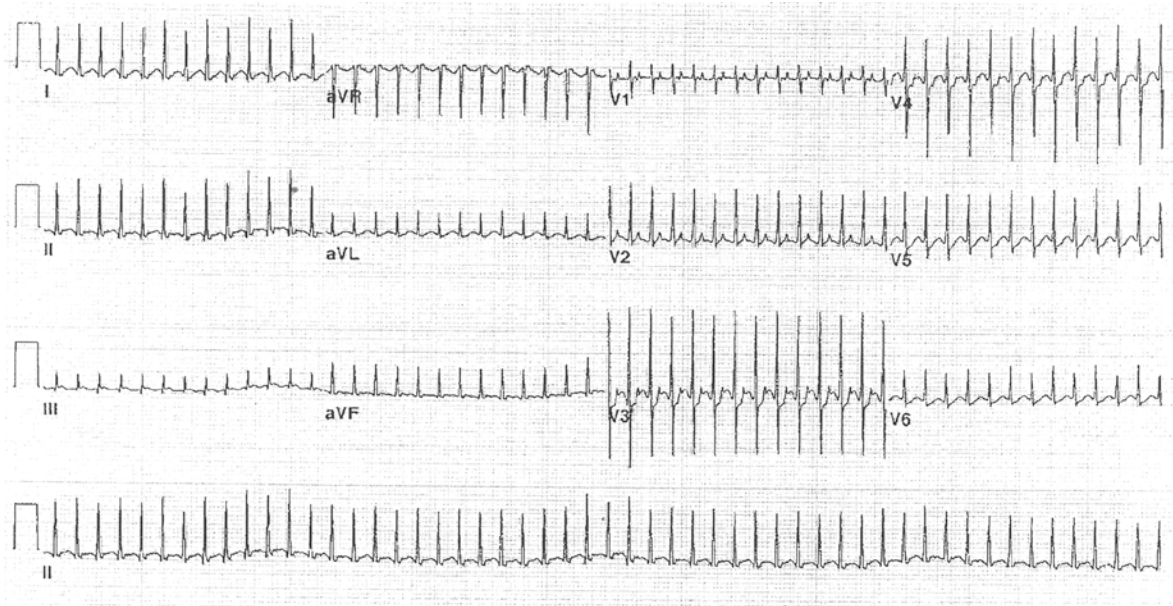


Fig. 53.8 (a) Supraventricular tachycardia. Note regular narrow complex tachycardia at a rate of 300 bpm

heart disease. Any patient undergoing cardiac surgery who has the substrate for re-entry SVT may have a recurrence in the postoperative state. This may cause significant and rapid hemodynamic distress in the setting of compromised myocardial function. Paroxysmal SVT can be easily recognized on the bedside monitor by the abrupt increase in heart rate to 180–300 bpm. This type of re-entry tachycardia is either mediated through an accessory pathway (AV re-entry) or via dual AV node pathways (AV node re-entry). An accessory pathway consists of myocardial fibers bridging the fibrous AV annulus. These may be manifested with anterograde conduction resulting in pre-excitation and constituting the WPW syndrome recognized by a delta wave in sinus rhythm (Fig. 53.9). However, these pathways often conduct only in a retrograde fashion, sometimes referred to as URAPs (unidirectional retrograde conducting accessory pathways) [5]. Therefore, they are not evident during sinus rhythm, but may still participate in a tachycardia circuit. Accessory pathway-mediated paroxysmal SVT predominates in younger individuals less than 10 years of age. After this age, AV node re-entry utilizing fast and slow AV node pathways becomes more prevalent [5–7]. Regardless of the mechanism, the re-entry circuit involves the AV node and this tachycardia is sensitive to any maneuver or drug that blocks conduction through the AV node. Although the mechanism of the SVT does not affect acute treatment choices, the use of the 12 lead ECG and an atrial recording can elucidate whether or not the

SVT is mediated by an accessory pathway or AV node re-entry. If retrograde P waves are seen on the ST segment of the 12 lead, or if the R-P interval on the atrial electrogram is greater than 80 ms, this implies the re-entry circuit is relatively large involving an accessory pathway. A very short RP interval where the P wave occurs within the QRS generally indicates AV node re-entry as the mechanism.

Treatment: If there is hemodynamic embarrassment, immediate synchronized cardioversion should be performed. If the situation is less critical, various vagal maneuvers can be tried such as the diving reflex with exposure of the face to ice water in a plastic bag. Adenosine is the drug of choice and is almost universally effective, at least transiently interrupting the tachycardia. However, in the presence of a high adrenergic state there may be a tendency for immediate recurrence of the SVT. This requires use of longer acting medications such as digoxin, beta blockers, procainamide or amiodarone. Although digoxin should not be used for a long term in individuals with Wolff Parkinson White because of its risk in enhancing AV conduction during atrial fibrillation, it is safe to use in the monitored critical care setting for paroxysmal SVT. Intravenous verapamil may be useful in patients over 1 year of age and who have preserved systolic ventricular function. Overdrive atrial pacing with an esophageal pacing lead or atrial leads placed the time of surgery is also very effective in acutely terminating this arrhythmia.



Fig. 53.9 Wolff Parkinson White Syndrome. Note the short PR interval and slurred upstroke of the QRS typical of ventricular preexcitation.

Junctional Ectopic Tachycardia (JET): This is the most common hemodynamically important arrhythmia seen in the cardiac ICU [11–14]. JET generally has its onset in the first 24 to 48 h postoperatively and is usually transient, lasting 2–5 days. The incidence ranges from 5 to 8% and risk factors include: age less than 6 years, complex intraoperative repairs, duration of cardiopulmonary bypass, and requirement for relatively high dose inotropic support. The defects that have most commonly been associated with postoperative JET include Tetralogy of Fallot, total anomalous pulmonary venous return, transposition of the great arteries (arterial switch procedure), ventricular septal defect, AV septal defect, and hypoplastic left heart (stage 1 Norwood Procedure). The mechanism remains unproven but is thought to be related to a combination of traction or trauma to the AV node and His bundle during surgery. The hallmark of the diagnosis includes a junctional rhythm greater than 170 bpm usually associated with AV dissociation with the junctional rate being greater than the atrial rate. There may be occasional sinus

capture beats causing irregular and shorter RR cycles. Occasionally there may be 1:1 VA conduction. The QRS morphology should be identical to the sinus QRS for this diagnosis to be made confidently. Figure 53.10 shows tracings of JET, and Fig. 53.4a shows the use of an atrial electrogram to define the VA relationship.

Treatment: Adenosine is *ineffective* in eliminating the tachycardia but may produce transient VA dissociation with continuation of the tachycardia distinguishing it from a re-entry SVT. The approach to this tachycardia should initially include avoiding hyperthermia, optimizing sedation and pain control, and minimizing inotropic support. Every effort should be made to normalize blood gases and electrolytes including calcium and magnesium. If this does not result in a decrease of the junctional rate, other maneuvers including drug therapy and cooling should be employed [11, 13, 15]. Our approach (outlined in Table 53.4) is to use amiodarone first with cooling added as necessary to decrease the junctional rate to a range that allows temporary atrial or AV sequential pacing to restore AV synchrony.

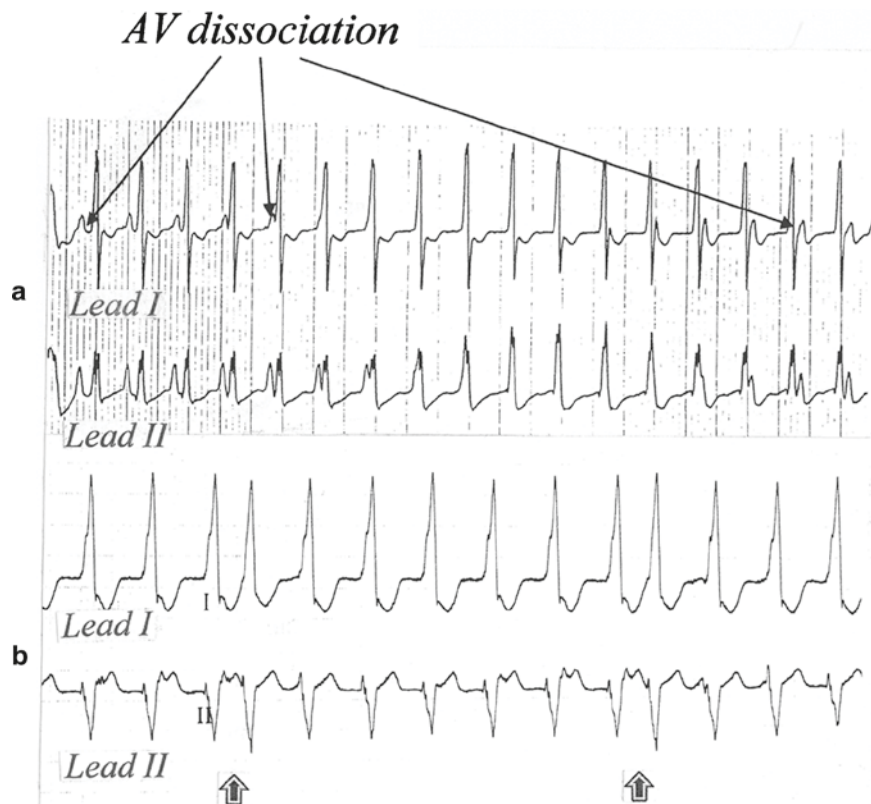


Fig. 53.10 (a, b) Junctional Ectopic Tachycardia (JET). (a) Rhythm strip demonstrates JET with AV dissociation (arrows identify P waves), (b) rhythm strip of JET with intermittent short RR intervals (double arrows) due to sinus capture beats

Table 53.4 Management of Junctional Ectopic Tachycardia

-
1. General measures
 1. Optimize sedation/hemodynamics
 2. Decrease exogenous catecholamines
 3. Correct fever, establish normo- or mild hypothermia
 2. Rate control
 1. Drugs – intravenous amiodarone
 2. If needed – moderate hypothermia, 35–36°C
 3. Persistent tachycardia and/or side effects from amiodarone – intravenous procainamide
 3. Establish AV synchrony
 1. Rate reduction plus atrial pacing, or AV sequential pacing if AV block present
-

R wave synchronized atrial pacing may also be attempted. Other medications have been used such as digoxin, intravenous beta blockers, and procainamide. Although there is a risk of hypotension with intravenous amiodarone [16], this can be minimized by giving the bolus doses relatively slowly. It is important to remember that an ectopic rhythm such as JET usually does not abruptly terminate and convert to sinus rhythm with the above maneuvers, and the goal of therapy is to gradually suppress the rate to a tolerated level which allows overdrive atrial pacing. Generally, therapy needs to be continued for only 1–2 days as this arrhythmia usually resolves with gradual improvement in the underlying hemodynamic status of the patient. Dexmedetomidine has arisen as a potentially useful drug but requires further prospective studies.

53.5.1.2 Ventricular Arrhythmias

Transient ventricular arrhythmias are not uncommon in the postoperative state or in the critically ill patient. Numerous conditions in this setting predispose the patient to ventricular irritability including electrolyte abnormalities (particularly potassium, calcium, and magnesium), hypoxia, mechanical irritation from catheters, drugs, edema, or acute inflammatory changes related to surgical manipulation. Furthermore, these patients often require inotropic drugs to support cardiac output, which enhance ventricular automaticity. The first approach to any ventricular arrhythmia is to try to correct any of the aforementioned causes.

Ventricular ectopics: This category includes isolated premature ventricular complexes (PVC), bigeminy and couplets. Premature ventricular complexes (Fig. 53.5a) are recognized by their aberrant QRS, absence of a preceding P wave, occasionally a fully

compensatory pause, and a morphology that is not typical for a bundle branch block pattern. A true compensatory pause (interval between the preceding normal QRS and post PVC normal beat being twice the normal RR interval) is frequently not seen because of underlying sinus arrhythmia. Morphology features favoring a ventricular origin include a very wide QRS, concordance of positivity (or negativity) of the QRS across the precordium, and an Rsr' pattern in V1 with the R amplitude greater than the r.' Supraventricular origin of an aberrant complex is more likely when the QRS has a typical right bundle branch block or left bundle branch block morphology.

Treatment: Although isolated premature ventricular complexes do not merit antiarrhythmic therapy, certain features are worrisome and suggest the possibility of progression to a more complex and hemodynamically compromising ventricular arrhythmia. These include multiform morphology, increasing frequency of ectopy, R on T pattern and nonsustained ventricular tachycardia.

Ventricular Tachycardia (VT): Nonsustained VT is defined as a run of 3 or more consecutive ventricular ectopics that spontaneously converts to sinus rhythm within 30 seconds. Sustained VT (Fig. 53.11) is a tachycardia that lasts greater than 30 s or requires immediate treatment because of hemodynamic collapse. VT may be monomorphic or polymorphic, and can occur transiently in the postoperative state related to the predisposing factors mentioned above. *Monomorphic VT* is more likely to occur when there is a discrete scar focus related to underlying structural myocardial disease or prior cardiac surgery. The highest risk population of patients who have had previous cardiac surgical repair include those with Tetralogy of Fallot, transposition of the great arteries or related lesions such as truncus arteriosus or double outlet right ventricle; and the risk increases proportionally to the time since surgery. *Polymorphic VT* is most often associated with acute ischemia or an acquired or congenital repolarization abnormality with prolongation of the QT interval. There are a number of congenital channelopathies in addition to the Long QT Syndrome that may present with life threatening ventricular arrhythmias, including catecholaminergic polymorphic VT and Brugada's syndrome [7]. In addition to VT, the differential diagnosis of a wide QRS tachycardia includes supraventricular tachycardia with aberrant conduction and antidromic SVT (anterograde conduction over an accessory

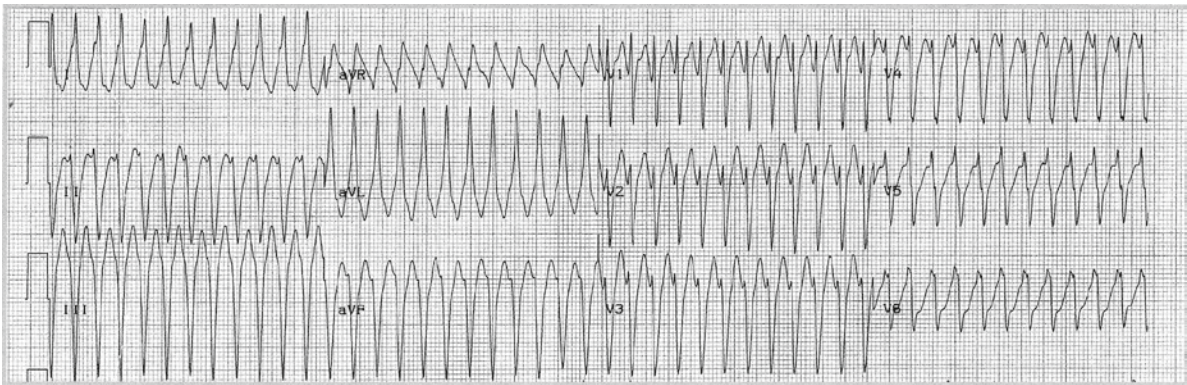


Fig. 53.11 Ventricular tachycardia. Note regular wide QRS tachycardia. P waves are not seen

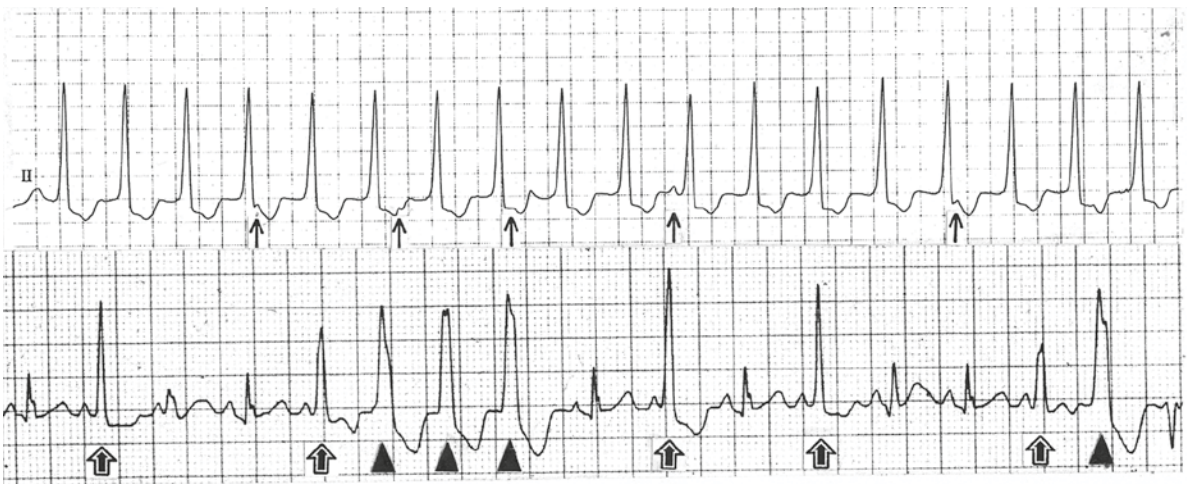


Fig. 53.12 Characteristics of ventricular tachycardia. (a) Rhythm strip of wide QRS tachycardia with AV dissociation showing P waves (arrows) are dissociated from ventricular activity. (b) rhythm strip showing frequent ventricular ectopics and a 4 beat run of nonsustained ventricular tachycardia. Note

difference in morphology between pure PVC's (triangles) and fusion beats (double arrows), the latter beats representing ventricular depolarization from both the ectopic site and conduction through the normal AV conduction axis. PVC premature ventricular complex

pathway). The key diagnostic features indicating ventricular origin include AV dissociation, fusion, and capture beats (Fig. 53.12a, b). AV dissociation is not necessarily present, as each ventricular complex may retrogradely activate the atrium through the AV node resulting in a 1:1 VA relationship. Adenosine may be useful in this situation as it will transiently cause VA block confirming the ventricular origin of the tachycardia. Fusion beats represent dual activation of the ventricle from the ectopic site as well as capture of a portion of the myocardium from a nearly simultaneously conducted supraventricular impulse. Capture beats are infrequently noted, but are recognized as a normal QRS complex within a relatively

slow run of ventricular tachycardia. The most likely cause of a very rapid irregularly irregular wide QRS tachycardia is atrial fibrillation associated with an accessory pathway (Fig. 53.13). Polymorphic ventricular tachycardia may take the typical pattern of Torsade de Pointes with undulating variation in the QRS complexes (Fig. 53.14). This distinctive form of VT is almost always due to prolongation of the QT interval, either as a primary genetic channelopathy involving the sodium and potassium channels, or secondary to drugs or electrolyte abnormalities such as low potassium, magnesium, or calcium.

Treatment: Treatment depends on the hemodynamic state of the patient. In the setting of hypotension and

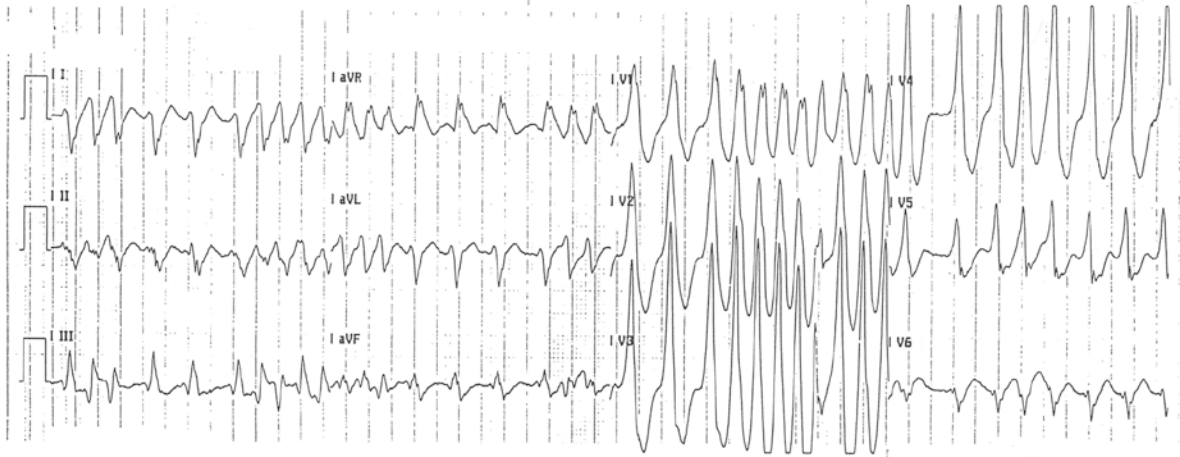


Fig. 53.13 Atrial fibrillation with WPW syndrome. Note the very rapid irregularly irregular wide QRS tachycardia in a patient with WPW syndrome. QRS complexes are wide due to antero-

grade conduction across an accessory pathway. The shortest RR intervals are 170–200 ms indicating a risk of deterioration of rhythm into ventricular fibrillation. *WPW* Wolff Parkinson White

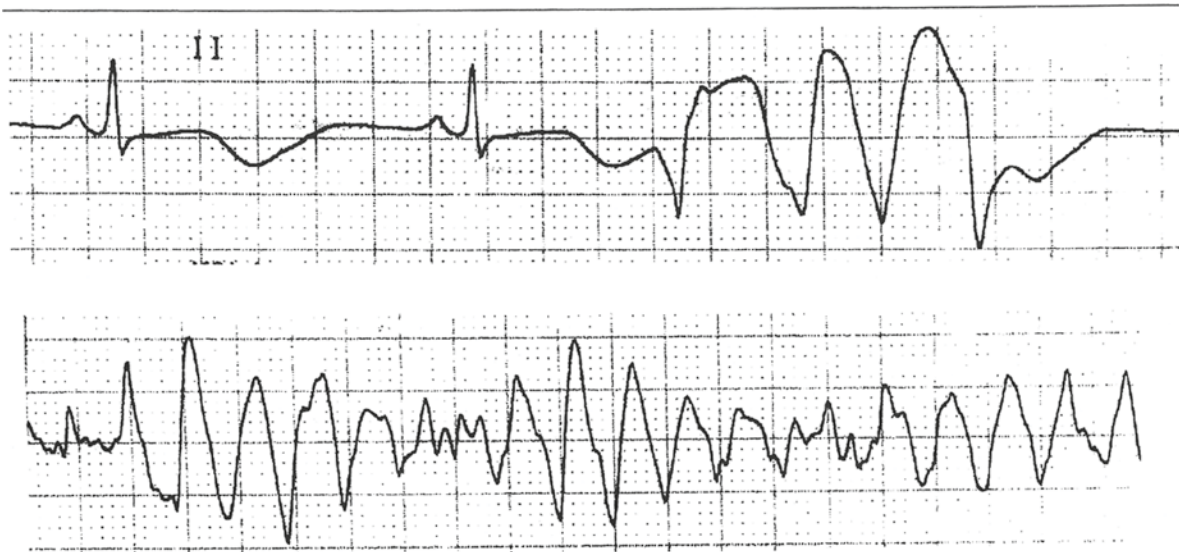


Fig. 53.14 Torsade de Pointes. Note the prolonged QT interval on first 2 sinus beats on top tracing with initiation of the arrhythmia with R on T premature ventricular complex.

cardiovascular collapse immediate synchronized cardioversion is indicated with a dose of 1–2 J/kg. If the patient remains relatively well perfused, a trial of medications is warranted. Intravenous magnesium is the treatment of choice for polymorphic ventricular tachycardia or Torsade de Pointes. Drugs available for acute treatment of ventricular tachycardia include lidocaine, procainamide, and amiodarone. It is generally worth an initial trial of lidocaine, as the side effects

are minimal and the effect will be immediately apparent. If this is unsuccessful, our next choice would be intravenous amiodarone, although there is potential for hypotension if infused too rapidly. Amiodarone is generally tolerated better than the other alternative, intravenous procainamide, in the setting of compromised myocardial function.

Ventricular flutter and fibrillation: These arrhythmias are usually the end result of sustained ventricular

tachycardia with degeneration into a nonperfusing arrhythmia. Occasionally ventricular fibrillation will occur as a primary event.

Treatment: These lethal arrhythmias must be immediately treated with defibrillation (asynchronous delivery of 2 J/kg) as opposed to synchronized cardioversion.

53.5.2 Bradyarrhythmias

53.5.2.1 Sinus Node Dysfunction

Sometimes referred to as “sick sinus syndrome,” this is a rhythm disturbance related to abnormal sinus node automaticity or perinodal conduction resulting in sinus bradycardia, long sinus pauses, sinoatrial exit block or a junctional escape rhythm. This condition rarely occurs as a primary event in the pediatric population, but is not infrequently seen in postoperative patients. Acute sinus node dysfunction may be seen after any procedure involving manipulation of the right atrium including sinus venosus and atrial septal defect repairs, Fontan procedure, total anomalous pulmonary venous return, or orthopic heart transplantation. Chronic sinus node dysfunction is common during long-term follow up of patients who have had a Mustard or Senning repair for transposition of the great arteries, a Fontan procedure, or closure of a sinus venosus atrial septal defect.

Treatment: Isuprel infusion, temporary or permanent atrial pacing.

53.5.2.2 Atrioventricular Block (AVB)

1) First Degree AV Block

This consists of 1:1 AV conduction, but the PR interval is longer than normal for age and rate (Fig 53.15a).

Treatment is not required.

2) Second Degree AV Block

This consists of conduction of some, but not all, atrial beats. There are two types of second degree block:

- a) Mobitz I (Wenckebach) Block: There is progressive lengthening of the PR interval before a single blocked P wave, with the next impulse conducted with a relatively short PR interval (Fig. 53.15b). This block occurs in the AV node and is due to

the property of decremental conduction inherent to nodal tissue. The etiology may be increased vagal tone, AV nodal injury or ischemia or drugs (particularly, beta or calcium channel blocking agents or digoxin).

Treatment is not necessary as long as an acceptable ventricular rate is maintained. If treatment is required, atropine, isoproterenol, and discontinuing offending medications are effective maneuvers.

- b) Mobitz II Block: There are intermittent nonconducted P waves without any change in the PR interval of the conducted beats, before or after the blocked impulses (Fig. 53.15c). This block arises distal to the AV node, from the His bundle or below, and is an ominous sign of impending complete failure of AV conduction. It may be due to direct surgical injury, ischemia, or diffuse myocardial disease.

Treatment is indicated and urgent with a temporary pacemaker. If prolonged episodes of asystole are occurring before a pacemaker can be inserted, isoproterenol, or transcutaneous pacing should be instituted.

Note: It is not possible to definitively determine whether a 2:1 block is Mobitz I or II. Indirect evidence favoring Mobitz I would be a normal QRS and absence of serious underlying heart disease, since Mobitz II block is usually associated with diffuse ventricular myocardial disease and aberrant QRS morphology.

3) Third Degree (Complete) AV Block

There is no conduction of any atrial impulses to the ventricle (Fig. 53.15d, e). Congenital AV block may occur in the absence of other structural abnormalities and may be related to maternal lupus antibodies. Certain types of congenital defects are highly associated with AV block including congenitally corrected transposition of the great arteries or the complex heterotaxy syndromes. Acquired AV block is more common in the intensive care setting and is usually related to surgical injury to the AV conduction axis. Other causes of acquired heart block include myocarditis or acute rheumatic fever. A narrow QRS escape rhythm indicates block above the His bundle with a usually stable junctional rhythm (Fig 53.15d), while a wide QRS escape generally indicates block below the His bundle, which is less stable (Fig. 53.15e). However, a wide QRS may be due to a bundle branch block rather than block below the His bundle.



Fig. 53.15 (a–e) Types of AV block. (a) PR interval is prolonged, but every P wave is conducted, (b) Second Degree, Mobitz Type I (Wenckebach), block shows progressive prolongation of PR interval before a blocked P wave, (c) Second Degree, Mobitz Type II, block shows no change in PR interval before the blocked P wave. Note wide QRS which is frequently

associated with more distal AV block, (d) Third Degree or Complete AV Block characterized by complete dissociation of atrial and ventricular activity. Narrow complex junctional escape rhythm suggests block is above the His bundle, (e) third degree AV block with slow wide QRS escape rhythm indicates block is below His bundle and is an indication for urgent intervention

Treatment is similar to that for sinus node dysfunction and includes temporizing measures with medication such as atropine or isoproterenol, followed by transcutaneous or temporary pacing. If the block is symptomatic or persistent, permanent transvenous or epicardial pacemaker implantation is necessary. Postoperative AV block is effectively managed by temporary pacing

utilizing surgically placed atrial and ventricular pacing wires. If block persists greater than 7 days, implantation of a permanent pacing system is generally warranted. Pacemaker therapy and indications for pacing are discussed in site chapter in this book.

Note: It is important to understand the term “AV dissociation,” as it is often used inappropriately.

Table 53.5 Common uses for antiarrhythmic medications

1) AV nodal blocking agents
Digoxin, beta blockers (esmolol), calcium channel blockers (diltiazem)
2) Ectopic (automatic) arrhythmias
Amiodarone, procainamide, beta blockers
Lidocaine (for ventricular arrhythmias)
3) Paroxysmal (re-entry) arrhythmias
Atrial: amiodarone, procainamide
AV node: adenosine, verapamil or diltiazem, digoxin, beta blockers, procainamide, amiodarone
Ventricular: lidocaine, amiodarone, procainamide
4) Differential diagnosis
Adenosine
Unmasking atrial tachyarrhythmias
Wide QRS tachycardia: SVT versus VT

Table 53.6 Dosages of common antiarrhythmics

Drug	Dose (intravenous doses)
Adenosine	Bolus: 100–300 µg/kg IV, up 12–15 mg
Amiodarone	Bolus: 5 mg/kg over 20 min, up to 20 mg/kg load Infusion: 5–20 µg/kg/min (10–15 mg/kg/24 h)
Esmolol	Bolus: 500 µg/kg Infusion: 50–200 µg/kg/min
Digoxin	Bolus: 20 µg/kg, up to 0.5 mg TDD: 40 µg/kg/24 h, up to 1–1.5 mg
Diltiazem	Bolus: 0.25 mg/kg, up to 25 mg Infusion: 0.1–0.3 mg/kg/h, up to 10–15 mg/h
Lidocaine	Bolus: 1 mg/kg, up to 100 mg, repeat every 10 min × 2 Infusion: 20–50 µg/kg/min
Procainamide	Bolus: 15 mg/kg over 30 min, up to 1 g (under one year reduce dose to 10 mg/kg) Infusion: 20–80 µg/kg/min
Propranolol	Bolus: 0.01 mg/kg, up to 0.5 mg, repeat up to 0.1 mg/kg if tolerated
Verapamil	Bolus: 0.1 mg/kg, up to 5–10 mg; repeat in 15 min

AV dissociation may be due to complete AV block, but it may also be due to isorhythmic (isochronic, interference) dissociation. In the latter situation, a lower focus, arising in the AV node or ventricle, demonstrates an intrinsic rate faster than the sinus rate. Therefore, most of the atrial complexes will encounter the AV node after it has already depolarized and is in a refractory state. This rhythm is usually characterized by intermittent short RR intervals due to sinus capture beats. Typical examples of AV dissociation not due to AV block include accelerated junctional or ventricular rhythm, and junctional ectopic or ventricular tachycardia.

53.6 Summary

Arrhythmias are a commonly encountered problem in the intensive care setting and in patients after cardiac surgery. Rapid and accurate diagnosis is required, particularly when hemodynamic compromise occurs. Multiple treatment modalities are available including optimizing the hemodynamic state and metabolic environment, medications (see Table 53.5 for doses of commonly used drugs), pacing and cardioversion or defibrillation.

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Chapter 54

Pacemakers (Temporary and Permanent), Implantable Cardioverter Defibrillators (ICDs) and Cardiac Resynchronization Therapy

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Cardiac output is dependent on normal mechanical function of the heart, which in turn is dependent on normal functioning of the cardiac conduction system. When derangements of cardiac conduction occur, this can result in poor cardiac output acutely as well as poor cardiac reserve chronically. These derangements can occur as a result of bradycardia, tachycardia, or electrical dyssynchrony (atrioventricular (AV) or interventricular) of the heart.

Different therapies have been developed to augment cardiac performance in times of electrical derangement, which include pacemakers (temporary or permanent) for bradycardic rhythms, antitachycardia pacemaker and implantable defibrillator devices for tachycardic rhythms and, most recently, cardiac resynchronization therapy (CRT) for patients with evidence of dyssynchrony causing poor cardiac output.

54.1 Basic Pacemaker Terminology and Definitions

Pacing can be performed in the atrium, the ventricle or in both chambers sequentially. In addition, pacemakers can respond to intrinsic myocardial electrical activity or can operate without regards to native depolarization (asynchronous modes). The basic modes of pacing are based on a combined North American Society for Pacing and Electrophysiology (NASPE) and British Pacing and Electrophysiology Group

(BPEG) consensus group, which formulated the generic pacing (NBG) nomenclature. An adaptation of the most revised version of this code is presented in Table 54.1 [1].

Successful pacing requires that electrical energy is successfully delivered from the generator to the myocardial tissue, allowing for electrical activation of the myocardium. Thus, failure in any part of the system (generator, lead, lead/myocardial interface) can lead to failure of pacing.

Common user-adjustable parameters in pacing include the lower and upper rates as well as the generator output. The threshold is defined as the lowest amount of energy required to successfully depolarize the myocardial tissue. Also, the sensing thresholds (level at which intrinsic depolarizations are sensed) can be adjusted. The timing of the heart rate is governed by setting of the atrioventricular (AV) delay (mimicking the native PR interval) as well as the post-ventricular atrial refractory period (PVARP). These factors govern the allowable upper rate based upon the total atrial refractory period (TARP), which is the sum of the AV delay and PVARP. A full discussion of these parameters is beyond the scope of this text but may be read in any basic pacing textbook.

Leads may be unipolar or bipolar. Briefly, unipolar pacing occurs between the electrode tip and a ground electrode (either subcutaneous or the pacemaker generator). Bipolar pacing, on the other hand, occurs between two electrodes which are in close proximity (typically both at the tip of the lead). It is also helpful to know that unipolar pacing results in a larger stimulus artifact on the electrocardiogram or monitor, while a bipolar pacing spike is usually small in amplitude or inapparent.

With application of magnets, most pacemakers will revert to asynchronous pacing, while defibrillators

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Table 54.1 Basic generic pacemaker code (NBG); adapted from [1]

I	II	III	IV	V
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation	Multisite pacing
O=None	O=None	O=None	O=None	O=None
A=Atrium	A=Atrium	T=Triggered	R=Rate modulation	A=Atrium
V=Ventricle	V=Ventricle	I=Inhibited		V=Ventricle
D=Dual (A+V)	D=Dual (A+V)	D=Dual (T+I)		D=Dual (A+V)

will typically temporarily disable therapies. However, devices respond differently to magnet applications so the specific response of each device must be confirmed before application of a magnet.

54.2 Pacemakers (Temporary and Permanent)

For over 50 years, pacemakers have been used in patients with bradycardic rhythms. In the current era, pacing can be accomplished temporarily or permanently. The primary methods for temporary pacing are transcutaneous, transvenous, or with epicardial wires, typically postoperatively. Permanent pacing involves implantation of a permanent pacemaker using either transvenous endocardial or epicardial leads.

Pacing requires a generator or battery to deliver electrical energy and a conduit to allow electrical energy to reach the heart. In most cases, the conduit takes the form of leads that are physically in contact with the heart.

54.2.1 Temporary Pacing

Typically, those patients who require temporary pacing are patients in whom a bradycardic rhythm is not tolerated hemodynamically but in whom recovery of normal rhythm is expected. Another major category would be patients with infected pacing systems that need to be explanted until the infection has been completely cleared. Indications for temporary pacing are listed in Table 54.2.

Temporary pacing can be accomplished transcutaneously in an emergency.

Transcutaneous pacing relies on an external generator, which is typically an external defibrillator. Energy is

Table 54.2 Indications for temporary pacing

Postsurgical bradycardia
– Atrioventricular (AV) block
– Sinus node dysfunction
– Overdrive suppression of arrhythmias (atrial flutter)
– Restoration of AV synchrony (e.g., junctional ectopic tachycardia)
Myocarditis
Endocarditis
Lyme disease
Rejection in post-transplant patients
Myocardial infarction
Active infection in patients needing permanent pacing

delivered to the heart using two external pads. The primary limitation to this approach is patient discomfort, as transcutaneous pacing is painful. In addition, the pads necessarily have a finite lifespan and need to be changed frequently. When using transcutaneous pacing, generator output is set at the minimum threshold required to have stimulation of superficial chest muscles. Successful pacing is measured by assessment of cardiac output, either via manual pulse check or invasive measures such as arterial blood pressure monitoring. With transcutaneous pacing, there are no lead-based parameters (e.g., sensitivity) to adjust. Thus, transcutaneous pacing is generally reserved for emergent resuscitation situations.

Temporary transvenous pacing is the preferred mode for patients requiring temporary pacing for hours to days. Pacing is usually performed in the right ventricle and is continued until a sustainable perfusing rhythm is restored or another pacing modality is established. In most cases, the generator used for temporary transvenous pacing is a specifically designed temporary pacemaker (Fig. 54.1). Various leads can be used for temporary transvenous pacing. In an emergency setting, balloon-tipped pacing catheters may be used for placement of a right ventricular pacemaker. In a more controlled setting, transvenous temporary leads with screw-in mechanisms to increase lead stability



Fig. 54.1 Temporary pacemaker (reproduced with permission of Medtronic, Inc.)

can be used. Temporary leads can be inserted through a standard percutaneous approach with or without an intravenous sheath. The subclavian and internal jugular veins are most often utilized since the right ventricle can often easily be entered without fluoroscopy. The femoral venous approach is available, but often requires fluoroscopy, though echocardiography may be helpful in lead placement. If permanent transvenous pacing is anticipated, the subclavian vein should be avoided to prevent thrombosis.

In the postoperative setting, the most common approach to temporary pacing is via the use of epicardial wires, which are placed directly onto the myocardium at the time of surgery. These wires can be placed in the atrium or ventricle, allowing for isolated single-chamber pacing or dual-chamber synchronous pacing. The atrial wires can also be used to obtain recordings of direct myocardial activity during arrhythmias for diagnostic purposes. These wires may also be used for atrial overdrive pacing for atrial tachyarrhythmias, which are not uncommon in the

postoperative setting (see Chapter 53 on “Arrhythmias in the Intensive Care Unit”). Again, the same generator used for temporary transvenous pacing may be used for temporary epicardial pacing (Fig. 54.1). In patients requiring temporary pacing longer than 7 days, consideration should be given to implantation of a permanent pacemaker (see Section 2.2).

With both transvenous and epicardial temporary pacing, the pacemaker output is based on the threshold that can be measured. In temporary pacemakers, output is measured in milliamps (mA) which is different than permanent pacemakers, where output is measured in volts (V). By convention, the output is set at twice the threshold to ensure an adequate safety margin. Thresholds will increase over time so they should be checked at least daily in all patients. In addition, the batteries in temporary pacemakers should be changed routinely, especially in patients who are pacemaker-dependent. Spare batteries should be readily available and it should be ensured that staff is familiar with battery replacement. Alternatively, for patients who are pacemaker dependent, a spare temporary pacemaker with new battery should be kept at the bedside in case of failure of the in-use temporary generator.

54.2.2 Permanent Pacemakers

Common indications for permanent pacing in young patients are given in Table 54.3 and are based on the consensus guidelines for pacing [2].

The primary modalities for permanent pacing are transvenous and epicardial systems. The choice of systems is based on patient size, anatomic issues (e.g., intracardiac shunts) vascular access, expected duration of pacing, and operator and center experience.

For patients with a permanent pacemaker who will be undergoing cardiac operations, knowledge of their pacemaker parameters before operation is essential to their postoperative care. As a generalization, patients should have their devices interrogated before and after their surgery to ensure normal device function. In addition, the medical team caring for the patients should be aware of their device parameters (mode of pacing, lower rate, upper rate) in order to properly troubleshoot any issues that may arise, especially the magnet response of that specific device.

Table 54.3 Common indications for permanent pacing in young patients

Advanced second- or third-degree AV block associated with symptomatic bradycardia, ventricular dysfunction or low cardiac output
Postoperative advanced second- or third-degree AV block not expected to resolve or persistent at least 7 days after cardiac surgery
Congenital AV block with wide QRS escape rhythm, complex ventricular ectopy or ventricular dysfunction
Congenital AV block in an infant with a structurally normal heart and heart rate <50 bpm
Congenital AV block in an infant with congenital heart disease and heart rate <70 bpm
Pause-dependent VT
Congenital AV block beyond 1 year of life with average heart rate <50 bpm, abrupt pauses in ventricular rate that are 2–3x basic cycle length, or with symptoms secondary to chronotropic incompetence
Long QT syndrome with AV block
Asymptomatic sinus bradycardia in the child with complex heart disease and pauses longer than 3 s or resting heart rate <40 bpm
Patients with congenital heart disease and impaired hemodynamics due to sinus bradycardia or loss of AV synchrony
Sinus node dysfunction and symptomatic bradycardia

54.3 Implantable Cardioverter Defibrillators (ICDs)

In patients with potentially unstable tachyarrhythmias, defibrillators may be potentially lifesaving. Currently, the most common application of this technology is implantable cardioverter-defibrillators, or ICDs. These may be implanted for secondary prevention in those patients who have sustained a life-threatening ventricular arrhythmia or as primary prevention in individuals at-risk for such arrhythmias. Consensus guidelines for ICD implantation relevant to pediatric patients are summarized in Table 54.4 [2].

Though ICDs are potentially lifesaving, their potential benefit must always be weighed against the known risks, which include infection, complication related to device placement, pneumothorax or hemothorax, lead fracture, inappropriate ICD shocks, other device malfunction, possible pro-arrhythmia and potential psychological impact on patients [3].

In pediatric electrophysiology, much of the current debate involves primary prevention of sudden death in patients with structural heart disease. It is clear that patients with repaired or palliated structural heart disease are at risk for sudden death. The lesions with

Table 54.4 Indications for implantable cardioverter-defibrillator (ICD) therapy

Cardiac arrest due to ventricular fibrillation (VF) or ventricular tachycardia (VT) not due to a transient or reversible cause
Spontaneous sustained VT in association with structural heart disease
Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study when drug therapy is ineffective, not tolerated or not preferred
Nonsustained VT in patients with prior myocardial infarction, LV dysfunction and inducible VF or sustained VT at electrophysiological study that is not suppressible by a – Class I antiarrhythmic drug
Spontaneous sustained VT in patients without structural heart disease not amenable to other treatments
Adult patients with LV ejection fraction of less than or equal to 30%, at least 1 month postmyocardial infarction and 3 months postrevascularization surgery

highest risk for late onset life-threatening arrhythmias include tetralogy of Fallot, transposition of the great arteries status post atrial switch and left-sided obstructive lesions [4]. However, there are no consensus guidelines for risk stratification in patients with structural heart disease. In addition, the patient population is quite heterogeneous, making it more difficult to have a unified approach based on type of heart disease. A prototype model for sudden death risk in patients with structural heart disease is patients with tetralogy of Fallot. Earlier data identified absolute QRS duration as well as QRS rate of change over time as risk factors for sudden death [5]. Recent published data advocate the use of invasive electrophysiology testing for risk-stratification [6]. However, study limitations and lack of wide acceptance have left each practitioner and center to formulate their own strategy for primary prevention.

54.4 Cardiac Resynchronization Therapy (CRT)

Electrical dyssynchrony results in dyskinetic ventricular activation, which reduces left ventricular efficiency. This is often seen in patients with advanced heart failure. Recent adult data have shown that pacing can be used to restore electrical synchrony to hearts with significant dyssynchrony, termed CRT [7–11]. CRT involves placement of a lead in the left ventricle,

typically via the coronary sinus, allowing for more uniform ventricular activation than by apical right ventricular pacing alone (Fig. 54.2). This has been shown to improve left ventricular ejection fraction, exercise tolerance and all-cause mortality in various adult studies. To date, there has been no prospective pediatric trial of CRT. The largest pediatric study is an international multi-center retrospective study that evaluated the potential benefits of CRT in a population of pediatric and congenital heart disease patients [12]. In a heterogeneous population, chronic CRT was associated with improvements in ejection fraction and QRS duration. The other proposed use of CRT is in the acute postoperative setting to temporarily augment cardiac output. Published reports have shown temporary benefits in patients with right ventricular dysfunction as well as single ventricle patients [13, 14].

The role of CRT in the management of pediatric and congenital heart disease patients is evolving and

further studies are necessary to elucidate any consensus approach.

54.5 Troubleshooting

Device troubleshooting is a voluminous topic worthy of textbooks in their entirety. In this chapter, we will review two of the most commonly seen device issues and their management. For a more extensive discussion, please consult a pacing textbook.

With pacing, a failure to capture the myocardium may occur, which results in a missed depolarization and a subsequent pause in the ventricular rate. This is termed pacemaker noncapture. It is characterized on the monitor and electrocardiogram by the visualization of pacing artifact with no resultant electrical activity following. This may occur either in the atrium or the ventricle.

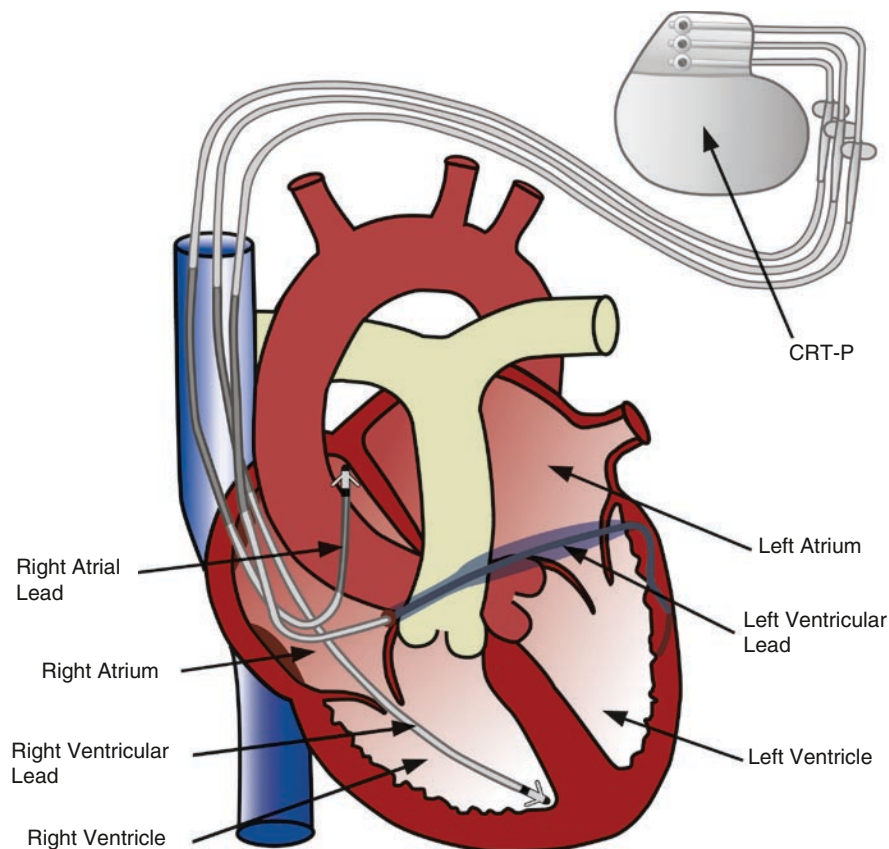


Fig. 54.2 Illustration of lead insertion in typical locations for cardiac resynchronization therapy (CRT). Locations include right atrium, right ventricle, and coronary sinus for left ventricular activation. (Reproduced with permission of Medtronic, Inc.)

When it occurs in the ventricle, the consequences are more severe as complete loss of cardiac output may ensue (Fig. 54.3). Once this is seen, the pacemaker (temporary or permanent) should be interrogated to evaluate the lead thresholds and device output. If the device output cannot be adjusted to provide an adequate safety margin, consideration should be given to the establishment of a more secure pacing modality.

Pacemaker oversensing can be similar in effect to noncapture. Pacemakers are often set to inhibit their activity in response to a sensed event. If the pacemaker falsely believes that an intrinsic depolarization has occurred, it will erroneously inhibit, resulting in a lack of depolarization and a resultant pause. This is deemed oversensing and can be distinguished from noncapture (Fig. 54.3) by the absence of pacemaker stimulus artifact compared to pacemaker noncapture where a stimulus artifact will be visualized.

As mentioned above, the upper heart rate is governed by the TARP. Many pacemakers have default settings which limit the upper rate limit to 180 beats per minute. In addition, some temporary pacemakers have default settings with a lower default upper rate (sometimes 110 bpm). When the upper rate is violated, pacemaker Wenckebach may ensue (Fig. 54.4). This is characterized by intermittently dropped P waves, similar to native Wenckebach. A P wave eventually falls in the PVARP and the ventricular lead is unable to respond to this P wave. If this occurs, the AV delay and PVARP should be adjusted to allow increase in the upper rate. The most important step to avoid this is to ensure that pacemakers are set based on age-appropriate parameters. In the case of temporary pacing, it is mandatory that the treating physician set the pacemaker based on each patient's individual case, and not rely on default settings.

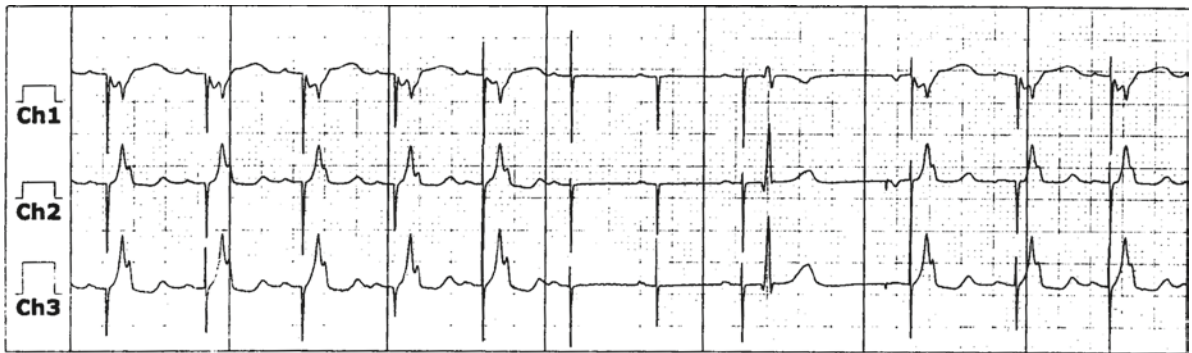


Fig. 54.3 Ventricular noncapture. Pacing spikes are initially followed by wide QRS complexes, indicating successful ventricular depolarization. In the middle of the strip, note the pacing spikes without QRS complexes, indicating noncapture. This is followed by a junctional escape beat (narrow complex)

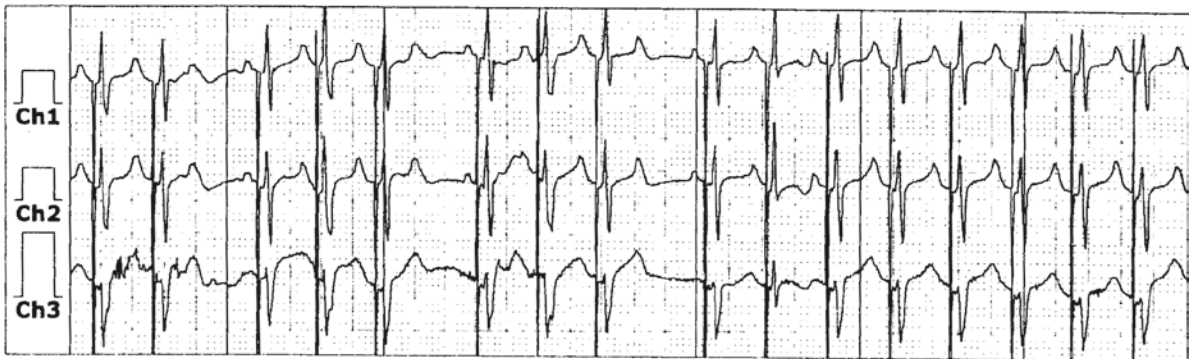


Fig. 54.4 Pacemaker Wenckebach. Initially atrial sensing with ventricular pacing (P waves followed by pacing artifact and QRS complexes). Occasional dropped beats indicate P waves that fall into the refractory period and are not responded to

54.6 Summary

Electrical therapies, including pacemakers, implantable cardioverter-defibrillators, and CRT are an important therapy for pediatric and congenital heart disease patients.

Current usage is dictated occasionally by published guidelines but is often dependent on center and physician preference. Further studies are necessary to assist in formulation of a consensus approach to management of these entities.

Understanding of the basic indications and functioning of these therapies is imperative for anyone involved in the care of these patients, particularly in the intensive care unit setting.

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Chapter 55

Discontinuation of Life: Ethical and Legal Issues

Denis Devictor and Pierre Tissières

This chapter addresses some ethically challenging situations that can occur especially in Pediatric Intensive care Units (PICUs) and Pediatric Cardiac Intensive Care Units (PCICUs). It begins with an overview of some principles of Medical Ethics. It continues with a discussion on decision making. Finally it broaches the difficult question of End-of-Life (EOL). This chapter aims at helping cardiac intensivists to resolve moral dilemmas.

55.1 Principles of Medical Ethics

There are several ethical theories that are useful in resolving moral dilemmas. Perhaps the best known is called Principlism. In a classic textbook on modern medical ethics, Tom Beauchamp and James Childress advocate four principles on which to base ethical analysis: respect of autonomy, beneficence, non-maleficence, and justice [1].

Beneficence: This principle refers to a moral obligation to act for the benefit of the patient. This may seem self-evident but the experience has shown that conflicts of interest can influence medical decisions. For example, caregivers might have the temptation to test new treatments or procedures as rescue therapies, even if their expected benefits have not been proved so far.

Non-maleficence: According to this notion, doctors have the duty to avoid harming patients. Again, this idea may seem obvious, but in practice, it is highly complex. When considering which treatment will best help the patient, doctors must balance benefits against

harm. For example, when deciding whether to use ventricular assist device for a desperately ill infant with cardiogenic shock, caregivers must consider the possibility that technology will extend the infant's life only by several days, without long-term benefit.

Respect for autonomy: This principle suggests the obligation to respect the decision-making capacities of autonomous persons. In pediatrics this obligation raises difficult dilemmas. For instance neonates and small children cannot be considered as autonomous persons. Therefore parents are often considered as their surrogates. However, the fact that parents must give legal consent for medical treatments does not mean that the opinion of the children and adolescents should be considered irrelevant or ignored, and that parents know what is the best for their child.

Justice: This principle raises the most challenging dilemmas for modern medical care. Namely, this principle exhorts caregivers to use medical services fairly, to avoid decisions that accept or reject candidates for therapies based on factors that are irrelevant to their medical situation (such as their religion, origins, social conditions for instance).

It can be safely stated that principlism is an overly simplistic theory to resolve many ethical dilemmas that arise in clinical practice. A number of alternative theories, more or less complex exist. Nevertheless, the principlism has the virtue of being clear, useful and educational.

55.2 Essential Elements of Medical Decision Making

Decision making is one of the most challenging issues in intensive care because it confronts the values of patients, families, health care professionals, and the society.

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A major shift in patient-families-doctors-society relations has occurred in recent years. Doctors now have less freedom to make paternalistic decisions about treatment according to their own beliefs. They must take into consideration the patient's, and family's perspectives. This shift has embodied in the doctrine of informed consent.

55.2.1 Informed Consent

The doctrine of informed consent assumes the right of a reasonable person to accept or refuse offered treatment. To make a valid choice, the patient or his or her surrogate need understandable information regarding the medical situation so any choice will reflect the range of alternatives and their consequences. This choice should occur voluntarily, that is, free of any undue pressure, especially from health care providers. Informed consent must satisfy at least three requirements: competency, information, understanding, requirements which are especially meaningful in PCICU.

Competency: A competent individual has the capacity to understand the medical situation, consider the risks and benefits, make a choice among the alternatives, decide upon a course of action, and appreciate the consequences of the choice. In most circumstances, minors are legally incompetent. As a consequence, their parents as surrogates must give legal consent for medical treatments. Moreover they are considered to know what is the best for their child. This does not mean that the opinions of the children should be considered irrelevant or ignored. Children as young as 6 or 7 years of age are often able to have reasoned opinions about certain aspects of their care. Moreover physicians must assess the decision making capacity of the parents.

Information: The concept of information remains a central component of informed consent. Assuming a patient or his or her surrogate has an appropriate decision-making capacity, the decision maker needs information about patient's condition, prognosis, and alternative treatments. Ethical and legal considerations require that the information is understandable. The information must allow the decision-maker to weigh the pros and cons of the therapeutic alternative. One can easily imagine situations in which understanding does not occur despite a competent decision maker and full information.

Understanding: Understanding is unlikely if the physician uses excessive medical jargon or the patient is ignorant of basic medical concept. This is particularly true in cardiology and PCICUs because of the complexity of the medical situations. Research suggests that physicians routinely overestimate what patients and family members understand. Similarly, parents may not hear what is said because of the stress induced by their child's illness. Moreover, in some cases, parents may not have enough time to consider alternatives. Time limitations might influence the decision and might invalidate full consent.

55.3 Special Issues in Pediatric Intensive Care

55.3.1 Family Access to Their Child

Access to their child is one of the most important issues for a family. Similarly, for the child, the family provides a reassuring constant in the unfamiliar PICU environment. To decrease family anxiety and the shifting of parental roles, access should be supported 24 h a day, with clear communication related to the importance of parental involvement. Parents should be viewed as partners in care rather than visitors [2].

55.3.2 Family-Centered Care

Family-centered care is an approach to the planning, delivery, and evaluation of health-care that is grounded in mutually beneficial partnerships among health care providers, patients, and families.

Family is acknowledged as expert in the care of their child, and the perspectives and information provided by the family are important to clinical decision-making. This concept is demanding since it imposes to recognize the family as a constant in the child's life, to facilitate parents-professionals collaboration, to share complete and unbiased information with families, and to satisfy child and family needs. There is a range of potential benefits and difficulties associated with the provision of family centered care [3].

55.3.3 Shared-Decision Making

A significant controversy persists regarding the role of parents relative to physicians in decision-making. Schematically, two scenarios are opposed. The first emphasizes that parents are the surrogate of their child and should be the main decision-makers. The second scenario argues that parents may not have their whole decision-making capacities because they are too stressed for instance. In this case the physicians bear the sole responsibility of the final decision. Between these extremes many countries have adopted the concept of shared-decision. The purpose is to reach consensus on a process that is in accordance with family's values and to build a collaborative relationship with the family. The shared decision paradigm allows for variations in family wishes regarding participation in the decision making process. In any cases, decisions should be well documented in the patient's chart.

55.3.4 Participation in Care

Parents better take part in care when their role as caregiver is maintained. Providing care can be alienating for some parents because they feel incompetent or too stressed. Staff, especially nurses, can help delineate the kind of care the parents can provide. Parents may feel frightened by their child's appearance or overwhelmed by the technology. Parents' participation may be as simple as holding the child's hand. They can participate more actively as well, such as assisting with tracheal suctioning, bathing, positioning, or massage.

55.3.5 Presence of Parents in Rounds

The presence of parents in physician rounds is encouraged in some institutions. However, the drawbacks would be to increase the time spent rounding and the presence of parents might inhibit open discussion among staff. Moreover, rounds may not be the best place to convey information and solicit family input in decision-making. Families may be too intimidated by the medical staff or their own lack of medical training, to actively participate [4]. Despite these drawbacks, it has been shown that nearly 85% of families request involvement

in rounds when given the option. Similarly, parental presence on rounds does not seem to interfere with the communication process within the staff [5].

55.3.6 Presence of Family Members During Cardiopulmonary Resuscitation (CPR)

The presence of family members during CPR is a controversial issue. Concerns in the literature are centered on three points. The first is the potential for family members' presence to affect the performance of resuscitation staff. The second is that witnessing a traumatic event, relatives may experience negative emotional and psychological consequences. Third, many studies have identified that members of the public would like to be given the choice whether or not to be present. These concerns are not supported by the literature, even if research on this topic is particularly scarce. Nevertheless, the general tendency is that all patients have the right to have family members present during CPR, and the patients' family members should be offered the opportunity to be present during CPR of a relative.

55.4 Essential Elements of End of Life Care

Pediatric intensivists and PICU personnel play a crucial role in EOL care [6].

55.4.1 Optimal Care for Children Dying in the PICU

The goal is the achievement of the best possible quality of life for patients and their families. Palliative care must begin from the moment the child enters the unit. The objectives of palliative are:

- To provide relief from pain and other distressing symptoms
- To intend neither to hasten nor to postpone death
- To affirm life and regard dying as a normal process

- To integrate the psychological and spiritual aspects of patient care and his or her family
- To offer support system to help patients live as actively as possible until death
- To offer support system to help family cope during the patient's illness and in their bereavement

These issues have the most relevance for those patients whose goals of care have been redirected from life-sustaining curative goals to palliative goals. These are usually children with terminal illnesses or other conditions for which the benefits of further life sustaining therapy are in question. Implicit in the phrase "redirecting the goals of care" is that care is never withdrawn from a patient, only life-sustaining treatment. Indeed, the withdrawal of care is one of the greatest fears of patients and families in these situations.

55.4.2 Forgoing Life-Sustaining Treatments

Physicians who care for patients in a PICU will be called upon to discontinue life support from dying children. In these often tragic circumstances, the question then becomes how best to manage the child during the dying process. The management of children at the end of life can be divided into two phases. The first concerns the shared decision making process as described above. The second concerns the actions that are taken once decision has been made to forgo life-sustaining treatments. Recommendations have been published to provide advice for clinicians who deliver EOL care in ICUs and PICUs. They give information on the successive interventions of EOL care.

55.4.2.1 Preparation of the Child, His or Her Family, and the Clinical Team

This preparation is based on the knowledge of child and family's needs. The needs of the child must be the primary focus of caregivers. They could be summed up in a few assertions such as to be with his or her parents and family, to have no pain, to have tender loving care, to respect his or her body, to respect his or her parents' wishes. Family needs could be summarized in a couple of priorities such as to obtain honest and complete

information, to have ready access to staff, to have better communication, to maintain parents child relationship, and to respect faith and cultural background. The needs of the clinical team are also crucial and excellent care at the EOL should be recognized as an institutional priorities. Clinical teams need to have the opportunities for bereavement and debriefing.

55.4.2.2 Providing Palliative Care

In the curative model, the criteria are related to the degree to which the procedure will contribute to the patient's recovery from illness. In the palliative model, the criteria are related to whether the intervention will improve symptom relief, improve functional status, or ameliorate emotional, psychological, or spiritual concerns [6]. Palliative care gives pain relief a high priority. The increased use of pain scales has provided for better quantification even in neonates and small infants. Patients' comfort can be improved with non pharmacologic or pharmacologic approaches. One crucial issue is the question of double effect. When an action has two effects, one of which is inherently good and the other of which is inherently bad, it can be justified if certain conditions are met. For example, the administration of morphine to a dying child has both a good effect (relief of pain and suffering) and the potential for a bad effect (hastening the child's death through respiratory depression). The key difference lies in the intention of the physician. As long as the physician's intention is treatment of the child's pain and suffering, the administration of analgesics and sedatives is non-controversial. When the physician's intention is to kill the child, then the red line between accepted practice and euthanasia has been crossed.

55.4.2.3 Withholding and Withdrawing Life Support

Physicians are much more comfortable in withholding treatments than in withdrawing them. In other words, they believe there is a difference between deciding not to intubate a patient because they do not think that he or she will recover, and extubating a patient who has failed to recover despite a period of ventilation. In practice each therapy may be continued or discontinued, depending on the clinical characteristics of the

patient and the type of life support that is being withdrawn or withheld. It has been shown that parents who were with their child at the time of death, did not regret having been present, whereas parents who were not present later wished they had been.

55.4.2.4 Communication

The quality of communication consistently emerges as an important, and indeed perhaps the most critical determinant of the satisfaction of parents with the care of their dying children. In some studies, parents rated parents-doctors communication as the principal determinant of high-quality physician care. Problems in communication lie at the heart of many conflicts that occur between families and clinicians in the PICU. Families often experience physicians not being sufficiently available. Parents always welcome the opportunity for scheduled meetings with clinicians. Some parents want to reduce the potential for contradictory information by having a single point person to communicate with. Other, actually prefer to hear from multiple perspectives.

55.4.3 Legal Issues

The legal issues involved in discontinuation of life sustaining treatment are highly dependant upon the legislation of the country. In many Western countries there is consensus in the law that parents have the authority to determine the best interest of their children and to make decisions in accord with their own values. However, pediatric intensivists must be thoroughly familiar with their legal duties to their pediatric

patients, independent of parental viewpoints about life-sustaining treatments.

55.5 Conclusion

Advances in pediatric intensive and critical care have led to ethical and legal issues of profound concern to all critical care providers. One of the most striking changes is that the majority of deaths in the PICUs occur following the decision to withdraw or withhold life-sustaining treatments. This fact heightens the importance of competence in EOL decision-making and palliative management by all practitioners working in PICUs and PCICUs.

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Part IV
The Challenge of Extra-Cardiac Complications

Chapter 56

Respiratory Complications: Acute Respiratory Distress Syndrome, Chylothorax, Diaphragmatic Palsy, and Functional and Respiratory Physiotherapy

Jennifer Exo and Ricardo Muñoz

56.1 Acute Respiratory Distress Syndrome (ARDS)

56.1.1 Introduction

Acute respiratory distress syndrome (ARDS), also called noncardiogenic pulmonary edema, is an uncommon postoperative complication after pediatric cardiac surgery, heart transplantation, and cardiopulmonary bypass. Several large prospective trials studying ARDS in medical and surgical patients have been completed, but postoperative cardiac patients were not specifically studied. Despite this, it is necessary for those caring for critically ill children with heart disease to understand the pathophysiology, clinical course, and therapies used to treat ARDS.

56.1.2 Definition

The definition of ARDS has evolved with the understanding of the disease. Originally called “adult respiratory distress syndrome,” the title was changed to “acute respiratory distress syndrome” after being recognized in newborns and children, though controversy over the incidence and pathology made ARDS difficult to define. In 1994, the American-European Consensus Conference Committee developed the widely accepted definition for ARDS and acute lung injury (ALI) [1]. As such, ALI is currently defined as

an acute onset of respiratory distress and hypoxemia (defined as a $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio ≤ 300), bilateral infiltrates on chest X-ray, pulmonary wedge pressure ≤ 18 mmHg, or absence of clinical evidence for left atrial hypertension. ARDS is characterized by the same chest X-ray and pulmonary wedge pressure findings, but with more severe hypoxemia (defined as a $\text{PaO}_2/\text{F}_i\text{O}_2$ ratio ≤ 200). The diagnosis of ALI and ARDS remains clinical, but the adoption of a consensus definition has helped standardize research studies and facilitated earlier recognition of these diseases.

56.1.3 Pathophysiology

The pathophysiology of ARDS is not completely understood, but several contributing mechanisms have been identified (Fig. 56.1). Neutrophils migrate into the alveolar compartment, and produce several proinflammatory substances, including leukotrienes, proteases, reactive oxygen, and nitrogen species that serve to propagate lung damage. Changes in capillary endothelial integrity allow protein-rich fluid to leak from the plasma into the lung interstitium and airspaces. Similarly, alveolar epithelial injury causes necrosis and sloughing of Type I alveolar cells.

Next, protein influx and damage to Type II alveolar epithelial cells alters the production and function of surfactant, which in turn alters alveolar function. Neutrophils also release the platelet-activating factor (PAF) along with other pro-coagulant inflammatory factors. The balance of coagulation and fibrinolysis is altered, resulting in the development of systemic microthrombi. In particular, occlusions of small pulmonary vessels by thrombi contribute to vascular remodeling and the development of pulmonary hypertension.

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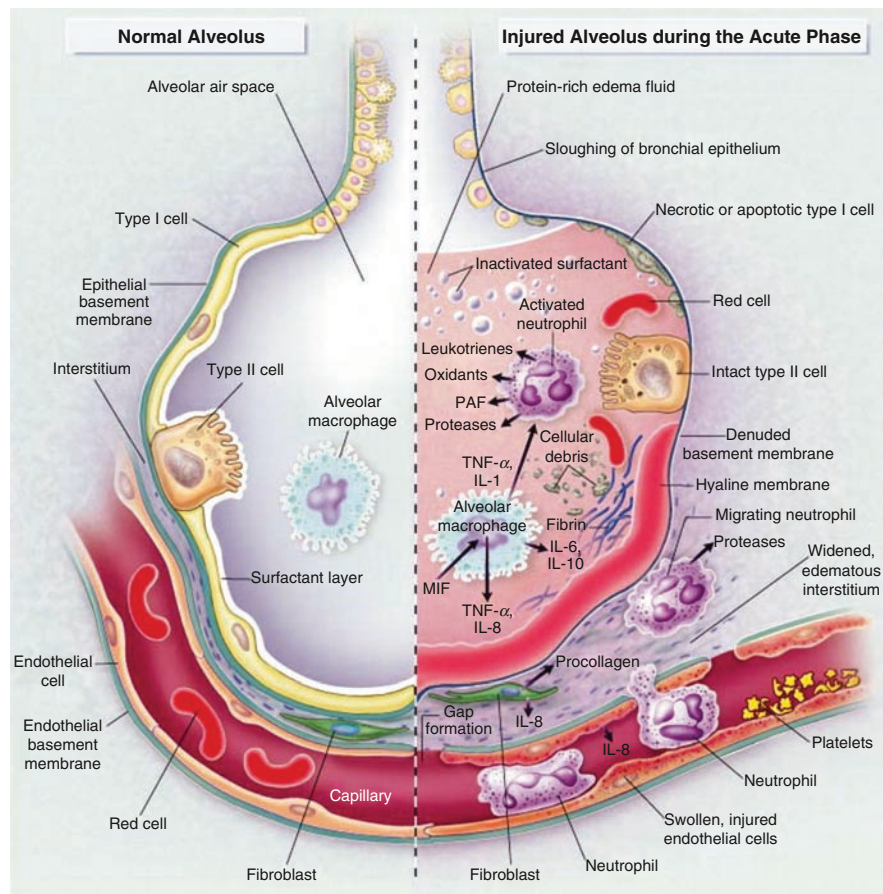


Fig. 56.1 The normal alveolus (*left side*) and injured alveolus in the acute phase of Acute Lung Injury and the Acute Respiratory Distress Syndrome (*right side*). The damaged alveolar epithelium and capillary endothelium allows leakage of inflammatory substances and cells into the airspace. The collection of fluid and protein in the alveolus inactivates surfactant. Release of cytokines, interleukins, and tumor necrosis factor α (TNF- α)

from alveolar macrophages activate and induce migration of neutrophils to the lung. Neutrophils adhere to the damaged capillary endothelium and move into the alveolus, which is filled with proteins and fluid. Upon their arrival, they secrete pro-inflammatory substances, including reactive oxygen species, leukotrienes, and platelet-activating factor (PAF) (By permission from Ref. [23])

Finally, mechanical ventilation itself can contribute to lung damage. Besides the toxic effects of prolonged ventilation with high fractions of inspired oxygen, mechanical stress is applied to susceptible alveoli amplifies inflammation. Since the amount of lung available for oxygenation and ventilation is greatly reduced, the volume and pressure applied by mechanical ventilation causes overdistension of uninjured alveoli. Repeated collapsing and reopening of alveoli also stimulates the release of inflammatory cytokines. Together, these changes cause the impaired gas exchange and altered lung mechanics that characterize the acute phase of ARDS.

56.1.4 Clinical Course

The onset of ARDS is characterized by rapid development of respiratory distress, hypoxemia that responds poorly to oxygen, bilateral infiltrates on chest X-ray (Fig. 56.2), and pleural effusions. Alveolar and interstitial edema can worsen the work of breathing by increasing resistance to airflow and decreasing lung compliance. When combined with respiratory muscle fatigue, intubation, and mechanical ventilation are often necessary. Computed tomography of the chest of an ARDS patient often reveals areas of normal lung interspersed with areas of consolidation and collapse (Fig. 56.3). The

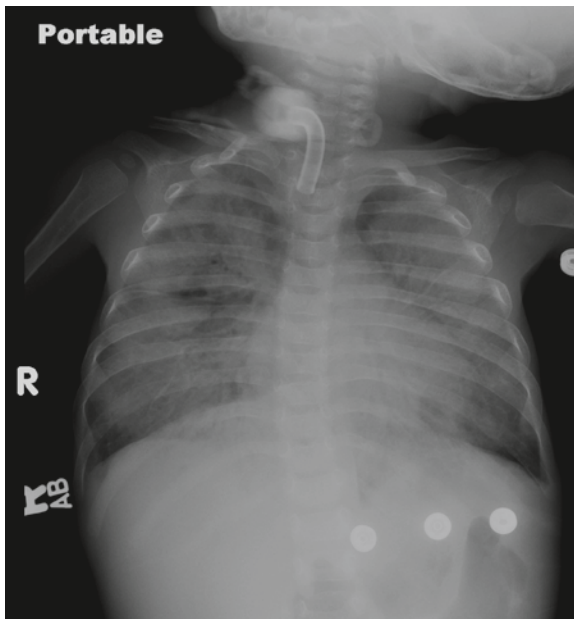


Fig. 56.2 Radiographic findings in the acute phase of Acute Lung Injury and the Acute Respiratory Distress Syndrome. This figure shows an anterior-posterior chest radiograph of an 18 month-old child with acute respiratory failure. The diffuse bilateral opacities are consistent with the diagnosis of acute respiratory distress syndrome (Courtesy of Dr. Rajesh Aneja)

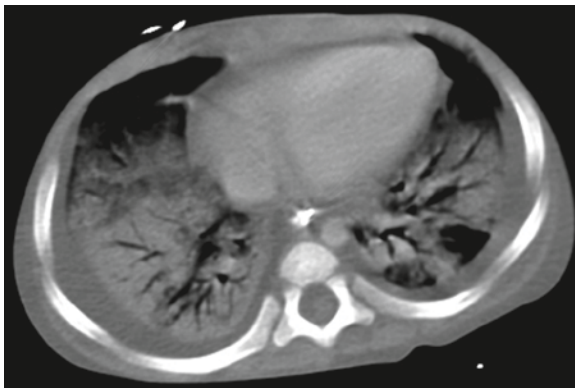


Fig. 56.3 Computed Tomographic (CT) Findings in the acute phase of Acute Lung Injury and the Acute Respiratory Distress Syndrome. This figure shows a CT image of an 18 month-old child with acute respiratory distress syndrome. Bilateral pleural effusions and alveolar opacities are present in the dependent areas of the lungs (Courtesy of Dr. Rajesh Aneja)

areas of lung with normal compliance can become overdistended as more of each breath is delivered preferentially to them instead of their stiff, damaged counterparts. This reduces lung functional residual capacity and increases intrapulmonary shunting. The

application of PEEP can recruit a portion of these collapsed areas.

Persistent pulmonary endothelial dysfunction, progressive fibrosis, and hypoxic vasoconstriction can increase pulmonary vascular resistance. Elevated pulmonary capillary and arterial pressures contribute to the development of pulmonary hypertension, which can cause shunting of blood from the right to the left side of the heart if a direct connection is present, or compromise cardiac output if no such connection exists. Prolonged pulmonary hypertension also contributes to the development of right ventricular dysfunction and failure.

Timely resolution of these pathologic processes is required for recovery. Excess neutrophils undergo apoptosis and phagocytosis by lung macrophages. Active transport of sodium and chloride from the alveoli into the interstitium facilitates resolution of alveolar edema. Water passively follows these ions through aquaporins, located primarily on Type I alveolar cells. Insoluble proteins are then removed by local cell endocytosis and phagocytosis, making it possible to rebuild the alveolar hyaline membrane framework. Type II alveolar cells multiply on the damaged framework, and then differentiate into type I cells. The type I cells restore alveolar structure and the alveolar-capillary barrier, new blood vessels form, and normal gas exchange and lung mechanics are restored.

Many patients experience substantial improvement within the first week of ARDS, while others develop fibrosing alveolitis. Progression to fibrotic lung disease usually occurs 5–10 days after disease onset; excessive fibrosis is associated with increased mortality. In the fibrotic phase, alveolar edema and inflammation become less prominent. Instead, granulation tissue, rich in collagen and fibrin, is deposited. This tissue, along with fibroblasts and procollagen III peptide, fill the alveolar spaces, making the lungs less compliant and susceptible to further injury. The fibrotic phase is usually prolonged, increasing the risk of developing nosocomial infections, organ failure, and respiratory muscle deconditioning. The progressive fibrosis further reduces lung compliance, rendering PEEP less effective for recruitment of collapsed areas and contributing to carbon dioxide retention. Patients in this stage often require weeks of mechanical ventilation, and after recovery, are at risk of increased bronchoreactivity and extrapulmonary complications (muscle wasting and weakness). Most patients who survive ALI and ARDS

do not have long term lifestyle limitations or severe, chronic pulmonary disease, but lung abnormalities, particularly involving gas exchange, may persist for an extended period of time.

56.1.5 Treatment

56.1.5.1 Ventilation and Oxygenation Strategies

Survival of ARDS often requires intubation and mechanical ventilation. Experimental and human research suggests using specific oxygenation and ventilation strategies. Traditionally, mechanical ventilation is titrated to achieve normal arterial blood gases; this is often accomplished by using tidal volumes measuring 10–15 ml/kg of predicted body weight. Numerous studies have shown excessive tidal volumes damage consolidated (low volume) lungs. Trials using lower ventilator settings at the expense of gas exchange were undertaken, and a landmark ARDS network study demonstrated low tidal volume, lung protection strategies improved outcome [2]. To summarize this study, the NIH ARDS network lower tidal volume strategy compared ventilation with tidal volumes of 4–6 ml/kg and positive plateau pressure less than 30 cm H₂O (lung protective arm) with tidal volumes of 11–12 ml/kg and positive plateau pressure less than 50 cm H₂O (control arm). Oxygen saturation was maintained between 88 and 95% by adjusting PEEP to maintain minimal FiO₂. Levels of arterial carbon dioxide were allowed to rise, as long as arterial pH remained higher than 7.15 (permissive hypercapnia). The pH was maintained by increasing ventilator respiratory rate and titration of a sodium bicarbonate infusion. The patients ventilated with the lower tidal volume strategy had significantly reduced mortality, increased ventilator-free days, and reduced incidence of extrapulmonary organ failure in the first 28 days of their hospital stay when compared with the traditional ventilation group (control arm). This study was criticized for using supranormal tidal volumes in the control arm, since, all but one other study showed no significant difference in mortality when lower tidal volumes were compared with tidal volumes of 10 ml/kg.

An important consequence of using lung protective strategies is the development of hypercapnia. Ideally, the PaCO₂ is allowed to raise no more than 5 mmHg/h.

PaCO₂ levels of 65–85 mmHg are considered acceptable, and bicarbonate is used to maintain a desirable pH. Increasing amounts of sedation may be required to reduce patient dyspnea and air hunger that result from rising levels of carbon dioxide. Hypercapnia can increase pulmonary vascular resistance and mean pulmonary arterial pressure, which is an important consideration in patients with heart disease.

Manipulation of positive end-expiratory pressure (PEEP) has been shown to improve outcome in ARDS [3]. Application of PEEP minimizes oxygen toxicity by maximizing alveolar recruitment and decreasing the need for high fractions of inspired oxygen. However, excessive levels of PEEP can overdistend areas of normal lung and negatively impact hemodynamic function. This has led researchers to seek the “ideal” PEEP, in which compliance and oxygenation are maximized, while overdistension and undesirable hemodynamic effects are minimized.

Prone positioning can also be used to recruit collapsed alveoli. This position is also thought to improve ventilation–perfusion matching, increase end-expiratory lung volume, create positive changes in chest-wall mechanics, and enhance oxygenation. Despite these positive effects, it has not been shown to improve survival [4].

High-frequency oscillatory ventilation (HFOV) can be used to minimize hypercapnia and maximize lung inflation and oxygenation. By adjusting the amplitude of the oscillation, lung ventilation is improved and hypercapnia is reduced. The mean airway pressure can be adjusted to maximize oxygenation and minimize the inspired fraction of oxygen. By using smaller tidal volumes and maintaining alveolar volumes, HFOV has been shown to improve survival and decrease the incidence of persistent lung disease after ALI [5].

56.1.5.2 Other Therapies

Several other therapies are useful in the treatment of ARDS. Because patients with bronchiolitis, pneumonia, and sepsis are more likely to develop ARDS, prompt initiation of antibiotic therapy is important.

Nitric oxide, a known pulmonary vasodilator, is also used in the treatment of ARDS. Inhaled nitric oxide increases pulmonary blood flow to normal lung tissue, and therefore improves ventilation–perfusion matching. Nitric oxide can be used to reduce pulmonary artery pressures and improve the oxygenation index (OI) in

ARDS patients, but has not been shown to improve mortality rates [6]. Assessment and management of fluid status is also important in the treatment of ARDS. Aggressive volume resuscitation is often necessary in the treatment of concomitant septic shock, and the development of capillary leak can increase extravascular lung water.

Diuresis is useful for treating persistent pulmonary edema, although this must be done carefully, since rapid diuresis can compromise cardiac output and tissue perfusion.

Because levels of surfactant are reduced, and the surfactant produced is functionally abnormal, administration of exogenous surfactant may improve lung compliance and allow recruitment of collapsed alveoli. A multicenter, prospective, randomized study demonstrated that patients with ALI or ARDS treated with surfactant had improved oxygenation and decreased mortality when compared with the control group [7].

Steroids are also used to treat the inflammation associated with ARDS, although the benefit of steroid administration in ARDS remains controversial. High-dose, short-course corticosteroids given in early ARDS failed to improve survival in several research trials [8–11]. Two trials showed moderate-dose steroids improved lung function and survival in persistent ARDS [12, 13]; while the ARDS network late steroid rescue study showed late administration of steroids did not improve survival [14].

56.1.6 Conclusion

Although relatively uncommon, it is necessary to understand the physiology and treatment of pediatric patients with ARDS. For patients with concomitant heart disease, gentle ventilation strategies and adjunctive therapies can be applied with special consideration of their cardiovascular effects, thereby hastening recovery from ALI and ARDS.

56.2 Chylothorax

Development of a chylothorax is a potential complication following surgery to correct heart disease [15]. A tear in the thoracic duct allows the leak of chylous fluid into the hemithorax. The development of a large chylous

effusion can result in compromised pulmonary function, significant loss of immunoglobulins, T-lymphocytes, albumin, and important electrolytes. Chest tube drainage may be persistent and creamy in appearance if the patient is receiving enteral nutrition with long-chain fatty acids. Fluid triglyceride levels >1.2 mmol/L and total fluid cell count >1000 cells/ μ L (predominantly lymphocytes) confirm the diagnosis of chylothorax. In fasting patients, drainage may appear serosanguineous with a normal triglyceride level.

Treatment includes:

- a) Decreasing chyle production
- b) Draining pleural fluid
- c) Providing appropriate nutrition and fluid replacement.

Placement of a thoracostomy tube allows continuous evacuation of chyle from the pleural space, while changing to a total parenteral or fat-restricted oral diet with medium chain fatty acid supplementation decreases chyle production. Somatostatin and its synthetic counterpart octreotide, have also been used successfully to treat chylothorax [13]. By acting on splanchnic vascular receptors, octreotide decreases chylomicron synthesis and transfer into the lymphatic duct, decreasing chyle leak into the pleural space. A chylothorax resistant to dietary and medical management may require surgical intervention [16, 17]. Ligation of the thoracic duct, placement of a pleuroperitoneal shunt, and pleurodesis with talc or fibrin are among several surgical techniques.

56.3 Diaphragmatic Palsy and Paralysis

Injury to the phrenic nerve (usually left) can occur during surgeries involving dissection of the branch pulmonary arteries and manipulation of the aortic arch and superior vena cava. Reoperations in the presence of adhesions and scarring, which obscure landmarks, can also make inadvertent injury to the phrenic nerve more likely. Phrenic nerve injury resulting in diaphragmatic palsy (reduced motion) and paralysis is a cause of respiratory failure in the postoperative period. Neonates and young infants are particularly at risk for respiratory failure from diaphragm palsy and paralysis. This population relies heavily on the diaphragm to breathe, whereas older counterparts use intercostal and accessory muscles to assist in the work of breathing. Injury to the phrenic nerve is part of the differential

diagnosis of a postoperative patient struggling to wean from positive pressure ventilation. Symptoms include increased work of breathing on low ventilator settings and persistent atelectasis and oxygen requirement. An elevated hemi-diaphragm may be visible on chest X-ray, although a film taken during peak positive ventilation may obscure this finding. Ultrasonography or fluoroscopy can be used to identify evidence of reduced or paradoxical diaphragm movement. Evoked responses and diaphragmatic electromiography may also provide useful diagnostic information. It is important that these tests are performed in the absence of positive pressure ventilation, as this can cause a false negative test result. Recovery from phrenic injury often occurs spontaneously, but surgical plication may be necessary when repeated extubation failures occur in patients with optimized cardiovascular function, particularly in patients with confirmed paralysis [18, 19]. Diaphragmatic palsy or paresis may also benefit of medical treatment including respiratory physiotherapy, CPAP, and the use of oral xanthines.

56.4 Respiratory Physiotherapy

Clearance of respiratory secretions and prevention and treatment of atelectasis are crucial components of postoperative recovery. Prolonged intubation, acquisition of pulmonary infections, respiratory muscle weakness, and inadequate nutrition can make this difficult. Chest physiotherapy and tracheal suctioning are often initiated for patients who are intubated or are unable to cough effectively. Tracheal suctioning allows clearance of tracheal secretions, but may cause arrhythmias and hypoxia. Chest physiotherapy consists of postural drainage and chest percussion or vibration. Fresh chest wounds, coagulopathy, and a tenuous cardiovascular status may be prohibitive. Several new devices are being used in conjunction with suctioning and traditional chest physiotherapy. These include an intrapulmonary percussive ventilator (IPV), intermittent positive pressure breathing (IPPB), and a mechanical insufflator–exsufflator (CoughAssist) [20–22]. These devices, in conjunction with tracheal suctioning, traditional chest physiotherapy, and inhaled mucolytics, can be helpful in the maintenance of pulmonary hygiene and increase the chance of respiratory recovery.

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Chapter 57

Gastrointestinal Complications: Necrotizing Enterocolitis, Malrotation, and Protein Losing Enteropathy

Joanne K. Snyder, Katherine Barsness, and Ricardo Muñoz

57.1 Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is an acute inflammatory disease with a multifactorial and controversial pathogenesis. NEC is a disease of newborns that is characterized by variable damage to the intestinal tract ranging from mucosal injury to full-thickness necrosis and perforation. The terminal ileum and proximal ascending colon are the most common sites of NEC. The disease may involve a single isolated lesion, multiple discontinuous areas or in rare instances pan-necrosis.

The pathogenesis of NEC is still incompletely understood. Several factors are involved in the pathophysiology of NEC, including: immaturity of the neonatal gut mucosa, mesenteric ischemia, tissue hypoxia, enteral alimentation, and presence of infectious or toxic agents [1].

The incidence of NEC is 1–3 cases per 1,000 live births. Male and female infants are equally affected. The disease is more prevalent among very low birth weight infants. NEC is also reported among term infants who have an additional risk factor that predisposes them to bowel ischemia, such as perinatal asphyxia, intrauterine growth retardation (IUGR), or congenital heart disease (CHD) [2]. The most commonly associated congenital heart defects are hypoplastic left heart syndrome (HLHS), truncus arteriosus, and aortic arch anomalies [3].

A high index of suspicion for NEC is critical in infants with CHD, ranging from patent ductus arteriosus (PDA) to HLHS. Surgical intervention to correct

any form of CHD may be a predisposing factor for NEC. Intestinal mucosal ischemia, although frequently transient, can occur in infants during and after cardiopulmonary bypass [4]. In contrast, patients with coarctation of the aorta may have reperfusion intestinal injury after the surgical repair, a defined component of postcoarctectomy syndrome [5].

The presence of PDA is also a risk factor for the development of NEC. Indomethacin is the pharmacological agent most frequently used for non surgical closure of PDA in premature infants. Indomethacin induces a reduction in mesenteric blood flow, which further compromises bowel perfusion in the presence of a hemodynamically significant ductus [6].

57.1.1 Clinical Presentation

The clinical presentation of NEC includes nonspecific findings, such as vomiting, diarrhea, and feeding intolerance. More specific symptoms include abdominal distension and frank or occult blood in the stools. With disease progression, abdominal tenderness, abdominal wall edema and erythema, or palpable bowel loops may become apparent. Apnea, bradycardia, lethargy, labile body temperature, hypoglycemia and shock are signs of advanced disease.

57.1.2 Diagnosis

57.1.2.1 Laboratory Test

In any infant with a suspicion for NEC, initial laboratory tests should include a complete blood count

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(CBC), basic metabolic panel (BMP), and blood cultures. A CBC may demonstrate elevated, normal, or low white blood cell (WBC) counts. An elevated hemoglobin level and hematocrit may mark hemoconcentration due to notable accumulation of extravascular fluid. However, the infant may be anemic if clinically significant gastrointestinal (GI) blood loss has occurred secondary to hemochezia. Thrombocytopenia is the most frequent hematologic abnormality; more than 80% of patients have platelet counts of less than 150,000/ μ L. Thrombocytopenia appears to be a reaction to gram negative bacterial endotoxin. Patients with platelet counts less than 50,000 warrant a platelet transfusion.

Obtaining a blood culture is recommended before beginning antibiotics in any patient presenting with signs or symptoms of sepsis or NEC. Although blood cultures rarely grow positive in NEC, sepsis is one of the major conditions that mimics NEC and should be considered in the differential diagnosis.

A blood metabolic profile may show electrolyte abnormalities consistent with metabolic acidosis. This is common and may represent intestinal ischemia, hypoperfusion, and hypovolemia.

57.1.2.2 Radiography

Plain abdominal radiographs are the mainstay in confirming the diagnosis of necrotizing enterocolitis. Pneumatosis intestinalis with an appropriate clinical presentation is diagnostic of NEC. Pneumatosis is present in over 50% of patients with NEC [7]. Pneumatosis may occur as a cystic form, which has a foamy appearance, or as the linear form, in which the gas accumulates in the sub-serosal layer. The gas is principally hydrogen, secondary to bacterial metabolism in the bowel wall.

Pneumoperitoneum is pathopneumonic for intestinal perforation and is best seen on an abdominal film performed in the left lateral decubitus position [7]. Free air may also be identified as the “football sign” on supine views, as free air outlines the falciform ligament.

Portal-vein gas is seen as linear branching streaks overlying the liver. It is caused by gas produced by bacteria in the portal veins or by the transmigration of gas from the bowel wall, through mesenteric veins and into the portal vein [7].

Although nonspecific, distended loops of small bowel are one of the most common radiographic findings in NEC. Air-fluid levels and bowel wall edema may also develop. Serial radiographic studies are important to monitor the degree of distension and to observe for any fixed or dilated loops of bowel.

Ascites can occur in advanced cases of NEC. The ascites is often purulent and may contain succous. Ascites is suggested by a generalized opacification of the abdomen with medial displacement of bowel loops. A paracentesis with a positive gram stain for gram negative bacteria is an operative indication for NEC.

Contrast-enhanced radiographic studies are not usually performed in infants with suspected NEC. However, an upper GI tract study can be useful for the infant with an equivocal presentation. Water-soluble contrast should be used to avoid the risk of barium extravasation through a perforated viscus. Signs of NEC include irregular or ulcerated mucosa, separated bowel wall loops, pneumatosis, and bowel wall spiculation.

Abdominal ultrasonography (US) is useful for identifying gas in the portal venous system as well as pneumatosis intestinalis and has been reported as more sensitive than plain radiography for the detection of these findings [7]. Ultrasonography appears to be most useful in neonates with an equivocal clinical picture for NEC and normal or nonspecific plain radiographic findings. In addition, ultrasonography can assist in the identification of ascites or abscess. Ultrasonography can also facilitate localization for paracentesis and percutaneous abscess drainage [7].

57.1.3 Treatment

57.1.3.1 Nonoperative Management

The mainstay of treatment for patients with early stage NEC is medical management. The typical course of treatment consists of cessation of enteral feeds, nasogastric decompression, and broad spectrum antibiotics. Historically, antibiotic coverage has consisted of ampicillin, gentamicin, and either clindamycin or metronidazole, although the specific regimen used should be tailored to the most common nosocomial organisms found in the particular Neonatal or Cardiac Intensive Care Unit. In addition, a strong index of suspicion for fungal septicemia must be maintained, especially in

the infant with a deteriorating condition and negative bacterial cultures.

Infants with early stage disease, improved abdominal symptoms and a negative sepsis workup will resume feedings in 7–10 days. The infant should be fed slowly with careful monitoring for distension, emesis, and other signs of intolerance or recurrent NEC. Large-volume feedings and highly concentrated formulas should be avoided when feeds are initiated.

Patients with more extensive NEC and those who do not demonstrate clinical improvement may need intense supportive care, including ventilatory support and aggressive resuscitation. These patients require urgent surgical evaluation and management.

57.1.3.2 Surgical Management

Surgery is indicated in the medically treated patient whose clinical condition deteriorates. The signs of deterioration include frank peritonitis, worsening abdominal cellulitis, progressive and intractable acidosis, persistent thrombocytopenia, rising leukocytosis or worsening leukopenia, and hemodynamic instability.

Surgical options for advanced NEC include peritoneal drainage and formal abdominal exploration. Peritoneal drainage is often selected for the very low birth weight infants (<1,000 g) or those infants too ill to tolerate a formal laparotomy [8]. For infants with multi-segmental disease and pan necrosis, peritoneal drainage is often inadequate and these infants will require subsequent abdominal exploration.

Peritoneal drainage is performed at the bedside with systemic narcotics and local anesthesia. The site of drainage is usually in one or both lower quadrants. A Penrose® drain is passed from the right to the left lower quadrant and secured in place. Upon entering the peritoneum, there is often a rush of air and/or succus. The drain will remain in place until drainage ceases. It is not unusual for a drain site to mature into an enterocutaneous fistula that will require subsequent surgical resection to restore intestinal continuity.

Abdominal exploration is performed through an upper quadrant transverse laparotomy incision. Upon entry into the peritoneal cavity, the liver is quickly identified and gently retracted out of the field of view. A sub-capsular liver hematoma can be a fatal complication of abdominal exploration in an infant. Therefore, it is imperative that there is a minimal manipulation of the liver.

The bowel is eviscerated from the peritoneal cavity and inspected for necrosis and perforation. Although the terminal ileum is the most common site of necrosis and perforation, the entire length of bowel must be evaluated due to a high incidence of discontinuous necrosis. The surgical goal is resection of all nonviable intestine with preservation of overall intestinal length. Bowel with liquifactive necrosis and/or frank perforation must be resected. Questionably viable bowel is often left in situ for second-look evaluation within 24–48 h of the original laparotomy. A proximal enterostomy is created at the most proximal site of intestinal resection. Distal discontinuous segments can be left in situ or re-anastomosed.

Primary anastomosis is advocated in select cases of isolated intestinal perforation. In these infants, there is minimal peritoneal contamination and overall excellent bowel viability.

Enterostomy closure to restore intestinal continuity is usually performed 6–8 weeks after the initial surgical intervention. All bowel distal to the stoma must be imaged with a contrast enema before closure of the stoma to ensure no distal strictures of the remaining bowel.

Abnormally high ostomy output may indicate a need for early ostomy closure. A patient with a high jejunostomy may have substantial loss of fluid and electrolytes, with consequences such as failure to thrive and peristomal skin injury. These patients may benefit from early ostomy closure with attendant colonic water absorption. However, infants with a high ostomy and extensive ileal resection, particularly the ileocecal valve, who undergo ostomy closure may have considerable secretory diarrhea. Regardless, patients must be monitored after ostomy closure for stool output and electrolyte abnormalities. All patients with remaining large intestine after an initial operation for NEC must be examined with contrast-enhanced enema of the colon to identify any areas of stricture before ostomy closure. If any strictured areas are present, they will need to be resected when the re-anastomosis is performed.

57.1.3.3 Postoperative Management

The most common complication after NEC is intestinal stricture. It occurs when an area of intestinal ischemia heals with resultant fibrosis and scar formation that impinges on the diameter of the lumen. The most common

site of stricture is the left colon, followed by the terminal ileum. Intestinal stricture is most common in infants treated nonoperatively. It should be suspected in any infant who receives nonoperative treatment for NEC and who fails to tolerate enteral feeds and/or has recurrent bloody stools or bowel obstruction after resumption of feeds.

Intestinal malabsorption is caused by loss of bowel length with decreased absorptive surface area, vitamin B-12 deficiency, bile salt deficiency, bacterial overgrowth, and intestinal hypermotility. Short gut syndrome is the most serious postoperative complication, occurring in as many as 27% of patients after intestinal resection [9]. Cholestatic liver disease is a multifactorial condition caused by prolonged fasting and total parenteral nutrition. It is characterized by hepatomegaly and elevated aminotransferase and direct bilirubin levels. The treatment is initiating enteral feedings as early as possible to stimulate bile flow. Patients with intestinal failure requiring chronic parental nutrition should be managed closely by a multidisciplinary team consisting of a nutritionist, gastroenterologist and pediatric surgeon.

57.1.4 Long-Term Outlook

Infants who survive NEC are at increased risk for developmental delay. According to one study infants with NEC were significantly more likely than infants of similar age and gestation who did not develop NEC to be neuro-developmentally impaired including a higher risk of cerebral palsy, visual, cognitive and psychomotor impairment [10]. NEC is associated with significantly worse neurodevelopmental outcome than prematurity alone.

57.2 Malrotation

Malrotation is an anatomical defect during embryonic development of intestinal rotation and fixation within the abdomen. Intestinal rotation and fixation begins in the fifth gestational week, with completion by the tenth gestational week [11].

There have been several different categorizations of the exact steps involved in this process, but it is logical

to consider the event as a continuum rather than occurring in distinct phases. Most simply, the embryonic gut begins as a short, straight continuous tube. The entire intestine must rotate counterclockwise for a total of 270° around the axis of the superior mesenteric artery (SMA). The duodeno-jejunal loop originates anterior to the SMA. It initially rotates to the right of the artery, then under and finally across the spine and upward, so that the duodeno-jejunal junction lies to the left of the SMA and spine. The ceco-colic loop originates beneath the SMA and also must rotate counterclockwise. It must initially rotate to the left of the SMA then above it and finally to the right and downward, to create the typical configuration of the colon. After normal development, the mesenteric root extends along the retroperitoneum from the Ligament of Trietz (LT) to the cecum [12]. Incomplete rotation results in a shortened distance between the LT and cecum, and therefore a narrowed mesenteric root. Fixation is initiated during rotation but continues even after rotation is complete. Fixation ensures the secure anchoring of the intestine to the posterior abdominal wall. Arrest of development anywhere along this continuum will result in incomplete rotation with varying degrees of intestinal fixation, termed “malrotation” [13].

57.2.1 Clinical Presentation

The diagnosis of malrotation is usually made in the neonate or young infant, with up to 50% of symptomatic patients being neonates, and up to 75% being less than 1 year old [14]. Bilious emesis with or without abdominal distention is the classic clinical manifestation of malrotation in newborns. If acute midgut volvulus develops, hematemesis, hematochezia, and abdominal guarding may occur in addition to the bilious emesis and abdominal distention. Patients with persistent symptoms of malrotation with volvulus may develop signs of peritonitis and shock. Intestinal malrotation can result in midgut volvulus, a condition that is usually fatal if not surgically corrected within several hours.

Malrotation is frequently observed in patients with situs inversus or heterotaxia, a syndrome associated with complex congenital cardiovascular defects. Intestinal malrotation has been observed most frequently in patients with single ventricle physiology [15].

57.2.2 Diagnosis

Early diagnosis is of the utmost importance, to avoid bowel necrosis associated with volvulus. The first priority for the clinician is to recognize the child who is at risk for malrotation, based on the history and physical findings. Abdominal radiographs may reveal a gasless abdomen or dilated intestinal loops, indicating only some form of obstruction.

The upper gastrointestinal (GI) series is the gold standard for radiographic diagnosis of malrotation and volvulus [16]. Normal rotation is present if the duodenal C-loop crosses the midline and places the duodeno-jejunal junction to the left of the spine at a level greater than or equal to the pylorus. If contrast ends abruptly or tapers in a corkscrew pattern, the differential diagnosis should include midgut volvulus. Some authors have recently described abnormalities in the orientation of the SMA and superior mesenteric vein (SMV) on ultrasonography (US) in patients with malrotation and have suggested that this may be an alternative way to establish this diagnosis [17]. The highest sensitivity for accurate diagnosis with ultrasound is achieved when inversion of the SMA and SMV can be visualized.

57.2.3 Treatment

57.2.3.1 Preoperative Management

Malrotation is a surgical emergency in all cases. The risk of midgut volvulus with attendant intestinal necrosis mandates immediate pediatric surgery consultation and treatment. A nasogastric tube should be placed to decompress the stomach. Volume resuscitation should also be initiated in preparation for operative intervention.

57.2.3.2 Surgical Management

The Ladd's procedure remains the cornerstone of surgical treatment for malrotation [18]. The abdomen is opened with a transverse upper abdominal incision. All bowel is eviscerated from the abdomen and inspected for ischemia and volvulus of the mesenteric

root. If volvulus is identified, this can be corrected with counterclockwise rotation of the bowel at the mesenteric root. Once the bowel has been devolvulized, it is further inspected for viability. When there are no concerns for intestinal ischemia and necrosis, the operation proceeds with division of the adhesive bands ("Ladd's bands") that originate from the cecum, cross over the duodenum and ultimately adhere to the right lateral abdominal wall. These bands are a source of duodenal obstruction if not properly divided. The mesenteric root is then widened at the root of the mesentery, allowing for a broader root and thereby decreasing the risk of subsequent volvulus. Finally, an appendectomy is performed.

If bowel viability is a concern in the setting of volvulus, a temporary silo may be placed with a planned second look operation the following day. Questionably viable bowel may recover within the first 24 h. All obviously necrotic bowel must be resected. If the entire midgut (Ligament of Treitz to the transverse colon) is necrotic, the only sustainable option for subsequent nutrition and intestinal rehabilitation will often be parenteral nutrition bridging into intestinal transplant.

In recent years a laparoscopic approach to the Ladd's procedure has been shown to be a safe and effective technique in patients with malrotation without volvulus. It can be performed with operative times equivalent to standard open techniques, and may allow for earlier return to feeds and decreased hospital stays [19].

57.2.3.3 Post-Op Management

There are several complications of malrotation, especially if midgut volvulus occurs. Patients suffering from midgut volvulus with intestinal loss often have a delay in recovery of bowel motility and function. Postoperatively, patients require bowel rest and nasogastric decompression until the return of bowel function. It is recommended to obtain central venous access and provide parenteral nutrition in the patients with volvulus and expected delay of bowel function [20]. If a significant portion of ischemic bowel is excised, they are at high risk for malabsorption and can require long-term parenteral nutrition. Patients with short gut syndrome are at risk for central line complications, including sepsis, liver failure, and death.

57.3 Protein Losing Enteropathy

Protein losing enteropathy (PLE) is a disease of unknown etiology, which has been associated with numerous cardiac and extracardiac disease states (Table 57.1). Conditions such as constrictive pericarditis, congestive heart failure, and cardiomyopathy, as well as post-Fontan, have been associated with PLE, with clinical signs surfacing months to years after the Fontan procedure. An abnormal leak of serum proteins into the intestinal lumen leads to the physical abnormalities and serologic/hemodynamic derangements. Multiple factors have been associated with PLE including a low cardiac output state, venous hypertension, an abnormal response to proinflammatory mediators, and severe infection or sepsis. The hallmark of PLE is a failure to maintain intact intestinal epithelium. Recent published data suggest that there is a specific loss of heparin sulfate proteoglycans from the basolateral surface of intestinal epithelial cells during episodes of PLE. Elevated venous pressures and inflammatory mediators such as interferon-gamma and tumor necrosis factor-alpha predispose the intestinal epithelial cells to leak proteins into the lumen [21].

Patients who have undergone a Fontan procedure are susceptible to a chronic low cardiac output state. This condition is believed to activate the inflammatory cascade, neurohormonal mediators, and the sympathetic nervous system. In addition, there is an increase in endoelin and angiotensin II levels. One of the most relevant consequences of the mentioned “stress response” is an increase in mesenteric vascular resistance with

mesenteric hypoperfusion and, the subsequent break in intestinal mucosa integrity (a predisposing factor for PLE) [22].

57.3.1 Clinical Presentation

There is a wide range of clinical signs and symptoms that vary in degree from mild to severe. Common symptoms of the disease include low grade fever, diarrhea, gastrointestinal discomfort, protuberant abdomen, and poor enteral tolerance. Hypoproteinemia, due to the enteric loss of protein that exceeds the normal rate of 1–2% of the plasma pool, leads to peripheral edema and to ascites. Conditions, which lend themselves to lymphatic obstruction, such as constrictive pericarditis and post-Fontan states, have been shown to be associated with lymphopenia and loss of immunoglobulins, while inflammatory states do not have this as a feature. The lymphopenia, which develops in response to lymphatic obstruction and as a consequence of the “leaky” intestinal epithelium, lends itself to potential dysfunction of the immune system. Patients with PLE also have an abnormal coagulation profile making them more susceptible to thrombotic phenomena. The procoagulant state is probably secondary to deficiencies of protein C, protein S, factor V, and factor VII. Fat malabsorption can also occur due to dilation and rupture of intestinal lacteals, leading to deficiencies of vitamin A, D, E, and K, and presents clinically as noninfectious diarrhea [23].

Table 57.1 Diseases associated with excessive enteric protein loss

Loss from intestinal lymphatics	Loss from an abnormal mucosa
Cardiac disease	Infection
– Congestive heart failure	– Invasive bacterial infection
– Constrictive pericarditis	– Parasitic infection
– Post-Fontan procedure	Inflammatory conditions
– Cardiomyopathy	– Gluten sensitivity
Obstructed lymphatics	– Graft-versus-host-disease
– Malrotation	– Crohn disease
– Lymphoma	– Necrotizing enterocolitis
– Malignancy	Vasculitic disorders
– Tuberculosis	– Systemic lupus erythromatosis
	– Henoch–Schönlein purpura

57.3.2 Diagnosis

The diagnosis of PLE is made by clinical history of a Fontan operation or other predisposing conditions and noting the signs and symptoms mentioned above. It is further aided by measuring the alpha-1-antitrypsin (A1-AT) concentration in the stool and performing an A1-AT clearance on a 24 h stool collection. A1-AT is an endogenous protein not present in the diet, and has a molecular weight similar to albumin. It is neither actively secreted, absorbed, nor digested, properties that make it an ideal marker for evaluating protein loss. In addition, liver function tests, including total serum

protein and albumin concentration, are informative and must be obtained [23].

57.3.3 Treatment

Patients with PLE may be admitted to the intensive care unit due to low cardiac output state, arrhythmias, overwhelming sepsis and/or edema secondary to low oncotic pressure and severe hydro-electrolyte imbalances. The ICU management should be tailored to manage the cardiac complications, with careful consideration for the extracardiac manifestations of disease, such as sepsis, water and electrolytes abnormalities, hypoproteinemia and thrombosis.

57.3.4 Cardiac Complications

All patients who are admitted to the intensive care unit with PLE must have an exhaustive investigation of the Fontan status. An echocardiogram and cardiac catheterization must be performed to assess ventricular function, cardiac output, atrioventricular or semilunar valve regurgitation, Fontan baffle or conduit, pulmonary arteries, patency of the fenestration and aortopulmonary or venous collaterals. Arrhythmias must be treated aggressively; some patients may need atrial pacing to improve the efficiency of the Fontan circulation. If the fenestration is closed, some patients may benefit from re-opening it in a cardiac catheterization laboratory or in the operating room. Distortion of the pulmonary arteries must be treated by interventional catheterization or surgery. A golden rule is that the caregiver must eliminate any anatomic, hemodynamic, and electrophysiological abnormality in the Fontan circuit [23, 24]. Nevertheless, it is worthwhile to mention that even an optimal surgically created Fontan may develop PLE. From the hemodynamic point of view, the perfect Fontan never exists, because the baffle pressure is always above the physiologic value. Heart transplantation is the final option for a failing Fontan, nevertheless, PLE has not consistently improved after heart transplantation. In addition, the immediate postoperative care of patients after heart transplantation and PLE is challenging. These patients are malnourished and may

develop third space syndrome associated with their previous hypoproteinemia.

57.3.5 Sepsis/Fluids and Electrolytes

Patients with PLE have lymphopenia and hypo-gammaglobulinemia which increase the risk for bacterial, fungal, and viral infections. Despite a lack of data linking PLE to new onset opportunistic infections, appropriate fluid resuscitation and broad spectrum antibiotics to cover bacterial and fungal infections should be initiated in the setting of suspected infection [25]. These patients may require more fluids and colloids due to loss of oncotic pressure than those patients with sepsis without PLE. A central venous catheter should be placed to monitor central venous pressure, to facilitate fluid replacement, and to monitor fluid administration. Diuretics should be carefully administered once the septic syndrome improves. Hyponatremia, hypokalemia, and hypomagnesaemia may not be of rare occurrence.

57.3.6 Hypoproteinemia

Nutritional management is a mainstay of therapy in patients suffering from PLE. While enteral therapy is recommended, the severity of the underlying disease may preclude that route. The diet should be rich in proteins and medium chain triglycerides (MCTs). MCTs, while not shown to decrease inflammation, are favorable because they are not absorbed via the lymphatic system, and thus do not put extra pressure on the lacteals. Intravenous protein supplementation can be accomplished with albumin 25% and/or parenteral nutrition, with the understanding that there is ongoing intestinal protein loss which can complicate and lengthen the time until correction.

57.3.7 Protein Loss

Loss of heparan sulfate and syndecan-1 (the predominant heparan proteoglycan) from the basolateral surface of intestinal epithelial in combination with elevated inflammatory mediators and high venous pressure, are the main triggering factors for developing PLE [21, 22, 24].

Currently, there are two main therapeutic strategies to stabilize intestinal cell membranes: steroids and heparin [23, 26].

Steroids stabilize the intestinal capillary and lymphatic cell membranes, treating the possible inflammatory component of PLE. There have been several reports of using steroids for treatment of PLE after a Fontan operation in adults and children. The studies have shown differing degrees of success with steroid therapy in patients with PLE. The response ranges from no response, to an almost complete disappearance of all symptoms of PLE, to frequent episodes of relapse. Side effects of steroids that include Cushing's syndrome, hypertension, and immunosuppression, are significant limiting factors for the long-term use of the drug.

It has been hypothesized that unfractionated heparin works because it is lipophilic and has a strong negative ionic charge. [26, 27]. Both of these properties are important in maintaining intestinal mucosal integrity. The negative ionic charge is of paramount importance in avoiding loss of proteins across the intestinal barrier. It appears that high molecular weight heparin reduces the effect of inflammatory cytokines (interferon-gamma and tumor necrosis factor-alpha) in inducing protein leak from the intestinal epithelial cell. Inhibition or reduction of this effect depends on the molecular size of the heparin. Recent research data suggest that low molecular weight heparin is less effective in preventing protein leak by the enterocyte when compared to high molecular weight heparin. Another mechanism to explain the potential benefit of heparin in PLE is that heparin might decrease chronic microemboli in the mesenteric circulation, in the setting of higher vascular resistance and increased pressures.

Clinical data have shown that unfractionated-high molecular or low molecular weight heparin may have some beneficial effects in patients with PLE after Fontan operations [22]. Similar to steroids, heparin has significant side effects such as undesirable anticoagulation, heparin induced thrombocytopenia with thrombosis, and decrease bone mineral density, seen with chronic exposure. The side effects appear to be decreased with the low molecular weight heparin, but this however should be weighed in combination with the potentially reduced efficacy.

In summary, PLE occurs in a variety of clinical settings and is commonly seen in patients after a Fontan procedure, with a frequency of approximately 3–15%. While the exact etiology remains unknown, a multifactorial

linkage is most likely. These factors include a combination of a low cardiac output state, high venous pressure, increased mesenteric vascular resistance, and an abnormal response of the intestinal epithelial cells to inflammatory cytokines. The resultant abnormal protein loss appears to be facilitated by the loss of heparin sulfate and syndecan-1 on the intestinal epithelial cell. Clinical symptoms of edema and ascites result from a proinflammatory state in conjunction with hypoproteinemia. Therapeutic strategies related to a pre-existing cardiac condition include investigation and treatment of abnormalities in the Fontan circuit (interventional cardiac catheterization and atrial pacing), high protein diet, high MCT diet, and intravenous protein supplementation with albumin 25% or parenteral nutrition. Corticosteroids and heparin remain valuable therapeutic modalities, however results are not consistently favorable. Finally, heart transplantation has been shown to reverse the effects of PLE in pediatric patients [28].

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Chapter 58

Malnutrition and Feeding Difficulties: Guidelines for Enteral and Parenteral Nutrition

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Nutrition is an important factor in critically ill pediatric cardiac patients, which has been shown to affect morbidity, wound healing, infection, and length of hospitalization [1, 2]. Pediatric patients hospitalized with congenital heart disease are at increased risk of becoming malnourished for a number of reasons. These patients often have poor enteral intake originating from fatigue and dyspnea. Anorexia is also common in patients with congenital heart disease, and it is greatest in infants with cyanotic cardiac defects [3]. Many of these children experience malabsorption due to decreased cardiac output, hypoxia, elevated right-sided cardiac pressure, and gastrointestinal dysfunction. These feeding limitations are often compounded by increased energy expenditure often associated with tachycardia and tachypnea [3, 4]. Infants and children undergoing cardiac surgery may be especially at risk of malnutrition due to fluid restrictions as part of their preoperative and postoperative management [5]. Previous studies have shown that protein malnutrition alone can result in poor outcomes in patients with cardiovascular disease [4].

The preferred method of nutritional supplementation is the enteral route; however, there are specific indications when enteral feeding is not appropriate and parenteral nutrition (PN) must be considered. Patient specific conditions that necessitate PN include chronic diarrhea, inflammatory bowel disease, short gut syndrome, intestinal failure, pancreatitis, neonatal necrotizing enterocolitis, chylothorax, persistent vomiting, surgical gastrointestinal conditions that have a prolonged postoperative recovery, and malabsorption syndromes. There are also signs of malnutrition that are independent of a

disease process, which necessitate the commencement of PN. If a patient demonstrates an inability to maintain normal weight gain, weight loss of more than 10%, a body weight that is less than 70% of ideal weight, the inability to take enteral feeds for more than 5 days, and/or a serum albumin less than 3.5 g/dl, PN may be indicated. Certain patients may have special situations that warrant therapy with parenteral formulations specially designed for trauma, hepatic failure, or renal failure [6].

PN is an important factor in ensuring that patients maintain appropriate nutritional requirements. PN should be used in a structured manner with an awareness of the risks and potential complications. It is imperative to be able to estimate the total energy expenditure to accurately calculate the patient's caloric need prior to prescribing PN. This allows the patient's baseline to be established, nutritional goals to be set, nutritional deficiencies to be noted, and changes in the patient's status to be monitored. Components of a nutritional assessment should include: clinical evaluation, anthropometric evaluation for age (weight, height, triceps skin fold thickness, mid-arm circumference, midarm muscle area, and body composition), and laboratory studies. Serum albumin is measured to assess visceral protein status. Triglycerides and essential fatty acids are measured to assess lipid metabolism.

58.1 Elements of Parenteral Nutrition

The components of PN that comprise adequate nutrition include protein, carbohydrates, fat, vitamins, and minerals. The goal is to provide adequate calories, while providing a balance in electrolytes, vitamins, and minerals to fulfill the patient's daily requirements. The caloric requirement for premature

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infants is approximately 100–120 cal/kg/day. This need is often elevated in patients in the cardiac intensive care unit due to increased metabolic demand; for example, a pre-term infant following cardiac surgery may require 120–140 kcal/kg/day to demonstrate adequate weight gain and healing.

Protein provides the patient both essential and nonessential amino acids. The essential amino acids include leucine, isoleucine, valine, methionine, lysine, phenylalanine, tryptophan, threonine, and histidine. Tyrosine, cysteine, taurine, and glycine are considered essential for premature and newborn infants. There are special formulations, such as Trophamine®, available for this patient population. Calories derived from protein are usually not included in PN calculations because in children, the amino acids should be utilized for growth. Protein has a caloric density of 4 kcal/g. One gram of protein is equivalent to 0.16 g of nitrogen or 6.25 g of protein is equal to 1 g of nitrogen. To ensure the maximum energy utilization of nonprotein calories is supplied, the calorie-to-nitrogen ratio should be at least 150 nonprotein calories per gram of nitrogen. The daily recommended amino acid intake for children in PN varies depending on the age of the patient. Premature infants require 3 g/kg/day of amino acids. Term infants need 2.5–3 g/kg/day, and children of 1–12 years need 1.5–2 g/kg/day. Protein requirements for children of more than 12 years range from 0.75 to 1.5 g/kg/day [7, 8].

Carbohydrates compose approximately 45–55% of the total caloric intake in a normal diet. Dextrose is the component that provides approximately 60–75% of the nonprotein calories in PN solutions. Dextrose monohydrate, as used in PN solutions, has a caloric density of 3.4 kcal/g. While providing additional calories through elevated dextrose content, close monitoring of glucose infusion rates (mg/kg/min) is important to prevent hyperglycemia. Usually the rate may begin at 5–6 mg/kg/min with gradual increases by 2 mg/kg/min/day to reduce the risk of hyperglycemia. The maximum glucose infusion rate varies by age. Pre-term infants may tolerate an infusion rate up to 18 mg/kg/min, while a toddler should be limited to an infusion rate below 14 mg/kg/min. The glucose infusion rate in mg/kg/min may be calculated using the formula below:

$$\frac{[\text{Total volume of dextrose infusion} \times 0.01] \times \text{dextrose concentration} \times 1000}{\text{Child's weight (kg)} \times 1440 \text{ minutes}}$$

The maximum concentration of dextrose that may be infused through a peripheral line is 12.5%. Solutions with osmolarities greater than 900 mOsm/L may cause inflammation and sclerosis of peripheral veins. If infused peripherally, these solutions with dextrose concentrations greater than 12.5% are very irritating and will cause tissue damage, if extravasation occurs. Central venous catheters are typically used for administration due to this limitation of dextrose infusion concentrations in peripheral venous lines. These catheters may be temporary internal jugular, subclavian, right atrial or femoral vein catheters, tunneled Broviac or Hickman catheters, implantable ports, or peripherally inserted central catheters (PICC).

Fat is also a crucial element to nutritional support of the critically ill patient. Lipid emulsions provide additional calories and prevent essential fatty acid deficiency by providing fundamental fatty acids such as linoleic and linolenic acids [6]. Approximately 25–40% of calories are delivered as fat. Infants are started on with 0.5–1 g/kg/day of lipids and advanced to a maximum of 3 g/kg/day. A 20% lipid emulsion is typically utilized, as opposed to a 10% emulsion, due to its lower phospholipid to triglyceride ratio, which provides improved fat clearance [9]. These lipid emulsions are soy-based with egg yolk phospholipids [6]. Currently, new sources of intravenous fat are being investigated in the United States, such as an omega-3 based solution, which in preliminary studies has shown to decrease cholestasis in patients on chronic PN.

58.2 Risks and Complications

For many patients, PN is necessary for growth and healing. Clinicians must remember that there are risks associated with this method of nutritional support. Several risks exist with the placement of central venous catheters for PN infusions: the patient receives anesthesia for the line placement, and during placement of these catheters, subclavian artery or carotid artery puncture, hemothorax, pneumothorax, brachial plexus injury, or cardiac tamponade may occur [10, 11]. Subclavian vein thrombosis may occur at the tip of the catheter, the tip of the catheter may break, or the line may puncture through the lumen of the vessel, causing the contents to infuse into the pleural space or mediastinum. Despite sterile technique employed in

the insertion, catheter-related sepsis is also a risk. The most common pathogens are *Staphylococcus epidermidis* and *Staphylococcus aureus*.

One of the major complications is parenteral nutrition-associated liver disease (PNALD). This broad term can be divided into cholestasis, steatosis, and gallbladder sludge or cholelithiasis. Cholestasis and gallbladder sludge are most common in infants and children. Premature infants may have an even worse outcome due to their still immature liver. Gallbladder sludge may be a result of decreased cholecystokinin (CCK) production from lack of enteral stimulation. Steatosis, due to increased fat synthesis, may be seen in pathologic examination of the liver. This is considered to be the result of the infusion of excessive carbohydrate calories, which exceed the patient's energy demand or expenditure [12]. Due to these potential complications, close monitoring of liver function tests are required.

Other possible complications are nutritional deficiencies such as electrolyte imbalances, hypoglycemia, hyperglycemia, essential fatty acid deficiency, or vitamin and/or trace mineral deficiencies. Recent studies have demonstrated that excessive glucose infusions have been noted to increase carbon dioxide (CO₂) and therefore require increased ventilatory support [13, 14]. It is imperative to maintain a balance of dextrose and fat of approximately 60–75% of calories from carbohydrates and 25–40% of calories from fat. This is used to promote growth while preventing essential fatty acid deficiency.

The risk of these complications may be minimized with attention to the individual patient and their needs along with close monitoring. Due to the dynamic status of an intensive care patient, the estimated total energy expenditure and required caloric demand must be reassessed daily. A daily nutritional assessment as described above, including clinical evaluation, anthropometric evaluation, and laboratory evaluation, must also be constantly reevaluated. Electrolytes should be monitored daily and as needed until stable. Liver functions tests such as aminotransferases, alkaline phosphatase, gamma glutamyl transpeptidase (gGTP), and conjugated and unconjugated serum bilirubin levels should be followed. Gallbladder sludge and cholelithiasis may be visible on ultrasound. If a patient is receiving PN for an extended period of time (typically defined as greater than 2–3 weeks) vitamin and trace mineral levels, such as selenium, carnitine, manganese, zinc, and copper

levels should be obtained. Essential fatty acid panels and triene and tetraene ratios may also be drawn to detect essential fatty acid deficiency and ensure an adequate balance of nonprotein calories to fat.

58.2.1 Initiation of Enteral Feeds

Initiation of enteral feeds is related to the overall condition of the patient. Patients should preferably be off epinephrine and/or norepinephrine as these agents notably constrict splanchnic blood flow. Dopamine in doses less than 5 µg/kg/min does not affect blood flow to the GI tract, and thus feedings can be initiated while the patient is weaning off dopamine. On otherwise stable patients, enteral feeds can be initiated within 24–48 h of admission to the cardiac ICU. Enteral feeds can be provided via oral or nasoduodenal route or via an endoscopically/surgically placed gastrostomy tube. Most awake patients will tolerate oral feeds. A notable exception is infants with congenital heart lesions prior to surgical correction in which the work of sucking and swallowing may exceed their respiratory and cardiac reserves. In infants incapable of tolerating oral feeds and older patients in whom oral feeds are undesirable (see below), a nasoduodenal tube is easily placed blindly at the bedside or under fluoroscopic guidance.

Few evidence-based guidelines exist on how fast to escalate oral or nasoduodenal tube feedings; consequently, the process is largely empiric at this time. When initiating oral feeds, we usually start at 2–5 cc every 3 h and escalate to goal feeds (see below for caloric requirements) by 2–5 cc every second or third feeding. Total fluid requirements and restrictions for each patient should be kept in mind while escalating feeds, and increase in the caloric content of the formula may be required if sufficient energy is to be provided within the allowed total volume. Signs of feeding intolerance include significant residual volume in the stomach (greater than 30–50% of the feeding volume), abdominal distention, diarrhea, and abdominal pain. In one study evaluating transpyloric feedings in children after cardiac surgery, abdominal distention and excessive residues were noted in 9–10% of patients and diarrhea in 7–8% [15]. Of note, necrotizing enterocolitis was also observed in two patients, associated with concomitant presence of both cardiogenic and septic shock. If a patient develops signs of feeding intolerance, reduction

in the volume or caloric content of feedings may be required. Occasionally, patients cannot tolerate enteral nutrition at full volumes. In these cases, an attempt should be made to provide so-called “trophic” feeds at 2 ml/h or less; the provision of minimal enteral feeds is thought to prevent the breakdown of intestinal mucosa and bacterial translocation, despite being inadequate for full nutritional support [16].

58.2.2 Estimation of Caloric Needs

Nutritional support for critically ill children ultimately aims to provide sufficient energy, and substrates to support healing and growth. To that end, energy requirements of children with congenital heart disease have been explored in multiple studies. However, a cohesive picture of caloric requirements before corrective surgery, during the immediate postoperative period and during long-term recovery has yet to emerge, as most studies involve a small number of patients with a variety of cardiac lesions and preexisting conditions. A recent meta-analysis by Nydegger and Bines (2006) suggests that total energy expenditure in infants with congenital heart disease (2 weeks–3 month of age) is approximately 100–115 kcal/kg/day prior to surgical correction [17]. This energy requirement is similar to that of healthy infants. However, many patients with congenital heart disease are malnourished or suffer from significant growth retardation [18], and thus catch-up nutrition may be beneficial preoperatively. Caloric intake of 135–150 kcal/kg/day, albeit delivered continuously over 24 h, has been associated with weight gain and increase in growth parameters in children with heart disease [19, 20].

A number of equations aimed at predicting energy expenditure in critically ill children have been developed, with varying degree of success. Traditional process recommends increasing the predicted basal metabolic rate (Table 58.1; WHO 2004) by a stress correction factor of 10–30% [21]. However, several studies have demonstrated that in critically ill, mechanically-ventilated children, the actual energy expenditure measured by indirect calorimetry is lower than that predicted by stress-related correction of the resting energy expenditure [22, 23]. Furthermore, immediately after surgical correction of a congenital heart lesion, the energy requirements are at or below

Table 58.1 World Health Organization: Equations to predict energy expenditure

Infants Birth–12 months	TEE (kcal/kg/d) = (-99.4 + 88.6 x W)/W
Children and adolescents	
Boys: TEE (kcal/kg/d) = (310.2 + 63.3 x W - 0.263 x W ²)/W	
Girls: TEE (kcal/kg/d) = (263.4 + 65.3 x W - 0.454 x W ²)/W	

W weight in kilograms

Adapted from WHO, 2004

the predicted resting energy expenditure in children [18, 24], although metabolism shifts towards fat oxidation and gluconeogenesis [24]. Caloric requirements and energy source utilization return to baseline within several days of corrective surgery [18].

In mechanically-ventilated children hospitalized in an ICU, an equation developed by White et al. in 2000 [25] appears to correlate closely with energy expenditure measured by indirect calorimetry:

$$EE \text{ (kcal/day)} = [(17 \times \text{age in months}) + (48 \times \text{weight in kg}) + (292 \times \text{body temperature in } ^\circ\text{C}) - 9677] / 4.184$$

Once mechanical ventilation is discontinued, accurate prediction of caloric needs becomes less feasible, since muscle activity and work of breathing increase with spontaneous breathing. A realistic goal is to target caloric intake towards the predicted basal metabolic rate. The most recent population-based update to the estimation of energy expenditure in infants, children, and adolescents has been produced by the World Health Organization (Table 58.1)

58.2.3 Factors Complicating Enteral Feedings in Cardiac Patients

58.2.3.1 Gastroesophageal Reflux Disease (GERD)

GERD is quite common in cardiac ICU patients and may present a significant obstacle to initiation of enteral feeds. Although, all infants have gastroesophageal reflux (GER) to some extent, a number of clinical signs manifest the pathological nature of GERD in cardiac patients. Vomiting of oral or nasogastric (NG) feeds, occasionally associated with transient hypoxemia noted on pulse oximetry, represents a warning sign that

reflux is significant enough to result in aspiration. Back or neck arching associated with feeds is another strong indicator of clinically significant GER. Arching is often severe enough to resemble opisthotonic-like posture. Less frequently, stridor and/or mild respiratory distress with retractions are observed when reflux occurs frequently enough to irritate the posterior pharynx and the upper airway.

Evaluation of GERD consists of a multi-step approach and varies by institution. The simplest method relies on the therapeutic trial of anti-reflux medications described below. Resolution of symptoms within days to weeks justifies continued use of pharmacotherapy. The gold standard for diagnosis of GERD relies on continuous measurement of esophageal pH using a probe. Detection of acidic pH above the lower esophageal sphincter provides the diagnosis. This technique is rarely used since patients in the cardiac ICU often have indwelling esophageal atrial leads or NG/nasoduodenal (ND) tubes.

Radiologically, definitive diagnosis is made preferably with a nuclear medicine "milk" gastric scan using Technetium-99 labeled sulfur colloid added to regular milk-based formula. During the milk scan, radioactive contrast is instilled into the stomach via an NG tube, the tube is withdrawn, eliminating a potential artifact of a foreign body impairing the function of the lower esophageal sphincter, and the contrast is then imaged in cinematographic fashion over the course of 1–2 h. Data provided by the scan are frequency of regurgitation into the esophagus and the esophageal level reached by the regurgitated material. Additionally, the time constant for elimination of contrast from the stomach into the duodenum is obtained, which allows for independent evaluation of gastric motility. Normal motility results in elimination of approximately 50–60% of the contrast from the stomach within 1 h. Reduced motility has been associated with increased frequency and severity of GER in the pediatric population.

An upper GI series is another radiologic tool for evaluation of GER. During this study, a radio-opaque contrast is instilled into the stomach via an NG tube, the tube remains in place, and the contrast is then imaged using static radiographic images at 10–15 min intervals. Although often used to diagnose GERD, an upper GI series tends to be inferior to the milk scan in sensitivity and specificity. Available data suggest that almost everyone has some degree of reflux observed on upper GI, partly related to the presence of a foreign

body passing through the lower esophageal sphincter. Additionally, since the images are obtained at a much lower frequency during an upper GI series than during the milk scan, the ability to detect infrequent reflux events and to assess their severity is quite limited.

Treatment of GERD relies primarily on inhibition of acid production in the stomach with an occasional added emphasis on enhancing gastric motility. Histamine receptor type-2 antagonists such as ranitidine orally or famotidine intravenously are inexpensive and readily available. Ranitidine can be used at doses as high as 3 mg/kg/dose orally 3 times daily whereas famotidine is usually dosed at 0.5 mg/kg/dose intravenously every 12 hours. Famotidine dosing requires adjustment when renal impairment is present. Profound acid inhibition is provided by the proton pump inhibitor (PPI) class of pharmacologic agents, such as pantoprazole, lansoprazole, or omeprazole. Pantoprazole is given intravenously at a dose of 0.5–1 mg/kg as a single daily dose. Lansoprazole is given orally at doses of 7.5, 15, and 30 mg for children weighing less than 10 kg, 10–30, and greater than 30 kg, respectively. Lansoprazole possesses an additional advantage for the pediatric population in that it is available as an orally disintegrating, pleasant-tasting tablet that may also be dissolved in water and administered through a feeding tube. Omeprazole is also available as an oral formulation; the dose is 10 mg daily for children weighing less than 20 kg, and 20 mg daily for children greater than 20 kg in weight.

Pro-motility agents such as metoclopramide and erythromycin ethylsuccinate have become second-line agents in the treatment of GERD. Metoclopramide is given intravenously or orally at a dose of 0.1–0.2 mg/kg/dose every 6 hours. It is also occasionally used for several days to facilitate progress of a feeding tube from the stomach through the pylorus into the duodenum. Rarely, extrapyramidal side effects can occur within 24–48 h of administration of metoclopramide; unwanted cardiac complications include blood pressure instability, supraventricular tachycardia, and A-V dissociation. Neurologic side effects of metoclopramide have been well characterized. It should also be noted that metoclopramide has been implicated in bone marrow suppression which is important in the setting of transplantation.

Erythromycin ethylsuccinate is effective at improving gastric motility in doses of 10 mg/kg/dose every 8 h. Oral administration route is strongly preferred as intravenous administration of erythromycin has been

associated with fatal cardiac complications. Additionally, administration of erythromycin to neonates 0–2 weeks of age for greater than 14 days in duration increases the risk of hypertrophic pyloric stenosis 10-fold. Thus, H₂-receptor antagonists and PPI agents remain the mainstay of GERD treatment in children.

58.2.3.2 Chylothorax

Postoperative chylothorax occurs in approximately 0.5–5% of children after open heart surgery [26, 27] and is associated with prolonged ICU stay [28]. The majority of cases are related to surgical manipulation of the thoracic duct or intraoperative traumatic injury. Rarely, superior vena caval thrombosis or elevated SVC pressures underlie the etiology of chylous effusion. Symptomatically, patients are likely to become tachypneic and tachycardic with a corresponding free-flowing effusion on chest radiography or ultrasonography. If the child has been fed a diet containing long-chain fatty acids, the effusion will likely contain elevated triglyceride levels (>1.2 mMol/L). In children who have been fasting, the fluid may appear serosanguinous – the diagnosis is then made when feedings are initiated. Conservative treatment requires switching to enteral nutrition based on a formula enriched with medium-chain-triglyceride oils (e.g., Portagen®) [29]. Alternatively, a low-fat diet may be used if patient is taking food by mouth. An effusion occupying greater than 20–30% of the hemithorax requires chest tube-mediated drainage. If chylothorax persists despite these measures for longer than 7–10 days, the treatment progresses to enteral rest and PN. These measures will lead to resolution of the chylous effusion in 80–90% of the cases [29]. The remaining 10–20% of patients with a chylothorax may require treatment with octreotide starting at 10 µg/kg/day as a continuous infusion or in divided doses and titrating up to 40 µg/kg/day [30, 31]. In remarkably recalcitrant cases, surgical interventions such as thoracic duct repair or ligation, pleurodesis, or pleuroperitoneal shunting may be necessary.

58.2.3.3 Laryngopharyngeal Dysfunction and Aspiration

Swallowing difficulties and airway abnormalities are quite common in children with heart disease and present

a significant obstacle to successful oral feeds and timely discharge from the hospital. Incidence of swallowing dysfunction after cardiac surgery in children has been reported at about 4% [32]. However, the nature of the procedure significantly impacts the probability of postoperative swallowing dysfunction. For instance, incidence of laryngopharyngeal dysfunction after Norwood procedure can reach almost 50% [33]. Diagnosis of laryngopharyngeal dysfunction is made with a modified barium swallow or a salivogram, which shows abnormal passage of the food bolus through the oropharynx or frank aspiration of the material past the vocal cords. Bedside consultation by a trained speech pathologist is essential to evaluating the respiratory effort during feeding and oral-motor mechanics. Clinically significant difficulty is evident when stridor, choking, coughing, and/or oxygen desaturation develop during oral feeding. Interventions may include positional change during feedings, modifications of the nipple/bottle, and limiting food textures to those that demonstrated no evidence of aspiration on the modified barium swallow [34]; In the most refractory cases, a gastrostomy tube may be required to provide adequate enteral nutrition.

The incidence of airway abnormalities in children with congenital heart disease is also approximately 3%, with laryngeal paralysis and subglottic stenosis comprising the majority of diagnoses [35]. Diagnosis requires direct laryngoscopy and bronchoscopy by an otolaryngologist familiar with pediatric airway problems. Most common presentation is intolerance of feeds or failure of extubation [36]. Surgical intervention may be required in up to 40% of children with a defined airway abnormality [35].

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Chapter 59

Hematological Aspects: Anticoagulation, Heparin-Induced Thrombocytopenia, Plasma Exchange

Peter H. Shaw

59.1 Anticoagulation

Cardiac ICU patients are at risk for thromboses due to their cardiac anatomy or because of iatrogenic procedures (e.g., cardiac bypass; catheterization). There are several anticoagulants used in the care of pediatric cardiac patients, each with unique mechanisms of action, methods of monitoring, and most have antidotes for rapid correction of anticoagulation.

59.1.1 Indications

All of the indications for anticoagulation are too extensive to include in this chapter. The most comprehensive evidence-based overview is in “Antithrombotic Therapy in Children” from the eighth ACCP conference on antithrombotic and thrombolytic therapy from 2008 [1].

59.1.2 Medications and Monitoring

59.1.2.1 Heparin

Heparin is an anticoagulant, which works by binding to antithrombin III, amplifying 1,000-fold its ability to inactivate clotting factors II, VII, IX, X, XI, and XII. It prevents new clots and the extension of existing

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clots while allowing the body’s own clot lysis mechanisms to work. It is administered subcutaneously (SQ) or intravenously (IV). It has a biologic half-life ($T_{1/2}$) of approximately 1 h.

Heparin effect is monitored by the partial thromboplastin time (PTT).

If long-term anticoagulation is required, particularly in the outpatient setting, heparin is often used to commence anticoagulation therapy until the oral anticoagulant coumadin is therapeutic. An alternative to coumadin for long-term outpatient anticoagulation is low molecular weight heparin (LMWH).

Dosing and Monitoring

At the start of anticoagulation with heparin, the patient should be bolused with a dose of 75 units/kg IV over 10 min and then started on a continuous infusion at the following doses:

Age ≤1 year: 28 units/kg/h

Age >1 year: 20 units/kg/h

Four hours after initiating heparin, check the first PTT. The goal is 60–85 s and should be adjusted as follows:

PTT (s)	Bolus (units/kg)	Hold (minutes)	Rate change (units/kg/h)	Repeat PTT (h)
<50	50	0	Increase 20%	4
50–59	0	0	Increase 10%	4
60–85	0	0	No change	24
86–95	0	0	Decrease 10%	4
96–120	0	30	Decrease 10%	4
>120	0	60	Decrease 15%	4

Adapted from Monagle et al [4]

Once PTT is therapeutic, check a CBC, PT, and PTT daily

Correction of Anticoagulation

If a patient is bleeding while on heparin and the PTT is supratherapeutic the heparin should be stopped and *protamine sulfate* should be given immediately. Protamine neutralizes heparin within 5 min, but can cause hypotension, bronchoconstriction, and pulmonary hypertension from histamine release. To minimize these side effects it should be given very slowly, IV in doses *not to exceed 50 mg* in any 10-min period. The dose is based on the amount of heparin administered within 2 h as follows:

Time since last heparin dose (minutes)	Protamine dose per 100 units heparin received (mg)
<30	1
30–60	0.5–0.75
60–120	0.375–0.5
>120	0.25–0.375

Adapted from Monagle et al [4]

Obtain a PTT 15 min after protamine sulfate dose given

Side Effects

Short-term side effects of heparin include bleeding and heparin-induced thrombocytopenia (HIT). HIT will be discussed more extensively in the following section. Long-term side effects include alopecia and osteoporosis.

59.1.2.2 Low Molecular Weight Heparin

The pharmacokinetics of LMWH is more predictable than unfractionated heparin. LMWH targets anti-factor Xa activity rather than anti thrombin (IIa) activity, so the anti-Xa level is monitored instead of the PTT.

Dosing and Monitoring

LMWH is given SQ at the following doses:

Age \leq 2 months:

Treatment dose: 1.5 mg/kg/dose every 12 h

Prophylactic dose: 0.75 mg/kg/dose every 12 h

Age 2 months to 21 years:

Treatment dose: 1 mg/kg/dose every 12 h

Prophylactic dose: 0.5 mg/kg/dose every 12 h

Four to six hours after at least the second dose, draw an anti-Xa level.

Target anti-Xa levels:

Treatment: 0.5–1 units/ml

Prophylactic: 0.1–0.3 units/ml

Adjust the dose of LMWH as follows:

Anti-Xa level (Units/ml)	Hold (minutes)	Dose change	Repeat anti-Xa level
<0.35	0	Increase 25%	4 h after next dose
0.35–0.49	0	Increase 10%	4 h after next dose
0.5–1	0	No change	Once in a week, 4 h after dose
1.1–1.5	0	Decrease 20%	4 h after next dose
1.6–2	0	Decrease 30%	4 h after next dose
>2	Until level anti-Xa <0.5, check q12 h	Decrease 45%	4 h after next dose

Adapted from Monagle et al [4]

Correction of Anticoagulation

If a patient has bleeding complications while on LMWH, the drug should be promptly stopped. Protamine sulfate has *not* been shown to completely correct the anticoagulant effects of LMWH.

If protamine sulfate is given within 3–4 h of the last dose of LMWH, a maximum of 1 mg of protamine per 100 units (1 mg) of LMWH should be infused over 10 min.

Side Effect

Short-term side effects include bleeding and HIT, although the rate of HIT is lower than with unfractionated heparin [2,3]. HIT will be discussed more in the following section. Other side effects include mild local reactions, pain, and bruising at the injection site. Late side effects include alopecia and osteoporosis.

59.1.2.3 Vitamin K Antagonists (Coumadin, Warfarin)

Coumadin inhibits the synthesis of active forms of the vitamin K-dependent clotting factors: II, VII, IX, and X, as well as regulatory factors proteins C, S, and Z.

Dosing and Monitoring

Coumadin loading dose on the first day of therapy – 0.2 mg/kg PO as a single dose. If the patient has liver dysfunction, dosing would start at 0.1 mg/kg. Maximum dose can be 10 mg (5 mg for patients with liver disease).

Coumadin is monitored by the INR (International Normalizing Ratio). The goal in most instances is 2–3, but for patients with mechanical valves the goal INR is 2.5–3.5.

Loading doses on days two to four – Daily dose based on day daily INR as per following chart:

INR	Coumadin Adjustment
1.1–1.3	Repeat initial loading dose
1.4–1.9	50% of initial loading dose
2–3	50% of initial loading dose
3.1–3.5	25% of initial loading dose
>3.5	Hold until INR <3.5 then restart at 50% less than the previous dose

Adapted from Monagle et al [4]

Correction of Anticoagulation

The main antidote for Coumadin is vitamin K, but fresh frozen plasma (FFP) is also used. Here are guidelines:

Patient is Not Bleeding

If the patient will be restarted on Coumadin in the near-future: Treat with phytonadione (vitamin K1) at a dose of 0.5–2 mg IV or SQ. If the patient will NOT be restarted on Coumadin in the near-future: Treat with phytonadione (vitamin K1) at a dose of 2–5 mg IV or SQ.

Patient Has Bleeding That is Not Life-Threatening

Treat with phytonadione (vitamin K1) at a dose of 0.5–2 mg SQ or IV and give FFP at 20 ml/kg IV.

Patient Has Bleeding That Is Life-Threatening

Treat with phytonadione (vitamin K1) at a dose of 5 mg IV over 10–20 min and give FFP at 50 ml/kg IV.

Elective Reversal of Coumadin

If the INR is less than 1.5, no reversal is needed for most surgery. For neurosurgery, it is ideal for the INR to be 1.

When there is a *HIGH* risk of thrombosis:

- Hold coumadin 3 days before surgery.
- Twenty-four hours before surgery, initiate heparin therapy as an infusion without a bolus.
- Stop IV heparin 6 h before surgery and check PTT 3 h before surgery – it should be normal.
- If INR remains >1.5 twelve hours before surgery, give 0.5 mg of phytonadione (vitamin K1) SQ and recheck INR 6 h later.
- Once cleared by surgeons, heparin IV is restarted at the earliest of 8 h postoperatively at the previous rate. Once therapeutic for 24 h, restart oral coumadin. Once INR is therapeutic stop heparin.

When there is a *LOW* risk of thrombosis:

- Hold coumadin 3 days before surgery.
- Check INR the day before surgery. If INR is >1.5, give 0.5 mg of phytonadione (vitamin K1) SQ and recheck INR 6 h later.
- Once cleared by surgeons, restart oral coumadin if patient can take PO medications on post-op day one.

Guidelines adapted from Monagle et al. [4].

Side Effects

Short-term side effects of coumadin include bleeding and necrosis. Bleeding can manifest as hemoptysis, excessive bruising, bleeding from mucosal surfaces, or hematuria or hematochezia. The risk of bleeding is greater if the INR is supratherapeutic.

A rare complication of coumadin is necrosis, which can occur shortly after starting therapy in patients with protein C deficiency and is clinically identical to purpura fulminans. This risk is decreased if the patient is therapeutic on heparin. Osteoporosis is a risk of long-term coumadin use.

Drug Interactions

In addition to oral vitamin K intake, there are many drugs that affect the metabolism of coumadin and can adversely affect the INR (please consult your

hospital's formulary or pediatric dosing references). It is important to review all medications a patient is taking concurrently with coumadin, as stopping or starting medications can affect the INR.

Direct Thrombin Inhibitors

The use of direct thrombin inhibitors (DTIs) are now used almost exclusively in the management of HIT in children.

The most commonly used DTIs are *Lepirudin* and *Argatroban*.

Dosing and Monitoring

If a patient is treated for HIT or presumed HIT, *heparin should be stopped* first.

In patients with normal renal function:

Lepirudin – To avoid initial overdosing, do not start *Lepirudin* if PTT is above therapeutic range (60–85 s).

Initial dose: IV bolus: 0.4 mg/kg and then start continuous IV infusion at 0.15 mg/kg/h.

Check PTT 4 h after starting infusion. The target is 60–85 s. Adjust dose as per heparin chart above.

In patients with abnormal renal function:

Argatroban – To avoid initial overdosing, do not start *Argatroban* if PTT is above therapeutic range (60–85 s).

Initial IV infusion rate: start at a dose of 0.75 µg/kg/min.

Check PTT 2 h after starting infusion. The target is 60–85 s. Adjust dose as per heparin chart above. Once a stable dose is achieved draw PTT every 24 h. INR and PT may be elevated, but should not be used for monitoring.

Administer via a dedicated line because *Argatroban* is not compatible with other drugs.

Conversion to an Oral Anticoagulant

Coumadin (Warfarin) may be introduced when platelet count starts to increase, but DTI should be continued until platelet count normalizes. After 4–5 days of coumadin, if platelet count is normal and PT is therapeutic, stop DTI for a few hours and recheck INR. If it is between 2 and 3, it is safe to discontinue DTI.

Correction of Anticoagulation

There is no antidote or reversal agent for *Argatroban* or *Lepirudin*. Half-life of *Argatroban* is short at 39–51 min and that of *Lepirudin* is slightly longer at 1.3 h.

Side Effects

The most common side effect of both DTIs is bleeding.

59.2 Heparin-Induced Thrombocytopenia

59.2.1 Description and Pathophysiology

Heparin-induced thrombocytopenia (HIT) occurs when autoantibodies form against platelet factor 4 (PF4), neutrophil-activating peptide 2 (NAP-2), and interleukin 8 (IL-8). This causes platelet aggregation and consumption of coagulation factors which can lead to both thrombosis and bleeding.

HIT can occur shortly after heparin is given (even in IV fluids) but usually occurs 5–15 days after the initiation of heparin. It is important to substitute for heparin when HIT is suspected or confirmed. Even when HIT's only manifestation is thrombocytopenia and heparin is stopped, risk of thrombosis in subsequent 30 days approaches 50% unless alternative anticoagulant is used.

59.2.2 Diagnosis

HIT can be diagnosed by the detection of the PF4 anti-platelet antibody in the patient's blood by one of two assays: washed platelet activation assays and commercial enzyme immunoassays (EIAs).

A negative test generally rules out HIT. However, because weak antibodies can also be detected (especially by EIA), a positive test does not necessarily confirm HIT. There may be false positive results and low diagnostic specificity, because HIT antibodies can be detected by EIA in about 50% of patients 1 week after cardiac surgery.

59.2.3 Management

If there is no risk for thrombosis, discontinue heparin and the platelet count is normalized. If there is risk for thrombosis or a thrombosis is being treated, follow guidelines above for the using DTI's.

59.3 Antifibrinolysis

59.3.1 Aminocaproic Acid

Its use is indicated in the case of excessive bleeding caused by fibrinolysis and as prophylaxis in patients on ECMO or after cardiopulmonary bypass.

59.3.1.1 Dosing and Monitoring

- *Children:* loading dose of 100–200 mg/kg IV, followed by 100 mg/kg/dose every 6 h or by a continuous infusion of 30 mg/kg/h (maximum 30 g/day)
- *Adults:* 4–5 g IV over the first hour followed by a continuous infusion of 1–1.25 g/h for 8 h or until bleeding ceases.

Dose should be reduced to 25% in case of renal failure.

59.3.1.2 Side Effects

Hypotension, bradycardia, arrhythmia, headache, seizures, rash, hyperkalemia, nausea, vomiting, decreased platelet function, agranulocytosis, leucopenia, myopathy, acute rhabdomyolysis, glaucoma, deafness, renal failure, dyspnea, and pulmonary embolism. Contraindicated in hypersensitivity to the drug, disseminated intravascular coagulation, and ongoing intravascular clotting process.

59.3.2 Aprotinin

This drug is used in the adult population to prevent hemorrhage after cardiopulmonary bypass interventions

and liver transplantation. It is also widely used throughout the world for post-CPBP patients, particularly in the case of reoperation and in neonates and in those with preexisting coagulopathies. In the USA, it has recently been removed from the market based on a number of reports regarding adverse effects in the adult population.

59.3.2.1 Dosing and Monitoring

- *Infants and children:* Test dose of 0.1 mg/kg IV (maximum 1.4 mg); *body surface less than 1.16 m²:* loading dose of 240 mg/m² IV, 240 mg/m² into the pump priming, then 50 mg/m²/h as a continuous infusion IV during the surgery; *body surface greater than 1.16 m²:* loading dose of 280 mg/m² IV, 280 mg/m² into the pump priming, then 70 mg/m²/h as a continuous infusion IV during the surgery.
- *Adults:* Test dose of 1 ml (1.4 mg) IV, followed by a loading dose of 2 million KIU (280 mg) IV, 2 million KIU (280 mg) into the pump priming and 2,50,000 KIU/h (35 mg/h) continuous infusion IV during the surgery.

In Europe and in Australia, Aprotinin is also used in the postoperative period at 1,000–4,000 KIU/kg/h IV.

59.3.2.2 Side Effects

Anaphylaxis, arrhythmia, heart failure, myocardial infarct, cerebrovascular events, chest pain, hypotension, pericardial effusion, pulmonary hypertension, fever, seizures, dizziness, hyperglycemia, hypokalemia, acidosis, nausea, vomiting, constipation, diarrhea, gastrointestinal hemorrhage, hemolysis, anemia, thrombosis, liver insult, phlebitis, arthralgia, renal failure, bronchoconstriction, pulmonary edema, and apnea. Contraindicated in: hypersensitivity to the drug, previous exposure within a 12-month period.

59.3.3 Tranexamic Acid

This drug is used off-label after CPBP as a prophylaxis against hemorrhage and to reduce postoperative bleeding.

59.3.3.1 Dosing and Monitoring

Loading dose of 100 mg/kg diluted in 20 ml of 0.9% NaCl over 15 min, followed by a continuous infusion of 10 mg/kg/h IV.

59.3.3.2 Side Effects

Nausea, diarrhea, vomiting, hypotension, and thrombosis. Contraindicated in: hypersensitivity to the drug, subarachnoid hemorrhage or active intravascular clotting process.

59.4 Fibrinolytics

59.4.1 r-TPA

r-TPA (Alteplase®) may be used in case of acute ischemic stroke, pulmonary embolism, acute myocardial ischemia or infarct, and systemic thrombosis, also to treat occluded central venous or arterial indwelling catheters.

59.4.1.1 Dosing and Monitoring

- *Systemic thrombosis*: 0.1 mg/kg/h IV for 6 h; monitor bleeding and fibrinogen levels (keep above 100 mg/dl). If persistent thrombosis, increase dose by 0.1 mg/kg/h every 6 h to a maximum of 0.5 mg/kg/h.
- *Venous thrombosis*: 0.06 mg/kg/h in neonates, and 0.03 mg/kg/h in older children, IV.
- *Arterial spasm*: 0.1 mg/kg IV, then 0.5 mg/kg/h for 2 h.
- *Central venous catheters*: instill 110% of the internal lumen volume into the occluded catheter and let it dwell for 30 min. Recommended concentration is 1 mg/ml, maximum 2 mg in 2 ml in patients between 10 and 30 kg, and 2 mg in 2 ml in patients above 30 kg. If the catheter is functional aspirate 5 ml of blood out to remove the residual drug and clot, and then flush with normal saline. If the catheter remains occluded, let it dwell for a total of 2 h and repeat the above. If it remains occluded, a second dose can be administered.

59.4.1.2 Side Effects

Gastrointestinal or genitourinary hemorrhage, ecchymosis, nausea, vomiting, fever, retroperitoneal hemorrhage, gingival hemorrhage, epistaxis, intracranial hemorrhage, hemopericardium, and arrhythmias (reperfusion). Contraindicated in: hypersensitivity to the drug, active internal bleeding, cerebrovascular hemorrhagic event, intracranial neoplasm, aortic dissection, arteriovenous malformation or aneurysm, bleeding diathesis, severe hepatic or renal disease, hemostatic defects, and severe uncontrolled hypertension.

59.5 Plasma Exchange

Plasma exchange (also known as plasmapheresis) is the removal, treatment, and return of plasma into a patient's circulation. During plasmapheresis, blood is taken out of the body through a needle or catheter. The plasma is then removed from the blood by a cell separator. This can be accomplished in any one of three ways following:

- *Discontinuous flow centrifugation* – One venous catheter line is required. Typically, a 300-ml aliquot of blood is removed at a time and centrifuged to separate plasma from blood cells. The blood cells are returned to patient while the plasma is treated.
- *Continuous flow centrifugation* – Two venous lines are used. This method requires less blood volume to be out of the body at any one time as it is able to continuously spin out plasma.
- *Plasma filtration* – Two venous lines are used. The plasma is filtered using a standard hemodialysis equipment. This continuous process requires less than 100 ml of blood to be outside the body at one time.

In plasma exchange, the removed plasma is discarded and the patient receives replaced donor plasma. Heparin is used to prevent the line and circuit from thrombosing.

59.5.1 Indications

Plasma exchange may be used in the cardiac ICU setting if the patient develops a coagulopathy,

such as DIC (disseminated intravascular coagulation) or autoimmune hemolytic anemia (either IgM or IgG-mediated). In ABO-incompatible solid organ transplantation, the recipient may develop IgM antibodies against the donor ABO blood type. Plasma exchange can be used to remove these isohe magglutinins.

59.5.2 Utilization and Monitoring

Plasma exchange works by both removing pro-coagulant and hemorrhagic factors as well as antibodies from the blood and replacing the patient's clotting factors with FFP. This blood product contains clotting factors II, V, VII, VIII, IX, X, XI, and XIII. It also contains fibrinogen and von Willebrand factor. Cryoprecipitate contains higher concentrations of the latter two factors and may be used to supplement FFP.

59.5.2.1 Monitoring

The PTT as well as fibrinogen need to be monitored at least twice per day while the patient is undergoing plasma exchange. The heparin should be adjusted to keep the PTT between 60 and 85 s. The fibrinogen level should ideally be kept above 150 to minimize the

risk of bleeding. Cryoprecipitate (1 bag per 10 kg of body weight) can be used to replace fibrinogen.

59.5.2.2 Side Effects

While the patient is undergoing plasma exchange, there is the risk of both bleeding and clotting. Careful monitoring as stated above can minimize these risks. There may also be hypotension from fluid shifts, so the rate of fluid exchange has to be monitored closely.

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Chapter 60

Renal Failure and Replacement Therapy

Richard A. Orr, Rhonda Gengler, and Michael Moritz

Acute renal failure (ARF) is a common postoperative complication. General medical measures to treat this condition should include:

- a. Maintenance of an adequate renal preload (optimal circulating volume and cardiac output)
- b. Use of rapid onset diuretics
- c. Optimization of renal afterload (i.e., avoid high central venous pressures)
- d. Management of acute consequences of renal failure including systemic hypertension and hyperkalemia

Prevention of renal failure is crucial. This goal may be achieved by applying the above described principles and also by controlling any potential insult to the kidney. These concerns, among other measures require, the cautious use of nephrotoxic drugs and the aggressive management of rhabdomyolysis.

Many algorithms may be followed concerning the use of diuretics. Traditionally, furosemide is the first choice of administration as boluses or ideally as a continuous infusion. Alternatively, bumetamide may also be used. In case of unresponsiveness, a dose of mannitol is indicated. Other strategies include the use of other diuretics that may exert a synergistic effect: hydrochlorothiazide, metolazone, and ethacrynic acid. Xanthines may also be used. Nesiritide and Fenoldapan are also alternatives but the pediatric experience is still scarce and further studies will be required before concluding their usefulness in the pediatric population. The use of dopamine remains controversial.

Refractory renal failure should motivate caregivers to rapidly progress towards renal replacement therapy.

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60.1 Continuous Renal Replacement Therapy

60.1.1 Background

ARF that requires renal replacement therapy is a relatively common condition, with an annual incidence of approximately 30 cases per 1 million of population [1]. Severe ARF is a major complication of cardiac surgery and is associated with a very high mortality (60–100%) when treated with standard intermittent hemodialysis [2, 3]. More recently, continuous renal replacement techniques have been introduced, which circumvent the hemodynamic instability associated with intermittent hemodialysis and its limited ability to control the intravascular volume. Continuous veno-venous hemofiltration (CVVH) is one form of continuous renal replacement therapy (CRRT). When used early and intensively in the course of renal failure, it has the potential to substantially aid in the care of patients with severe ARF.

Hemofiltration was first described in the late 1970s as a means of removing extracellular fluid from patients with edema refractory to diuretics [4]. Continuous hemofiltration, combined with the administration of an appropriate fluid, is now recognized as a form of renal replacement therapy in ARF.

60.1.2 Basic Principles of CRRT

Hemofiltration and hemodialysis are similar in a few aspects. Both techniques require access to the circulation so that blood can pass through an extracorporeal circuit that includes either a dialyzer or a hemofilter.

The mechanism by which the composition of the blood is modified differs between the two.

During *dialysis*, blood flows along one side of a semipermeable membrane as a crystalloid solution is pumped along the other side of the membrane counter-current to the blood flow. Through the process of diffusion, molecules cross the membrane where the dialysis fluid is designed to produce as near normalization of the plasma as possible. This is affected by having the sodium concentration of the dialysis fluid physiologic, whereas the potassium concentration is lower than that of normal plasma to establish a gradient from the plasma to the fluid that promotes the removal of potassium ions from the patient's blood. Urea, creatinine, and phosphate substances that are to be removed completely are not found in the dialysis fluid. The removal of salt and water is accomplished by the creation of a transmembrane pressure gradient; the pressure being lower in the dialysis fluid compartment. In accordance with the laws of diffusion, the larger the molecule the slower is its rate of movement across the membrane. Urea, a small molecule, is cleared efficiently, whereas creatinine, a larger molecule, is cleared less well. Phosphate ions have very low rates of clearance across the membrane so that patients on intermittent dialysis have problems with hyperphosphatemia. (Fig. 60.1)

In contrast to dialysis, *hemofiltration* works by having blood under pressure pass down one side of a highly permeable membrane, which allows both water and substances of high molecular weight to pass across the membrane by convective flow (passive movement

of solute across a membrane along with water). This is what occurs in glomerular filtration. In contrast to hemodialysis, hemofiltration allows large molecules such as urea, creatinine, and phosphate to clear at similar rates. Profound hypophosphatemia can easily develop unless the patient's phosphate intake is supplemented or replaced via IV fluids. Larger molecules such as heparin, insulin, myoglobin, and vancomycin, cleared in only negligible amounts during dialysis, are cleared more efficiently by hemofiltration. (Fig. 60.2)

Current technology cannot reproduce the complex function of the kidney where glomerular filtration is selectively reabsorbed by the renal tubules. During hemofiltration, the filtrate is discarded and the patient receives replacement fluid. This replacement fluid is a solution where the major crystalloid components of the plasma are at physiologic levels. Fluid balance for the patient is determined by adjusting the rates of hemofiltration production and the replacement fluid. For example, if there is no need for the removal of fluid from the patient, the rate at which the replacement fluid is given is matched exactly with the rate of production of hemofiltrate. Generally, fluid removal is desired as patients with renal failure have total body fluid overload or the clinical need to administer fluids to a patient with oliguria. This is accomplished by replacing less fluid through the infusion of replacement fluid than is removed by hemofiltration.

Hemofiltration leads to an increase in the concentration of red cells and plasma protein in the blood. This increases the viscosity of the blood and induces a high colloid oncotic pressure at the distal end of the

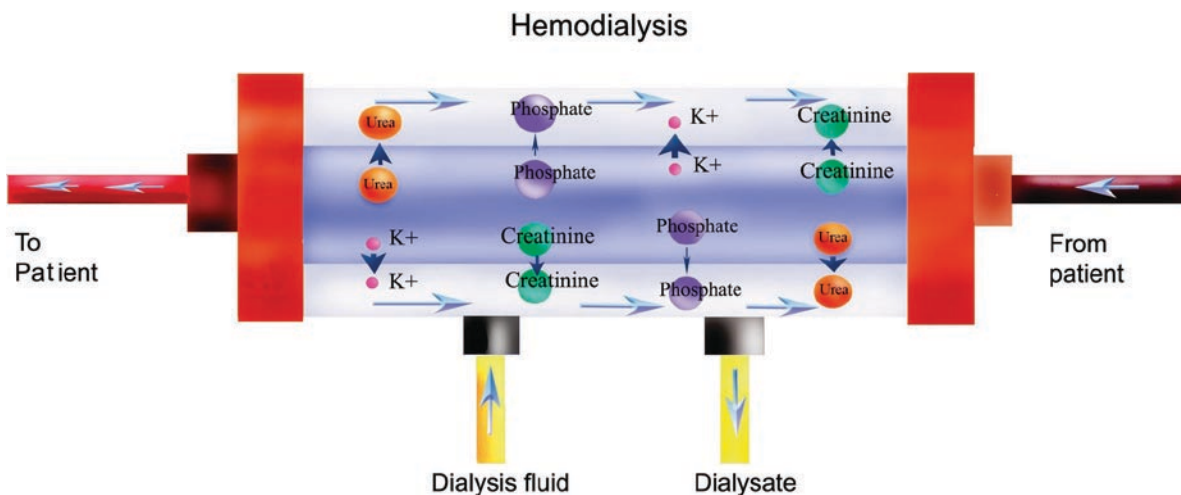


Fig. 60.1 Hemodialysis. The arrows that cross the membrane indicate the direction of movement of each solute through the membrane. The relative size of the arrows indicates the net amounts of the solute transferred. Other arrows indicate the direction of flow

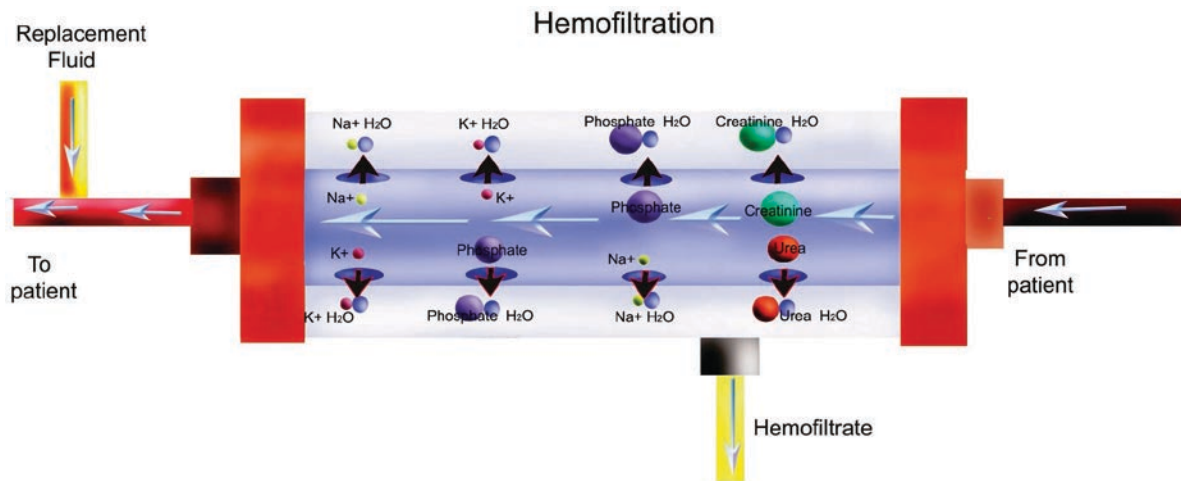


Fig. 60.2 Hemofiltration. The arrows that cross the membrane indicate the direction of movement of each solute through the membrane. The relative size of the arrows indicates the net amounts of the solute transferred. Other arrows indicate the direction of flow

hemofilter. Therefore, *the filtration rate should be no more than 30% of the blood flow rate.*

The continuous nature of hemofiltration is the most important contribution to the treatment of patients with ARF in intensive care units, where most have multisystem organ dysfunction. The majority of these patients has a negative nitrogen balance and are in dire need of appropriate nutrition. This task becomes difficult when

fluid restriction is necessary in the treatment of respiratory distress syndrome and renal failure. CRRT allows for both appropriate fluid removal and supplying the much needed nutrition.

60.1.3 Terms and Definitions

Dialysis	The separation of electrolytes and low molecular weight solutes from the blood across a semipermeable membrane.
Clearance	The ability of a filter to remove metabolic waste products from the blood. Occurs by diffusion, filtration, and convection.
Diffusion	Passive movement of solutes through a semipermeable membrane from an area of higher to lower concentration.
Ultrafiltration (convective transport)	The movement of water along with small solute across a semipermeable membrane.
Osmotic ultrafiltration	Passive movement of water from an area of lower concentration (blood) to an area of higher concentration (dialysate fluid). The common osmotic agent used is dextrose. The greater the difference in concentration between the two "compartments" the greater the fluid removal. Plasma proteins increase the plasma oncotic pressure and oppose fluid removal from osmotic ultrafiltration.
Hydrostatic ultrafiltration	The movement of water along with small solutes from the blood to the dialysate, via a hydrostatic pressure gradient between the two compartments.
Hemofiltration fluid	Sometimes referred to as "dialysate" or "bath."
Effluent	Fluid collected from the hemofilter that includes dialysate and fluid removed from the patient.
Predilution fluid	Replacement fluid that enters the circuit before the filter.
Postdilution fluid	Replacement fluid that enters the circuit after the filter.
Countercurrent flow	Hemofiltration fluid flows through the filter in the opposite direction as the blood. This provides increased clearance.

60.1.4 Variations on CRRT (Fig. 60.3)

60.1.4.1 Arteriovenous

Continuous Arteriovenous Hemofiltration (CAVH)

CAVH is the original and simplest form of the technique. An artery and vein are cannulated and the blood passes through the hemofilter under the influence of arterial pressure alone. No blood pump is used. The efficiency of hemofiltration depends on the difference between the

patient's mean arterial pressure and the venous pressure, a problem in patients who are hypotensive and/or with a high central venous pressure.

Continuous Arteriovenous Hemofiltration with Dialysis (CAVHD)

This configuration adds dialysis fluid to the CAVH system. This system adds diffusion as a mode of

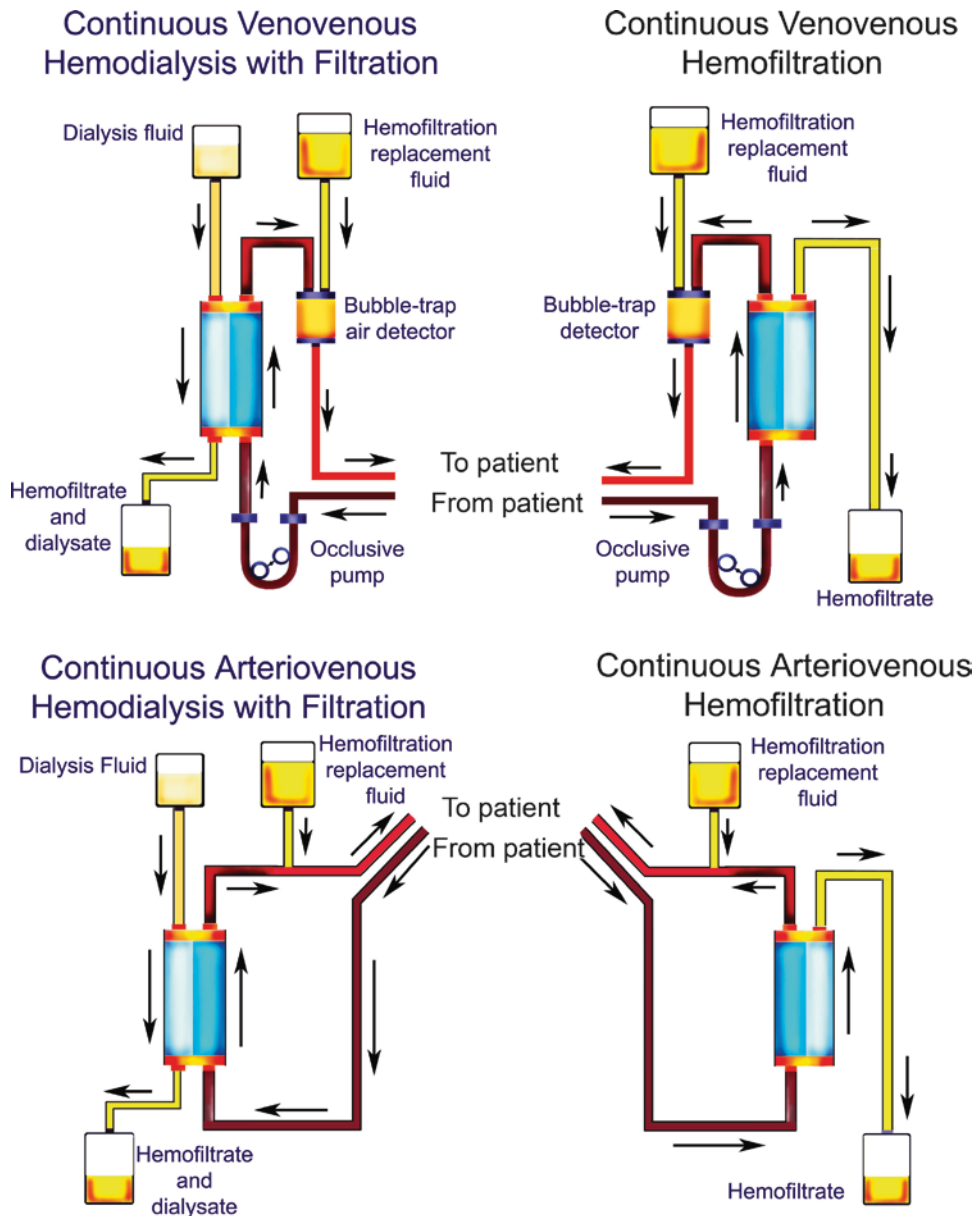


Fig. 60.3 Mechanisms of hemofiltration and hemodialysis with filtration

removing smaller molecules across the hemofilter. This configuration can also be referred to as continuous arteriovenous hemodialysis with filtration.

60.1.4.2 Veno-venous

Continuous Venovenous Hemofiltration (CVVH)

This configuration uses a double lumen catheter that is placed in a central vein (femoral, subclavian, or internal jugular), or alternatively, a single lumen catheter in each of the two central venous sites. An occlusive pump is placed into the filtration circuit that allows for control of the blood flow and the filtration rate, without the limitations imposed by relying on the arterial pressure to move the blood. Replacement fluid is used, often at high rates, to improve clearance. Water and small solutes are removed by filtration and convection.

Continuous Venovenous Hemofiltration with Dialysis (CVVHD)

This configuration adds dialysis to the CVVH system. Higher clearance rates of small solutes are achieved at any given blood flow by this modification. The majority of the required clearance needed can be achieved with CVVH alone, so the addition of dialysis is rarely needed in the authors' opinion. Acute hyperkalemia or hyperammonemia is one important indication for this configuration where additional clearance might be needed immediately at the inception of CRRT. This configuration can also be referred to as continuous venovenous hemodialysis with filtration.

Slow Continuous Ultrafiltration (SCUF)

This configuration is similar to CVVH except that there is no use of hemofiltration replacement fluid. Fluid removal is by hydrostatic ultrafiltration. *The fluid removal rate should not exceed 30% of the blood flow rate.* This configuration is selected when the only goal is to remove excess body fluid.

60.1.5 Indications for CRRT

The definition of ARF is not mutually agreed upon with the definition ranging from a change from baseline of >50% of serum creatinine, or a blood urea nitrogen >40 mg/dl, or not having enough urine output to match intake for medications, vasopressor agents, or "adequate" nutrition. Because these definitions vary considerably between programs or between clinicians, the decision or need for renal replacement therapy as well as the overall care of the child varies considerably. According to the author, the type of population the hospital serves, the presence or absence of a cardiac surgery program, ECMO program, bone marrow transplant, or solid organ transplant program influences the type of population that has ARF. It is not unusual that many children with ARF have been ill for a period of time before its diagnosis and are often malnourished, potentially effecting their treatment and outcome [5–9].

60.1.6 Indications

1. Patients who meet the criteria for hemodialysis or peritoneal dialysis, are hemodynamically deranged or have experienced abdominal trauma or surgery.
2. Symptoms of fluid overload in a hemodynamically deranged patient will not tolerate hemodialysis or CAVH due to a low blood pressure.
3. Patients with oliguric or anuric renal failure, frequently require administration of intravascular volume expanders such as salt poor albumin, packed red blood cells, fresh frozen plasma, and medications.
4. Patients with oliguric or anuric renal failure can be improved of their nutritional status by increasing fluid administration of TPN, intralipids, or NG feedings.
5. Patients with oliguric or anuric renal failure also have hepatic failure. CVVH may remove various toxins and small molecules. It has been well-documented that CVVH may improve overall survival of these patients.
6. Metabolic derangements where the production of noxious metabolic products is continuous. Hemodialysis is frequently insufficient in such cases because of its intermittent nature. For example, hyperammonemia and hyperkalemia

7. In certain cases of drug intoxication, the filters used for CVVH have larger pores than conventional hemodialysis filters, thus drug removal may be enhanced. The continuous nature of CVVH and the high rate of daily Ultrafiltration that is obtained make this therapy very useful.
8. Removal of fluid in volume overloaded patients who are resistant to diuretic therapy or with ARF.

60.1.7 Contraindications

There are no absolute contraindications for the use of CVVH except life-threatening bleeding, if one only uses systemic heparinization in the management of CVVH. The use of the citrate anticoagulation protocol is considered in this situation. In addition, one should not initiate renal replacement therapy while the patient is hypotensive. This can be ameliorated by ensuring adequate intravascular volume, a normal ionized serum calcium level, and the use of vasopressor agents.

60.1.8 Nutrition and CRRT

Hemofiltration prescriptions will result in significant amino acid depletion across the hemofilter membrane. In the non-dialytic setting of ARF, the standard recommendation for protein requirements is in the range of 1.5 g/kg/day. In patients on hemofiltration, protein administration may be in the range of 3–4 g/kg/day to maintain positive nitrogen balance. Since dialysate solutions are deficient in phosphorus unless added by

pharmacy, hypophosphatemia will occur, requiring that additional phosphorus be added to TPN. There is also loss of glutamine, an amino acid needed for protein production, regulation of signaling, trafficking of proteins, and sustaining immune function. It is essential to provide glutamine supplementation to all critically ill patients, and in particular, those who sustain losses through hemofiltration [10].

As mentioned earlier, the use of CRRT adds the benefit of optimizing nutrition during critical illness, since one has to be less concerned with restricting fluid intake. Fluid balance is now more easily controlled.

60.1.9 Vascular Access for CRRT

Vascular access for CRRT is decided upon by the size of the patient, the decision for what blood flows are needed, and the type of anticoagulation. Blood flow rates (BFR) through the hemofilter need to be maintained in the range of 3–5 mL/kg/min. This will translate into blood flows of 10–70 mL/min in patients <15 kg, 50–100 mL/min in patients 15–30 kg, and 100–250 mL/min in patients >30 kg. Dialysate or replacement fluid becomes saturated with solute at the prescribed rate of 2 L/h/1.73m². Therefore, higher BFRs have little effect upon solute clearance, and efforts to increase BFR increases the resistance in the circuit. Triple lumen access is helpful in patients where sites are limited and in those where citrate anticoagulation is being used, since a calcium infusion is needed to prevent hypocalcemia as a result of the chelating properties from citrate. Table 60.1 gives the suggested catheter sizes and sites of insertion for patient weight.

Table 60.1 Suggested catheter type and size for hemofiltration

Patient size	Catheter size (Product name)	Insertion site
Neonate	Single lumen 5.0 Fr (COOK) (need two catheters) Dual lumen 7.0 Fr (COOK, MEDCOMP)	Femoral artery or vein
3–6 kg	Check flow introducer sheath 4.0 Fr (COOK)	Internal jugular, subclavian, or femoral vein
	Dual lumen 7.0 Fr (COOK, MEDCOMP) Triple lumen 7.0 Fr (MEDCOMP, ARROW)	
6–15 kg	Dual lumen 7Fr, 8.0 Fr (KENDALL, ARROW, VAS-CATH)	Internal jugular, subclavian, or femoral vein
15–30 kg	Dual lumen 8.0Fr, 9.0 Fr (MEDCOMP, VAS-CATH)	Internal jugular, subclavian, or femoral vein
>30 kg	Dual lumen 10.0, 11.5 Fr, 12 Fr (ARROW, KENDALL, VAS-CATH)	Internal jugular, subclavian, or femoral vein

60.1.10 Machinery for CRRT

Industry sponsored machinery (Aquarius, Edwards Lifesciences, Mississauga, ON; PRISMA, Gambro, Lakewood, CO; BM-25, Baxter, Deerfield, IL; Diapact™, B. Braun Medical Inc, Bethlehem, PA; 2008 Hemodialysis and CRRT machine, Fresenius, NA) offer a variety of BFRs, warming systems, accurate ultrafiltration controllers, venous and arterial pressure monitor, and blood leak detectors. These systems allow for local prescriptions of hemofiltration including CVVH and CVVHD.

One could use adaptive machinery that includes a blood pump segment with an air leak detector. Unfortunately, adaptive machinery does not include the ability to regulate ultrafiltration and thermic controls, and increases nursing time and overall expense of performing CRRT.

60.1.11 Membranes

The choice of a hemofilter membrane for CRRT depends on the machine, the need for convective or diffusive clearance, and the size of the patient. The Baxter, Braun, and the Fresenius machines allow for individual choice of the hemofilter membrane, while the PRISMA uses a single membrane (AN-69) that has been found to improve survival rate in adult ARF [11]. This membrane has shown to be very biocompatible and can be used for either convective or diffusive clearance. The AN-69 hemofilter might be a better choice than polysulfone membranes for patients with sepsis. However, one problem that occurs with the AN-69 membrane is a bradykinin reaction when it interacts with acidotic plasma [12]. This problem can be avoided by using a priming solution of PLASMA-LYTE A (pH 7.4) with the addition of 20 mEq/L Sodium Bicarbonate and by ensuring a normal serum ionized calcium level before placing the patient on the circuit. Table 60.2 gives a summary of the available pediatric hemofilters and their properties. For venovenous hemofiltration, a larger circuit volume may be required depending on the volume of the blood lines. For the nonadapted systems (PRISMA), the filter is the Multiflow 60 and the circuit volume is fixed at 90 mL. The Multiflow 10 has a circuit volume of 45 mL.

Table 60.2 Choices for pediatric hemofilters and their properties

Hemofilter (Manufacturer)	Properties/surface area	Priming volume
AMICON(Baxter)	Polysulfone	15 mL
Minifilter Plus	0.07 m ²	
RENAFLO II (Minntech)	Polysulfone	28 mL
HF 400	0.3 m ²	53 mL
HF 700	0.7 m ²	83 mL
HF 1200	1.25 m ²	
Miniflow/Hospital	AN-69	3.5
Miniflow 10	0.04 m ²	44 mL
Multiflow 60	0.6 m ²	
PAN (Asahi)	Polyacrylonitrile	33 mL
0.3	0.3 m ²	63 mL
0.6	0.6 m ²	70 mL
1.0	1.0 m ²	
PRISMA (Gambro)	AN-69	50 mL
M10	0.04	84
M60	0.6	

60.1.12 Solutions

A variety of solutions can be used for CRRT. Some programs use saline or Ringers Lactate as an inexpensive form of replacement fluid while others use commercially available solutions for dialysis or pharmacy-made solutions. The decision to use replacement fluid is based on the overall solute and ultrafiltration clearance requirements of the patient as well as the local standard of care. The generally accepted rate of replacement and dialysate solutions for CRRT is 2 L/1.73 m²/h, though adequate metabolic control, and clearance can be achieved with lower rates. There are data to suggest that high clearance rates have a positive impact on mortality in adults [13]. Studies have shown that both lactate and bicarbonate-based solutions result in the same degree of clearance, but plasma lactate levels can be higher in patients on lactate-based solutions. This, obviously, raises the question in a critically ill patient as to whether the lactate is from the solution or from end organ malperfusion. In addition, patients with hepatic failure may not be able to metabolize lactate into CO₂ and hence, bicarbonate, exacerbating the lactic acidosis. Therefore, many programs have transitioned to using bicarbonate-based solutions. The first FDA approved bicarbonate-based solution for CRRT became available in 2000 (Normocarb®, Dialysis Solution Incorporated, Richmond Hills, ON, Canada).

This permitted programs to maintain a bicarbonate-based dialysis solution with less expense and risk of pharmacy error. Normocarb® and Accusol 30 2K 0Ca are also calcium-free, allowing the use of citrate anticoagulation instead of heparin. A list of commercially available solutions used for CRRT is given in Table 60.3. These solutions can be used in a diffusive or a convective mode.

60.1.13 Anticoagulation

Anticoagulation is needed to maintain the patency of an extracorporeal circuit. Before making the decision to provide systemic anticoagulation for CRRT, one should determine whether the patient needs it. Many patients with multisystem organ dysfunction have an underlying disease that results in systemic anticoagulation (e.g., septic shock with DIC).

One should consider not using anticoagulation if a patient has any one of the following:

- PT-INR more than 2.5, APTT more than 60 s
- Platelet count less than 60,000
- Active bleeding
- Patient is in the first 24 h postoperative

In these patients, vascular access with a large catheter and using a high blood flow rate through the circuit could be sufficient to maintain hemofiltration without systemic anticoagulation.

Traditionally, *heparin* has been the mainstay of anticoagulation for CRRT. The use of heparin loading between 10 and 30 units/kg as a bolus, and then 10–20 units/kg/h to maintain an ACT of 180–240 s or a PTT of 60–80 s is usually adequate for most patients. Bleeding is the obvious risk of systemic heparinization.

Citrate anticoagulation can be used as an alternative to heparinization [14]. Citrate is infused post-patient

(ACD–A solution) but before the hemofilter, to bind the calcium that is in the hemofiltration circuit. When calcium is bound with citrate, the blood loses its ability to coagulate and keeps the circuit patent. The result is an ionized calcium of 0.35–0.45 mmol/L within the circuit. In order to prevent citrate toxicity in the patient, calcium then is infused independent of the circuit and back to the patient to maintain a physiologic ionized calcium level of 1.1–1.3 mmol/L. The overall result is hemofiltration system anticoagulation without patient anticoagulation. Citrate anticoagulation requires a calcium-free dialysis bath to prevent any potential binding of calcium and any potential risk of coagulation in the hemofiltration system. Two primary side effects with the use of citrate are metabolic alkalosis and “citrate loc.” Since citrate is metabolized through the Krebs cycle, 1 mmol of citrate produces 3 mmols serum bicarbonate from the production of CO₂ from cellular respiration. This can be remedied by reducing the amount of bicarbonate in the replacement fluid and adding the difference with normal saline. The pH of normal saline is 5–5.4 and this offsets the development of metabolic alkalosis. “Citrate loc” is when citrate delivery exceeds citrate clearance. Citrate is metabolized and cleared in the liver and the hemofilter membrane. “Citrate loc” is seen clinically as rising total serum calcium and dropping serum ionized calcium. This gap is due to citrate being bound to the calcium. This can be remedied by holding the citrate dose for a period of time (usually 30 min) and then resuming at a lower infusion rate.

60.1.14 Writing the Prescription for CRRT

60.1.14.1 Physician Worksheet (Table 60.4)

The intensivist should be the physician in charge of CRRT because it is a dynamic process. Nevertheless, in

Table 60.3 Commercially available solutions for CRRT

Electrolytes mEq/L	Ringer's lactate	1.5% PD fluid	Normocarb	Prismasate	Accusol	Nxstage
Na	130	132	140	140	140	140
K	4	0	0	0, 2 or 4	0, 2 or 4	0, 2 or 4
Cl	109	96–102	105	108–120.5	109.5–116.3	109–113
HCO ₃	0	0	35	22 or 32	30 or 35	35
Lactate	28	40	0	3	0	0
Ca	3	3.5	0	0, 2.5 or 3.5	2.8 or 3.5	3.0
Mg	0	0.5–1.5	1.5	1.0 or 1.5	1 or 1.5	1.0
Dextrose g/L	0	15	0	0 or 0.11	0 or 0.11	0.1

Table 60.4 CRRT calculation sheet

1. Determine the patient's body surface area (BSA) using a nomogram or calculate using the Mosteller formula:

$$\text{BSA (m}^2\text{)} = ([\text{Height (cm)} \times \text{Weight (kg)}] / 3600)^{1/2}$$
 Answer: _____ m²

2. Calculate patient insensible fluid losses.
 For patients who are breathing humidified gas or who are being mechanically ventilated:

$$\text{Insensible loss per hour (mL)} = (300 \text{ mL/m}^2/24 \text{ h} \times \text{BSA}) / 24 \text{ h}$$
 For patients who are breathing room air:

$$\text{Insensible loss per hour (mL)} = (400 \text{ mL/m}^2/24 \text{ h} \times \text{BSA}) / 24 \text{ h}$$
 Answer: _____ mL/h

3. Calculate blood flow rate through hemofilter (start at 3–5 mL/kg/min)

$$\text{Blood flow rate (mL/min)} = \text{Patient weight (kg)} \times \text{___ mL/kg/min}$$
 Answer: _____ mL/min (minimum 30 mL/min)

4. Calculate counter current flow dialysate rate – *only if dialysis is used*

$$\text{Counter current flow dialysate rate (mL/h)} = 2000 \text{ mL} / 1.73 \text{ m}^2/\text{h}$$

$$\text{Counter current flow dialysate rate (mL/h)} = (2000 \text{ mL} \times \text{BSA}) / 1.73 \text{ m}^2$$
 Answer: _____ mL/h counter current dialysate

5. Calculate filter replacement fluid

$$\text{Filter replacement fluid rate (mL/h)} = 2000 \text{ mL} / 1.73 \text{ m}^2/\text{h}$$

$$\text{Filter replacement fluid rate (mL/h)} = (2000 \text{ mL} \times \text{BSA}) / 1.73 \text{ m}^2$$
 Answer: _____ mL/h (minimum 100 mL/h) filter replacement fluid

6. Calculation of electrolyte losses

- Calculate clearance in liters/24 h using filter replacement.

$$\text{Clearance (L/24 h)} = [\text{filter replacement fluid (mL/h)} \times 24 \text{ h}] / 1000 \text{ mL/L}$$
 Answer: _____ Liters clearance/24 h
- Potassium loss (mEq)

$$\text{Potassium loss (mEq)} = \text{liters clearance/24 h} \times [\text{Serum K}^+ \text{ (mEq/L)} - \text{replacement fluid K}^+ \text{ concentration (mEq/L)}]$$
 Answer: _____ mEq potassium loss/24 h
- Phosphorus loss (mmol)
 There is no accurate formula for calculating 24-h phosphate losses through CRRT. However, when one assumes a clearance of 2 L/1.73 m²/h, an acceptable guideline for initiation of sodium phosphate replacement would be 1 mmol/kg/day.
 Answer: _____ mmol phosphorus loss/24 h
- The daily losses for potassium (mEq) and phosphorus (mol) must be added to the 24 h maintenance prescription for these two elements (in either parenteral nutrition or maintenance fluids) to avoid hypokalemia and hypophosphatemia.

7. CRRT anticoagulation

- For CRRT using heparin anticoagulation
 If ACT is <165 s, give heparin IV bolus (15–20 Units/kg)
 Answer: _____ Units heparin load
 Begin heparin continuous infusion 5–15 Units/kg/h to maintain ACT range 165–215 s
 Answer: _____ Units/h
- For CRRT using citrate anticoagulation

$$\text{ACD-A infusion rate (mL/h)} = \text{blood flow rate through hemofilter} \times 1.5$$
 Answer: _____ mL/h ACD-A (Initial rate)

$$\text{Calcium chloride infusion (10 mg/mL in 0.9\% NaCl)} = \text{ACD-A rate} \times 0.3$$
 Answer: _____ mL/h (Initial rate)

Important: Use the ACD-A and Calcium Chloride titration scales on the order sheet to guide your therapy during the course of CRRT when using citrate anticoagulation.

many programs CRRT is ensured by a multidisciplinary team including intensivists and nephrologists. CRRT can potentially affect all organ systems, so it is important to provide the patient with continuous monitoring. Ideally, this should include continuous monitoring of at least ECG, pulse oximetry, arterial, and central

venous pressures. The physician in charge of CRRT must perform a series of calculations *before* writing the prescription and implementing CRRT. These calculations are found in Table 60.4 and will oblige the physician to carefully manage the patient's fluid balance, electrolytes, and nutrition.

60.1.14.2 CRRT Physician Order Sets (Fig. 60.4 and 60.5)

Order sets for both heparin and citrate anticoagulation are found in Fig. 60.4 and 60.5. Again, these should not be written until all of the calculations from the physician's worksheet have been completed. Net hourly balance reflects the difference between the total hourly fluid intake (all IV fluids, additional volume expanders and transfusions, calculated insensible loss, and filter replacement fluid), and total hourly fluid output (ultrafiltration, drains (pleural, mediastinal, gastric, peritoneal, CSF), and urine) from the perspective of the patient and not the circuit! This is accomplished through strict adherence to the CRRT flow sheet (Fig. 60.6). In the authors' experience, net hourly balance should be kept at zero for at least the first 2 h as the patient is adjusting to CRRT. Ideally, orders should be rewritten every 8 h for the first 24 h as the patient is adjusting to fluid and electrolyte shifts.

60.1.14.3 CRRT Flowsheet

The CRRT flowsheet (Fig. 60.6) is a necessary part of successful renal replacement therapy and becomes a part of the patient record. The flow sheet is designed to promote accurate hourly fluid and electrolyte balance through a simple and logical linear process that is clearly defined for the caregiver and operator of the circuit. CRRT flow sheets are renewed every 24 h. Fluid balance calculations for the previous 24 h can also be transferred to the patient's ICU flow sheet for completeness.

60.1.14.4 Nursing Considerations

A team approach is germane to the success of a CRRT program. Caregivers involved in the team should receive special training in the pathophysiology of renal failure, fluid and electrolyte balance, extracorporeal circuits, anticoagulation, aseptic technique and infection control, modes of CRRT and their indications, and setting up/troubleshooting the circuit. It is imperative that physicians, nurses, and technicians who are involved in the CRRT team be educated together through a training module that includes company product in-services, patient scenarios, and setting up the equipment for CRRT. The authors suggest the CRRT team successfully complete the educational module through testing and complete competency checks on a regular basis to stay current.

60.2 Peritoneal Dialysis in Cardiac Disease

60.2.1 Background

Peritoneal dialysis has been a main stay of renal replacement therapy for infants and children with renal failure for over 50 years. While hemofiltration and hemodialysis have largely supplanted peritoneal dialysis for the management of ARF and the treatment of fluid overload, it continues to play an important role and has certain advantages to therapies which require vascular access.

60.2.2 Advantages

Peritoneal dialysis has distinct advantages over other renal replacement therapies. Peritoneal dialysis catheters are relatively easy to insert and can be placed in virtually any sized child. It is a widely available therapy that is inexpensive and does not require specially trained personal or sophisticated dialysis equipment. Unlike other therapies, peritoneal dialysis does not require anticoagulation or anticoagulation monitoring. Peritoneal dialysis can be used as both a continuous and intermittent therapy, large amounts of volume can be removed without inducing hemodynamic instability and it can provide superior clearance to intermittent hemodialysis. Additives such as antibiotics, insulin, and potassium can also be administered in the peritoneal fluid and therapeutic blood levels can be obtained. Peritoneal dialysis also provides nutrition to the patients as the dextrose in the dialysate solution is absorbed across the peritoneum.

60.2.3 Disadvantages

The primary disadvantage of peritoneal dialysis is its lesser efficiency than vascular therapies and unpredictability of the amount of clearance and fluid removal. The volume of fluid that can be removed is not comparable to that of hemodialysis or hemofiltration and precise quantity of fluid removal cannot be achieved. Another disadvantage is that commercial peritoneal dialysate solutions are lactate based. Peritoneal dialysis



**CONTINUOUS RENAL REPLACEMENT THERAPY
ORDERS WITH HEPARIN ANTICOAGULATION**

Form CHP2189 Rev. 08/07

Patient
Name

Medical Record
Number

Birthdate

Date: _____ Time: _____ Height: _____ cm Current Weight: _____ kg Dry Weight: _____ kg

Allergies: _____

Place check <input checked="" type="checkbox"/> at order to be implemented.		ORDERS			
1. Therapy: _____ CVVH-D-F					
2. Place patient onto a bed with a scale					
3. Laboratory Studies:	Pre-Procedure	Q 4 Hrs.	Q 12 Hrs	QAM	
Electrolytes:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Phosphorus:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Calcium:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Magnesium:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Glucose:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
TCO ₂ :	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
BUN:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
Creatinine:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
CBC:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Platelets:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
4. Type and cross: 2 units of PRBC's (keep on unit at all times)					
5. Calculate insensible losses _____ ml/hr (300 ml/m ² /day for ventilated patient or 400 ml/m ² /day non-ventilated patients)					
6. Blood flow rate _____ ml/min (start at 3 - 5 ml/Kg/min, 30 ml/min minimum)					
7. Maintain net hourly balance of _____ ml/hr					
8. Preparing solutions:					
A. Rinsing: _____ 1 - 1L 0.9% Sodium Chloride + 5000 Units/L of Heparin					
B. Prime: _____ 1 - 1L Plasma - Lyte A Injection pH 7.4 + 20 mEq / L Sodium Bicarbonate					
C. _____ Calcium Chloride _____ mg IV Bolus (10 mg/Kg)					
D. _____ Calcium Chloride _____ mg/hr infusion (100 mg/ml) to run while attaching patient. (100 mg/Kg/hr) 50 cc syringe					
9. _____ Dialysate: Counter current flow					
Accusol 35 2K 2.5 L bag					
Dialysate Rate: _____ ml/hr					
10. _____ Prefilter Replacement Fluid					
Accusol 35 2K 2.5 L bag					
_____ ml/hr (minimum 100 ml/hr)					
11. Anticoagulation:					
_____ Pre-procedure ACT (Activated Clotting Time)					
_____ ACT Q 20 min until stable, then Q1 hr					
_____ Heparin IV Bolus (15 - 20 Units/Kg) _____ Units					
_____ Heparin Infusion (5 - 15 Units/Kg) _____ Units/hr					
_____ Titrate Heparin to Maintain ACT _____ to _____ seconds (Range 165 to 215)					
12. Notify CCM and/or Renal Attending for:					
_____ Net hourly balance not maintained _____ Phosphate < 2.5 mg/dl					
_____ ACT above or below set parameter (See #11) _____ MAP < _____ mm/Hg					
_____ Any alarms, which are unable to be corrected by nursing algorithm					

Name of Attending MD Notified: _____ Date/Time: _____

Signature MD: _____ Date/Time: _____

Signature RN: _____ Date/Time: _____



CHP2189

Fig. 60.4 Continuous renal replacement therapy (CRRT) orders with heparin anticoagulation

a



**CONTINUOUS RENAL REPLACEMENT THERAPY
ORDERS WITH CITRATE ANTICOAGULATION**

Form CHP0167 Rev. 08/07 Page 1 of 2

Patient
Name

Medical Record
Number

Birthdate

Date: _____ Time: _____ Height: _____ cm Current Weight: _____ kg Dry Weight: _____ kg

Allergies: _____

Place check at order to be implemented.

ORDERS

1. Therapy: ____ CVVH-D-F

2. Place patient onto a bed with a scale

3. Laboratory Studies:	Pre-Procedure	Q 4 Hrs.	Q 12 Hrs	QAM
Electrolytes:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Phosphorus:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Calcium:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Magnesium:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Glucose:	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
TCO ₂ :	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
BUN:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Creatinine:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
CBC:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Platelets:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Albumin:	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

4. Type and cross: 2 units of PRBC's (keep on unit at all times)

5. Calculate insensible losses _____ ml/hr (300 ml/m²/day for ventilated patient or 400 ml/m²/day non-ventilated patients)

6. Blood flow rate _____ ml/min (start at 3 - 5 ml/Kg/min, 30 ml/min minimum)

7. Maintain net hourly balance of _____ ml/hr

8. Preparing solutions:

A. Rinsing: _____ 1 - 1L 0.9% Sodium Chloride + 5000 Units/L of Heparin

B. Prime: _____ 1 - 1L Plasma - Lyte A Injection pH 7.4 + 20 mEq / L Sodium Bicarbonate

9. _____ Dialysate: Counter current flow

Accusol 30 2K 0Ca

2.5 L bag

Dialysate Rate: _____ ml/hr

10. _____ Pre-Filter Replacement Fluid

Accusol 30 2K 0Ca

2.5 L bag

Replacement Fluid Rate: _____ ml/hr (minimum 100 ml/hr)



CHP0167

Fig. 60.5 (a) and (b) CRRT orders with citrate anticoagulation

b



**CONTINUOUS RENAL REPLACEMENT THERAPY
ORDERS WITH CITRATE ANTICOAGULATION**

Patient
Name

Medical Record
Number

Birthdate

Form CHP0167 Rev. 08/07 Page 2 of 2

11. Anticoagulation with Anticoagulant Citrate Dextrose, Formula A (ACD-A):

- _____ Pre-procedure Ionized Ca
- _____ Ionized Ca from both the patient and the pump circuit at 30 minute intervals until the circuit's and patient's levels are within the No Adjustment range as noted below
- _____ Ionized Ca levels hourly after they are stable in the No Adjustment range
- _____ ACD-A infusion (blood flow rate X 1.5) _____ ml/hr
- _____ Titrate ACD-A infusion to maintain pump circuit's Ionized Calcium level 0.25 - 0.39 mMol/L (see chart below)
- _____ Calcium Chloride infusion (10 mg/ml in 0.9% Sodium Chloride) (ACD-A rate X 0.3) _____ ml/hr (1L/bag)
- _____ Titrate Calcium Chloride infusion to maintain Patient's Ionized Calcium 1.0 - 1.4 mMol/L (see chart below)

ACD-A TITRATION SCALE

Circuit Ionized Ca	Wt < 20 Kg	Wt ≥ 20 Kg
< 0.25 mMol/L	Decrease rate by 4 ml/hr	Decrease rate by 8 ml/hr
0.25 - 0.39 mMol/L	No adjustment	No adjustment
0.4 - 0.5 mMol/L	Increase rate by 4 ml/hr	Increase rate by 8 ml/hr
> 0.5 mMol/L	Increase rate by 8 ml/hr	Increase rate by 16 ml/hr

CALCIUM CHLORIDE TITRATION SCALE

Patient Ionized Ca	Wt < 20 Kg	Wt ≥ 20 Kg
> 1.4 mMol/L	Decrease rate by 4 ml/hr	Decrease rate by 8 ml/hr
1.0 - 1.4 mMol/L	No adjustment	No adjustment
0.9 - < 1.0 mMol/L	Increase rate by 4 ml/hr	Increase rate by 8 ml/hr
< 0.9 mMol/L	Increase rate by 8 ml/hr	Increase rate by 16 ml/hr

12. Notify CCM and/or Renal Attending for:


- _____ Net hourly balance not maintained
- _____ Total Ca > 12.5 mg/dl
- _____ Phosphate < 2.5 mg/dl
- _____ ACD-A Infusion Rate > 300 ml/hr
- _____ Calcium Chloride infusion > 150 ml/hr
- _____ MAP < _____ mm/Hg
- _____ Any alarms, which are unable to be corrected by nursing algorithm

Name of Attending MD Notified: _____ Date/Time: _____

Signature MD: _____ Date/Time: _____

Signature RN: _____ Date/Time: _____

Fig. 60.5 (continued)



PRISMA FLOW SHEET
CONTINUOUS RENAL REPLACEMENT THERAPY
RECORD WITH HEPARIN ANTICOAGULATION

Form CHP0166 Rev. 08/07

The following abbreviations are disallowed: u (unit), AS and MSO4 (morphine), MgSO4 (magnesium sulfate), mg (microgram), QD (every other day), IU, (International Units), State Prescribing Practices: Verify all orders by reading the order back to the prescriber. Do not use units (e.g., mg/hr). Order heparin in "mg" not "mg" doses.

PATIENT NAME: _____ UNIT NUMBER: _____ DATE: _____

NET CUMULATIVE BALANCE: _____ ml AS OF _____ / _____ / _____ DATE: _____

FLOW SHEET (CONTINUED)

MIDNIGHT TIME	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S		T		U	V
																			HEP	HEP	ACT	ACT		
00																								
01																								
02																								
03																								
04																								
05																								
06																								
07																								
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23																								

Fig. 60.6 CRRT nursing flow sheet. This flow sheet may be used for either CRRT with heparin or citrate anticoagulation

removes bicarbonate from the patient and exchanges it for lactate. Peritoneal dialysis can worsen lactic acidosis in the critically ill patient who cannot convert lactate to CO_2 and bicarbonate.

60.2.4 Principles of Peritoneal Dialysis

Peritoneal dialysis is performed via a single lumen catheter that is placed in the peritoneal membrane (Fig. 60.7). A dialysate solution is then instilled into the peritoneum. Solute and fluid removal primarily occurs via diffusion. The peritoneum is a semipermeable membrane to both large and small molecules. Uremic toxins, potassium, phosphorous, and proteins move across the peritoneal membrane over a concentration gradient into the peritoneal fluids. The greater the volume infused into the peritoneum and the more frequent the fluid is exchanged the greater the clearance. Dialysate solutions contain varying degree of dextrose which makes it hyperosmolar in relationship to the plasma. Water diffuses across the peritoneum

over a concentration gradient which results in osmotic ultrafiltration. Unlike hemofiltration, osmotic ultrafiltrate is slightly hypotonic in relationship to the plasma and hypernatremia can develop with rapid fluid removal.

60.2.5 Indications

Peritoneal dialysis is, a useful modality in infants following surgical repair of congenital heart disease. A peritoneal dialysis catheter is placed at the time of surgery and peritoneal dialysis is instituted if oliguria, fluid overload, or electrolyte disorders develop. Dialysis can be initiated immediately postoperative, if needed. Peritoneal dialysis is also a good choice for cardiac patients where:

- CRRT is not available
- Vascular access is limited
- Anticoagulation is contraindicated
- Prolonged dialysis may be required due to acute tubular necrosis or diuretic resistant edema due to severe heart failure

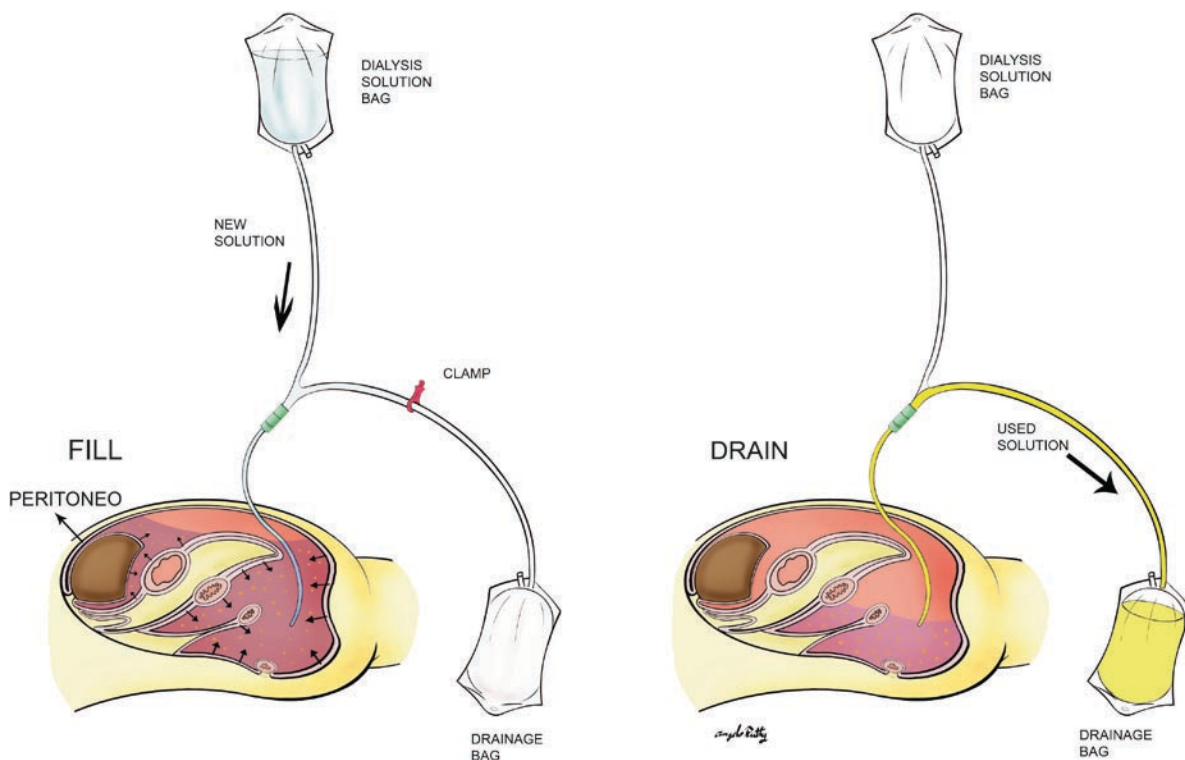


Fig. 60.7 Manual peritoneal dialysis using a Y set

60.2.6 Contraindications

The primary contraindication to peritoneal dialysis is recent abdominal surgery, abdominal drains, or abdominal wall defects. Peritoneal dialysis is also contraindicated if there is a communication between the abdominal cavity and the thorax. Peritoneal dialysis will not be successful if there are extensive abdominal adhesions or peritoneal membrane failure. Peritoneal dialysis can be instituted safely within 2 weeks following most major abdominal surgeries. Gastrostomy tubes, ileostomies, colostomies, and vesicostomies are not contraindications to peritoneal dialysis. A ventriculo-peritoneal shunt is a relative contraindication to peritoneal dialysis.

60.2.7 Access

Peritoneal dialysis catheters come in three sizes. An infant catheter is used in patients <3 kg, a pediatric catheter in children up to 5 years of age, and an adult catheter in children >5 years of age. Pediatric and adult catheters have the same internal diameter but differ in the length of the catheter.

Dialysis catheters can be cuffed or uncuffed, straight or coiled. An uncuffed acute peritoneal dialysis should not be placed for more than 72 h. A Tenckhoff single-cuffed acute dialysis catheter is most often used in children. If chronic dialysis is a possibility, a double-cuffed catheter should be placed.

60.2.8 Apparatuses for Dialysis

Acute peritoneal dialysis is easy to initiate and can be done manually. All that is needed is a “Y set” that connects to the peritoneal dialysis tubing (Fig. 60.7). One end of the Y connects to the dialysate solution and the other end to a drain bag. Manual peritoneal dialysis can be initiated with this set up. For infants, a special manual dialysate set called “Dialy-Nate®” is available. This is a closed system with a burretrol to administer small volumes of dialysis and multiple connectors for dialysate bags. Many centers will use an automated peritoneal dialysis machine called a “cycler” for acute peritoneal dialysis in children. This machine performs

continuous cycled peritoneal dialysis (CCPD). Some cyclers can be used in infants because they can deliver a dwell volume as low as 60 mL.

60.2.9 Dialysis Prescription

There are various components for writing a peritoneal dialysis prescription: (a) dialysate +/- additives, (b) dialysate dwell volume, (c) dwell time and number of exchanges.

60.2.10 Dialysate

Dialysate solutions have the same electrolyte composition (Table 60.5), but vary in the dextrose concentration. The dialysate type is referred to by the dextrose concentration as 1.5, 2.5, or 4.25%. These concentrations may slightly vary within countries. The standard dialysate used to initiate acute peritoneal dialysis is 1.5%. Dialysate concentrations can be increased if fluid removal is not adequate with a 1.5% dialysate. When initiating acute peritoneal dialysis 200 units/l of heparin is usually added to the dialysate to prevent the development of fibrin. Heparin does not result in systemic anticoagulation as it does not cross the peritoneum. If hypokalemia develops, 2–4 mEq/L of potassium chloride can be added to the dialysate.

60.2.11 Dwell Volume

Acute peritoneal dialysis is usually initiated at a low dwell volume of 10 mL/kg. A low volume is used to prevent leakage of fluid around the catheter from

Table 60.5 Peritoneal dialysis solution composition

Dextrose	1.5, 2.5, and 4.25%
Sodium	132 mEq/L
Chloride	98 mEq/L
Calcium	3.5 mEq/L
Magnesium	0.5 mEq/L
Lactate	40 mEq/L

increased intraperitoneal pressure. The dwell volume is then progressively increased to as much as 40–50 mL/kg. A dwell volume of 30–40 mL/kg can safely be reached within 10–14 days of catheter insertion.

60.2.12 Dwell Time

A standard dwell time for acute peritoneal dialysis is every hour. If dialysis is initiated within 24 h of catheter insertion, the dwell time can be decreased to 20–30 min to prevent leakage from around the catheter. More rapid dwell times are also useful for aggressive fluid removal or in the case of hyperkalemia. Continuous dialysis is used for optimal fluid removal. Intermittent dialysis with hourly exchanges for 8–10 h/day is usually sufficient when a dwell volume of 40–50 mL/kg is achieved.

60.2.13 Complications

There are a variety of complications that can occur with acute peritoneal dialysis. The most common complications of acute peritoneal dialysis are a dialysate leaking around the catheter exit site and infections.

A dialysate leak can be best avoided by:

- a. Waiting 1 or 2 days after catheter placement to initiate dialysis
- b. Using a cuffed dialysis catheter
- c. Using a low dwell volume of 10 mL/kg with rapid exchanges.

Peritoneal dialysis should be temporarily interrupted and the dwell volume decreased if a dialysate leak develops. Fibrin glue can be placed to the exit site.

Peritonitis and a peritoneal catheter exit site infection are the other common complications. The diagnostic criteria for peritonitis are a cloudy dialysate with a white blood cell count $>100/\mu\text{L}$ and $>50\%$ neutrophils. Peritonitis is not a reason to discontinue dialysis and can be treated by adding antibiotics to the dialysate.

Problems with filling and draining can occur with dialysis. This can be either due to poor positioning of the catheter, fibrin obstruction of the catheter, constipation, or omentum wrapped around the catheter.

Experience dialysis personal should be consulted if any complications arise.

60.3 Conclusion

ARF continues to be a significant factor contributing to the morbidity and mortality of critically ill infants and children. Although there is no true consensus regarding an absolute definition for ARF, it is generally accepted that ARF is characterized by an abrupt decline in glomerular filtration rate and an inability of the kidneys to appropriately regulate fluid, electrolytes, and acid–base homeostasis. Unfortunately, multicenter prospective outcome studies for critically ill children with ARF are largely deficient. The pediatric ARF outcome literature has been beset with retrospective data from single center, anecdotal experiences, without stringent stratification of various CRRT modalities. Because of these issues, the *Prospective Pediatric CRRT Registry Group* has been established to accumulate data from numerous pediatric centers across the United States to evaluate the impact of various CRRT prescriptions/modalities on circuit life and function, and to assess the effect of clinical variables on overall patient outcome [15]. The reader is encouraged to review the current literature on the topic ARF in infants and children and CRRT [16, 17].

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Chapter 61

Neurological Complications: Intracranial Bleeding, Stroke and Seizures

Robyn A. Filipink and Michael J. Painter

Within the first 12 months of life, approximately one-third to one-half of the 30,000–40,000 infants born in the United States each year with congenital heart disease (CHD) will undergo cardiac surgery [1, 2]. This large infant group is an accessible population for detailed assessment of medical and surgical techniques as well as outcome measurements. Over 50 years ago, before the advent of cardiopulmonary bypass, which allowed for open heart surgery, survival was the goal not often realized for these patients. Each decade has heralded surgical and medical advances that have decreased mortality. Intraoperative strategies now favor low-flow bypass over deep hypothermic circulatory arrest, and acid–base management prefers the acidotic pH-stat approach to the alkalotic alpha-stat strategy. In recent years, there has been a shift in emphasis to neurological morbidity. As neurological outcomes have become more important, cardiac intensive care unit (CICU) care is increasingly including the neurologist to help detect, manage, and offer prognosis for neurological complications. A full appreciation of the unique vulnerability of the cerebral vasculature and brain anatomy, along with understanding the major neurological complications of CHD, will guide comprehensive care for this special pediatric population.

A useful division to understand risk and neurological complications is the partition of the medical course into the preoperative, perioperative, and postoperative periods. Before entering the operating room, the CHD patient has accumulated risk starting from the prenatal period. Their genetic predisposition to central nervous system (CNS) problems may include brain dysgenesis

and malformations. Infants with CHD have a higher incidence of cranial ultrasound abnormalities [3]. Hypoplastic left heart syndrome (HLHS) is a common heart defect, and a retrospective investigation of this population found that 29% had minor or major CNS anomalies [4]. These included microcephaly, immature cortical mantle formations, holoprosencephaly, and agenesis of the corpus callosum [4]. Other common CHD, carry neurologic abnormalities in varying ranges: Tetralogy of Fallot 5–10%, truncus arteriosus 4–10%, and coarctation of the aorta 4–9% [4]. The combination of coarctation of the aorta and ventricular septal defect has a 70% incidence of brain lesions among full-term infants [3]. These CNS anomalies may cause seizures and abnormal cerebral blood flow leading to intracranial hemorrhage and vaso-occlusive insults. The specific cardiac defect may also predispose the patient to hemodynamic shock, hypoxemia, and acidosis in the newborn period. If the cardiac disease is serious, the patient may suffer cardiac arrest, further contributing to hypoxic-ischemic injury.

The perioperative time continues to carry risk of cardiac and systemic collapse. Chronic hypoxia has become less of a concern as early cardiac repair decreases this exposure. However, the immature cerebral vasculature and parenchyma are vulnerable to injury from surgical intervention. Fragile vasculature has difficulty in compensating for the metabolic and circulatory changes which occur during cardiac bypass. Low or absent cerebral blood flow during bypass leads to global hypoperfusion, which is likely the main cause of hypoxic-ischemic and reperfusion injury. Risk is also present during the core cooling and rewarming phases of deep hypothermic cardiac surgery. Complications include focal ischemia from embolic and thrombotic insults and hemorrhage from bypass-induced coagulation disturbances.

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In the postoperative period, the CHD patient faces cardiopulmonary dysfunction, hemodynamic instability, and continued cerebral vaso-dysregulation. Effects from surgery may become apparent as they were masked by paralytics and sedation. Cerebral insults occurring in the pre- and perioperative periods may lead to seizures during the recovery time. Hemorrhage and vaso-occlusive insults continue to be complications.

The major neurological sequelae present throughout the three important risk time periods are stroke, hemorrhage, and seizure. It is important to recognize these acute neurological issues and, when possible, exercise primary and secondary prevention to avoid long-term complications. This chapter reviews these three neurological manifestations of neurological injury facing pediatric cardiac patients and discusses prevalence, physical signs and symptoms, and work-up strategies and treatment (see Figures 61.1-61.3).

61.1 Hemorrhage

The intrinsic circulatory disturbances associated with congenital cardiac disease can predispose the brain to hemorrhage. This injury can occur anytime during the continuum of care, but age is a major risk factor. Sites of hemorrhage vary as full-term infants are more likely to have intraparenchymal and subdural hemorrhage, while premature neonates more commonly have intraventricular, intracerebellar, and subarachnoid hemorrhages [5]. The immature germinal matrix is especially predisposed to injury because of its structural and physiologic vulnerability. In the general newborn population, 90% of intraventricular and periventricular hemorrhage occurs during the first 36 h of life [5]. CHD neonates are susceptible to hemodynamic instability, and up to 24% may develop hemorrhage [6]. Surgery compounds risk as patients are exposed to changes in blood pressure, cerebral blood flow, and anticoagulation. One-third of neonates who underwent surgery with varying cardiac disease had new parenchymal hemorrhage diagnosed by magnetic resonance imaging (MRI) [7].

Additional risk factors include delivery complications, maternal coagulopathy, evolution of ischemic lesions, and infection. Identifying specific cardiac patients who carry a greater risk for hemorrhage is an important tool. These populations are HLHS [8] and coarctation of the aorta, the latter of which has an associated increase in intracranial aneurysms and hypertension [5, 9].

Symptoms of hemorrhage are wide ranging, depending on the mental status of the cardiac patient as sedation and paralytics needed for stabilization can mask neurological deficits. Physical signs include weakness, pupillary changes with increased intracranial pressure, acute vital sign changes, and clinical seizures. In contrast, some hemorrhages can remain clinically silent. An MRI study comparing pre- and postoperative asymptomatic intracranial hemorrhages in full term CHD neonates revealed that 43% had extension of hemorrhage, 26% had decreased hemorrhage, and 30% remained unchanged [10]. Sites of hemorrhage were the choroid plexus, subdural space, intraparenchymal, and occipital horn [10].

Caregivers should have a low threshold to evaluate for intracranial hemorrhage. The most widely used modality is *cranial ultrasound* (US). Portability with availability at the bedside makes this modality most useful in patients who are unstable and unable to be moved from the intensive care unit. *Computerized tomography* (CT) is the next technique employed for patients who may be transported, as it gives better spatial resolution and requires short scanning time. *MRI* is the best modality for dating hemorrhage and differentiating primary hemorrhage from transformed hemorrhagic infarct. Limitations on MRI include contraindication for ferromagnetic devices (e.g., pacemakers and valves) and patient transport issues [11]. Other criteria for performing preoperative cranial US include birth weight less than 1500 g, hemodynamic compromise sufficient to cause metabolic acidosis, coagulation disturbance, and certain cardiac lesions such as hypoplastic left-heart syndrome and coarctation of the aorta [1].

Complications from hemorrhage include seizure, as blood itself represents an irritant, stroke involving stasis of blood flow, and long-term neurological disability. Recently, the postmortem neuropathology of 405 pediatric cardiac patients who underwent transplantation revealed extraparenchymal hemorrhage in 31% with obstructive cardiac lesions and 16% of the total population with varied cardiac defects [12].

Management of hemorrhage employs serial imaging to survey extension. In the acute setting, transfusion and fresh frozen plasma may be used, if not contraindicated by cardiac vulnerability. Some patients may be on aspirin therapy, which increases the risk of bleeding and must be taken into account. The coagulable state of the patient can be precarious when balancing cardiac disease and risk of bleeding with

possible serious neurological sequelae. An important issue that arises once a patient is found to have an intraventricular–periventricular hemorrhage preoperatively is the timing of surgery. The main concern is to avoid extension of injury. Small subependymal hemorrhages should not delay surgery [1]. Intraventricular or intraparenchymal hemorrhages may call for waiting at least a week before cardiopulmonary bypass can be performed, however [11].

61.2 Stroke

Congenital heart disease is the leading known risk factor for childhood stroke. Estimates of the incidence of stroke per 100,000 children range from 2.5 [13] to 13 [14], including both ischemic and hemorrhagic strokes. From 25 to 30% are associated with CHD [13, 15, 16]. Realizing the high incidence of stroke allows for risk stratification based on age, specific cardiac disease, presence of thrombotic or embolic sources, inherent or acquired hypercoagulable states, and vascular anatomy.

An ischemic event specific to neonates is periventricular leukomalacia (PVL). This manifests as necrosis in the white matter surrounding the lateral ventricles and involves injury to immature oligodendrocytes. Vascular immaturity combined with hemodynamic instability from cardiac defects and surgery plays an important role. In general, preterm infants are at greater risk for PVL. The association between cerebral blood flow and the occurrence of PVL was examined preoperatively in 25 term infants with a variety of congenital heart defects. Decreased baseline cerebral blood flow was associated with PVL, which was present in 28% of this cohort [2]. In a study of full-term CHD infants, MRI uncovered 16% with PVL before surgery and 48% with new PVL in the postoperative period [7]. Another recent study found PVL through MRI in more than 50% of neonates after cardiac surgery [17]. These studies underscore the susceptible time periods for CHD patients.

HLHS patients are a particularly vulnerable group. An association of up to 25% has been reported between HLHS patients and the occurrence of PVL [8]. Among those who undergo Fontan operations, there is a 2.6 [18] to 8.8% [19] prevalence of stroke, and the risk may extend up to 15 years [20]. Additionally, postmortem evaluation after cardiac transplantation revealed that infarct was the primary CNS pathology in HLHS patients [12].

Embolic sources require cardiac anatomy that allows for passage into the cerebral circulation. Endogenous sources include intracardiac and systemic emboli, such as deep vein thrombosis and pulmonary emboli. Emboli may be induced by stasis, altered vascular pressure, surface interactions and circulation induced by cardiopulmonary bypass, deep hypothermic circulatory arrest, and immobilization. Septic emboli can occur in up to 50% of patients with infective endocarditis [21–23] and show a predilection for the middle cerebral artery territory [24]. Exogenous emboli are related to surgery and include synthetic debris, air, platelet, and fat. Thrombotic insults can involve both the arterial and venous systems and are related to possible systemic inflammatory vascular changes and increased central venous syndrome, respectively [1]. The role of prosthetic materials in altering blood flow pathways is another contributor to embolus and thrombosis formation. Hypercoagulable states secondary to cardiac disease [25–27] and additional coagulation pathway abnormalities contribute to stroke. Lutterman et al highlighted the association between Moyamoya syndrome, a chronic cerebrovascular disease of progressive stenosis and eventual occlusion of the internal carotid arteries, and congenital heart disease [28]. Additional risks for stroke include venous thrombosis [29], intracranial aneurysms, and large vessel dissection [30].

The signs and symptoms of stroke are similar to those of hemorrhage. Focal signs are related to the anatomy in the infarct area and can include motor and sensory deficits, alterations in consciousness, acute changes in vital signs, language disturbance, or visual field defects. Seizures can also be a cardinal sign of cerebral dysfunction. Age is a factor that can help guide the evaluation of a patient with suspected stroke. Infants often present with focal seizures [15, 31, 32], whereas older children more readily show language, motor, and visual deficits. As mentioned earlier, physical signs can easily be disguised by medication and recovery state.

Brain imaging reveals the presence of infarct, areas and extent of involvement, and hemorrhagic components. Cranial US is limited by low spatial resolution and the inability to detect acute and evolving ischemic areas, but may be the only modality available for an patient in critical condition. CT detects the presence of blood, but subtle findings in acute stroke such as loss of gray-white matter differentiation may not be detected until 6 h after infarction has occurred [33]. MRI using diffusion-weighted imaging (DWI) is a superior in

detecting cerebral ischemia [34] within 30 min from onset [33]. Magnetic resonance angiography (MRA) visualizes intra and extracranial vasculature to detect occlusion, dissection, and vascular anomalies. Alternatively, computed tomography angiography (CTA) and conventional angiography may give better visualization of vascular anatomy, but have the added risk of radiation exposure. Conventional angiography allows for vascular intervention, but is also limited by the stability of the patient to undergo anesthesia and the procedure. Newer techniques to assess perfusion aim to determine if there is reversible ischemia and salvageable brain tissue.

These include xenon-enhanced CT, CT perfusion, MR perfusion, and diffusion imaging. Each has its own advantages and disadvantages, but tolerability of scanning time is the main limiting factor for patients in the CICU.

Stroke complications include seizure, progression to hemorrhage, and apparent and subtle long-term neurological deficits. The interplay between these major complications is exemplified by the relationship of some antiepileptic medications and anticoagulants used to prevent primary or further strokes. For example, warfarin's effectiveness can be decreased by phenobarbital, a widely used anti-seizure medication.

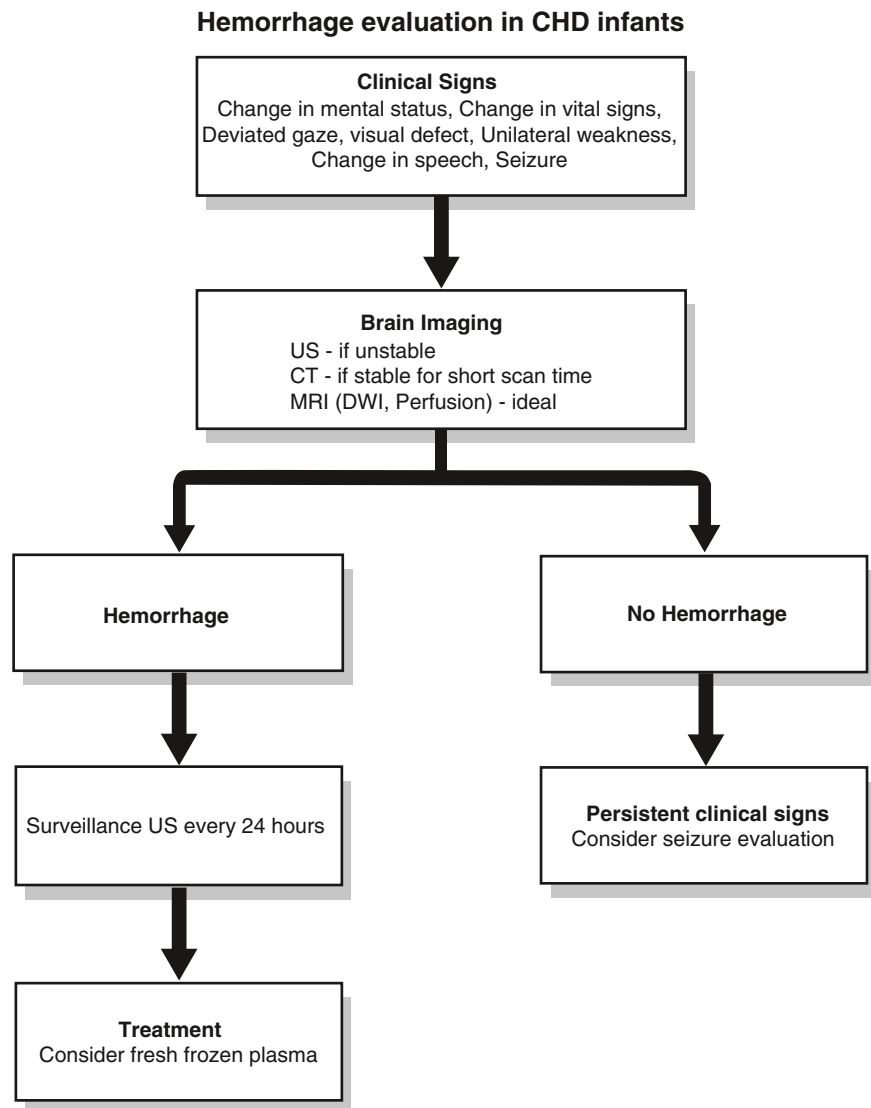


Fig. 61.1 Hemorrhage evaluation in CHD infants

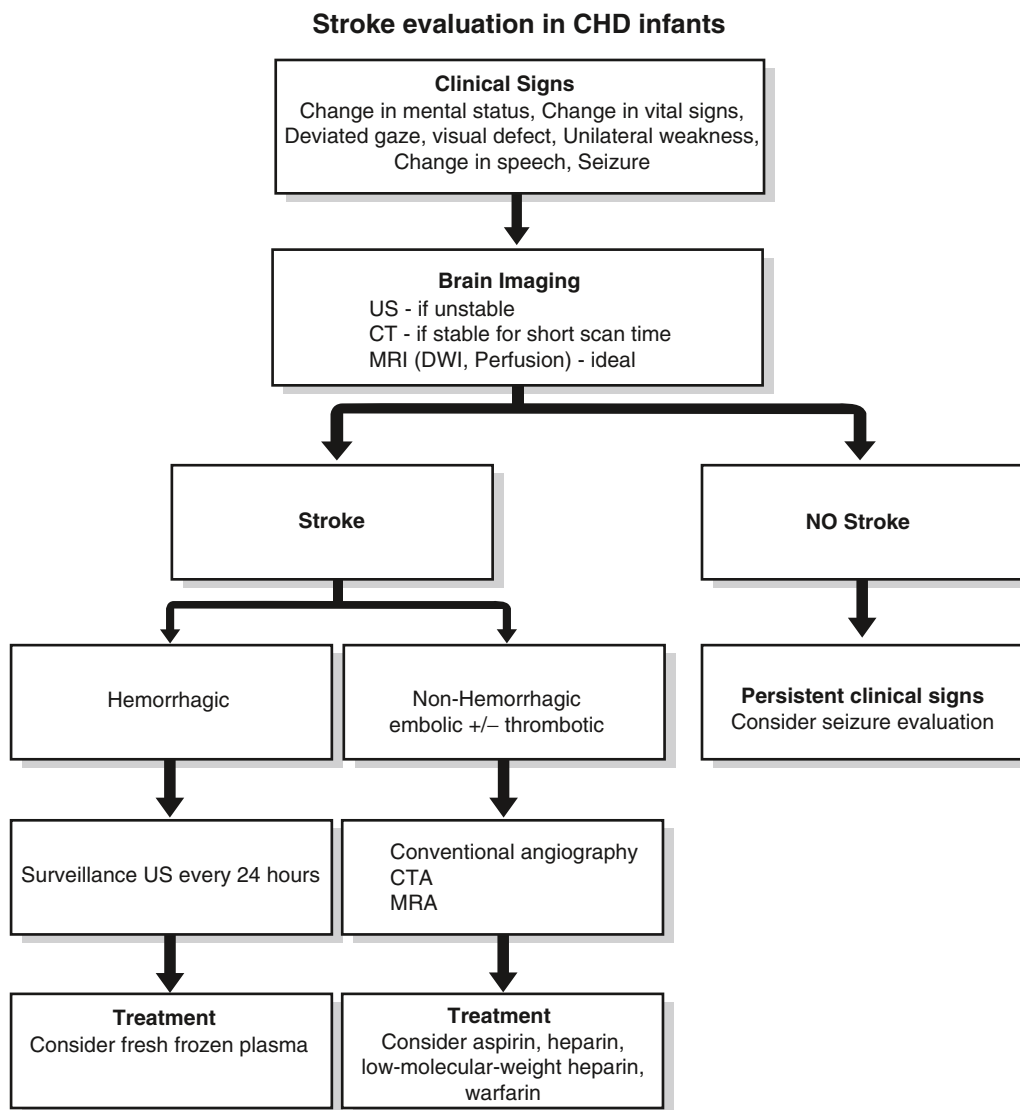


Fig. 61.2 Stroke evaluation in CHD infants

Unfortunately, in contrast to adults, there is minimal epidemiological evidence and no acute intervention studies on children to guide treatment. Acute therapy for adults ranges from revascularizing ischemic areas with thrombolytics either remotely by intravenous administration or directly by intra-arterial administration or invasive neurosurgical intervention such as vascular stents or angioplasty. The first national estimate of the use thrombolytic therapy for ischemic stroke in children reported that less than 2% of children received this treatment [35]. None of the patients receiving thrombolytics had CHD, and as a matter of practice, thrombolytics are

rarely, if ever, given to this high risk population. This highlights the need for further investigation into acute stroke interventions for pediatric CHD patients.

Primary preventative care aims to provide prophylactic treatment, while secondary prevention aims to stop hemorrhagic conversion of the infarcted area or avoid future strokes. Indications for primary prophylaxis include prosthetic heart valves, dilated cardiomyopathy, intracardiac thrombus, and prolonged immobility. Therapies include anti-platelet medications such as aspirin and plavix, and anticoagulation medications such as warfarin and low-molecular-weight heparin.

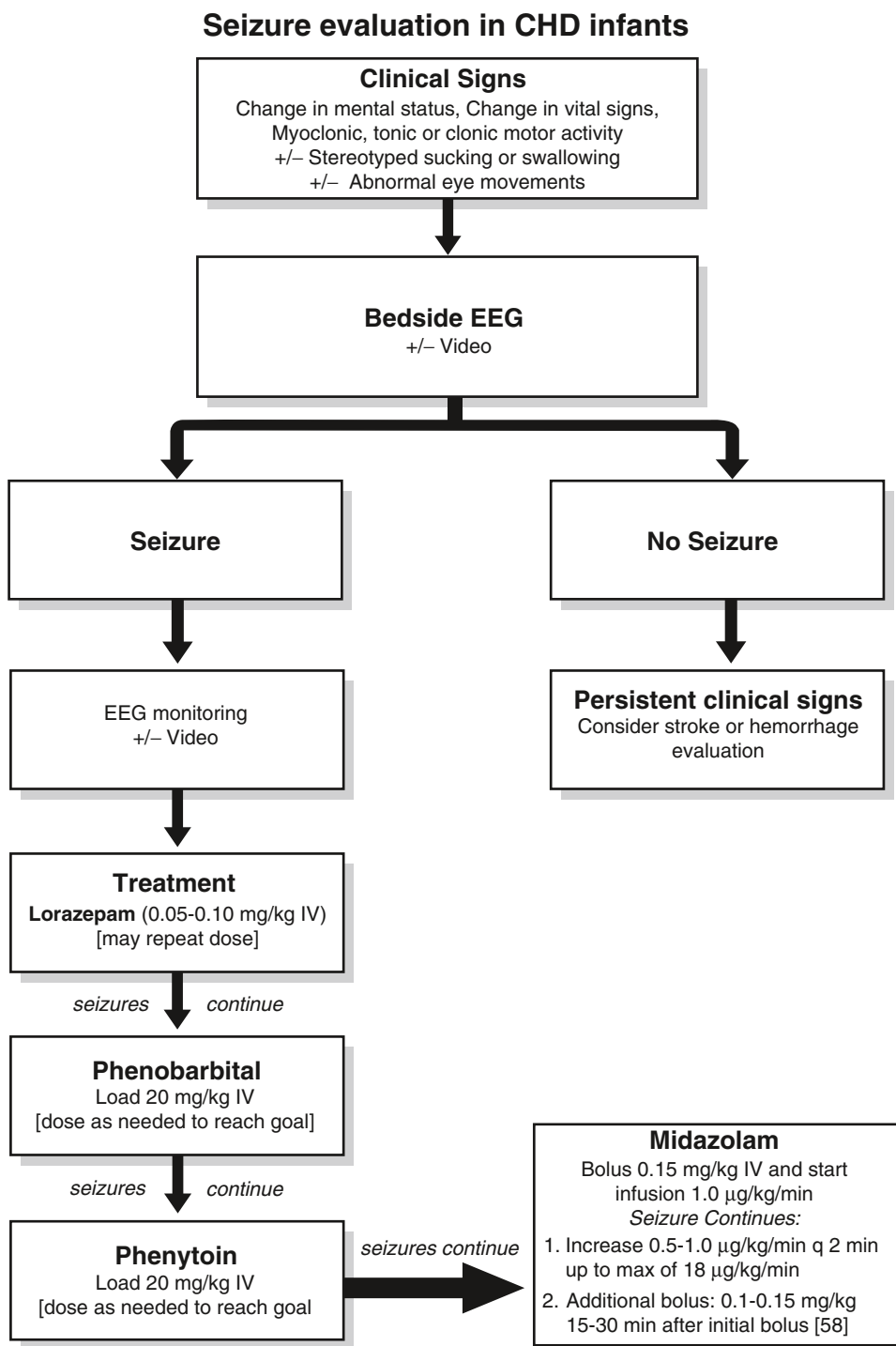


Fig. 61.3 Seizure evaluation in CHD infants

Hemorrhage is the primary side effect. Decisions require careful assessment of risk and benefit. Although the precise risk for children with CHD is unknown, adult

studies again serve as guides and offer information on surgical timing. Large infarcts in adults, involving a cerebral lobe or more than 30% of a hemisphere, have

greater risk for hemorrhage [36–38]. Within the first 48 h, 70% of adult strokes evolve to hemorrhagic transformation [37]. This data helps formulate a logical stepwise approach to stroke in the CICU.

61.3 Seizures

Seizures are common manifestations of neurological dysfunction in CHD patients. The neonatal period is the time of highest seizure incidence [39–41]. Even before cardiac surgery, patients may have seizures that reflect their underlying brain dysgenesis. Seizures are also a common complication after surgery. Incidence varies depending on the mode of seizures identification. Electrographic seizures, detected by video-EEG monitoring for 48 h postoperatively, occurred in 11.5% of CHD infants, and none had clinically visible seizures [42]. In contrast, another study noted a seizure incidence of 1.2% for CHD infants after surgery, and these seizures were diagnosed clinically [43].

A risk factor for increased seizures in infants is the duration of deep hypothermic circulatory arrest (DHCA). DHCA duration of more than 40 min significantly increases incidence of electrographic seizures [44]. Hemorrhage and stroke predispose a patient to seizure. Cyclosporine toxicity is another etiology, which is particular to CHD patients on immunosuppressants [43]. As discussed earlier, Moyamoya syndrome should be considered when the presentation includes both stroke and seizure [28].

Identification of seizures in the newborn period can be very difficult to detect clinically. Physical signs can include behaviors and movements that are very different from the typical tonic–clonic epileptic movements of older children. Episodic autonomic changes may be the only sign of a seizure [45–47]. Clinical signs of focal seizure can vary from rhythmic shaking of an extremity, twitching of one side of the face or eye deviation, to subtle change in mental status. Generalized seizures may present as whole body rhythmic shaking with loss of consciousness. Electrographic seizures may not have a clinical correlate, however, as mentioned earlier. Therefore, a low threshold of clinical suspicion is needed for evaluation of seizures.

EEG is the definitive test to detect seizures and quantify their frequency. EEG is performed at the bedside where a trained technician can apply electrodes and run a recording even on unstable patients. Video-EEG

helps determine if clinically suspicious movements, behaviors or autonomic changes are a sign of seizure activity. Abnormal EEG background is a strong predictor for concomitant and subsequent seizures in the following 24 h [48]. Burst suppression patterns, which are a markedly abnormal background, are highly indicative of chronic static encephalopathy [49]. Epileptogenic discharges, such as excessive sharp waves, can indicate a lowered seizure threshold. Therefore, the EEG is a valuable tool to identify seizures and help predict future seizure risk, as well as, to some extent, neurological outcome.

The underlying cause for seizures determines prognosis. Infants with brain dysgenesis have a high chance of developing epilepsy, but there are other associated risk factors. A retrospective review of childhood stroke reported that 49.3% of patients developed at least one seizure and 28.8% developed recurrent seizures [31]. Stroke occurring in the newborn period carries the lowest risk for epilepsy [50]. Additional information has emerged from studies following congenital cardiac patients. West syndrome, defined by the combination of infantile spasms, hypsarrhythmia, and developmental delay, has been reported in a small group of CHD after surgery [51].

The importance of this manifestation of cerebral disturbance is underscored by a study, which associated poorer cognitive outcome with seizures. It revealed that preoperative seizures in a group of children with HLHS predicted lower full-scale IQ [52]. In survivors of corrective surgery for D-transposition of the great arteries, perioperative seizures were associated with poor neurodevelopmental outcome at 1 [53] and 4 [54] years after surgery. Conversely, recent outcome data on a group of 178 neonates and infants after cardiac surgery showed that the occurrence of seizures was not predictive of worse development at one year of age [55].

Acute treatment for seizures is related to the underlying cause. Correcting electrolyte abnormalities and identifying toxic medication levels are important steps in the approach to the seizing child. The commonly used medication *algorithm* outlined by du Plessis [11] first employs lorazepam at an infusion dose of 0.05–0.1 mg/kg and the dose may be repeated twice if needed. If seizures continue, phenobarbital is loaded at a dose of 20 mg/kg to a maximum of 40 mg/kg. Higher doses may be required, but blood levels will help determine appropriate dosing (goal level 40 mg/L). Administration of phenobarbital leads to a 50% or more reduction in less than half of infants experiencing seizures [42].

Phenytoin is the next step for continued seizures. The loading dose is 20 mg/kg, with repeat dosing if necessary. Both phenobarbital and phenytoin have been reported to be equally, but incompletely, effective in controlling seizures in less than half of neonates. Their combined use led to a slight improvement in seizure control in 57–62% of neonates [56].

Prolonged seizure activity unresponsive to these medications may be treated next with an infusion of IV midazolam. Favorable response to midazolam in this situation has been reported using an IV bolus of 0.15 mg/kg, followed by continuous infusion (1 µg/kg/min) increasing by 0.5–1 µg/kg/min every 2 min until a favorable response or a maximum of 18 µg/kg/min. A second bolus of 0.10–0.15 mg/kg may be administered 15–30 min later if seizure activity continues [57]. As many patients will not go on to develop epilepsy, the duration of anti-epileptic medications must be considered for each patient based on etiology for seizures, brain imaging, and timing of seizures to other events such as stroke. After this approach, the likelihood of seizure recurrence can dictate management and, in most cases, medication can be weaned within 2 months.

61.4 Conclusion

Three interconnected neurological complications encountered in the pediatric CICU are hemorrhage, stroke, and seizure. As risk follows a patient throughout their hospitalization and beyond, the physician must be ever vigilant. By employing the discussed detection, surveillance, prevention, and treatment strategies, one can effectively treat the pediatric patient with congenital cardiac disease and promote an improved neurological outcome.

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Chapter 62

Infections in the Cardiac Intensive Care Unit

Glenda V. Wright and Marian G. Michaels

Children in the cardiac intensive care unit (CICU) are at a high risk for infections. This may be due to underlying immunodeficiency, iatrogenic alterations in the immune system or due to invasive procedures. Some patients are admitted to the CICU primarily due to an infection, while others develop secondary infections once they are in the CICU setting. This chapter reviews the types of infections that can occur in the pediatric CICU to give an understanding of predisposing factors, primary and secondary infections.

62.1 Predisposing Factors

The child's immune status is a critical factor influencing the risk for infection while in the CICU setting. Age itself affects the child's immune capacity. Infants with congenital heart defects (CHD) are often admitted to the CICU shortly after birth. Their immature immune system coupled with the absence of immunizations puts them at risk for infections with consequential morbidity and mortality.

Routine vaccinations should be given to the infants as soon as possible. This is particularly important for heart transplant candidates, as they may not respond adequately to vaccines after they receive anti-rejection immunosuppressive agents. Hepatitis B vaccine can be given at birth followed by second and third doses at one and 6 months of age. Other vaccines can be started at 6 weeks of age.

Some congenital cardiac defects are associated with immunodeficiencies such as asplenia or syndromes such as Di George syndrome involving full or partial deletions of chromosome 22q11⁻. Thymic development is abnormal in Di George syndrome affecting the T-cell arm of the immune system leaving children at severe risk for opportunistic infections such as transfusion or breast milk associated cytomegalovirus (CMV), and *Pneumocystis jiroveci*. Blood products should be CMV negative or leukocyte depleted to decrease this risk. In addition, after 4 weeks of age prophylaxis against *P. jiroveci* pneumonia (PCP) should be given in the form of trimethoprim/sulfamethoxazole. These infants are also at risk for partial engraftment of leukocytes that contaminate blood cell transfusions leading to graft versus host disease with its immunosuppressive effects. For this reason, irradiated blood products should be administered to all infants in whom the diagnosis of Di George syndrome is considered [1]. In our institution, all neonates receive CMV safe (filtered) and irradiated blood products.

Poor nutritional status is another risk factor for infections that can affect patients in the CICU. Children with uncontrolled heart failure or other defects, which result in impaired feeding or increased caloric needs, may be malnourished with increased susceptibility to infections [2]. In addition, the nutritional impairment contributes to poor wound healing, increasing the likelihood of surgical-site infection.

Nosocomial infections are a significant concern for children in a CICU setting. Infants and children in the CICU often have surgical wounds, and invasive catheters that interrupt the normal protective barriers of the body. The presence of sternal wounds, central line catheters, chest drains, and pacing wires put these patients at risk for nosocomial bacterial and yeast infections [3]. Intubation of the trachea and ventilatory

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support put the patient at risk for tracheitis and ventilation associated pneumonia. Use of bladder catheters, often necessary for accurate measurement of urine output, is also a risk for urinary tract infections.

Extracorporeal membrane oxygenation (ECMO) is required at times to provide cardiovascular support in patients undergoing cardiac surgery or as a bridge to cardiac transplant. A retrospective review of nosocomial infections associated with ECMO over a 4-year period found increased infections in children with CHD (29/75) compared to other underlying diseases (8/66) [4]. The authors postulated that this increased risk for nosocomial infection may partly be due to longer cannulation times as well as increased likelihood of undergoing major procedures or having an open sternum. Left ventricular assist devices (LVADs) have only recently been used in children but represent an important bridge to heart transplantation in patients with end-stage heart failure [5]. Infection is a common complication of LVAD's in adults and likely affect children as well [6].

Finally, circulating nosocomial infections that are particular to a time of year such as respiratory syncytial virus, or in a specific institution, such as vancomycin resistant enterococci, may be additional risk factors for children requiring CICU care. While every hospital should employ good hospital infection control policies, it is clear that nosocomial infections can occur. Accordingly, it is important to know the epidemiologic risks for individual institutions.

62.2 Types of Infections

62.2.1 Surgical Site Infections

Surgical site infections (SSI) may occur following any surgical procedure including cardiac surgery. There is considerable variation in regimes for prophylactic antibiotics, in terms of antibiotic choice and duration [7]. To decrease SSI, protocols for administration of antibiotics just prior to surgery and for 24 h afterwards have been employed [8]. Guidelines for prevention of SSI include preoperative bathing with chlorhexidine gluconate, to reduce the cutaneous bacterial colony count [9]. Likewise, it is recommended to use appropriate antimicrobial agents that will maintain therapeutic levels within the serum and tissues throughout the operation

and a few hours after closing the incision. Prolonged use of antibiotics is not required. Use of vancomycin as prophylaxis is discouraged unless the patient is known to be colonized with methicillin resistant *Staphylococcus aureus*. Despite these measures, infections can occur at the wound site that may be superficial, involving the skin or subcutaneous tissue, deep, involving deep soft tissues or organ space or the most severe form – mediastinitis. This latter infection involves the sternum and the organ tissues outside of the incision. Mediastinitis can occur despite preoperative prophylactic strategies [10]. The highest risks groups are those with delayed sternal closure following repair and those requiring re-exploration surgeries for bleeding [10, 11]. Surgical debridement is often necessary along with specific antimicrobial treatment aimed against the infecting organisms. Gram-positive organisms, particularly *S. aureus* and coagulase negative staphylococci are prominent. *Pseudomonas aeruginosa* is the most frequently implicated Gram-negative organism [11, 12].

62.2.2 Catheter-associated Infections

Line-associated bacteremias are frequent complications with the use of long-term vascular catheters. Infection may occur locally at the site of catheter insertion or in the blood stream. Clinical findings may be minimal as they may manifest only as fever [13]. Most patients in the CICU regardless of their underlying condition will have a central intravascular catheter placed. Data are limited regarding the management of catheter-related infections in children [14]. Accordingly, guidelines are derived from adult data. Measures to reduce catheter-associated infections include strict adherence to sterile techniques during catheter placement, including gowning, gloves, and sterile drapes. Chlorhexidine/isopropyl alcohol solutions to prepare the skin before placement also assist in prevention of infection [15]. Finally, reassessment of their need and prompt removal of catheters after they are no longer required, helps to minimize the rate of infections [14]. Antibiotic locks to prevent infection have been evaluated in critically ill neonates. Garland showed that prophylactic use of a heparin-vancomycin lock solution for 20 or 60 min twice daily, significantly reduced the incidence of catheter-related blood stream infection in this population. Unfortunately, the utility of antibiotic locks is often hampered

in the critical care setting where central lines are often required for continuous infusion of medications or parenteral nutrition. In Garland's study, interruption of continuous infusion of total parenteral nutrition resulted in hypoglycemia in some infants [16].

Indwelling urinary catheters are associated with nosocomial urinary tract infections (UTI). Interestingly, Levy et al. [3] reported this in <1% of pediatric CICU patients. However, this low incidence may be explained by their study being limited to patients after cardiac surgery with relatively short-term use of urinary catheters.

62.2.3 Respiratory Tract Infections

Tan et al. [17] found nosocomial pneumonia in infants after cardiac surgery to occur more frequently in children with underlying complex congenital heart disease (CHD) compared to children with simple CHD. The authors suggest that this may be due to previous recurrent pneumonia, longer surgical procedures, and prolonged postoperative mechanical ventilation [17]. As noted previously, all children requiring mechanical ventilation are at increased risk for tracheitis and for lower respiratory tract infection. While endotracheal colonization increases with prolonged intubation, it does not require antibiotic treatment. To distinguish colonization from true infection, three elements should be evaluated:

1. Clinical signs and symptoms such as a change in the respiratory status and change in the color, consistency, and volume of tracheal secretions
2. The Gram stain of the secretions which should show neutrophils, as well as moderate to heavy staining of a single type of bacterium
3. Growth of moderate to heavy amount of bacteria.

To ascertain the cause of pneumonia deep suctioning or a bronchoalveolar lavage may be required.

62.2.4 Transfusion-Transmitted Infections

Patients in the CICU often receive multiple transfusions of blood products. Blood product safety has improved significantly over the past several decades.

Transmission of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) decreased substantially particularly with the introduction of polymerase chain reaction (PCR) based assays [18]. The American Red Cross voluntary blood supply estimates HIV and HCV transmission risks of 1:1,525,000 and 1:1,390,000 respectively. The risk of transmission of hepatitis B is higher at 1:144,000, but is anticipated to decrease further as rates of universal immunization increase in the United States [19]. Leukoreduction techniques for packed RBC have decreased transmission of viruses such as CMV and EBV [20]. Still of concern is transmission of infections with a long incubation periods such as human T-cell leukemia virus (HTLV) and Creutzfeldt-Jacob disease. Emerging infections such as West Nile virus also can be transmitted with transfusions. Bacterial contamination of platelets is currently the most frequent transfusion associated infection.

Prevention of transfusion-associated infections relies on appropriate screening of blood donors and proper techniques for collecting and storing blood products. The use of a designated donor unit can reduce some risk for infants who require repeated transfusions by avoiding exposure to multiple donors. Judicious administration of blood products may also decrease infection risk.

62.2.5 Myocarditis

Myocarditis is an important cause of morbidity and mortality in children (see specific chapter in this book). Affected children are often managed in the CICU. Enteroviruses, in particular Coxsackie B virus, have long been recognized as important causes of myocarditis in children. Adenovirus has been found frequently in more recent studies [21, 22]. Parvovirus B19, Influenza, and CMV have also been implicated [23–25].

The clinical features of viral myocarditis may range from self-limited illness with subclinical myocardial dysfunction to severe cardiac failure or even sudden death [26]. The diagnosis is often based on clinical findings, with evidence of ventricular dysfunction on echocardiogram and viral culture or serology [27]. Endomyocardial biopsy is the gold standard, providing histology, culture, and PCR material but has significant risk and is not performed at all centers. Treatment involves supportive measures, which may include inotropic agents, mechanical ventilation, and in severe

cases mechanical devices such as ECMO or ventricular assist devices. While many centers use intravenous immunoglobulin (IVIG) therapy for myocarditis in children, controlled pediatric trials are lacking [28]. Drucker et al. [29] reported a non-controlled case series of pediatric myocarditis where 1-year survival and ventricular function in IVIG treated children was superior (N=21). However, a large controlled study done in adults by McNamara failed to show benefit [30]. Pleconaril an antiviral agent with activity against enteroviruses appeared to have favorable response when used under compassionate use protocols in patients with life-threatening enterovirus infection [31]; however, this medication is not currently available. A multicenter study supported by the National Institutes of Allergy Immunology and Infectious Diseases, (NIAID) Collaborative Antiviral Study Group (CASG) using pleconaril versus placebo for infants with myocarditis or disseminated enterovirus disease is ongoing.

62.3 Specific Infections

62.3.1 Viral Infections

Patients in the CICU setting are at increased risk for disease from viruses due to their underlying condition; however, several viruses deserve particular mention.

62.3.1.1 Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) infection is a significant problem in patients with CHD [32]. In particular, acquisition of RSV just prior to being admitted for cardiac surgery is associated with an increased rate of lower respiratory tract disease in the postoperative period with increased morbidity. Advances in medical care have resulted in significant reduction in mortality in this group of patients, but morbidity remains a serious concern [33]. Unlike healthy infants where RSV is rarely severe after the first 6 months of life, children through 2 years of age with CHD continue to develop serious disease due to RSV [33]. Transplant recipients are at increased risk for serious RSV disease if they are under 1 year of age or within the first post transplant month [34].

62.3.1.2 Cytomegalovirus

CMV is less of a risk for CICU patients since the institution of leukoreduction of RBC transfusions, but it still causes infection in 25–50% of heart transplant recipients. The highest risk occurs in patients who are CMV seronegative at the time of transplant and receive organs from CMV seropositive donors. Infection usually occurs 1–6 months after transplantation, although it may occur later if patients receive prophylaxis. The use of ganciclovir, as well as monitoring protocols have decreased the incidence of CMV disease following transplantation [35]. Pharmacokinetic studies are in progress for the use of oral valganciclovir in pediatric recipients.

62.3.1.3 Epstein-Barr Virus

Post transplant lymphoproliferative disorder (PTLD) is a potentially fatal condition after transplantation usually associated with EBV infection. The term PTLD encompasses a wide range of clinical syndromes – from non-specific viral illness to malignant monoclonal non-Hodgkins lymphoma [36, 37]. Seronegative EBV status prior to transplantation is a major risk factor for PTLD [38]. Young children and infants, therefore, are particularly vulnerable as most are EBV naive prior to transplantation. The degree of immunosuppression also influences the development of PTLD [39]. The risk of developing PTLD is highest during the first year following transplantation often associated with donor transmission. Numerous treatment strategies have been employed but reduction of immunosuppression is a critical component [36, 40, 41].

62.3.1.4 Influenza Virus

Children undergoing cardiac surgery during influenza season are at risk for community-associated infection prior to hospitalization or nosocomial acquisition [42]. In addition, influenza A infection of children with underlying CHD frequently leads to hospitalization. Depending on the severity of illness, these children may be managed in the CICU [43]. Children with heart disease should receive annual influenza vaccination. Likewise, family members and all health care workers should be vaccinated against influenza [44]. While vaccination is critical before and after heart transplantation,

recipients have a lower response rate compared to immunocompetent individuals [45]. Studies are underway to investigate the use of oseltamivir as prophylaxis for these individuals during the influenza season.

62.3.2 Bacterial Infections

Bacteria remain a problem in the CICU due to nosocomial wound and catheter associated infections. Attention to hand washing, strict sterile technique for central line insertion, and removal of all catheters as soon as they are not medically needed are all measures which help to decrease this risk. It is important to have knowledge about the local epidemiology of resistant organisms in each CICU to know the risk of vancomycin resistant enterococci or MRSA. *Clostridium difficile* is a potential pathogen in the CICU setting as patients are often exposed to multiple antibiotics and nosocomial spread can occur.

62.3.3 Fungal Infections

Fungal infections, particularly *Candida* species complicate the care of children in the CICU. Risk factors for candidemia include the use of total parenteral nutrition and prolonged antibiotic therapy [46]. Immunosuppression also increases the risk for disseminated candidiasis [47, 48]. Removal of intravenous catheters is often required for clearance of candidemia, although newer studies are evaluating the use of amphotericin or ethanol based lock therapy. Fluconazole is often used as empiric therapy. Newer classes of antifungal agents such as echinocandins have excellent activity against yeast and fungi and are being increasingly studied in pediatric populations. Lipid-based amphotericin B products, however, are still often required for unstable patients or resistant isolates. Children undergoing heart lung transplantation may also be at risk for aspergillus infections [49].

62.3.4 Parasitic Infections

Parasitic infections are infrequent causes of disease in CICU patients in the United States. *Toxoplasma gondii*

can cause disease after heart transplantation particularly in a child who is seronegative prior to transplantation and receives an organ from a seropositive donor. The use of immunosuppressants to prevent graft rejection and the propensity of the organism to infect cardiac muscle confer a unique risk of infection in these patients [50]. Cases of fulminant infection have been well described well in [51, 52]. Pyrimethamine and sulfadiazine in combination are well established as effective treatment for toxoplasmosis [53]. Trimethoprim-sulfamethoxazole is also effective prophylaxis against toxoplasmosis [54].

62.4 Prevention of Infections

Mortality and morbidity in the CICU can be impacted by reduction of infections using preventive strategies. Infection control measures for prevention of nosocomial spread of infections should be a priority. Intense monitoring of hand-washing, sterile barriers as well as glove and gowning for procedures where soiling can occur should be done routinely. One study on a *Serratia marcescens* outbreak in a pediatric CICU found that the nosocomial infection rate most strongly correlated with patient census, and the nursing hours to patient day ratio. The authors postulated that this increased CICU activity reflected a greater risk for breaks in aseptic techniques [55]. Accordingly, attention to hospital staffing can be important for infection control.

Optimizing the infant's immune system with routine immunizations can decrease the risk of infection for infants with underlying cardiac disease. Infants with associated asplenia or immune defects will particularly benefit from immunization against *S. pneumoniae* and *H influenzae*. Palivizumab given monthly during the RSV season can decrease the risk of severe RSV disease in infants with hemodynamically significant CHD [55–57].

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Chapter 63

Skin Protection

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The skin has been established as one of the largest organs of the human body as the skin provides a multitude of protective functions. Because the skin is easily accessible, assessing the integumentary system can provide a wealth of information. Illness and internal organ dysfunction are apparent by assessing the appearance of the skin. Critically ill children with cardiac disease processes are at risk for skin breakdown because of significant risk factors such as hypotension, hypoperfusion, and poor nutrition that place them at risk for developing wounds that cannot heal without expertise. Disruptions in skin care integrity places a compromised child at further risk for developing significant complications including infection. To aid in skin protection that will improve patient outcomes, several steps can be taken to ensure that the integrity is not further compromised including: (1) practicing routine skin care; (2) optimizing wound healing; and (3) managing surgical wounds proficiently.

63.1 Integumentary Structure and Function

Understanding functioning of the skin as a protective barrier, thermal regulator, and immune defense mediator begins with understanding the three layers of the skin – the *epidermis*, *dermis*, and *subcutaneous tissue*. The avascular epidermis is the outer layer of the skin

that is comprised of five different cell layers each with a separate function. “The inner basal cell layer of the epidermis is nourished by the blood supply of the dermis and is responsible for epithelial cell division. As basal cells multiply, they are pushed up by the remaining layers of the epidermis and are gradually filled with keratin, a waterproofing protein” ([1]; sic 512). Keratinization results in creating the outermost layer of the epidermis. Keratinization helps to facilitate the shedding and rejuvenation of keratinocytes, which help to prevent colonization on the epidermis. Included in the epidermis are specialized epidermal cells such as melanocytes which produces melanin, Langerhans’ cells which is the primary defense of the immune system, and Merkel’s cells in which the function is unclear. In newborns and infants, the epidermal layer is much thinner than that of an adult, which facilitates increased water loss. In addition, since the skin surface area is disproportionately greater than body weight, there is an increased risk for dehydration and systemic toxicity related to increased absorption rate of transcutaneous chemicals. Damages to the epidermis can be a result of mechanical trauma or adhesives.

The highly vascular layer of the skin that lies beneath the epidermis is the dermis. The dermis varies in thickness depending on the location and is comprised of three types of tissue that are present throughout the body. Tissue types include:

1. Collagen
2. Elastic tissue
3. Reticular fibers

Fibroblasts and macrophages create collagen which provides the skin with mechanical strength and elasticity. The vasculature of the dermis supports both the dermal and epidermal cells not only by aiding in

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thermal regulation but also by using sebaceous glands to secrete sebum which helps to keep the skin hydrated. Infants and children generate less sebum and the dermis is thinner. “Dermal thickness increases slowly after 1 year of age and doubles between the ages of 3 and 7. Sebaceous glands are functional at birth, but sebum production remains low until 8–10 years of age, providing less protection against evaporation and drying” ([1]; sic 512).

Subcutaneous tissue serves as the supporting layer of the skin in that this layer is comprised of the same structures found in the dermis plus the sweat glands. Subcutaneous tissue provides cushion to skin trauma, regulates the temperature, and metabolizes energy. Infants and children are at risk for thermal instability because they have less subcutaneous tissue. Located within the subcutaneous tissue are sweat glands. Not only is thermoregulation through sweat production essential for life but also sweat removes acids and toxins from the body.

63.2 Phases of Wound Healing

Most critically ill children not only experience wounds from surgery or invasive procedures but also from intravascular access. Wound healing, although difficult at times, is defined as “the process in which injured tissue is replaced through regeneration or repair” ([1]; sic 512). To have regeneration occur, tissue is replaced with similar tissue except in some tissues, such as subcutaneous and muscle; these must heal by forming new connective tissue or scar tissue to fill in the wound bed.

The three phases of the cellular process involved in wound healing are as follows:

1. Inflammatory phase
2. Proliferative phase
3. Maturation phase

The defensive or inflammatory phase function is to debride dead cells and bacteria from the wound bed and to initiate the healing process. Cellular activities occurring during the inflammatory phase include:

- *Vasoconstriction* that causes platelets to aggregate next to the injured blood vessels which results in fibrin clot formation. Vasoconstriction decreases

blood flow to the injured blood vessels and aids in hemostasis [1].

- *Vasodilation* succeeds vasoconstriction, promoting bradykinin and histamine release and increasing vascular permeability. “Fluid, protein, and enzymes normally found in the intravascular compartment leak through the vessel walls into the extracellular space, causing edema and erythema” ([1]; sic 513).
- “*Macrophages* orchestrate the healing process through ingestion of debris, angiogenesis, and the release of a protein that stimulates the formation of fibroblasts necessary for the next phase of wound healing” ([1]; sic 513).
- A persistent decrease in cardiac output can delay the onset of the inflammatory phase which generally lasts 4–6 days.

Epithelization, angiogenesis, and granulation tissue are the primary components in the next phase of wound healing which is the proliferative phase. First, epithelial cells move in a pattern to restore the normal layers of the epidermis. Angiogenesis allows for cell migration and capillary formation. The granulation phase and tissue deposition require nutrients supplied by the capillaries, and its failure to occur results in a chronically unhealed wound. The granulation tissue formation is the last step in the proliferative phase.

The most important cellular process is the maturation or remodeling phase, because collagen synthesis occurs in this phase. Diet and impaired cardiac functioning can impede collagen synthesis. Collagen that forms in injured skin is thinner, has a decreased tensile strength, and will never become as organized as undamaged skin [2].

63.3 Factors in Wound Healing

In the cardiac population, disturbances in tissue perfusion and nutrition can add to the complexity of wound healing. Tissue perfusion disturbances can be categorized as local (small vessel occlusion-emboli or external compression). Cardiac insufficiency, inotropic infusions, large vessel disruptions, inadequate tissue perfusion, and decreased circulatory volumes are classified as general tissue perfusion disturbances. Inadequate tissue perfusion leads to tissue hypoxia [2].

63.4 Promoting Skin Integrity and the Braden Q

Because critically ill children have an increased risk of skin impairments, the key to healthy, intact skin is knowledgeable healthcare providers. Promoting skin integrity by using established skin care guidelines can maximize patient outcomes. Diligent assessments of all skin areas confirm the need for individualized plans of care. Patients should be bathed with a pH-balanced cleanser. Water, not creams and lotions, lubricate the skin. Creams and lotions should be applied only after hydrating the skin with water, as creams and lotions seal moisture in the skin. Bath oil should not be added until the end of the bath to enable hydration of the skin to occur first, and then, the hydration can be sealed into the skin with the bath oil.

To promote skin integrity in the cardiac intensive care unit, nurses should minimize the impact of medical devices in such a way that the nurse alters pressure points regularly, pads persistent pressure areas, and frequently assesses the affected areas. Early initiation of nutritional support via enteral or parental feedings will maximize nutritional status and promote wound healing. “Capillary leak and hypoalbuminemia contribute to interstitial edema, which impedes the skin’s fragility by stretching collagen fibers” [1]. Protein, caloric, and vitamin deficiencies have an adverse effect on wound healing. Adequate pressure reduction enhances capillary blood flow to the skin and underlying soft tissues. Routine assessment for pressure ulcer risk in pediatric patients is necessary to track at risk patients and initiate skin care prevention measures.

A method to assess pressure ulcer risk in pediatric patients is by using *Quigley and Curley’s Modified Braden Q Scale*. “The Modified Braden Q scale demonstrates the unique developmental needs of the pediatric patient, the prevalence of gastric/transpyloric tube feedings, and the availability of blood studies and non-invasive technology in pediatric settings” ([3]; sic 23). Nurses must acquire adequate knowledge to use the Modified Braden Q scale accurately. The Braden Q has seven subscales which include: mobility, activity, sensory perception, friction and shear, and tissue perfusion/oxygenation. Each of the Braden Q’s subscales are score from 1 (more risk) to 4 (less risk). Therefore, the minimal pressure ulcer risk assessment score that a patient can receive is 7 and the maximum score is 28.

Any score obtained on a patient that is 16 or less for three consecutive days, places that patient at a greater risk for developing pressure ulcers. Therefore, preventive skin care measures that were previously discussed must be instituted to optimize patient outcomes.

63.5 Special Populations at Risk – Ventricular Assist Devices

Ventricular assist devices (VADs) are used in patients with severe end-stage heart failure as a bridge to transplant or recovery. The incidence of infection has been shown to be around 35% in the pediatric population. The incidence of infection across pediatric and adult population of those requiring VADs has been shown to be anywhere from 19–60%. Infection decreases the overall chance for patient survival. If a patient has an overt clinical infection, transplant is not possible until the infection is clear. These infections include but are not limited to blood, urine, and VAD drive line infections. In order to decrease VAD infections close attention to infection control and meticulous surgical site care is imperative [4].

Initially, VAD drive line site dressings are changed every 24 h. Once the drainage decreases from the sites, then the dressing change frequency is decreased. The goal is to change the dressing once a week. The dressing is also changed when its integrity is compromised. This is indicated if more than a quarter size of drainage is noted on the dressing. Also, if the patient develops fever, the dressing must be changed to assess the site. If purulent drainage is noted then a surface culture of the drainage is sent.

A non-adherent type occlusive dressing is applied using sterile technique. The person performing the procedure must wear a sterile gown, gloves as well as mask, and a surgical cap. Any person present in the room during a dressing change should wear a surgical cap and mask. The old dressing is removed using sterile gloves and a new pair of gloves should be worn to finish the dressing (see Fig. 63.1 for exposed drive line sites for cleaning). The driveline sites are cleansed with a 1/2 saline and 1% chlorhexidine solution (see Fig. 63.2 for cleansing of drivelines). They are rinsed with saline solution and thoroughly dried with sterile gauze prior to applying the dressing insuring that all



Fig. 63.1 Exposed drive lines for cleaning

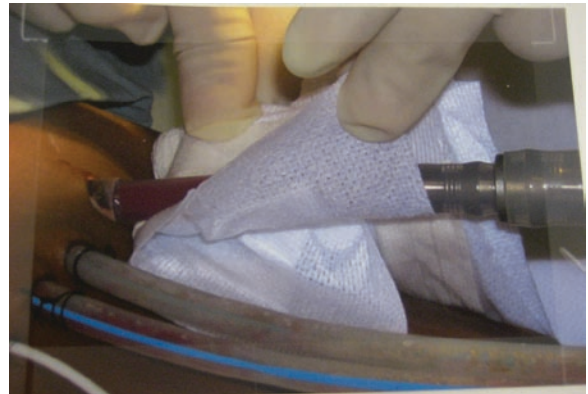


Fig. 63.4 Applying a sterile telfa island dressing under the driveline



Fig. 63.2 Cleansing of drive lines



Fig. 63.5 Applying a sterile telfa island dressing on top of driveline



Fig. 63.3 Drying the drive lines

residuae is removed (see Fig. 63.3 for drying driveline sites). If purulent drainage is present, a calcium/sodium alginate dressing is wrapped around the driveline site prior to applying the above noted dressing (see Fig. 63.4 and 63.5 for applying a sterile telfa island dressing under and on top of the driveline to create an occlusive dressing). An immobilization binder should be applied over the dressing. This should be worn at all times to help ensure maturation of the exit sites.

Strict adherence to sterile technique and monitoring for infectious complications will decrease the mortality and morbidity of children and adults with VADs [5].

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