Enhanced Recovery after Surgery

Ryoji Fukushima
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Editors

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Preface

Today, "team medical care" and "standardization of medical care" are both trends in the medical profession, and we are required to be able to provide the same level of medical care all over the country. As an example of team medical care, nutrition support teams have been in operation at many institutions and have shown the great clinical effect of nutritional therapy, which has become widely accepted as an essential supportive therapy. In addition, the various academic societies are making efforts so that various surgical procedures can be designated as the standard surgical procedure for given conditions. Perioperative management is not universalized to the degree that surgical procedures are, and traditional surgical perioperative management continues to be at a great advantage. Although there are many wonderful methods in accordance with these traditional clinical experiences, there are also management methods described in senior commentaries that are not suitable for today's surgery. The enhanced recovery after surgery (ERAS®) protocol originating in Northern Europe is soon to be introduced into Japan as a "standardization" tool for perioperative management, but simply incorporating this protocol into the clinical process will not lead to its successful use in daily clinical practice. Because we are involved in surgery, it is important to always think about the metabolic fluctuation of patients who have undergone the stress of surgery in a rational way. Above all, the perioperative management we provide must be acceptable to the patient.

The "postoperative recovery ability program," which reduces the physical burden of patients who undergo surgery, is the first line of effort in Japan in the field of surgery. The content of the program is said to range from presurgical meals to medication, intraoperative anesthesia, drip infusion, and rehabilitation after surgery, which will shorten the length of stay. By doing this, the patients themselves will be able to restore their physical fitness in a shorter period of time and will be able to return to work earlier. For medical institutions as well, it is thought that by expediting discharge from the hospital earlier, this program is advantageous in that it makes it possible to receive more patients.

The Essential Strategy for Early Normalization After Surgery with Patient's Excellent Satisfaction (ESSENSE) project, which we have been working on for several years at the Japanese Society for Surgical Metabolism and Nutrition, is equally important to both the theory of biological response to surgical invasion and the satisfaction level of patients.

ESSENSE is planned to be a trigger initiative for all surgeons in all areas, anesthesiologists, rehabilitation doctors, nurses, and co-medical staff in their respective positions. We anticipate that it will help to develop highly satisfying surgical management for patients.

Tokyo, Japan Ryoji Fukushima
Hirakata, Japan Masaki Kaibori
July, 2017

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Introduction

Chapter 1
ESSENSE Project for the Sound Recovery of the Patient

Go Miyata

Abstract Postoperative patient recovery continues to improve with the adoption of the enhanced recovery after surgery (ERAS) program established in 2005 in Northern European countries. The Japanese Society for Surgical Metabolism and Nutrition launched the ESSENSE project to introduce this program in Japan and to demonstrate its effectiveness. “ESSENSE” is an acronym for ESsential Strategy for Early Normalization after Surgery with patient’s Excellent satisfaction.

With the premise of alleviating the biological response to surgical invasion, physical restoration is inevitably promoted by stimulating early physical activity autonomy, early nutrition intake independence, anxiety mitigation, and recovery motivation. It is also important to set evaluation items so that the surgical clinical team staff can share these goals. The ESSENSE project is an evaluation method that takes into account the patient’s preferences, rather than a procedure focused on the medical provider.

Keywords ERAS • Patient’s satisfaction • Surgical invasion

1.1 Surgeon’s Nature and Postoperative Management

When thinking about improving perioperative management, we can consider surgical treatment from the point of view of the surgeon, rather than from the patient’s point of view. Many surgeons regard surgery as their primary task, and perioperative management is an appendix to the job.

In this era, especially when the difficulty of surgery is also increasing, such as endoscopic surgery, the sense of accomplishment of surgery itself is often the enjoyment of modern surgeons to live.

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“Good surgery” is, of course, the most important factor leading to a good postoperative course and a satisfactory outcome for patients. However, no matter how good the operation may be, a traditional approach to postoperative management such as long-term bed rest and long-term nil per os (NPO or nothing by mouth) may be an inhibiting factor to physical recovery. To date, the rationale behind “postoperative bed rest” is avoiding tension to the wound site and avoiding pain enhancement, while “postoperative NPO” is employed to avoid tension on the bowel anastomotic site and prevent vomiting due to intestinal paralysis. In modern times, however, evidence pointing to disadvantages of the tradition approach such as disuse atrophy of the skeletal muscles and intestinal tracts is increasing. Recent developments in anesthesia and preemptive analgesia make it possible to rehabilitate and use the intestinal tract from the early postoperative period. If we were able to overcome the difficulties of surgical insults by careful and rational postoperative management, the resulting sense of accomplishment will guide the surgeon in the next surgery.

1.2 Introduction of ERAS®

In recent years, fast-track surgery, or enhanced recovery after surgery (ERAS®), a keyword originating in Northern European countries, has gained popularity in the Japanese clinical surgery environment. Perioperative management, especially for colon cancer patients, is the starting point in promoting the physical recovery of the patient. Perioperative management consists of no preoperative bowel preparation, very short preoperative fasting period, abolition of nasogastric tubes, early oral ingestion after surgery, and early mobilization implemented through practical programs. The ERAS protocol, which changes the previously accepted traditional approach in the field of gastrointestinal surgery, was proposed to improve patient care.

Since patient recovery is obviously affected by the perioperative management method, the conventional approach to perioperative management was modified.

The ERAS® protocol, established in the 2005 consensus review [1], consists of approximately 22 recommendations.

Regarding the outcome obtained by complying with these recommendations, not only does the clinical experience give a strong impression about quick recovery of patients, but also the effect of reducing the length of hospital stay and reducing complications was demonstrated in the Cochrane Review meta-analysis [2].

In Japan, the number of institutions adopting ERAS® has increased. The use of ERAS not only for colon cancer but also for other surgical procedures has been reported at various surgical conferences.

Although some elements are already accepted as the standard in Japan, some authors claim that it would be difficult to implement all ERAS® protocols.

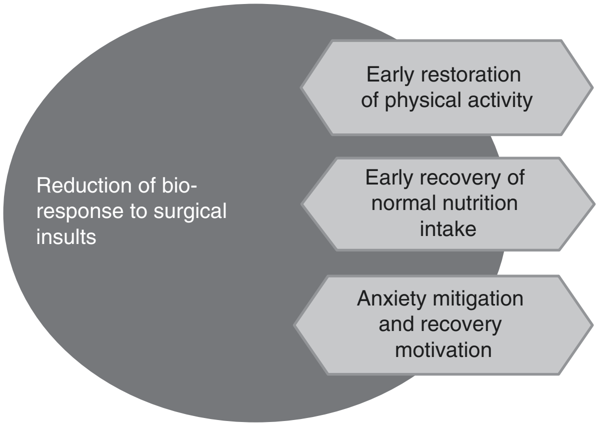

Fig. 1.1 Four directions for ESSENSE project. Based on the element "reduction of bio-response against surgical insult," the other three targets should be directed toward quick patient recovery after surgery

1.3 ESSENSE Project for the Sound Recovery of Patients

In line with the medical situation in Japan, to better understand ERAS®, and to further improve perioperative management, the Japanese Society for Surgical Metabolism and Nutrition, with a history of over 50 years, has been working on a perioperative management project since 2010. We decided to call it the ESSENSE project to represent the ESsential Strategy for Early Normalization after Surgery with patient's Excellent satisfaction.

The mission of the project is "to improve the safety of surgery, to examine the essence of postoperative recovery promotion measures accompanied by patient satisfaction, and to provide scientific information."

We rearranged and refined the direction for the medical provider by examining 22 elements recommended in ERAS®, their mutual relationships, and purpose: (1) modulation of the host response to surgical insults, (2) early restoration of physical activity, (3) early recovery of normal nutrition intake, and (4) perioperative anxiety reduction and excitation of recovery motivation. In particular, we believe that "reduction of the bio-response against surgical insult" should be the base for the other three conditions (Fig. 1.1).

The significance of the ERAS® protocol and the relationships of the elements with each other are described below using an example for the "abolishment of preoperative bowel preparation."

Bowel preparation induces systemic potential dehydration, and a consequent cascade will occur as shown in Fig. 1.2. Because intraoperative blood pressure decreases, intravenous massive fluid replacement is required. This causes intestinal

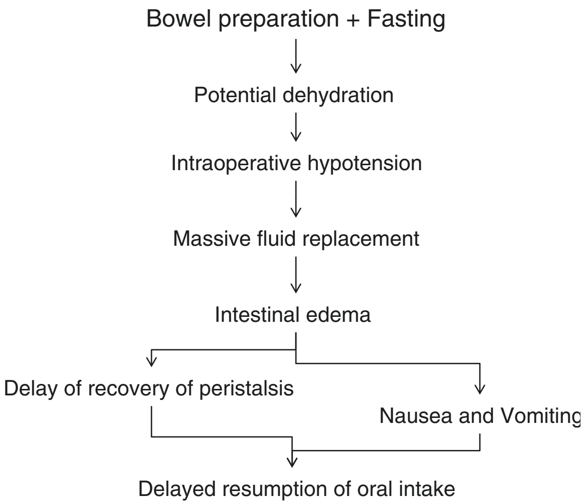

Fig. 1.2 Relationship and significance of "abolishment of bowel preparation." Avoidance of preoperative bowel preparation alleviates the "bio-response against surgical insults" of dehydration and intraoperative blood pressure reduction, which contributes to "early nutritional intake autonomy." "Measures for postoperative nausea" and "postoperative peristalsis stimulation measures" can be interpreted as "early nutrition ingestion independence"

edema and delays peristalsis recovery. Postoperative nausea delays the resumption of oral intake.

In other words, abolishment of preoperative bowel preparation alleviates the "bio-response against surgical insults" of dehydration and intraoperative blood pressure reduction, which contributes to "early nutritional intake autonomy." "Measures for postoperative nausea" and "postoperative peristalsis stimulation measures" can be interpreted as measures for "early nutrition ingestion independence." The 22 ERAS® items can be summarized as recommendations aimed at achieving the above four patient states.

The difference between ERAS® and ESSENSE is that the ESSENSE project stipulates and organizes "the state and direction of the patient as a target," whereas ERAS® prescribes "intervention items." By doing this, we anticipate further development at each facility.

In the ESSENSE project, the following four points are proposed as the target patient states to be attained during postoperative management:

1. To attain an analgesic condition to the extent that the patient can at least take a deep breath and, if possible, can cough effectively
2. Preventative measures for nausea so that the patient can at least drink some water from the first day after surgery
3. An ambulation program that allows the patient to move at least from the first postoperative day
4. Using a pedometer as an additional incentive to increase the patient's willingness to recover and to set goals until discharge

1.4 Rethinking the Role of Surgeons in Perioperative Management

When we think about what is necessary to create a system that can help improve perioperative management and how surgeons need to work, it is necessary to refer to the characteristics of the surgeon in the medical field.

The work of doctors, not only surgeons, has diversified, resulting in specialized differentiation for organs and procedures. With the rise of team medical care such as the nutritional support team (NST) and perioperative management teams, cross-sectional work redistribution to medical staff and new task assignments are becoming easier. The surgeon should recognize this and prepare accordingly.

One common trait found in doctors that perform general surgery is a strong sense of responsibility "Who will do it if I do not do it?" This perspective persists despite the continued professional differentiation of medical departments and specialization in limited areas. The surgeon's sense of responsibility sometimes tends toward the direction of "If I do not do it myself, I do not feel comfortable." It is also likely that the surgeon is headed in the direction of specialized differentiation, so authority delegation and collaboration are necessary.

Perioperative medical care is accomplished through teamwork rather than individual effort. As the adoption of team medical care increases, it is expected to build a collaborative system that takes into consideration the four aspects of ESSENSE. Unifying the goal and revitalizing medical staff-staff and staff-patient communication not only promotes recovery but also leads to patient satisfaction with surgical treatment.

1.5 Standardized Evaluation Value for Cooperation Among Professions

We believe that sharing evaluation indices is necessary for communication between professions. Several evaluation indices have been proposed. For pain evaluation, rather than simply digitizing pain using tools like the Visual Analog Scale or the Prince Henry Hospital Pain Scale [3], we proposed a purpose-oriented pain assessment of behavior that can be completed in the absence of pain. Early activity independence can be determined by the number of steps walked in 1 day, measured using a pedometer, while early nutrition intake autonomy focuses on the daily calorie intake (kcal/day). We believe that these factors can be used by surgical doctors, anesthesiologists, nurses, physiotherapists, nutritionists, pharmacists, etc., to understand the patient's problems and to create a system that naturally encourages improvement.

Setting up the new system may seem like a daunting task. However, at each facility, a wide variety of team medical care systems should already have been implemented, and we can find a way to add practical benefits to these systems and to organize them.

Modifying the critical paths for each type of surgery by incorporating ESSENSE is a realistic improvement method. The assessment of nutritional intake is performed by the NST, which collaborates with the anesthesia department and the surgery department effectively, using the World Health Organization safe surgery checklist [4]. In addition, it is possible to ensure an effective flow of information by incorporating some items in perioperative management.

In Japan, the word "rehabilitation nutrition" is rapidly increasing in popularity [5]. If it is possible to share information and goals between rehabilitation physicians, physiotherapists, occupational therapists, speech therapists, and dietitians, the convenience of information sharing due to the spread of the electronic medical record should also be the tailwind of this movement. Making full use of existing methodologies and organizations benefits each job category and contributes to growth.

1.6 Evaluation of Perioperative Management with the Balanced Scorecard

There was an era when the only corporate achievement of a company was the "financial income." However, in modern times, it is not possible to evaluate the positives and negatives of a company based on the financial income alone. Therefore, a method to evaluate and manage the wide variety of enterprises is necessary.

One of the methods currently available is the balanced scorecard (BSC) [6]. BSC captures company management from four perspectives: (1) financial perspective, (2) customer perspective, (3) business process perspective, and (4) learning and growth perspective of staff. The idea behind BSC is that striving to maintain balance between these four aspects is the key to maintaining a sound company with continuous growth. I think this method is easy to understand as a way to evaluate work and improvements in perioperative management.

In companies, the financial point of view means "profit." However, in perioperative management, as shown in Fig. 1.3, profit is replaced with safe and high-quality medical treatment such as "the number of complications" and "the length of hospital stay."

The customer's viewpoint is represented by the degree of the biological response, early physical activity independence, early nutrition intake independence, degree of anxiety resolution, degree of motivation, and so on.

For the business process point of view, intervention items such as the creation of an early ambulation program as indicated by ERAS® and the abolition of preoperative fasting can be used.

For the staff's point of view, we mention the techniques, knowledge, and qualifications for involvement.

I introduced the BSC here because I think it is easy to explain the differences between the viewpoints of ERAS® and those of ESSENSE. While ERAS® prescribes intervention measures, ESSENSE highlights the expected patient state changes.

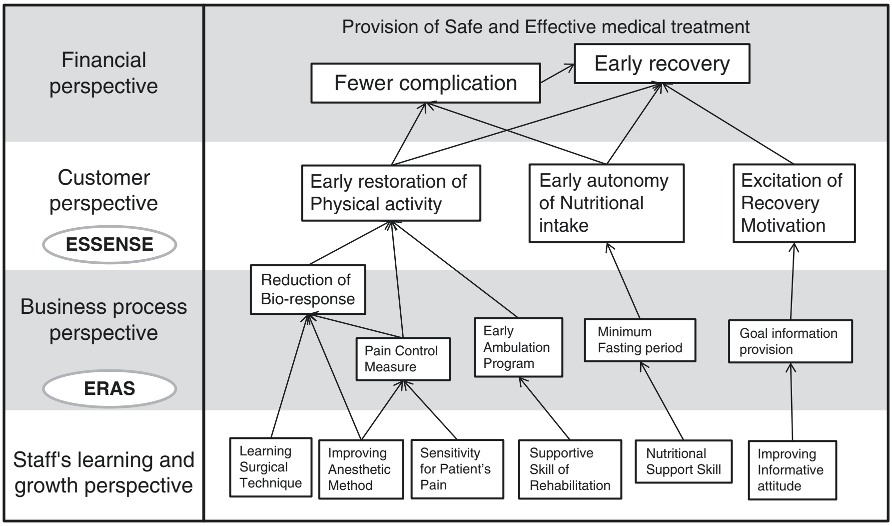

Fig. 1.3 Evaluation of perioperative management using balanced scorecard. When BSC is employed as the evaluation method for the company's performance, it is possible to understand the difference between ERAS and ESSENSE in perioperative management

In BSC, we propose that each indicator for each intervention measure should be included in each step. This will allow us to evaluate the weight of each intervention measure in the final outcome. For example, if the quantitative evaluation of "wound pain during the postoperative period" is performed with an established pain scale, if the progress for rehabilitation is expressed based on the daily number of walking steps, and whether pain is an inhibitory factor of activity recovery can be determined in terms of numerical values.

In regulating "intervention measures" like ERAS®, there is a concern that staff satisfaction may be ignored. However, setting a goal of the "state of the patient" as the outcome can also motivate the patient to recover.

The ESSENSE project outlines the roles played by surgeons in organization management related to perioperative care.

In order to create a better surgical management system, it is necessary to draw out the power of each medical profession. I think the surgeon has a responsibility to put together each profession's abilities and inevitability to promote this integrated power of team.

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Part II
Mitigative Methods for Biological Invasive Reaction

Chapter 2
Minimizing the Length of the Preoperative Fasting Period to Prevent Stress and Dehydration

Hideki Taniguchi and Keiko Ushigome

Abstract By reducing the duration of preoperative fasting, patients' physical and mental stress can be reduced. Furthermore, by preventing preoperative dehydration, stabilization of circulation dynamics during anesthesia becomes possible, thereby increasing safety. By shortening the duration of fasting, the duration of not ingesting carbohydrates is also shortened, suppressing the increase in postoperative insulin resistance. Based on all these findings, shortening of the preoperative fasting period is expected to contribute to the promotion of patient postoperative recovery. In this article, we introduce fasting guidelines of each country and scientific basis and outline about eating and drinking before surgery. And we would like to aim for management to minimize the length of the preoperative fasting period to prevent stress and dehydration in enhanced recovery after surgery.

Keywords preoperative fasting • ERAS • clear fluids • carbohydrate loading • oral rehydration solution

2.1 Introduction

To prevent vomiting and aspiration in patients receiving general anesthesia, patients are routinely requested to fast for a long time prior to the procedure. In recent years, however, it has been shown that there is no clear evidence or scientific basis to implement prolonged preoperative fasting and that safety can be achieved by implementing a preoperative oral ingestion method that strictly follows evidence-based recommendations on type and time of ingestion. Furthermore, oral ingestion is physiologically advantageous in that stress during the perioperative period can be minimized by avoiding preoperative dehydration [1–3].

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Table 2.1 Preoperative fasting duration recommended by guidelines from various anesthesiology societies

Country	Duration of fasting (h)	
	Beverages: clear fluids[a]	Solids: light meal[b]
United Kingdom	3	6–8
Canada	2	6–8
United States	2	6
Norway	2	6
Sweden	2	From midnight the night prior to the procedure
Germany	2	6
Japan	2	No consensus recommendations

These guidelines exclude patients with emergencies and gastrointestinal obstruction
[a]Clear fluids: transparent fluids such as water, tea, apple or orange juice (no pulp or dietary fiber), coffee (no milk), and carbohydrate drinks (sports drinks and oral rehydration solution)
[b]Light meal: toast with clear fluids or equivalent

2.2 American Society of Anesthesiologists, European Nation, and European Society for Clinical Nutrition and Metabolism Guidelines on Preoperative Fasting

Many randomized controlled trials (RCT) in patients from various age groups undergoing planned general anesthesia have shown that shortened time of limited oral ingestion maintains patient safety, as measured by the absence of changes in gastric juice volume and pH and in incidence of aspiration pneumonia [2]. The American Society of Anesthesiologists (ASA) published clinical guidelines for preoperative fasting in 1999 [1], and several European nations have published similar guidelines over the last several years [3]. Excluding emergencies and cases where delayed gastric emptying is expected, these guidelines indicate that ingestion of clear liquids (water, carbohydrate drink, coffee or tea without milk, and juice without dietary fiber) up to 2–3 h or a light meal (toast and a meal without fat) up to 6 h prior to an anesthetic procedure is permitted (Table 2.1) [1–3]. Similarly, the guidelines on perioperative intravenous nutrition published by the European Society for Clinical Nutrition and Metabolism (ESPEN) in 2009 state that preoperative fasting is unnecessary in most cases (advisability A): ingesting liquids preoperatively does not increase the risk of aspiration, but does prevent the sensation of thirst in many patients [4].

2.3 Cochrane Library's Recommendations on Preoperative Fasting

The purpose of preoperative fasting is to prevent regurgitation and aspiration by avoiding increases in gastric content and acidity. However, many RCTs have shown that by following strict time and type of ingestion recommendations, preoperative oral ingestion can be done safely. The 2003 Cochrane Library review reports that in healthy people, the incidence of regurgitation and aspiration did not differ between those who fasted overnight before a procedure and those who had a shortened fasting period. There was also no change in associated mortality. The authors proposed that the standard practice of fasting overnight prior to an anesthetic procedure should be corrected based on in situ evidence [2].

2.4 Preoperative Fasting by Fast-Track and Enhanced Recovery After Surgery (ERAS) Protocols

In both the fast-track program [5] proposed by Cotton in the United States and the ERAS protocol reported by Fearon et al. in Northern Europe [6], the main objective is to improve the postoperative recovery of patients. These protocols recommend active intake of high carbohydrate-content (CHO) beverages up to 2 h prior to an anesthetic procedure based on evidence that ingestion of 800 mL of 12.5% CHO the night prior and 400 mL at least 2 h prior to anesthesia resulted in reduced postoperative insulin resistance. Many safety studies on 12.5% CHO have been published, including one using a radioisotope and MRI imaging [7].

2.5 Japanese Guidelines

In July 2012, the Japanese Society of Anesthesiologists published *Preoperative Fasting Guideline* (Table 2.2) (http://www.anesth.or.jp/guide/pdf/guideline_zetsuinshoku.pdf). Similar to recommendations by anesthesiology societies of other nations, drinking clear water is deemed "safe until 2 h before the operation for any age." For both general anesthesia and local anesthesia, the amount and rate of liquid ingested can be freely modified. On the other hand, there are no clear fasting time recommendations for solid food for the following reasons: compared to liquids, the evidence on solid food is insufficient; the distinction between solid food and a light meal is unclear; and there are large variations in food nutritional content.

Table 2.2 Japanese Society of Anesthesiologists "preoperative fasting guidelines"

Preoperative fasting time	
Ingested item	Fasting time (h)
Clear fluids	2
Breast milk	4
Artificial milk/milk	6

Source: http://www.anesth.or.jp/guide/pdf/guideline_zetsuinshoku.pdf

2.6 Preoperative Beverages to Be Ingested

2.6.1 Liquid Drinks

As discussed in a previous section, preoperative drinking guidelines in the United States and EU member nations indicate that ingestion of clear liquids 2–3 h before an anesthetic procedure is permitted [1–3]. However, it should be noted that all guidelines exclude cases of emergencies and gastrointestinal diseases. It is worth noting that ingestion of an oral nutritional supplement (ONS) that contains amino acids and vitamins takes 3 h to empty the stomach, even if the amount is reduced [7]. For this reason, in the fast-track and ERAS protocols, the only drinks deemed safe are CHO beverages up to a concentration of 12.5%, as studies have shown that CHO beverages up to this concentration have a gastric emptying time similar to that of other clear liquids [5, 6]. Because there is no evidence regarding the safety of beverages other than ONS and CHO beverages with concentrations higher or lower than 12.5%, large-scale studies on the use of other beverages are needed.

2.6.2 Selection Method for Preoperative Drink

Surgeons and anesthesiologists select a beverage from those classified as clear liquids based on the following objectives: (1) suppression of decline in postoperative insulin sensitivity and (2) supply of water and electrolytes. There is evidence supporting the safety and effectiveness of clear water for meeting objective, the use of 12.6% carbohydrate drink (preoperative carbohydrate loading) for meeting objective (1) [5, 6], and the use of preoperative oral rehydration solution (ORS) for meeting objective (2) [8, 9]. The objectives and indications for the various types of beverages are shown in Table 2.3.

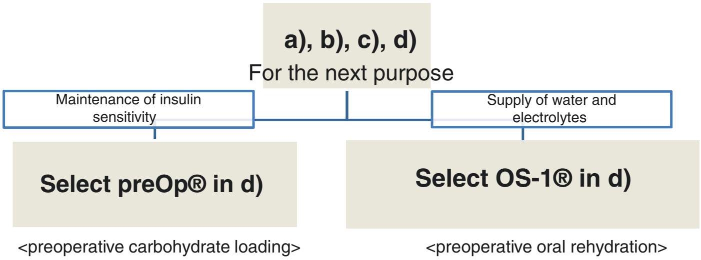
2.6.3 Preoperative Oral Rehydration Therapy (PO-ORT)

It is reported in the ERAS protocol that postoperative insulin resistance can be reduced by taking carbohydrate (CHO loading), leading to an increase in postoperative recovery ability [5, 6]. However, the products which have similar evidence of safety and efficacy as the CHO product recommended by the ERAS protocol (Table 2.4) are not commercially available in Japan. Instead, "preoperative oral rehydration therapy (PO-ORT)" using an oral rehydration solution (ORS), classified as a carbohydrate-containing drink and generally called "clear" fluids, has been introduced in many hospitals in Japan (Table 2.4) [8, 9], and a shortened hospital stay and discontinuation of parenteral treatment in preoperative periods are commonly realized in these hospitals [10]. We investigated the occurrence of intravenous

Table 2.3 Drinks classified as clear fluids and selection method based on the purpose

【Clear fluids*】

a) water, tea, and carbonated beverages
b) coffee/tea without milk (fat)
c) juice without dietary fiber
d) carbohydrate drinks (preOp®**and OS-1®***)



* Safe to ingest prior to an anesthetic procedure

* *preOp ®; NUTRICIA ***OS-1®; Otsuka Pharmaceutical Factory
Carbohydrate drink that has established safety as a preoperative drink

Table 2.4 Compositions of oral rehydration solution (ORS) and carbohydrate drink

Product	Unit	ORS (OS-1®[a])	Carbohydrate drink (preOP®)
Carbohydrate	%	2.5 (glucose 1.8)	12.6 (glucose 2.1)
Na^+	mEq/L	50	22
K^+	mEq/L	20	31
Mg^{2+}	mEq/L	2.0	0.0
$Lactate^-$	mEq/L	31	–
Cl^-	mEq/L	50	0.2
P	mmol/L	2.0	0.0
Osmolality	mOsm/L	Approx. 270	Approx. 240
pH	–	3.9	4.9

OS-1, classified as a food in Japan, Otsuka Pharmaceutical Factory, Inc., Tokushima, Japan
[a]OS-1® is a drink compatible with the approach to oral rehydration therapy advocated by the WHO (World Health Organization), and the formulation is based on oral rehydration guidelines endorsed by the American Academy of Pediatrics

infusion-related events in the 1-year periods before and after introduction of PO-ORT (i.e., we compared July 2006–2007 with July 2007–2008). Using PO-ORT for preoperative fluid management of surgical patients, the occurrence rate of such events noticeably decreased to reflect the effect of not using intravenous solutions (27 ± 9 vs 15 ± 9 events/month, $P < 0.01$). The workload of ward nurses was also reduced by using PO-ORT [11]. PO-ORT is mentioned in the guideline published by the European Society of Anaesthesiology ("Perioperative fasting in adults and children") in 2011. PO-ORT is as effective as intravenous infusion in terms of provision of water and electrolytes and can reduce thirst, hunger, anxiety, and physical restriction due to intravenous infusion. Also, it can allow for safe introduction of general anesthesia in surgical patients without increasing the volume of gastric fluid [2]. Although ORS is recommended as the carbohydrate-containing drink in the guideline, its effect on insulin resistance is not addressed. Yatabe et al. investigated insulin resistance in healthy subjects using the glucose clamp technique. Since the carbohydrate concentration of ORS used in the study is as low as 2.5% compared to CHO, its effect on insulin resistance is low, reflecting the concentration of carbohydrate. However, the results indicate that consumption of ORS may attenuate insulin resistance [12]. To position PO-ORT as one of the essential tools for postoperative enhanced recovery, its effect on enhancing postoperative recovery must be further studied [13].

2.7 Preoperative Solids to be Ingested

There are a limited number of large-scale surveys on solids as compared to liquids, producing little evidence on safety. Therefore, the recommended preoperative fasting time is set longer for solids than physiologic gastric emptying time for added safety. In the ASA guidelines for elective surgeries, a light meal is permitted up to 6 h, and fried food and other solid foods with fat are permitted up to 8 h prior to an anesthetic procedure [1]. In contrast to liquids, solids require physical digestion or pulverization to a diameter of 1 mm or less for passage through the pylorus. Solids that are broken down as such pass through the pylorus within 2–3 h after the meal, whereas solids that are larger than 1 mm remain within the gastric lumen for longer. For 2–3 h after a meal, gastrointestinal peristalsis occurs because of interdigestive migrating motor complex (MMC), resulting in gastric emptying. This means that theoretically, the stomach of a physiologically healthy person should be empty in about 180 min, even if the person ate solid foods. However, this area remains one that requires active investigation to study [14].

2.8 Stress Reduction Through Avoidance of Fasting and CHO Loading

2.8.1 Avoiding Fasting and Postoperative Recovery

Shortening the duration of fasting has been shown to be effective in improving the prognosis of patients. In patients who present with symptoms of dehydration, the use of local anesthesia for epidural analgesia or an anesthetic induction agent results in cardiovascular suppression that requires volume resuscitation, leading to an increased risk of fluid overload [15]. Fluid overload delays postoperative recovery due to decreased intestinal motility. In 2006, Lobo et al. showed that patients maintaining "normal fluid and electrolyte balance" upon arriving at the operating room had a faster postoperative recovery [16]. The authors therefore concluded that the preoperative fasting period should be minimized. On the other hand, there is also a report that states that fasting from the night prior to the anesthetic procedure does not reduce circulating blood volume [17]. This highlights another area where more studies are needed.

In addition to the physiologic effects, the psychological effects of fasting must also be considered. In a reinforcement ERAS protocol, it is preferred that patients are relieved of psychological stress by reducing the length of preoperative fasting. It has been shown that patients who went through oral loading of a carbohydrate drink (carbohydrate loading: CHO loading) had less thirst and hunger than patients who fasted, resulting in relief of preoperative anxiety. Other advantages have been found such as not having to be confined to a hospital bed for administration of intravenous liquids [5, 6].

2.8.2 Preoperative Carbohydrate (CHO) Loading

Surgical stress intensifies the action of stress hormones, and increased surgical stress results in a reduction of postoperative insulin sensitivity. In contrast, in the reinforcement program, oral CHO loading with a high CHO concentration of 12.5% is recommended in an effort to maintain postoperative insulin sensitivity, in addition to postoperative chest epidural analgesia and therapeutic exercise. Patients are administered 800 mL of hydrocarbon drink the night before and 400 mL 2–3 h prior to the procedure. If oral ingestion is not possible, intravenous CHO loading is performed [5, 6]. However, it must be noted that the high-concentration CHO drink discussed here is limited to a concentration of 12.5%; there is no evidence of higher or lower concentrations being effective. Additionally, a double-blind study by Mathur et al. showed no difference in the length of hospitalization or degree of recovery from fatigue between a CHO drink and a flavored placebo drink in colorectal surgery and liver resection in a double-blind study [18]. Therefore, the effect of CHO loading needs to be further examined as it stands.

2.9 Conclusion

By reducing the duration of preoperative fasting, patients' physical and mental stress can be reduced. Furthermore, by preventing preoperative dehydration, stabilization of circulation dynamics during anesthesia becomes possible, thereby increasing safety. By shortening the duration of fasting, the duration of not ingesting carbohydrates is also shortened, suppressing the increase in postoperative insulin resistance. Based on all these findings, shortening of the preoperative fasting period is expected to contribute to the promotion of patient postoperative recovery.

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Chapter 3
Preoperative Bowel Preparation in ERAS Program: Would-Be Merits or Demerits

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Abstract For over a century, surgeons have used preoperative mechanical bowel preparation (MBP) to decrease fecal mass within the large bowel. However, over the past 2 decades, several randomized trials and a large meta-analysis have failed to demonstrate reduced rates of surgical site infection (SSI) after elective colorectal surgery in patients who received MBP alone. It was reported in 1971 that MBP removed gross feces but did not alter the number of microorganisms in the colonic lumen. MBP with oral antibiotics, but not alone, reduces the prevalence of SSI. MBP does not affect the prevalence of anastomotic leakage in colon surgery. However, we should not equate rectal surgery with colon surgery because the rate of anastomotic leakage is higher in the former. Also, omitting MBP may be a risk factor for anastomotic leakage in elderly patients. MBP does not reduce morbidity, including SSI, in patients undergoing digestive tract surgery (not for colorectal cancer), such as esophagocoloplasty, hepatectomy or pancreaticoduodenectomy. MBP can negatively affect intestinal motility after surgery. Of note, omission of MBP may negatively affect long-term survival; however, this hypothesis is controversial.

Keywords Mechanical bowel preparation • Enhanced recovery after surgery • Surgical site infection

3.1 Introduction

For over a century, surgeons have used preoperative mechanical bowel preparation (MBP) to decrease fecal mass within the large bowel, theoretically decrease bacterial load within the operative field, and reduce the risk of postoperative surgical site infection (SSI). Over the past 2 decades, several randomized trials and a large meta-analysis have failed to demonstrate reduced rates of SSI after elective colorectal

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surgery in patients who received MBP alone compared with no bowel preparation [1–6]. Moreover, MBP has been reported to increase prevalence of SSI [7, 8]. However, many surgeons prefer MBP. Why do they prefer MBP? We should understand the merits and demerits of MBP.

3.2 MBP Reduce Feces but Not Microorganisms

It is thought that postoperative infectious complications are related to infective bowel content. However, there is no evidence to support this. MBP alone cannot reduce microorganisms. In 1971, Nichols et al. reported that MBP without antimicrobials removed gross feces but did not alter the number of microorganisms in the colonic lumen [9]. They also reported that MBP, with dietary restriction, cathartics, and enemas, significantly reduced the mean concentration of coliforms only. Obligate anaerobes, the major constituents of the colonic microflora, and other aerobic and microaerophilic intestinal bacteria were not significantly affected [10]. However, oral antibiotics in addition to MBP were shown to suppress aerobic and anaerobic microorganisms [11]. Therefore, theoretically, MBP alone cannot reduce the prevalence of SSI.

It is suggested that MBP can increase the incidence of *Clostridium difficile* infection [12]. However, this opinion is controversial. Kim et al. reported that MBP with oral antibiotics, but not alone, reduced the rate of *C. difficile* infection [13]. Several researchers have also reported that MBP is not associated with increased incidence of *C. difficile* infection [14–16].

3.3 MBP With Oral Antibiotics Reduces Prevalence of SSI in Colon Surgery

Patients who receive MBP plus oral antibiotics before colon surgery have a lower incidence of superficial SSI, deep SSI, organ space SSI, any SSI, anastomotic leakage, postoperative ileus, sepsis, re-admission, and reoperation compared with patients who receive neither [6, 17, 18]. Moghadamyeghaneh et al. reported that combination of MBP and oral antibiotics significantly decreased risk of overall morbidity, superficial SSI, anastomotic leakage, and intra-abdominal infections in patients undergoing resection of the left colon [19]. However, oral antibiotics alone have been reported to reduce SSI, anastomotic leakage, postoperative ileus, and major morbidity after elective colorectal surgery [20, 21]. Thus, the role of MBP is still unclear.

3.4 Effects of MBP on Anastomosis in Colonic Surgery

In many studies, MBP did not affect the prevalence of anastomotic leakage [3, 4, 22, 23]. No benefit of MBP has been found regarding morbidity and mortality after anastomotic leakage in elective colorectal surgery. Mortality rate, initial need for surgical re-intervention, and extent of bowel contamination do not differ between patients with and without MBP [24]. Bucher et al. reported that MBP did not reduce the incidence of anastomotic leakage and also did not reduce the incidence of septic complications [25]. Conversely, Elnahas et al. reported that MBP omission was associated with a higher rate of 30-day anastomotic leakage in elective left-sided colorectal resection [26].

3.5 MBP for Rectal Cancer

Only a few reports describe the effect of MBP in patients with rectal surgery. However, we should not equate rectal surgery with colon surgery because the rate of anastomotic leakage is higher in the former. Further research is warranted on patients undergoing elective rectal surgery, below the peritoneal verge, and laparoscopic surgery.

Bretagnol et al. reported that overall and infectious morbidity rates were significantly higher in the no-MBP than MBP group. However, there was no significant difference for anastomotic leakage and major morbidity rates between the 2 groups [27]. Ji et al. reported that anastomotic leakage rates did not differ. However, a significantly lower rate of clinical leakage requiring surgical exploration was observed in the no-MBP group. There were no significant differences in the clinical severity of anastomotic leakage as assessed by the length of hospital stay, time to resuming a normal diet, duration of antibiotic use, and rates of ileus, transfusion, ICU admission and mortality between the leakage without MBP and leakage with MBP groups [28].

Conversely, Pittet et al. reported that, compared with MBP, a simple rectal enema before rectal surgery was not associated with more postoperative infectious complications or higher overall morbidity. Overall morbidity, pelvic abscess formation, wound infection, extra-abdominal infection and non-infectious abdominal complications such as ileus and bleeding were also comparable [29].

3.6 MBP for Elderly Patients Undergoing Colon Surgery

The indications for MBP in elderly patients undergoing colon surgery should be judged carefully. MBP carries various risks including fluid and electrolyte imbalance for the elderly population. However, a database review of the American College of Surgeons National Surgical Quality Improvement Program reported that omitting MBP is a risk factor for anastomotic leakage in elderly patients, similar to ASA score III and IV, chronic obstructive pulmonary disease, diabetes mellitus, smoking history, weight loss, previous post-colectomy wound infection [30]. Dolejs et al. also reported that MBP and oral antibiotics reduced rates of anastomotic leakage, ileus, SSI, organ space SSI, and respiratory compromise, and reduced length of stay in elderly patients [31].

3.7 MBP for Patients With Digestive Cancer Not Involving Colorectal Cancer

MBP does not reduce the prevalence of morbidity including SSI in patients undergoing esophagocoloplasty, hepatectomy or pancreaticoduodenectomy. In esophagocoloplasty, omission of MBP has a positive impact on the incidence of postoperative complications. There was no significant difference between the groups in the rates of evisceration, colocolic or cologastric anastomotic dehiscence, and death. However, the incidence of cervical leakage in patients without MBP is significantly lower than that of patients with MBP [32]. In patients undergoing liver resection for hepatocellular carcinoma, MBP does not appear to affect the short-term outcome, such as overall and major complications (Clavien–Dindo grade ≥ 3), incidence of liver failure, and SSI [33]. In patients undergoing pancreaticoduodenectomy, MBP shows no clinical benefit. There are no differences in the rates of pancreatic fistula, intra-abdominal abscess, or wound infection in patients receiving MBP or clear liquid diet [12].

3.8 Merits of MBP

MBP may positively affect the prognosis of patients with colon cancer. Collin et al. reported that the 10-year cancer-specific survival rate of patients with MBP was significantly better than that of patients without MBP. They explained this finding as follows. MBP might cleanse the colon of any possible circulating cancer cells and reduce the risk of spread. Another possibility is that a mechanically prepared, empty colon is easier to handle during surgery, which should therefore be easier technically. This could lead to a more radical operation with more proximal division of the blood vessels and removal of more lymph nodes. The tumor might also be easier to identify in an empty colon and the resection margin therefore more accurate [34]. In contrast, MBP may result in more forceful mechanical cleansing of the colon, liberate cancer cells from the tumor, and thereby increase the risk of spread. Furthermore, MBP may not facilitate the operation because there is no difference in operating time between patients with and without MBP [23]. Two reports show that long-term survival is not improved by MBP before colonic cancer surgery [35, 36].

Ikehara et al. reported that MBP using polyethylene glycol (PEG) significantly reduced positive detection rate of exfoliated cancer cells in colon cancer surgery, which involved functional end-to-end anastomosis using a linear stapler. They washed the stapler cartridge using 100 mL of physiological saline, and the washing samples were promptly subjected to cytological analysis.

An interesting experiment on animals were reported. MBP increased working space during laparoscopy by reducing bowel content [37]. Obtaining enough working space is essential for good view and handling for laparoscopic surgery.

3.9 Demerits of MBP

MBP can negatively affect intestinal motility after colon surgery. Previously, we conducted an observational study of 282 patients with colon cancer. We showed that MBP with PEG negatively affects intestinal motility after open and laparoscopic colon surgery [23]. Jung et al. also reported that MBP delayed the first postoperative bowel movement in open colon surgery [38]. Similarly, Bucher et al. reported that PEG delayed the first postoperative bowel movement in left-sided colon surgery [7]. Murphy et al. reported that MBP is a risk factor for postoperative ileus, similar to smoking, weight loss, preoperative oral antibiotics, and open surgical approach [39]. Conversely, some researchers have reported that MBP with oral antibiotics reduces the prevalence of ileus [13, 16].

Bowel content in the resected specimens did not differ significantly. Counts of bacterial microflora, such as *Bifidobacterium* and total *Lactobacillus*, in intraoperative fecal material and first material after surgery were significantly lower in the MBP than no-MBP group. Levels of fecal organic acids, such as acetic, propionic and butyric acids, in intraoperative fecal material were significantly lower, and levels of lactic acid significantly higher, in the MBP than no-MBP group. The succinic acid level was significantly higher after surgery than before in the MBP group [40].

Two interesting experiment on animals are reported. MBP increased bile secretion and induced mild congestion, edema, and inflammation in the small and large bowel of rats [41]. MBP had a negative impact on cellular proliferation and intracellular transport of butyrate within the rat colon [42]. Congestion, edema and inflammation can negatively affect wound healing of anastomoses and intestinal motility. Low cellular proliferation may also have a negative impact on anastomoses.

3.10 Conclusion

MBP alone does not reduce enterobacteria and morbidity rate in digestive surgery. Thus, MBP alone is not recommended. MBP with oral antibiotics reduces SSI. However, it is unclear whether oral antibiotics alone or combined with MBP are desirable. Further study is needed about elderly patients and patients undergoing rectal surgery.

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Chapter 4
Objective and Quantitative Assessment of Postoperative Pain in Digestive Surgery

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Abstract *Background*: Pain is associated with subjective factors, making it difficult to assess. The PainVision™ system has been developed to quantitatively assess pain and compare postoperative pain intensity. We investigated the utility of PainVision in assessing postoperative pain in digestive surgery patients.

Methods: Pain scores were measured with the visual analogue scale (VAS), the PainVision™ system, and the short-form McGill Pain Questionnaire (SFMPQ) in patients undergoing open or laparoscopic hepatectomy, gastrectomy, and cholecystectomy.

Results: As measured by the PainVision™ system, postoperative pain intensity was lower in patients who underwent laparoscopic operations compared with open hepatectomy. Over 50% of patients who underwent open hepatectomy through a right subcostal incision had continuous dull, heavy, and tender postoperative pain per the SFMPQ. In open hepatectomy patients, pain intensity by the PainVision™ system was significantly lower on postoperative day (POD) 7 and 10 than POD 1; pain intensity was also influenced by other variables, including body mass index, length of the skin incision, and operative time. Preemptive use of nonsteroidal anti-inflammatory drugs significantly reduced postoperative pain in open hepatectomy patients.

Conclusions: PainVision effectively quantifies pain intensity after digestive surgery. Objective assessment of postoperative pain may lead to early mobility and improved quality of life.

Keywords Postoperative pain • PainVision™ • Digestive surgery • Hepatic resection • Preemptive nonsteroidal anti-inflammatory drugs

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4.1 Introduction

Pain relief in patients undergoing digestive surgery is provided by thoracic epidural analgesia or intravenous (IV) opioid analgesia. Although epidural analgesia is generally considered to represent the gold standard in the treatment of postoperative pain, it has contraindications and can be associated with complications, limiting its use. IV opioid analgesia may cause opioid-related side effects and sometimes produces inadequate analgesia. Thus, it is essential to investigate alternative approaches to traditional analgesic techniques.

Furthermore, an accurate assessment tool for postoperative pain is necessary to evaluate new approaches to postoperative pain relief. However, because pain is a sensation associated with subjective factors, it is difficult to measure and assess [1–3]. Accordingly, subjective assessments, such as the visual analogue scale (VAS) [4] and the face pain rating scale (FPRS) [5], have been the primary methods of measuring pain in clinical medicine. To the best of our knowledge, there are few objective methods of assessing pain used in clinical practice to date.

In recent years, the PainVision™ system (PS-2100; Nipro Corporation, Osaka, Japan), a device capable of quantitative pain assessment by substituting different sensory stimuli for pain, has been developed and used in Japan in the field of anesthesiology and in pain clinics [2, 3, 6]. In this study, we examined whether postoperative pain could be objectively and quantitatively assessed by the PainVision system, and we compared pain intensity in patients undergoing different types of digestive surgery including hepatic resection and also in patients with or without preemptive use of nonsteroidal anti-inflammatory drugs (NSAIDs).

4.2 Methods

We prospectively analyzed patients who underwent open or laparoscopic hepatectomy, laparoscopic cholecystectomy, and open or laparoscopic distal gastrectomy at Hirakata Hospital of Kansai Medical University (Osaka, Japan) between March 2012 and December 2014. All patients provided written informed consent for participation in this study, and the protocol was approved by the institutional review board.

General anesthesia was induced by IV propofol (1.5–2.0 mg/kg) and sufentanil (0.3 μg/kg). Endotracheal intubation was facilitated by the administration of IV rocuronium (0.9 mg/kg). After endotracheal intubation, intermittent positive pressure ventilation of both lungs was applied. Anesthesia was maintained with combined IV and inhalant anesthesia (propofol, remifentanil, and sevoflurane in oxygen). An infusion of remifentanil was started at 8 μg/kg/h and was titrated up to 12 μg/kg/h for the control of hemodynamic responses to pain during surgery. For laparoscopic hepatectomy or gastrectomy, a bilateral ultrasound-guided subcostal transversus abdominis plane block was performed as previously described [7] (with

20 mL of 0.375% ropivacaine on each side) after the induction of general anesthesia. In patients undergoing open hepatectomy or gastrectomy, a thoracic epidural catheter was placed between T8 and T9 before the induction of general anesthesia, with 4 mL of 1.5% lidocaine as a test dose. An initial loading dose of 5 mL of 1.5% lidocaine was administered before the induction of anesthesia, and 5 mL was infused every hour during surgery.

After the operation, patients received continuous epidural analgesia maintained by epidural infusion pumps, with a background infusion of 0.2% ropivacaine and 2.5 μg/mL fentanyl at 4 mL/h. Patients who underwent laparoscopic hepatectomy or gastrectomy received IV patient-controlled analgesia with fentanyl (1 mg bolus dose with a 5-min lockout time and no maximum dose). Intravenous and epidural analgesia were both maintained throughout the first 72 h postoperatively. Patients who underwent laparoscopic cholecystectomy received NSAIDs as rescue.

Patients were assessed on the day prior to surgery and on days 1, 2, 3, 5, 7, and 10 postoperatively. NSAID requirements and pain scores were recorded; pain was assessed 3–4 times/day (including at rest and on movement) using VAS scores, the short-form McGill Pain Questionnaire (SFMPQ) [8, 9], and the PainVision system (Fig. 4.1).

The PainVision system was used as previously described, with minor modifications [6]. Briefly, sensors transmitting an electric current were attached to the right medial forearm. The patient's level of pain is quantified using a stimulating electric current representing the pain sensation and comparing this with pain-free electric stimulation. A pulsing current wave not generating pain is applied to the skin, and the pain and stimulating sensations are compared while gradually increasing the pulse. The electric current giving a sensation equivalent to the pain intensity is defined as the pain current. The threshold of electric stimulation for the patient (the current at which the patient first perceived the increasing electric stimulation) is defined as the minimal perceptible current. The minimal perceptible current is used to eliminate individual differences generated by relative location of the electrode and the subcutaneous nerve system or by intracerebral cognition of the stimulation. The current perception threshold, which indicates each patient's pain threshold, was measured three times, and the mean values were used for subsequent calculations.

Pain intensity was calculated using the following equation: Pain intensity = 100 × (pain compatible electrical current − current perception threshold)/current perception threshold (Fig. 4.1c) [10].

After a series of examinations was completed, a subset of the patients who underwent open and laparoscopic hepatic resections were treated with NSAIDs (loxoprofen; 180 mg/day) from POD 1 through 10 and 7, respectively, as a preventive measure to control postoperative pain. Pain intensity and VAS scores for NSAID-treated patients who underwent open and laparoscopic hepatic resections ($n = 38$) were compared with those for patients who examined firstly without preemptive NSAIDs ($n = 34$).

Patients were questioned regarding the details of their pain using the Japanese version of the SFMPQ. Patients who underwent open hepatic resection with or without preemptive NSAIDs were questioned about the characteristics of their pain using the Japanese SFMPQ.

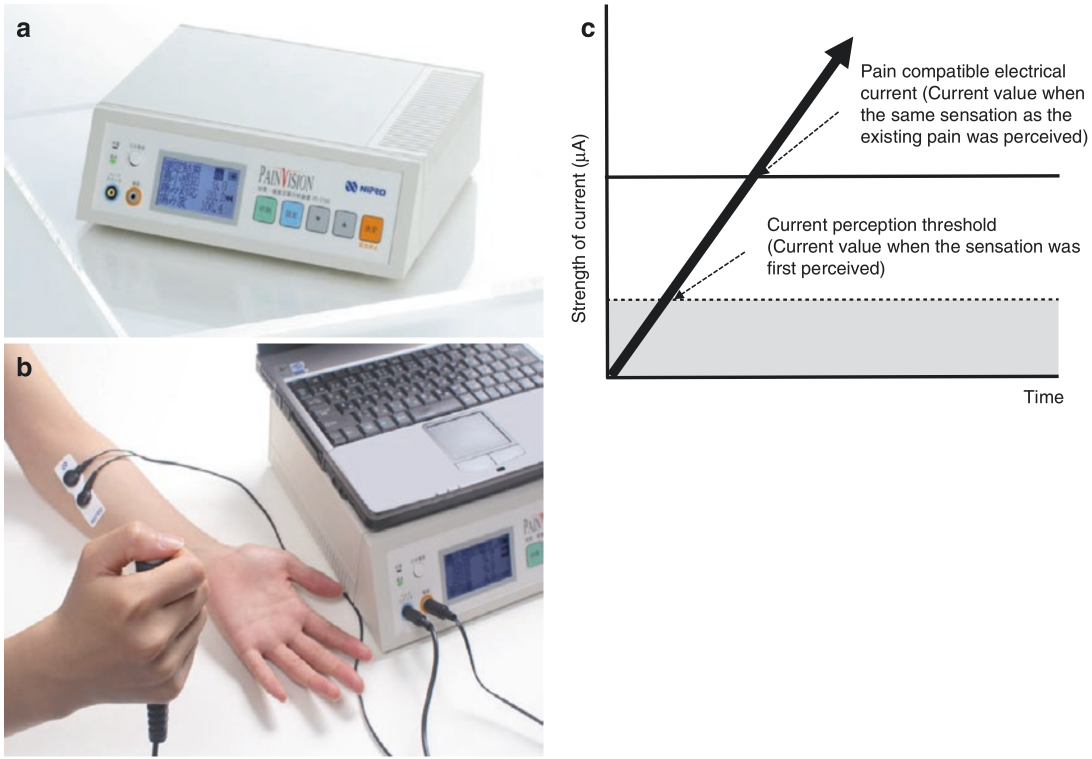

Fig. 4.1 Depiction of the PainVision™ system. (**a**) Main unit of the PainVision system. (**b**) Attach a bipolar electrode to the ulnar side of the forearm and have the subject hold the switch with the other hand. (**c**) Gradually increasing the strength of the stimulating current, the current value at when the subject first perceived the stimulation represents the current perception threshold, and the value at when the subject perceived the same intensity of pain as his/her existing pain represents the pain equivalent current. Because the magnitude of electric stimulation is equal to the pain experienced by the patient, the current administered is defined as the pain compatible electrical current; the pain compatible electrical current is represented by the mean value of three measurements. Pain intensity is calculated as follows: Pain intensity = 100 × (pain compatible electrical current − current perception threshold)/current perception threshold

4.2.1 Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD). The patients were divided into groups based on the median values of the continuous variables. The significance of differences between the groups or at different times within a group was assessed using the Mann–Whitney U test. For all analyses, $P < 0.05$ was considered to indicate statistical significance.

4.3 Results

We examined a total of 82 patients who underwent open or laparoscopic hepatectomy (n = 39), laparoscopic cholecystectomy (n = 26), and open or laparoscopic distal gastrectomy (n = 17). The 39 patients who underwent hepatectomy comprised 30 cases of hepatocellular carcinoma and 9 of colorectal liver metastasis. Open hepatectomy through a right subcostal incision was performed in 34 patients, and laparoscopic hepatectomy was performed in 5 patients. Laparoscopic cholecystectomy was performed in 19 patients with gallbladder stones and 7 patients with gallbladder polyps. Open distal gastrectomy through an upper median incision was performed in 5 patients; laparoscopic gastrectomy was performed in 12 patients. Thirty-eight and five of the patients who underwent open and laparoscopic hepatic resections, respectively, were treated with preemptive NSAIDs from POD 1 through 10 and 7.

When pain was assessed by VAS, there were no significant differences in pain intensity at different time points between the five groups (open and laparoscopic hepatic resection, laparoscopic cholecystectomy, and open and laparoscopic gastrectomy) (Fig. 4.2, right), although there was a tendency that open hepatic resection group had higher VAS levels than other groups at POD 3 and thereafter. In contrast, with the PainVision system, pain intensity in the open hepatic resection group was significantly higher than that experienced by patients in the other groups at PODs 3, 5, and 7 (Fig. 4.2, left). In open hepatic resection patients, the pain intensity on PODs 7 and 10 was significantly lower than on POD 1.

We compared pain intensity, as measured with the PainVision system in open hepatic resection patients (right subcostal incision), among patients with differing clinical characteristics and surgical variables (Tables 4.1 and 4.2). Pain intensity at PODs 2 and 3 was higher in patients who were <65 years old compared with patients aged ≥65 years. Patients with a body mass index (BMI) < 24 kg/m^2 experienced a significantly higher pain intensity than those with a BMI ≥ 24 kg/m^2 (POD 3). The pain intensity was significantly higher in patients with a history of alcohol abuse compared with those with none (POD 1). The pain intensity was significantly higher in patients with a skin incision length ≥ 25 cm compared with those with a skin incision <25 cm in length (PODs 5 and 7). The pain intensity with anatomic resection was significantly higher compared with nonanatomic resection (PODs 3 and 5). The pain intensity in patients with an operative time ≥300 min was

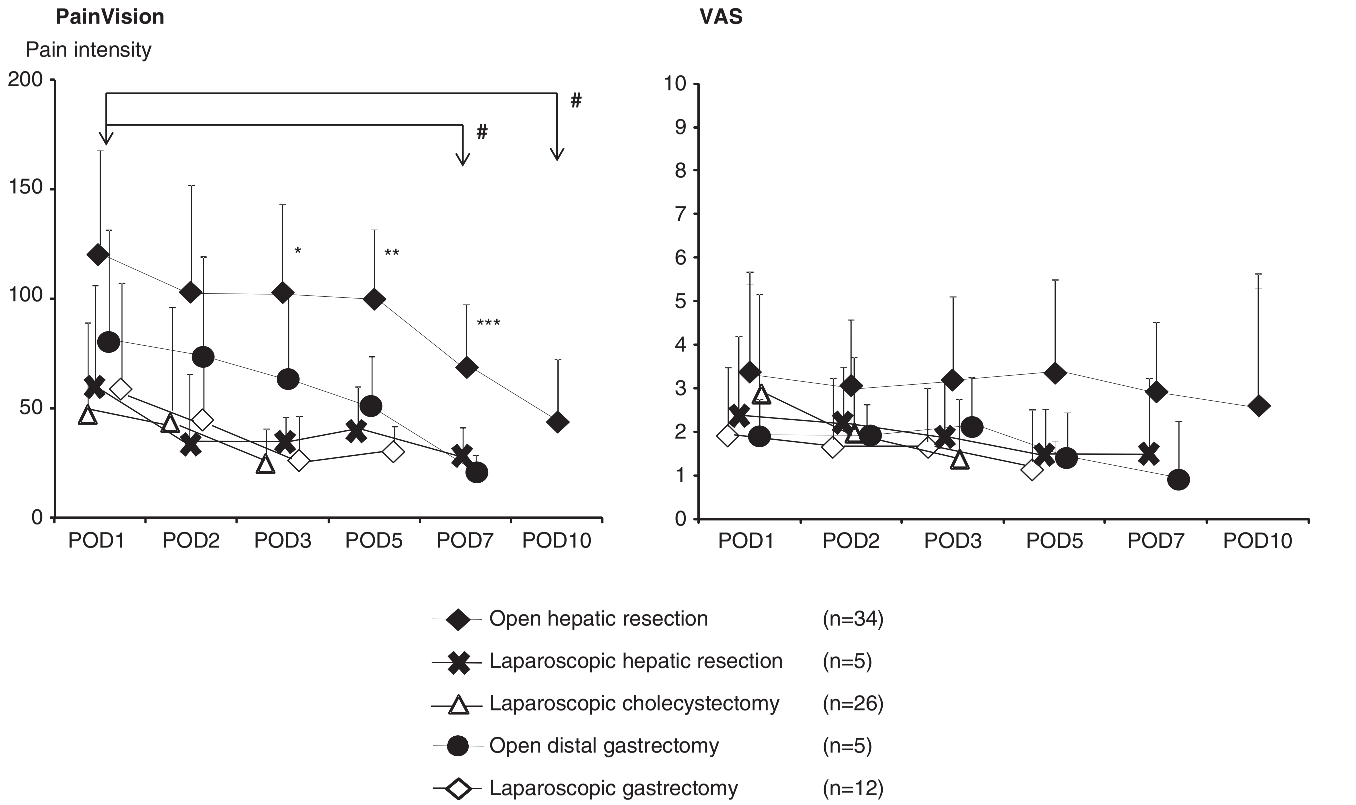

Fig. 4.2 Measurement of postoperative pain following digestive surgery using the PainVision system and the VAS. *, $P < 0.05$ between open hepatic resection ($n = 34$) and laparoscopic hepatic resection ($n = 5$) or laparoscopic gastrectomy ($n = 12$) at POD 3. **, $P < 0.05$ between open hepatic resection and laparoscopic hepatic resection or laparoscopic gastrectomy at POD 5. ***, $P < 0.05$ between open hepatic resection and laparoscopic hepatic resection or open distal gastrectomy ($n = 5$) at POD 7. #, $P < 0.05$ between POD 1 and POD 7 or POD 10 in open hepatic resection patients. *VAS* visual analogue scale, *POD* postoperative day

Table 4.1 Pain intensity over time with differing patient characteristics as measured with the PainVision™ system in open hepatic resection patients

	POD 1	POD 2	POD 3	POD 5	POD 7
Age (years)					
≥65 (*n* = 23)	117 ± 74	88 ± 38	73 ± 77	76 ± 69	70 ± 49
<65 (*n* = 11)	125 ± 85	121 ± 70	115 ± 70	105 ± 58	92 ± 29
P value	N.S.	N.S.	N.S.	N.S.	N.S.
Body mass index (kg/m^2)					
≥24 kg/m^2 (*n* = 14)	107 ± 77	97 ± 64	76 ± 40	79 ± 56	76 ± 51
<24 kg/m^2 (*n* = 20)	145 ± 94	124 ± 100	117 ± 70	115 ± 61	88 ± 60
P value	N.S.	N.S.	**0.04**	N.S.	N.S.
Alcohol abuse					
Present (*n* = 14)	168 ± 72	138 ± 76	124 ± 98	106 ± 84	89 ± 66
Absent (*n* = 20)	79 ± 68	71 ± 51	79 ± 65	78 ± 66	74 ± 50
P value	**0.04**	N.S.	N.S.	N.S.	N.S.

Values are represented as mean ± standard deviation. *POD* postoperative day

Table 4.2 Pain intensity over time with differing surgical variables as measured with the PainVision™ system in open hepatic resection patients

	POD 1	POD 2	POD 3	POD 5	POD 7
Length of the skin incision					
≥25 cm (*n* = 18)	135 ± 98	124 ± 84	118 ± 78	117 ± 62	105 ± 62
<25 cm (*n* = 16)	85 ± 55	80 ± 62	71 ± 50	60 ± 38	43 ± 20
P value	N.S.	N.S.	N.S.	**0.04**	**0.03**
Surgical procedure					
Anatomic resection (*n* = 13)	124 ± 102	124 ± 91	126 ± 74	120 ± 51	100 ± 68
Nonanatomic resection (*n* = 21)	110 ± 82	74 ± 48	59 ± 30	54 ± 25	54 ± 39
P value	N.S.	N.S.	**0.04**	**0.04**	N.S.
Operational time					
≥300 min (*n* = 18)	130 ± 110	124 ± 82	130 ± 58	119 ± 76	105 ± 50
<300 min (*n* = 16)	112 ± 106	75 ± 47	64 ± 30	69 ± 48	74 ± 43
P value	N.S.	N.S.	**0.04**	N.S.	N.S.
Tumor size					
≥5 cm (*n* = 13)	128 ± 109	120 ± 81	136 ± 85	126 ± 84	101 ± 54
<5 cm (*n* = 21)	108 ± 92	84 ± 50	72 ± 51	76 ± 38	74 ± 42
P value	N.S.	N.S.	N.S.	N.S.	N.S.

Values are represented as mean ± standard deviation. *POD* postoperative day

significantly higher relative to those with an operative time <300 min (POD 3). The pain intensity was higher with a tumor ≥5 cm in size compared with a tumor <5 cm in size (POD 3).

We also examined the effects of preemptive NSAIDs in patients who underwent open and laparoscopic hepatic resections (Figs. 4.3 and 4.4). In 34 patients who underwent open hepatic resection (conventional group), the average time with a thoracic epidural catheter was 3.1 ± 0.5 days (mean ± SD) after the operation; the mean flurbiprofen dose (IV) was 35 ± 35 and 30 ± 35 mg/day on PODs 1 and 2, respectively, and the mean loxoprofen dose as rescue was 20 ± 36, 30 ± 40, and 24 ± 42 mg/day on PODs 3, 5, and 7, respectively. In five patients who underwent laparoscopic hepatic resection (conventional group), the mean loxoprofen dose as rescue was 36 ± 33, 24 ± 33, and 12 ± 27 mg/day on PODs 3, 5, and 7, respectively.

An additional 38 and 8 patients (the preemptive NSAID groups) received preemptive loxoprofen (180 mg/day) after open or laparoscopic hepatic resections on POD 1 through POD 10 and POD 7, respectively, and pain intensity was compared between conventional and preemptive NSAID groups. Although the VAS score did not significantly differ between the two groups in open hepatic resection, the pain intensity as measured by the PainVision system was significantly lower in the preemptive NSAID group compared with the conventional group on POD 1 through POD 3 (Fig. 4.3). The additional mean loxoprofen dose as rescue was 14 ± 26, 6 ± 19, and 3 ± 14 mg/day at PODs 3, 5, and 7, respectively. In patients who underwent laparoscopic hepatic resection, both of the pain intensity by the PainVision system and VAS score did not significantly differ between the two groups (Fig. 4.4). The additional mean loxoprofen dose as rescue analgesia was 8 ± 21, 8 ± 21, and 0 mg/day at PODs 3, 5, and 7, respectively.

Patients who underwent open hepatic resection between conventional and preemptive NSAIDs groups were questioned about the characteristics of their pain using the Japanese SFMPQ (Fig. 4.5). More than 50% of patients who underwent hepatic resection (≥17 patients) complained of continuous dull, heavy, and tender pain from POD 1 through POD 7, whereas more than 50% of patients who underwent open hepatic resection with preemptive NSAIDs (≥19 patients) did not have any complaints.

4.4 Discussion

The VAS [4] and FPRS [5] are subjective methods of pain assessment currently used in clinical practice [1–5]. With these methods, pain intensity is determined by comparing the level of pain a patient is experiencing with a “pain of maximum intensity.” Because sensitivity to pain varies among individuals, it is difficult to quantitatively compare measurements obtained by subjective methods. Moreover, these modalities are even less reliable for the measurement of relatively weak pain. The PainVision system, intended for the quantitative analysis of perception and pain, has recently been used and evaluated in the fields of pain management and anesthesiology [2, 3, 6]. This system administers alternative, painless sensory stimulation equivalent to pain (mainly by stimulating the sensory nerve fibers A-beta and A-delta) and measures the intensity of this stimulation. Because individual pain thresholds are evaluated first (to enable accurate subsequent measurements with the

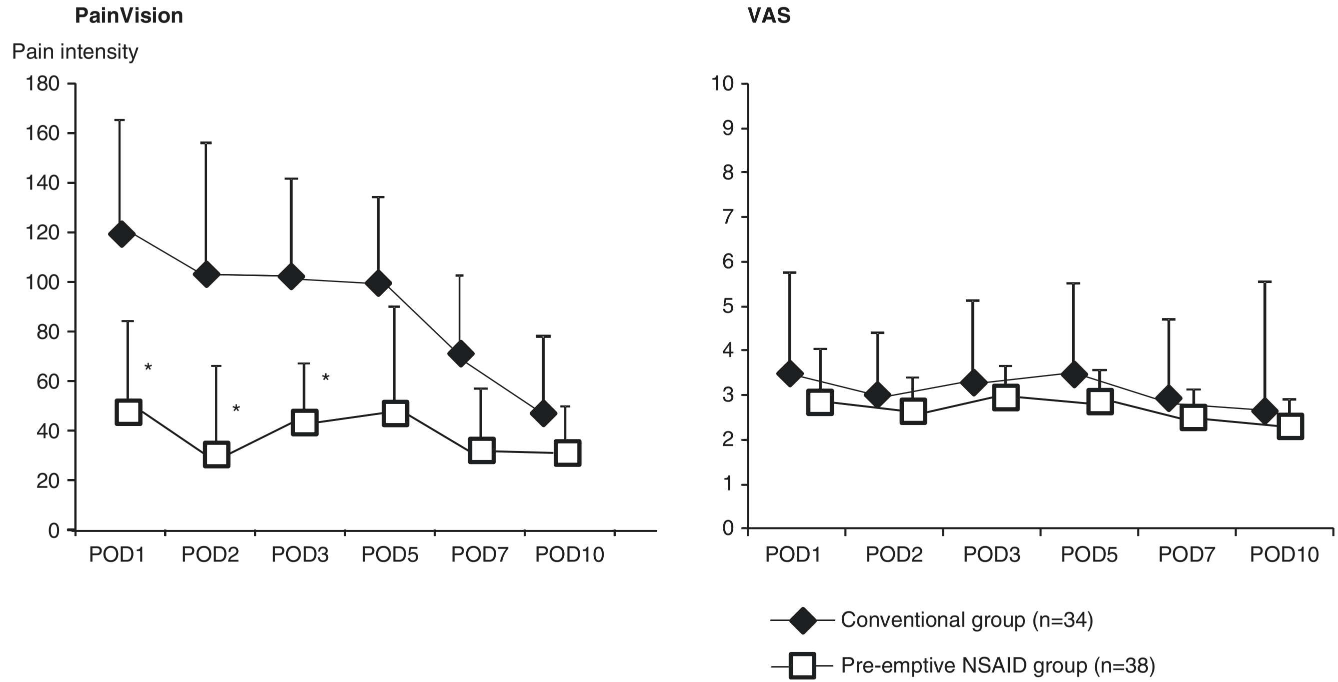

Fig. 4.3 Measurement of postoperative pain with the PainVision system and the VAS in patients who underwent open hepatic resection with or without preemptive NSAIDs. *, $P < 0.05$ between conventional (without NSAIDs, $n = 34$) and preemptive NSAIDs ($n = 38$) groups at PODs 1, 2, and 3. *VAS* visual analogue scale, *POD* postoperative day, *NSAID* nonsteroidal anti-inflammatory drug

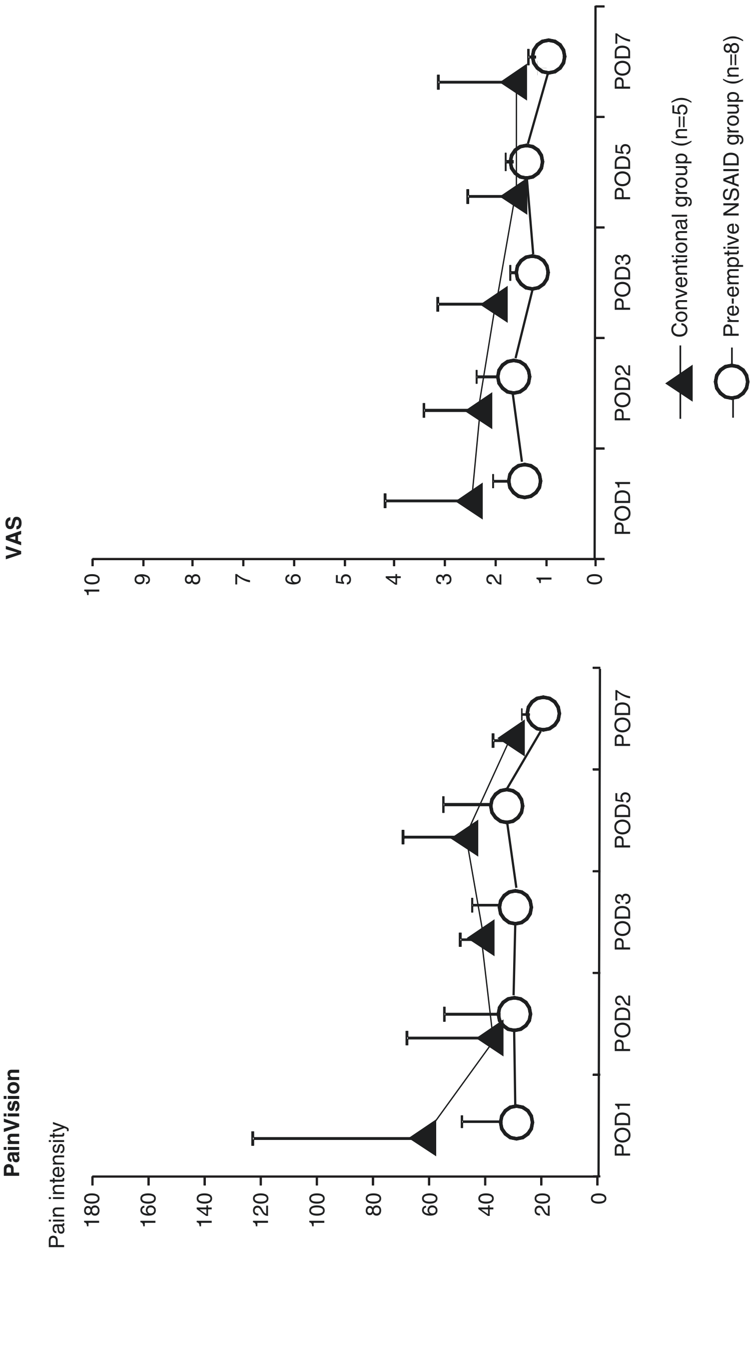

Fig. 4.4 Measurement of postoperative pain with the PainVision system and the VAS in patients who underwent laparoscopic hepatic resection with or without preemptive NSAIDs. Conventional (without NSAIDs, $n = 5$) and preemptive NSAIDs ($n = 8$) groups. *VAS* visual analogue scale, *POD* postoperative day, *NSAID* nonsteroidal anti-inflammatory drug

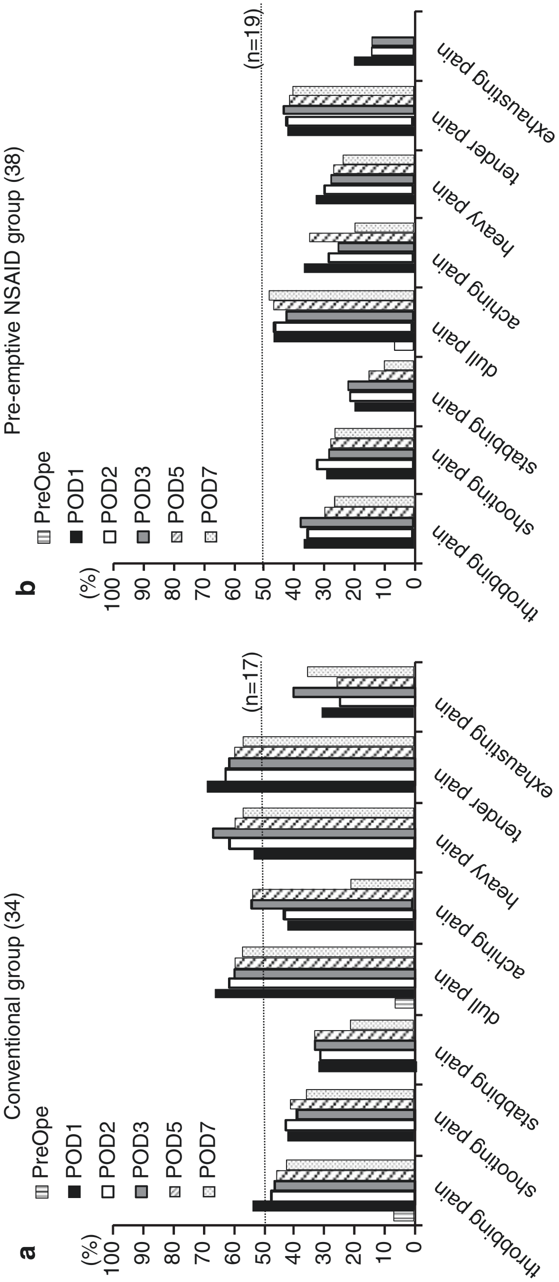

Fig. 4.5 Short-form McGill Pain Questionnaire results in patients who underwent open hepatic resection with and without preemptive NSAIDs. (**a**) Conventional (without NSAIDs, $n = 34$) and (**b**) preemptive NSAIDs ($n = 38$) groups. *POD* postoperative day

device), pain intensity can be quantitatively compared between patients. The device has been used in studies on persistent, chronic pain such as herpes zoster-associated pain [3].

In this study, we evaluated postoperative pain in digestive surgery patients by using VAS scores and the PainVision system. Although the postoperative VAS scores did not obviously differ between the five types of operations performed, postoperative pain intensity as measured by the PainVision system was lower in patients who underwent laparoscopic operations compared with open hepatectomy and gastrectomy. In particular, postoperative pain intensity as measured was significantly higher following open hepatic resection compared with the other four operations, after which patients' pain intensity markedly dropped in a time-dependent manner (Fig. 4.2).

In patients with compromised liver function, post-hepatectomy morbidity and mortality are always significant [11]. Early mobilization has proven to be very important in the short-term outcomes of these patients, but this is difficult to achieve in the presence of severe pain. Large doses of powerful opiates can be used to alleviate such pain; the use of the epidural route is effective in the postoperative care of high-risk patients and can achieve a decrease in the pain threshold for long periods of time. However, the decision to perform continuous epidural analgesia is made on an individual basis by weighing the risk/benefit ratio. Despite using a thoracic epidural catheter for patients undergoing open hepatectomy or gastrectomy, our postoperative doses of NSAIDs as rescue were relatively low. Patients were instructed to ask for additional pain relief if they felt any kind of pain postoperatively. However, most of our patients did not request NSAIDs for additional analgesia.

Our analysis of patients who received preemptive NSAIDs after open hepatic resection demonstrated that NSAIDs were effective for the reduction of pain intensity and more than 50% of patients have not complained postoperatively, although the study was not randomized or controlled and had a small sample size (Figs. 4.3 and 4.5).

In this study, postoperative pain intensity, as measured by the PainVision system in patients who underwent open hepatic resection, was associated with operative stress; a longer skin incision, more extensive hepatic resection (anatomic resection), and longer operative time were associated with greater pain intensity at some time points (Table 4.2). We also found that postoperative pain intensity was significantly higher in patients with a smaller BMI or history of alcohol abuse (Table 4.1). However, the reasons for these results are unknown at present.

In conclusion, postoperative pain intensity can be objectively measured with the PainVision system, enabling the quantification of pain and the comparison of pain between individuals following digestive surgery. In this study, pain intensity following laparoscopic operations appeared to be comparatively low, whereas the pain intensity following open hepatic resection through a right subcostal incision was critical, representing high surgical stress. The objective and quantitative measurement of postoperative pain may contribute to improvements in patients' quality of life.

Authors' Contributions

MK and HI contributed equally to this work. MK and HI conducted the data analysis and drafted the manuscript. MI, KM, and M. Kon conceived the study, participated in its design, and helped draft the manuscript. TS, HM, and JF participated in the study design and contributed to the data collection. KI participated in the study design and advised the analysis. YM contributed to study data collection. All authors contributed to the interpretation of the findings and read and approved the final manuscript.

Competing Interests

The authors declare that they have no competing interests.

Compliance With Ethical Standards

Disclosure of Potential Conflicts of Interest

The authors declare that they have no conflict of interest.

Research Involving Human Participants and/or Animals

1. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional with the 1964 Helsinki declaration and its later amendments.
2. This chapter does not contain any studies with animals performed by any of the authors.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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Part III
Early Independence of Physical Activity

Chapter 5
Pros and Cons of Abdominal Drain in Digestive Surgery

Morihiko Ishizaki, Kosuke Matsui, and Masaki Kaibori

Abstract The Consensus Guideline advocated by the Enhanced Recovery After Surgery (ERAS) Study Group does not recommend routine drain insertion. However, no well-established evidence of the need for abdominal drainage in gastrointestinal surgeries is available. In this article, the currently available evidence of the need for abdominal drains in gastrointestinal surgeries is reviewed. In fact, indwelling drains are not needed in all surgical cases. Since the publication of an overseas report that denied the preventive effects of abdominal drains and the need for indwelling drains, several studies on the appropriate use of drains have been performed in Japan. Although it is unclear whether sufficient discussions have been conducted regarding the selection of drains in other countries, the use of a selected drain for its maximum benefits, and appropriate withdrawal timing, it is necessary to first identify the optimal use of drains regardless of whether drains should be continued to be used in the future. Thus, we suggest that decisions regarding indwelling drains should be appropriately made by respective surgeons based on surgical findings. Finally, it should be noted again that a prophylactic drain should be promptly removed once it is no longer needed because an extended period of indwelling drainage may lead to retrograde infection.

Keywords Abdominal drain • Gastrointestinal surgery

5.1 Need for Drain Insertion in Gastrointestinal Surgeries

5.1.1 Introduction

Drainage refers to a basic surgical technique that constantly drains nonphysiological fluid accumulated in vivo, including blood, serum, lymph, digestive juice, and pus, out of the body to avoid biohazardous reactions, promote wound healing, and

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maintain homeostasis. The guideline for prevention of surgical site infection (SSI) published by the Centers for Disease Control and Prevention in 1999 [1] recommends using a closed sump drain if drainage is necessary, indwelling the drain at a site distant from the surgical incision, and withdrawing the drain as soon as possible. These drainage recommendations are rated as Category IB recommendations, which are “highly recommended to implement; supported by multiple experimental, clinical, or epidemiological research; and theoretically reasonable.” However, the recommendation regarding prompt drain withdrawal is based on research findings in the field of orthopedic surgery (total knee prosthesis and hip replacement surgeries) [2]. Characteristics specific to gastrointestinal surgeries should further be investigated.

The Consensus Guideline advocated by the Enhanced Recovery After Surgery (ERAS) Study Group does not recommend routine drain insertion. In fact, with the absence of abdominal drainage after surgery, patients must only pay attention to the intravenous route from their arm or neck region at the time of postoperative ambulation, which provides greater mobility to help establish early self-reliance in physical activities. Moreover, no well-established evidence of the need for abdominal drainage in gastrointestinal surgeries is available. Rather than merely following customs regarding insertion and maintenance of an indwelling drain during the postoperative period, it is necessary to accumulate and share evidence of various aspects of appropriate drain control. Popular drains used for gastrointestinal surgeries are abdominal drains, subcutaneous drains, percutaneous transhepatic cholangiography drains, and T-tubes. In this article, the currently available evidence of the need for abdominal drains in gastrointestinal surgeries is reviewed.

5.1.2 Purposes and Types of Drain Insertion

Three types of drains are available depending on the intended purpose: information drains, which help to identify and respond to postoperative intraperitoneal bleeding and anastomotic leakage; prophylactic drains, which remove effusion to prevent complicating diseases such as anastomotic leakage and internal organ/cavity SSI; and therapeutic drains, which provide a quick and complete cure of abscesses caused by anastomotic leakage and internal organ/cavity SSI (Table 5.1). A literature search in the field of liver surgery, which is the author’s specialized discipline,

Table 5.1 Purpose and types of surgical drains

1. Information drain	It could be checked the existence of bleeding or bile leakage, for the purpose of early detection of postoperative complication (e.g. drain for colecstectomy)
2. Prophylactic drain	It could be removed ascitic fluid from abdominal dead space according to intraoperative infection to prevent postoperative complication (e.g. drain for hepatopancreatobiliary and gastrointestinal surgery)
3. Therapeutic drain	It could be removed abdominal abscess or digestive juice according to panperitonitis, and also could be performed abdominal cavity irrigation (e.g. panperitonitis, abdominal abscess, acute pancreatitis)

revealed research findings that deny the preventive effects of drains (i.e., the incidence of anastomotic leakage and internal organ/cavity SSI does not change with or without the presence of an indwelling drain) [3–5]. However, these findings have not been exemplified by a sufficient number of cases. Another study even indicated that the presence of an indwelling drain increased the incidence of SSI [6]. Thus, insufficient numbers of studies have been performed regarding the necessity of prophylactic indwelling drains. In Japan, drains are usually used to obtain information rather than prevent complications as often seen in overseas surgical practices. In the event of anastomotic leakage, such information drains are indwelled as therapeutic drains for an extended period of time. When clinicians expect that the drain itself may become a medium for bacteria and prevent resolution of local inflammation due to prolonged indwelling, the drain should be promptly replaced.

This chapter presents an overview of drain types. Drain tubes are classified into three types depending on their indwelling part, shape, and drainage properties: film type, hollow type, and fluted type. Film type drain tubes are corrugated, film-shaped tubes with thin walls and drain fluid by utilizing capillary action. They are used as information drains because they effectively drain serous fluid. They are also used for delicate regions near solid organs (hepatic radial margin, pancreatic stump, superior pancreatic margin, pancreas-jejunum anastomotic region periphery, and anastomotic region periphery in case of rectal and other surgeries). Conversely, it is difficult to secure a linear drainage route with film type drains; they are unsuited for drain replacement. Moreover, film type drain tubes cannot be connected to closed or closed sump drainage bags for drain control, and they are necessarily used under semi-opened control with an opened pouch with a gauze pad (Fig. 5.1), which is associated with a risk

Fig. 5.1 Film type drain under semi-opened control with an opened pouch

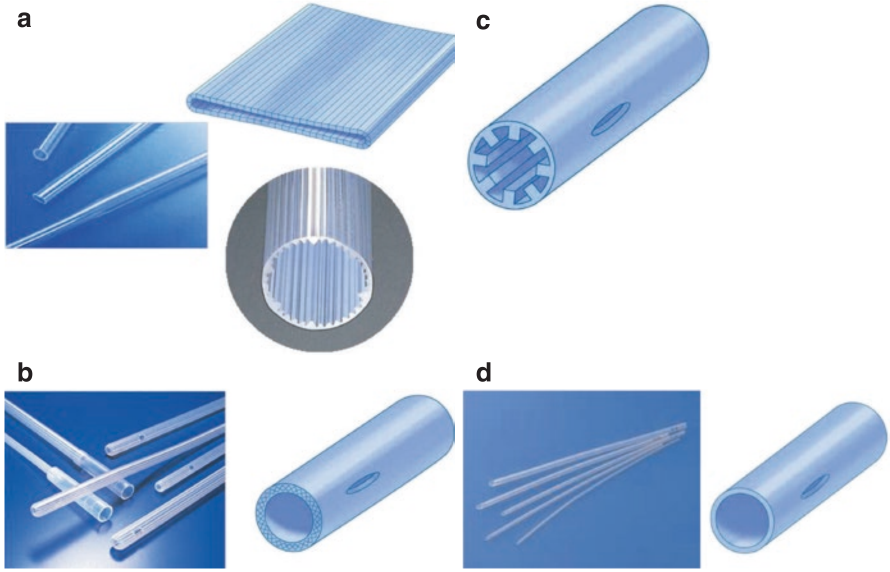

Fig. 5.2 (**a**) Film type drain (*Penrose drain*). (**b**) Hollow type drain (*Duple drain*) which have fine hollows on tube walls. (**c**) Hollow type drain (*Pleated drain*) which have a spiral structure. (**d**) Hollow type drain (*Nelaton tube*) with no processing on the tube walls

of reflux infection. The periphery of the drain insertion site is prone to become stained and cause patient discomfort; the complexity and inefficiency in nursing care management are also drawbacks of this type of drain tube. A representative film type drain is the Penrose drain (Fig. 5.2a). The hollow type has a hollow space within a silicone tube and is used for anastomotic regions in surgeries of the subdiaphragmatic, subhepatic, and colic regions, where highly viscous fluid such as blood, pus, and fecal juice accumulates. Other film type drains include Duple drains, which have fine hollows on tube walls (Fig. 5.2b), and pleated drains, which have a spiral structure (Fig. 5.2c). All are designed for effective drainage of serous fluid by capillary action. The Nelaton tube (Fig. 5.2d) is a typical example of a drainage tube with no processing on the tube walls. Although made of silicone, the tip of hollow type drains is hard, and care is required to avoid damaging organs or puncturing the intestinal canal during the indwelling process. Hollow type drains are generally connected to a closed drainage bag with no continuous suction, such as a Urobag (Fig. 5.3a). Hollow type drains were previously used with an open bag; however, closed drainage bags have rapidly gained popularity since 2000 because of the same circumstances described above for film type drains. The combination of a hollow type drain and a closed continuous suction drainage bag is not commonly used because a hollow type drain has only one opening at its tip, posing a risk of tissue involvement, tube clogging, and organ damage during suction. Fluted type drains have no hollow and are designed for drainage via their grooves by capillary action. A representative fluted type drain is the Blake drain, and both round and flat shapes are available (Fig. 5.3b). Normally, a fluted type drain is used in connection with a closed continuous suction drainage bag (Fig. 5.3c). Fluted drains are well

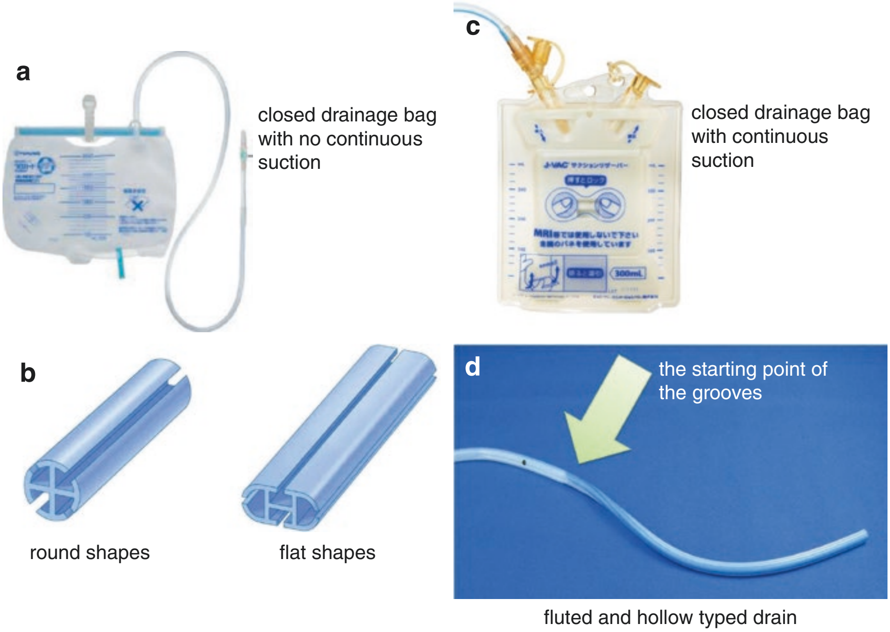

Fig. 5.3 (**a**) Closed drainage bag with no continuous suction (Urobag). (**b**) Fluted type drain (*Blake drain*). (**c**) Closed drainage bag with continuous suction (J-VAC). (**d**) Drainage reportedly begins at the starting point of the grooves (*Blake drain*)

suited to continuous suction and allow for proactive drainage of serous fluid. Additionally, fluting of the tube reduces the risk of tissue involvement by opening of the tube during suction as well as resultant occlusion and organ damage at the time of removal. However, the drainage properties of fluted and hollow type drains largely vary and require careful attention during the indwelling process. In the case of Blake drains, for instance, drainage reportedly begins at the starting point of the grooves (Fig. 5.3d) [7]. Additionally, the drainage area reportedly moves toward the tip as fluid around the tube is drained and the drain spaces are filled [8]. Thus, the drain is most effective at the starting point of the grooves, and this point should be located in a region where fluid accumulates. Therefore, a Blake drain is used for gastrointestinal surgery, and the black dot marked on the tube is often located in the body cavity, not on the peripheral skin of the drain insertion site. For hollow type tubes, however, the opening is located at the tip of the tube, and the tip should thus be located in the fluid accumulation site.

5.2 Need for Drains in Gastrointestinal Surgeries

Regardless of the type of surgery performed, drain insertion is clearly needed in patients with poor intestinal blood flow in the anastomotic region, a contaminated operation, absence of complete hemostasis, surgery performed by an inexperienced surgeon, or any other situation where the surgeon or supervising doctor deems it necessary. Additionally, there are certain perspectives regarding the need for routine use of drains. The need for drainage based on clinical tests for different surgeries is discussed below.

According to a systematic review [9] that conducted a meta-analysis of 11 randomized controlled trials (1803 cases) examining the benefit of drainage versus no drainage in elective colorectal surgery, the mortality rate was 3% (32 of 939 cases) versus 4% (31 of 864 cases), the rate of clinical findings of anastomotic dehiscence was 4% (31 of 769 cases) versus 3% (20 of 724 cases), the rate of radiographic findings of anastomotic dehiscence was 5% (32 of 669 cases) versus 5% (28 of 619 cases), the wound infection rate was 7% (65 of 939 cases) versus 6% (51 of 864 cases), the reoperation rate was 5% (32 of 762 cases) versus 4% (32 of 737 cases), and the respiratory complication rate was 5% (42 of 888 cases) versus 6% (46 of 816 cases), respectively. Overall, no benefit of prophylactic drainage was found. In contrast, Urbach et al. [10] reported that the odds ratios associated with indwelling drains were 1.38 for mortality, 1.47 for anastomotic leakage, and 1.70 for SSI. Thus, it is safe to say that there is no need for prophylactic drainage in elective open colectomy, which is a non-contaminated operation. But the another report of meta-analysis shows that the presence of a pelvic drain reduces the incidence of extraperitoneal colorectal anastomotic leakage and the rate of reintervention after anterior rectal resection [11].

Previous studies have revealed no evidence to support routine drain use after hepatectomy [12, 13]. According to a systematic review [14] that conducted a meta-analysis of six trials (665 cases) examining the benefit of drainage versus no drainage in uncomplicated hepatectomy, there is no evidence to support routine drain use after hepatectomy. Shwaartz et al. [15] reported about propensity score-matched cohorts of 1005 patients who underwent major hepatic resection with or without drain placement. They concluded that drain placement after major hepatectomy may lead to increased postoperative complications including bile leak, superficial surgical site infection, and hospital length of stay.

For cholecystectomy, whether laparoscopic or laparotomic, no cases involving a high risk of complications indicating drainage have been reported, suggesting that drains should be used at the surgeon's discretion only when there is a risk of intraoperative bilistasis and bile duct injury [16]. According to a Cochrane review [17] that conducted a meta-analysis of four randomized controlled trials (438 cases) examining the benefit of drainage versus no drainage in uncomplicated laparoscopic cholecystectomy, there is currently no evidence to support the routine use of drain after laparoscopic cholecystectomy.

For gastrectomy, previous studies have revealed no significant difference in the incidence of postoperative complications with or without drain use, and the need for routine use of drains has not been reported [18–20]. However, considering the insufficient number of cases and lack of examination of cases of total gastrectomy, extended lymph node dissection, pancreatic complication ablation, and similar procedures, a definite conclusion regarding the need for drains in high-risk surgeries cannot be drawn. According to a recent Cochrane review [21] that conducted a meta-analysis of four randomized controlled trials (438 cases) examining the benefit of drainage versus no drainage in gastrectomy, there was no evidence of a difference between the two groups in mortality, re-operations, and post-operative complications. However, the addition of a drain prolonged the operation time and post-operative hospital stay and led to drain-related complications.

A meta-analysis of postoperative risk–benefit assessments of closed drains in pancreatectomy did not confirm a significant difference in postoperative complications (odds ratio, 0.80) or mortality (odds ratio, 0.97) with versus without drains. However, in a comparison between early and late withdrawal (3–4 vs. ≥5 days, respectively), late withdrawal exhibited significantly lower odds ratios in relation to pancreatic leakage (0.13), abdominal fluid accumulation (0.08), and intraperitoneal abscesses (0.26) and resulted in shorter hospital stays (reduced by 2.6 days) [22, 23]. According to a recent Cochrane review [24] that conducted a meta-analysis of 3 trials (711 cases) examining the benefit of drainage versus no drainage in pancreatectomy, there was inadequate evidence to establish the effect of drains on mortality at 30 days (2.2% with drains versus 3.4% no drains; RR 0.78), mortality at 90 days (2.9% versus 11.6%; RR 0.24), intra-abdominal infection (7.3% versus 8.5%; RR 0.89), wound infection (12.3% versus 13.3%; RR 0.92), morbidity (64.8 versus 62.0%; RR 1.04), length of hospital stay (MD −0.66 days), or additional open procedures for postoperative complications (11.5 versus 9.1%; RR 1.18). There was one drain-related complication in the drainage group (0.6%). They concluded that active drainage may reduce hospital stay after pancreatic surgery, and early removal may be superior to late removal for people with low risk of postoperative pancreatic fistula (Table 5.2).

5.3 Conclusion

Since the publication of an overseas report that denied the preventive effects of abdominal drains and the need for indwelling drains [25], several studies on the appropriate use of drains (primarily in relation to the indwelling period) have been performed in Japan. Although it is unclear whether sufficient discussions have been conducted regarding the selection of drains in other countries, the use of a selected drain for its maximum benefits, and appropriate withdrawal timing, it is necessary to first identify the optimal use of drains regardless of whether drains should be continued to be used in the future.

In fact, indwelling drains are not needed in all surgical cases. Thus, we suggest that decisions regarding indwelling drains should be appropriately made by respective surgeons based on surgical findings. Finally, it should be noted again that a prophylactic drain should be promptly removed once it is no longer needed because an extended period of indwelling drainage may lead to retrograde infection.

Table 5.2 Systematic reviews that examing the benefit of drainage versus no drainage in gastrointestinal surgery

Author	Year	Number of trials	Number of patients (drain/no drain)	Surgical procedure	Results (drain vs. no drain)				Recommendation
					Mortality	Postoperative complication	Re-operation	Hospital stay	
Rondelli [11]	2013	8	1537/740	Colorectal resection	N.S.	N.S.	N.S.	NA	Routine drainage is recommended only in case of anterior rectal resection
Zhang [9]	2016	11	939/864	Colorectal resection	N.S.	N.S.	N.S.	NA	Routine use of prophylactic drainage in colorectal resection is not recommended
Gavriilidis [14]	2016	6	334/331	Liver resection	N.S.	Acitic leak was higher in the drain group	N.S.	N.S.	Routine abdominal drainage is not recommended in elective uncomplicated hepatectomy
Gurusamy [17]	2013	12	915/916	Laparoscopic cholecystectomy	N.S.	N.S.	N.S.	N.S.	The operating time was longer in the drain group. Routine use of drain after laparoscopic cholecystectomy is not recommended
Wang [21]	2015	4	220/218	Gastrectomy	N.S.	N.S.	N.S.	Longer in the drain group	The operating time was significantly longer than the no drain group. Routine abdominal drainage is not recommended in gastrectomy

Diener [22]	2011	4	139/129	Pancreatic resection	N.S.	In case of drain insersion, early compared to late drain removal reduced pancreatic fistulas, intra-abdominal abscesses, and hospital stay	Further randomised controlled trials are warranted to clarify whether drains are of any use. In case of drain insertion, early removal seems to be superior to late removal
Cheng [23]	2016	3	358/353	Pancreatic resection	N.S.	In case of drain insersion, early compared to late drain removal reduced pancreatic fistulas, and hospital stay	It is unclear whether routine abdominal drainage has any effect on the reduction of mortality and postoperative complications after pancreatic surgery. Early removal may be superior to late removal

N.S. not significant, *NA* not available

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Chapter 6
Avoiding Gut Starvation is Key to Early Recovery After Surgery

Kazuhiko Fukatsu

Abstract Making gut starvation period as short as possible is an important part of early recovery after surgery protocols. Even when nutritional requirements are fully supplied via venous route, lack of enteral delivery of nutrition causes various changes in host defense mechanisms against surgical insults. Gut-associated lymphoid tissue, hepatic mononuclear cells, and peritoneal resident and exudative leukocytes, all of these immune organ and cells are indispensable to the protection against hostile microbes. However, gut starvation rapidly decreases these immune cell numbers and impairs their functions. Gut starvation also leads to excessive activation of endothelial cells in vital organs, thereby worsening systemic inflammation. Clinicians should be aware of significance of gut as nutritional route for surgical patients' early recovery.

Keywords Gut associated lymphoid tissue • Hepatic mononuclear cell • Peritoneal leukocyte • Endothelial cell

6.1 Introduction

Total parenteral nutrition (TPN) can maintain nutritional status and prevent progression of malnutrition in patients whose gut is not tolerable to oral or enteral nutrition (EN). Without TPN, we could not have achieved many of the advances in modern surgery. Particularly, in the field of gastrointestinal tract surgery, patients sometimes may not consume diets orally or enterally during perioperative period. TPN is the only way to meet metabolic demands in such cases.

However, along with the marked progress on surgical techniques and devices, it is now safe to restart oral intake of diets very soon after surgery, and this has become a very important part of early recovery programs. Moreover, guidelines on preop-

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Table 6.1 Summary of influences of nutritional routes on host defense mechanisms

	Oral intake or EN	PN
GALT mass	++	+
Gut IgA levels	++	+
Respiratory tract IgA levels	++	+
Hepatic MNC number	++	+
Hepatic MNC function	Preserved	Blunted
Peritoneal leukocyte number	++	+
Peritoneal leukocyte function	Preserved	Blunted
Endothelial cell activation	Normal	Activated without stimulation
Resistance to gut ischemia reperfusion	Preserved	Impaired

erative fasting have been revised worldwide, allowing patients to drink clear liquids until 2 h before surgery, which is also a factor in early recovery [1].

Why then is it so important to make the period of no enteral delivery of nutrients shorter? Many clinical studies, though the size is small, have demonstrated early EN in severely injured patients to be favorable for reducing infectious complications and hospital stays [2]. Many experimental studies have clarified theoretical reasons for the advantages of EN over PN during the last several decades. Part of the data in this review are from basic research. Once surgeons become aware of the beneficial influences of EN on host response to surgical insults and host immunity against hostile microbes, they may find that prescribing EN for their patients accelerates recovery after surgery.

6.2 Concept of Gut Starvation

Malnutrition is known to impair host defense mechanisms against various surgical insults. Appropriate parenteral administration of nutrients can prevent malnutrition-induced changes in host defense. However, even when adequate nutrients are supplied parenterally, the gut cannot obtain nutrients directly via gut lumen without EN. This condition can be described as "gut starvation." Gut starvation has been demonstrated to cause the following unfavorable changes (Table 6.1).

6.3 Gut Barrier Function

There are tremendous numbers of microbes in the human gut lumen. Some exert beneficial influences, while others are detrimental. Maintaining a balance of gut microbiota has thus become an important topic in science.

Under healthy conditions, the body can prevent microbes invading and hampering the gut barrier through various mechanisms, i.e., gastric acid, gut motility, mucus, tight junction between the mucosal epithelial cells, and immunological components. However, these barrier functions are compromised under stressful conditions, such that microbes can easily pass through the gut epithelium and cause systemic inflammation and/or infections, so-called bacterial translocation. Therefore, critically ill or severely injured patients may suffer from sepsis even when there are no evident sources of infections other than the gut. To prevent bacterial translocation and promote recovery from surgical stress, maintenance of gut barrier functions is essential during the perioperative period.

The gut physical barrier is compromised in the state of gut starvation. Gut morphological structure, such as villous height and crypt depth, shows atrophy and gut permeability rises during TPN. These changes were reported to be reversed by giving small amount of a low residual diet corresponding to more than 15% of total energy [3, 4].

Gut immunological barrier consists of antimicrobial peptides and immunoglobulin A (IgA) secreted from gut Paneth cells and IgA-producing plasma cells, respectively [5]. Figure 6.1 summarizes the barrier system which is called "gut-associated lymphoid tissue (GALT)." Antigens in the gut lumen are sampled by M cells and transferred into dendritic cells. The dendritic cells sensitize naïve lymphocytes recruited from the systemic circulation to Peyer patches (PPs). Sensitized lymphocytes move to mesenteric lymph nodes where they undergo proliferation and maturation and then return to the systemic circulation via the thoracic duct. A portion of the lymphocytes homes to the gut intraepithelial spaces and lamina propria (LP) for gut mucosal defense. Intraepithelial lymphocytes (IEL) secret various cytokines and growth factors and clear infected epithelial cells to maintain mucosal integrity. LP lymphocytes also produce various mediators, and some are transformed into IgA-producing plasma cells. IgA secreted into the gut lumen neutralizes microbes without marked inflammation. Other lymphocytes which home to extraintestinal mucosa, such as the respiratory tract and the urinary tract, protect the mucosal barrier. Therefore, preservation of GALT is good not only for gut mucosal defense but also for extraintestinal mucosal defense.

Using murine feeding models, influences of nutritional routes and types on GALT have been examined [5, 6]. Mice fed TPN for 5 days via jugular vein catheter (IV-TPN) showed significant reduction of GALT lymphocyte number in PPs, IE spaces, and LP and IgA levels in the intestinal washings as compared with mice fed identical TPN via gastrostomy, complex enteral diet (CED) via gastrostomy, or oral intake of a normal chow diet. IgA levels in respiratory tract washings were also lower in the IV-TPN than in the other groups. Absence of glutamine in the standard TPN fluids, reduced secretion of neuropeptides and interleukin-7, unbalance of Th1/Th2 cytokines in the gut, low expression of MAdCAM-1 on venules in PPs, and so on have been demonstrated to possibly be mechanisms underlying IV-TPN-induced impairment of gut immunity [7–10].

Kinetic studies of the GALT revealed that lack of enteral delivery of nutrients causes GALT atrophy and reduction of mucosal IgA levels in a few days and that restarting oral feeding also rapidly, in a few days, normalizes such changes [5]. These findings may provide the theoretical basis for minimizing the period of no per os intake in the program for early recovery after surgery.

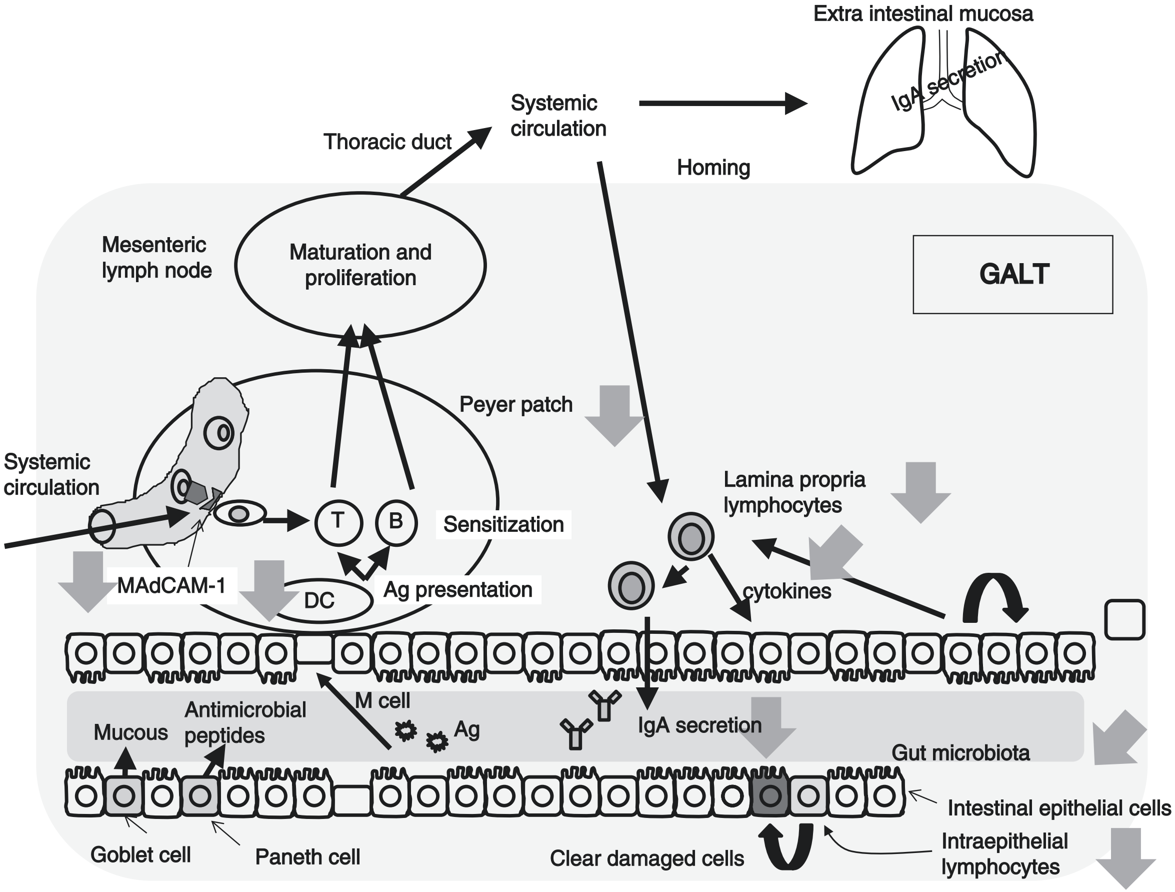

Fig. 6.1 GALT and influences of lack of EN. Lack of EN decreases GALT cell numbers (dendritic cells, PP lymphocytes, IE lymphocytes, lamina propria lymphocytes), MAdCAM-1 expression on venules in PPs, and IgA levels at mucosal sites, changes gut cytokine milieu and gut microbiota, and so on

Though gut morphological changes and permeability were completely normalized with small amount of enteral diet during TPN in rats, GALT atrophy may be improved EN dose dependently [11]. One of our animal studies demonstrated that supply of a higher ratio of EN/PN energy resulted in better preservation of GALT cell number when the total amount of energy given was the same.

These changes associated with lack of EN were confirmed in human as well [12]. Terminal ileum specimens from patients who underwent right colectomy for colon cancer treatment were analyzed using immunohistochemical staining. When patients were divided into two groups, oral feeding (OF) and no oral intake of food in those receiving only PN (PN) before surgery, the PN group showed significant loss of T cells in IE spaces and LP, IgA-producing cells in LP, and mature dendritic cells in LP as compared with the OF group. In association with the reduced GALT cell numbers in the PN group, the morbidity of postoperative infectious complications was higher in the PN than in the OF group.

Thus, avoiding gut starvation leads to preservation of gut physical and immunological barrier, which may prevent gut-origin systemic inflammation and infection. Moreover, extraintestinal mucosal defense is also maintained by using the gut as a nutritional route.

6.4 Hepatic Mononuclear Cells

The liver is the center of systemic metabolism but also acts as an important immune organ, because liver contains large number of immune cells, known as hepatic mononuclear cells (MNCs). Hepatic MNCs include T cells, NK cells, NKT cells, Kupffer cells, and so on, removing microbes and toxin which come from the gut via portal vein.

Animal studies have clarified that hepatic MNC numbers are markedly reduced during TPN as compared with EN, without significant differences in subpopulations [13]. In addition, hepatic MNCs isolated from parenterally fed animals cannot activate the intracellular signal pathway in response to lipopolysaccharide (LPS) stimulation, thereby showing blunted pro-inflammatory and anti-inflammatory cytokine production, while hepatic MNCs from enterally fed mice activate signaling and produce cytokines LPS dose dependently. These changes, attributed to lack of EN, were associated with poor survival and severe organ injury after intra-portal injection of live *Pseudomonas aeruginosa*.

Very interestingly, only 12 h of gut starvation results in reductions of hepatic MNC numbers [14]. In terms of the maintenance of hepatic immunity, avoiding gut starvation may also contribute to the prevention of infectious complications after surgery.

6.5 Peritoneal Leukocytes

Once an aseptic peritoneal cavity is contaminated with pathogens, peritoneal resident macrophages are activated through translocation of NFκB from the cytoplasm to the nucleus and produce pro-inflammatory cytokines and chemokines. These mediators cause massive influx of polymorphonuclear neutrophils from the systemic circulation to the peritoneal cavity. Exudative neutrophils phagocytize and kill pathogens employing superoxide and/or elastase production.

Absence of enteral delivery of nutrients decreases the numbers of peritoneal resident macrophages and exudative neutrophils as compared with EN [15]. Blunted NFκB activation in these cells and reduced peritoneal cytokine and chemokine levels were observed in TPN mice but not in those given EN, resulting in poor survival in cecal ligation and puncture-induced peritonitis models [16].

Therefore, avoiding gut starvation may serve to maintain the peritoneal host defense system against contamination by pathogens. Because macrophages and neutrophils are also important for preventing wound infection, EN might reasonably be expected to reduce the morbidity of surgical site infections.

6.6 Endothelial Cell Activation

In addition to the beneficial effects of EN on host defense against the infectious insults described above, EN may exert advantageous effects against noninfectious insults. When mice are fed EN, ICAM-1 and P-selectin expression on gut endothelial cells and E-selectin expression on lung endothelial cells remain low [17, 18]. However, TPN without EN significantly increases the expressions of these molecules. Since these adhesion molecules increase circulating neutrophil-endothelial cell interactions, eventually causing migration of neutrophils to tissue interstitium, increased expression of these molecules carry risks of tissue damage by excessively activated neutrophils. In fact, mice fed TPN showed higher vascular permeability in the lung and liver after gut ischemia reperfusion than enterally fed mice, resulting in shorter survival time [19]. Gut ischemia reperfusion is known to be an important mechanism underlying organ dysfunction following shock, massive bleeding, and major surgery. Taken together, these observations indicate that avoiding gut starvation may prevent tissue injury and organ dysfunction after severe hemodynamic disorders by controlling the expression of adhesion molecules on endothelium.

6.7 Conclusions

Avoiding gut starvation before surgery and early restart of oral diet or EN after surgery may maintain host defense mechanisms against both infectious and noninfectious insults, thereby promoting early recovery after surgery without severe postoperative complications.

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Part IV
Reduction of Perioperative Anxiety and Excitation of Recovery Will

Chapter 7
Reduction of Perioperative Anxiety Before Surgery and to Incentives to Get Well by Patients Themselves

Naohiro Washizawa

Abstract Consultation and education before admission to hospitalization are very important items of perioperative management. Anxiety related to surgery has a negative impact on the post-surgery recovery. The goal of a clinical course has to be as clear as a milestone must be understandable, because patients feel safe with that feeling of goal attainment. Surgical patients have to get not only understanding but also satisfaction for preparation to receive the surgical therapy.

Keywords Counselling • Education • Consultation • Anxiety

7.1 Introduction

Perioperative management, what is done empirically, the possible unnecessity, or what we mustn't do, is discussed. The ERAS (enhanced recovery after surgery) Protocol™ concept as a postoperative recovery strengthening protocol became popular in Europe [1], and it has become a hot topic along with fast-track surgery [2] as methods for eliminating negative factors involved in delaying recovery. There is inappropriate dissemination in Japan and in one's own environment, as well as with the Western world, as also in the ESSENSE (Essential Strategy for Early Normalization after Surgery with patient's Excellent satisfaction) project progress. Consideration of what is necessary to promote better recovery after surgery revealed the reduction of anxiety and providing patients with incentives to get well by themselves as voluntary rehabilitation.

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7.2 Consultation and Education Before Operation

Counseling before hospitalization is listed as one of the major items to be executed of in the ERAS Protocol™ [1], and it should include not only explanatory talk but also education to provide a positive effect of the perioperative course. Education, shared by medical staffs and practitioners such as counsellors, should be provided to promote early recovery or improvement. Such efforts can result in intrinsic satisfaction, with the expectation of a fast recovery. To promote a substantial early recovery, planners have to set the clinical goal of patients and medical staff.

Anxiety related to surgery has a negative impact on the post-surgery recovery. We can see situations of deterioration of wound healing due to rejected use of the affected area, as it would delay healing. If pain was a direct reason, the following [(1)–(3)] need to be analyzed for the relationships between cause and effect: (1) causes of pain in the affected area, (2) pathological abnormality in the affected area, and (3) delayed recovery of the affected area caused by factor (2). If the relationship can be identified, the use of painkiller might inhibit the recovery of the affected area. However, if factor (2) is independent of (3), the functional weakness, for example, limb muscle strength weakness, should be prevented by aggressive rehabilitation with medication.

After scientific verification of whether or not use would influence the affected area, aggressive perioperative management is planned. Patients have various anxieties before surgery. Doubt over whether the description of the disease and treatment information are correct or not, and whether one's clinical course is different from that of other patients, can affect to patients' anxiety. Incorrect disclosure of the clinical course of malignant disease caused by family misunderstanding can result in patient doubt.

Patients have fear not only of the disease and death, but they can also be anxious about complications that can lead to death. Mental anguish can cause the patient to be unable to see the apparent goals of treatment, and not knowing when suffering will end is a big problem. Mental stress triggers changes in immune function. Immune incompetence can lead to deterioration of wound healing and pain caused by the resulting physiological reactions [3]. Anxiety is enhanced by unknown situations caused by inadequate explanation of the preferable behavior of patients for their recovery.

Patients who feel less anxiety may have a lot of medical knowledge gathered from previous experiences. For example, experience from medical examinations of family members or previous surgical treatment of the patients themselves can prove informative for the next event. In other words, practical experience can encourage patients. "Preadmission information" and "counseling" in the ERAS Protocol™, written on paper as presented as oral information [1], should be made into a simulated experience. This requires detailed planning, and goal setting in a concrete plan should be presented base on policy decision.

Obtaining informed consent before medical procedures must be agreed upon and enforced if medical practice requires this. The information provided prior to treatment should advise patients of the risks involved; they should be fully briefed on the contents of the disease, treatment, duration of treatment, and healing of the surgery; and they should achieve an understanding that must be satisfied with the explanations. Furthermore, the next step of treatment, if the patient does not agree with the described plan and wants to transfer to another clinic, should also be attended by physicians. The legend might be to make the explanation uncomplicated to demystify the procedure in order to obtain the consent, but it cannot lead the patient's pure agreement because the physical experience is lacking.

To establish a simulated experience, the required education style should focus "when," "where," "who," "what," and "how" explanations. But, there has not been much prior research into this topic.

Accordingly, the practical subjects required for education concerning hospitalization are described below:

(a) When?

Consulting with someone and understanding the interval between prior to admission and the hospitalization day are essential. Education just before the surgery, just repeatedly describing the same content, is insufficient for allowing a deeper understanding. Information with different points of view can make the patient proactive during a period of reflection. On the other hand, although education on the operation date or postoperative day 1 or 2 can be understood as reality by the patients, it has the handicap of being less than convincing for the patients.

(b) Where?

For education before hospitalization, a communication room or outpatient examination booth is better than corridors because of less distracting noise and activity. After hospitalization, it is also better in a patient's single room than in a communication room.

(c) Who?

If the surgery itself causes anxiety, explanation by anesthesiologists and operating room nurses as representatives of the actual procedure in easy-to-understand terms is essential. If patients are concerned about the post-surgery recovery period, the surgeon or physician in charge of postoperative care and the ward nurse can explain the actual clinical resources. If some patients have an economic problem, clerical officers or social workers are adequate persons in charge of giving realistic explanations. Counselors will be needed to completely and skillfully settle the patient's anxiety before surgery.

This skill is important for stabilizing the patient's insecurity compared to explanatory skill in some cases. A clinical trial study focusing on coronary artery bypass surgery compared patients who were taken care of in rooms shared with another patient who had already undergone the same procedure and ones who were taken care of in single rooms. The anxieties in patients who were looked after in shared rooms were less severe than in those who were in single rooms [4].

Explanations by medical professionals in white coats or by description specialists are different from the education from a patient who underwent the same treatment in terms of a simulated experience. This is why a patient's talk is used to explain the method in folk medicine. Research on behavior without anxiety is guided by who can explain what is expected.

(d) What?

Whether or not it is reasonable to explain all events related to the surgery depends on the personality and/or social background of the individual cases. An explanation that is difficult to understand might give rise to growing uncertainty in recipient patients. However, it is difficult for us to recognize the patient's real understanding. Therefore, it is extremely important to teach the patient how to act in certain situations.

A report described 46 patients who underwent abdominal surgery and were educated about the types of postoperative pain and soothing techniques against pain by anesthesiologists, and they used about half the amount of pain-relieving medications compared to 51 abdominal surgery patients who had not received such education [5].

In the future, we need to make lists of the cases that caused inconveniences during their hospitalization by not understanding the explanations. The information should be as simple as possible. One of most items of education concerns postoperative intestinal paralysis, as delayed oral intake significantly affects the recovery time.

A clinical trial of intestinal peristalsis after gastrointestinal surgery was carried out. Forty patients were divided to two groups after receiving the general explanation for 10 min. One group (20 patients) received explanation of the pathophysiology of intestinal paralysis and physical therapy as solution for 5 minutes, and the other group was educated for 5 min without mention of the pathogenesis. There were significant differences in the starting time of postoperative intestinal peristalsis noise, gas flatus, drinking water, the date of removing away the nasogastric tube, and the duration of hospital stay [6].

Patients could take a postoperative care themselves in the recovery step which affects their clinical course. The new trial that the patients present their behavior toward recovery goal themselves and daily records should be made by themselves is starting in Japan.

(e) How methods?

Explanations written on paper or previously printed documents are commonly used. Diagrams and pictures can be good tools for removing fear of uncertain issues, as they can be supporting instruments for patients who cannot clearly understand the clinical course. Understanding can be expected to reduce anxiety, that is, bring one close to the actual experience as much as possible compared to theoretical content, and thereby increase the level of satisfaction, although this area of clinical research is still rare.

If the information is not changed to a useful style for the patients, their own comprehension cannot result in a medical benefit.

A study using a questionnaire about the recognition of perioperative management was carried out with 322 patients. There was a significant difference in the percentage of correct answers between the patients who had read the booklet before this survey (161 cases) and the other group (161 cases) who had not read the booklet [7].

The goal of a clinical course has to be as clear as a milestone must be understandable, because patients feel safe with that feeling of goal attainment. Medical staff should present the instruction of medical management after surgery based on a protocol that should be systematically ordered to provide a feeling of security. For example, the rehabilitation plan of walking three times around in the ward should be ordered as a much thinking plan as a personal observation. Comparable information documents across hospital policy in regard to general standards are needed because disparity between facilities might make a patient uneasy.

According to a meta-analysis, devices used in art education, booklets, manuals, tape recorders, and videotapes for low-budget education before operation reduced pain and decreased mental disability, with a tendency of many recovery indices also showing improvement [8]. A clinical study of the 74 patients (Group 1) who were educated indirectly with written paper worksheets between 2003 and 2008 and 74 patients (Group 2; 1998–2002) who were not given the worksheets reported that the hospitalization period was significantly longer in Group 2 compared to group 1 and pneumonia complications were significantly less in Group1 [9]. The goals of postoperative management will become clear by the movement of personnel and attitudes without direct explanations and must be also reassuring for patients.

The character or graphics and the verified effects of prior education based on photos and videos were expected also.

(f) Understanding and satisfaction

Because the operation is the treatment of obnoxious diseases. Incentives to get well from patients themselves are difficult to well up because the clinical goal differs from a delight. However, the result in a feeling of fullness when it approaches the envisioned goal as clear as acceptable can make the patient satisfied and pleasant. Satisfaction is required to be assessed as a halfway evaluation in the clinical process not only after the treatment.

Assessment tools should be standardized for uncomplicated recognition of each causal relationship in patients' understanding and psychological situation as well as actual behavioral indicators. Sometimes a "normal" answer is interpreted with low satisfaction in popular surveys of healthcare institutions caused by inappropriate evaluation.

When the treatment plan is operated by both patients and medical staffs with assessment of the achievement rate as a landmark and stress markers, the mutual psychological states of satisfaction affect each other, and this plan will make an ideal global recovery.

7.3 Summary

Concrete teaching of how to solve the problems of anxiety reduction and recovery drive will be effective. The education method should be executed regarding when, where, and who, about what tools are needed to be investigated for judgment of "satisfaction" not "understanding."

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Chapter 8
Perioperative Management for Early Recovery after Esophageal Cancer Surgery

Yoshihiro Nabeya, Isamu Hoshino, Matsuo Nagata, and Akio Sakamoto

Abstract The morbidity and mortality after esophagectomy remains high despite significant improvements in the surgical procedures and perioperative care over the last several decades. In the field of esophageal cancer surgery, enhanced recovery programs based on the enhanced recovery after surgery (ERAS®) or Japanese *ES*sential *S*trategy for *E*arly *N*ormalization after *S*urgery with patient's *E*xcellent satisfaction (ESSENSE) programs have recently been introduced and appear promising for achieving better outcomes. However, to date, such programs for early recovery after esophagectomy have lacked large-scale, prospective, multicenter evidence. At present, integrated perioperative care aiming at the prophylaxis and control of postoperative infectious complications (represented by anastomotic leakage as a surgical site infection and pneumonia as a remote infection) may be a top-priority component for not only early recovery from esophagectomy but also improvement of the long-term survival and postoperative quality of life. Among the available modalities, seamless enteral nutrition throughout the perioperative period is expected to play a central role. In addition, perioperative cancer rehabilitation and mental/social support should be kindly provided, particularly in elderly patients. Early recovery after esophageal cancer surgery may require the application of the latest knowledge and the perioperative practice of multi-occupational team medical care, according to the situation of each facility.

Keywords Esophageal cancer • Esophagectomy • ERAS® • Perioperative management • Postoperative infectious complication

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8.1 Introduction

Although endoscopic resection and chemoradiotherapy are widely performed today, esophagectomy remains a major means of treating esophageal cancer, especially as a part of multidisciplinary treatment [1–6]. Esophageal cancer surgery is known to be one of the most stressful gastrointestinal operations [2–9]. While minimally invasive esophagectomy (MIE) by thoracoscopic/laparoscopic approach has recently become widespread [6, 7, 10–12], three-field (cervical, mediastinal, and abdominal) lymphadenectomy (3FL), the standard operation in Japan, remains an extremely invasive surgery typically performed in high-risk patients [1–6], many of whom are heavy smokers and drinkers [6].

A recent development in gastrointestinal surgery is the implementation of enhanced recovery after surgery (ERAS®) programs [13]. ERAS® is a patient-centered, surgeon-led system provided by team medical care combining anesthesia, nursing, nutrition and psychology [13–17]. It aims at minimizing the surgical stress and maintaining the physiological function in perioperative management, thereby expediting recovery [13–17]. ERAS® programs were initially introduced for colonic surgery, and the implementation of ERAS® protocols has led to a reduction in the rate of postoperative complications and length of hospital stay [13]. However, the ERAS® theory is not commonly applied in esophageal cancer surgery, particularly 3FL, due to its surgical complexity and high morbidity rate [2–9], which limits the application of some ERAS® items. With the increasing prevalence of MIE or less-invasive surgical techniques, even for conventional open esophagectomy (OE) [2, 3], and perioperative care focused on enteral nutrition (EN), ERAS® has begun to be implemented in the field of esophageal surgery [14–17]. However, strong evidence of its advantages remains scarce, and there are little established data regarding which items should be achieved for such a stressful surgical procedure.

The "*ES*sential *S*trategy for *E*arly *N*ormalization after *S*urgery with patient's *E*xcellent satisfaction (abbreviated as ESSENSE)" is a project aimed at enhancing the physical recovery of patients after surgery in accordance with the actual situation in Japan [18] advocated by the Japanese Society for Surgical Metabolism and Nutrition (JSSMN). When deploying recommendations of 22 items in ERAS® protocols in Japan, the protocol should ideally not be adapted as it is but instead examined for the essential significance of each item in order to improve understanding of the basic components. The basic policy of the ESSENSE project is to "examine the essence of measures to promote postoperative recovery with patients' satisfaction while improving the safety of surgery." Its essential strategies are as follows: (1) Modulation of host response to surgical insults, (2) Early restoration of physical activity, (3) Early recovery of normal nutrition intake and (4) Encouragement of motivation for recovery with reduction of the anxiety [18]. Even in the management of esophageal surgery, these ideas should be shared among the medical staff.

Understanding perioperative management for early recovery after surgery requires clarifying the clinical goals and appropriate indicators of such management. Although the date (postoperative day: POD) of starting oral intake or the duration of hospital stay are often used as indices of early recovery [13–17], these indices may not always be appropriate. For example, the criteria of resumption of oral intake or discharge differ among the facilities, which can bias results. Such indicators may also depend on social factors or the wishes of the patient or their family and may therefore be indistinct. In clinical practice, the rate of postoperative complications should be kept as low as possible (physical early recovery), and the patient's satisfaction (spiritual early recovery) should be monitored carefully.

In this Chapter, recent topics of perioperative care are discussed in general. We also introduce the care delivered at the preoperative, intraoperative, and postoperative stage of esophageal cancer surgery.

8.2 Perioperative Management: General

8.2.1 Infection Control in Esophageal Surgery

The incidence of infectious complications after esophagectomy for cancer is still high in Japan [2–7]. In 5354 cases registered in the Japanese nationwide database (National Clinical Database: NCD) in 2011, superficial incision/deep incision/organ space surgical site infections (SSIs) developed in 7.7%/4.7%/9.2% of cases, respectively, and respiratory infection (pneumonia) as a remote infection (RI) occurred in 15.4% of cases after esophagectomy [6].

In gastrointestinal surgery including esophagectomy, incisional SSIs due to the exposure of digestive juice to surgical wounds and organ space SSIs mainly due to anastomotic failure may occur. MIE for esophageal cancer, the performance of which has begun to spread in recent years, may serve as a useful countermeasure against incisional SSIs because of the lower degree of exposure of digestive juice to the wounds as well as its lower invasiveness by minimizing the wound size. However, some contamination during operations may still occur, and the incidence of anastomotic leakage following esophagectomy is reported to exceed 10% [5–7, 12], causing SSIs (organ space) in MIE as well as in OE.

Thus, not only the prevention of anastomotic leakage (SSI) and respiratory infection (RI) but also the control of such infections once developed is important to achieve early recovery after esophageal cancer surgery [4–8, 12, 19]. However, the concept and operative procedures of esophageal cancer surgery differ markedly between the West and Japan, where 3FL is the standard procedure. Even in Japan, the surgical techniques and perioperative management differ widely among institutions and surgeons. Accordingly, there are few countermeasures against infections with high evidence levels, and it is difficult to establish a widespread standard of management. More realistic is the establishment of an infection control "bundle" that matches the surgical techniques and perioperative care of each facility and can be adapted to the condition of each case. Table 8.1 shows an example bundle against infectious complications (particularly SSIs) routinely performed at our institute now.

Table 8.1 Example bundle against infectious complications after esophagectomy for cancer (Division of Esophaogo-gastrointestinal Surgery, Chiba Cancer Center, as of 2017)

• Muscle-sparing thoracotomy without cutting the rib via short thoracic incision with endoscopic assist (intraoperative)
• Irrigation of wounds by saline before closing (intraoperative)
• Aggressive nutritional support for patients during NAC or at high risk before surgery (preoperative)
• Seamless enteral nutrition based on postoperative early enteral feeding via jejunostomy (pre- and postoperative)
• Individualization of postoperative nutritional support and meals based on the swallowing function (postoperative)
• Professional oral care by an expert dentist (pre- and postoperative)

NAC neoadjuvant chemotherapy

8.2.2 Perioperative Cancer Rehabilitation

For thoracic surgical patients, active intervention by the rehabilitation team before and after operation is necessary for early recovery [20–23]. Elderly patients with various co-morbidities and a low physical ability are particularly likely to develop several complications during the perioperative period. It is necessary to thoroughly evaluate and carry out training with "preoperative preventive" rehabilitation, and "postoperative restorative" rehabilitation should be started early after surgery to avoid waste atrophy due to lying down or the development of complications [20–23]. The surgical cancer rehabilitation for esophagectomy should be performed comprehensively by multi-occupational, team-oriented medical care [20–25].

Concretely, the perioperative rehabilitation for esophageal cancer patients should mainly aim at minimizing the surgical damage to the respiratory system, as "respiratory rehabilitation" [20, 21], as well as to resolving issues of dysphagia, as "swallowing rehabilitation" and oral care [22–26].

The aging of the population and aggression of surgical indications may increase the proportion of elderly patients undergoing esophagectomy for cancer. However, elderly patients have an insufficient physical/mental capacity and therefore may have an increased incidence of postoperative complications compared with younger patients. By reducing the rate of postoperative complications and preventing waste syndrome, aggressive perioperative rehabilitation may help improve the patients' quality of life (QOL) as well as shorten the hospitalization period, resulting in early recovery in elderly patients after esophagectomy. However, there has been no definite evidence supporting an effective rehabilitation approach and duration, and its implementation can often be difficult due to issues with personnel and the rehabilitation regimen.

8.2.3 Clinical Pathway

A clinical pathway (CP) including a rehabilitation program was recently introduced in the perioperative management of esophageal cancer surgery. However, the morbidity rate is high for the highly invasive surgery that elderly patients with a smoking and drinking history or co-morbid diseases often receive after preoperative chemoradiation therapy [1, 2, 5–7], and carrying out "standardized" care according to the CP prescribed beforehand in the days after operation can be difficult to apply in some cases. We often need "individualized" management throughout the perioperative period (Table 8.1) for early recovery after esophagectomy.

8.3 Preoperative Management

Esophageal cancer surgical patients should receive adequate preoperative treatment, including regular consultations by a dietician for the assessment of supplemental feeding [4, 27–31] and by a physiotherapist [20], especially from the start of neoadjuvant therapy [30].

8.3.1 Nutritional Care: When and How?

Many patients with esophageal cancer already have some passage disturbance and weight loss at the first visit. We must therefore make a nutritional assessment and consider the need for nutritional intervention, as well as accurately stage the cancer. In Japan, many esophageal cancer patients suffer from squamous cell carcinoma (SCC), and preoperative chemotherapy (neoadjuvant chemotherapy: NAC) has been employed as a standard treatment for patients with stage II/III esophageal SCC [1]. The start of proper nutritional support along with NAC may be mandatory, to maintain or improve the patients' general condition and ensure they undergo operations in a good condition [4, 27–30] (Table 8.1). Even if patients receive esophagectomy without NAC, they should still undergo a comprehensive nutritional assessment before any operation.

Attention must be paid to the continuation of oral intake in advanced esophageal cancer patients, especially those with stenosis at the upper part of the esophagus, who should be recognized as a high-risk group for developing aspiration. Such patients often need individualized meals of the appropriate amount, texture and content, or the restriction of oral feeding. The possibility of bleeding must also be considered. Therefore, physicians need to share information with other staff members, such as dietitians, nurses and pharmacists in charge of the patient, and plan to implement timely, appropriate nutritional management. The authors start nutritional intervention via EN or total parenteral nutrition (TPN) in cases with any of the following: (1) body weight loss ≥10%, (2) inability to ingest rice gruel meal sufficiently, (3) an extremely unbalanced diet (4) a possible risk of bleeding or perforation by eating, based on the findings of previous reports [28]. The serum albumin level may not necessarily low in cases of dehydration in advanced cancer patients at the first medical examination; as such, this factor may not necessarily be appropriate as an indicator of the nutritional status. In cases with a history of weight loss, we calculate the target energy requirements for improving the nutritional status (a simple formula of “ideal body weight × 30 kcal/kg/day” may be used [32]) and determine the amount of energy that can be ingested orally. The excluded portion is then administered with EN or TPN as artificial nutrition.

Physiological EN is thought to be excellent as a preventive measure against bacterial translocation and may play a role in infection control. Therefore, it is ideal to insert a nasogastric tube beyond the stenosis into the stomach or intestine and to perform nutritional management with EN. There are many doctors who think that TPN should be avoided whenever possible due to the risk of complications. However, supplying sufficient nutrients to surgical patients via the enteral route alone is sometimes unavoidable, and we must also consider the risks of discomfort with a nasal catheter, skin disorders due to fixation and aspiration. A previous study found that combined nutritional therapy (CNT), the concomitant use of EN with PN (by administering EN at 10–15% of total energy in addition to TPN of the excluded portion) and the administration of some nutrients such as Glutamine-Fiber-Oligosaccharide (GFO®) enteral formula in addition to TPN improved the morphological and functional changes in the intestinal mucosa associated with TPN [33–35]. Therefore, CNT centered on TPN plus a small amount of oral nutritional supplement should be considered in patients with esophageal stenosis. In addition, many patients are complicated with diabetes, so preoperative nutritional management and blood glycemic control using TPN with insulin may be safe in some cases. However, as the overall condition can change during preoperative therapy, the content, target, and method of nutritional support should also be revised as necessary.

The nutritional status and risk of infection must be monitored frequently during NAC, and medical care by a nutrition support team (NST) or infection control team (ICT) including dentists, nurses, dietitians and pharmacists, should be applied facility-wide at the start of NAC. Nutritional support by a dietitian during NAC has been reported to reduce the rate of postoperative complications after esophagectomy [29], and the significance of comprehensive team medical care for early recovery after esophageal cancer surgery is expected to increase further.

In recent years, bioelectrical impedance analyses (BIAs) have rapidly popularized body composition analyzers, and a body composition analysis can be performed relatively quickly [30, 31]. Changes in the body composition parameters during NAC or preoperative sarcopenia (low skeletal muscle mass) have been reported to be potential predictive markers of postoperative complications after esophagectomy for cancer [30, 31]. However, further analyses are needed to clarify whether or not nutritional intervention improves such parameters or skeletal muscle mass, contributing to a reduction in the postoperative morbidity. The necessity and indications of nutritional intervention for the prophylaxis of postoperative infectious complications has yet to be clarified using body composition analyses.

8.3.2 Immunonutrition: Useful for Reducing Infectious Complications?

The preoperative administration of an immune-modulating diet (IMD), used almost synonymously with immune-enhancing diet (IED; i.e. immunonutrition), has been highly anticipated for more than 10 years as a tool of nutritional intervention to prevent postoperative infectious complications [36–39]. Immunonutrition is also recommended in the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, particularly in the perioperative management of major gastrointestinal surgery, such as esophagectomy [40]. In Western studies, preoperative immunonutrition was reported to increase the host defense and decrease the rate of postoperative infections complications. However, no randomized controlled trial (RCT) of a large number of esophageal cancer surgical cases has been conducted in Japan, and previous studies have not demonstrated a positive effect of immunonutrition on reducing postoperative infectious complications in esophageal surgery [36–39]. Surgical techniques and perioperative management differ among the facilities or surgeons, making it difficult to conduct a prospective, multicenter cooperative RCT.

An RCT of 53 patients revealed that the pre- and post-operative administration of enteral formula enriched with eicosapentaenoic acid (EPA) was associated with the preservation of lean body mass after esophagectomy compared with a standard formula, but no significant difference in the incidence of major complications was shown [41]. While preoperative IMD suppressed the elevation of the TNF-α levels, no significant difference was observed in the levels of IL-6 or CRP or the rate of postoperative complications after thoracoscopic esophagectomy in patients with esophageal cancer [38]. The potential benefits of immunonutrition have therefore been suggested as a measure for early recovery. However, as esophageal cancer surgery has become considerably safer than in the past [9], there is currently insufficient evidence recommending the routine use of IMD in patients undergoing esophageal cancer surgery from a cost-effectiveness perspective. IMD may be worth trying in high-risk patients who can drink IED/IMD before surgery [39, 40].

8.3.3 Control of Blood Glucose Levels

Hyperglycemia may increase the risk of postoperative infections, but patients are often unaware of having impaired glucose tolerance (IGT), including diabetes mellitus (DM). The levels of blood sugar and urinary sugar at the first visit should always be checked for potential IGT. In esophageal cancer patients as well as general surgical patients, fasting blood glucose <140 mg/dL, urine sugar <10 g/day, urinary ketone body-negative status and hemoglobin (Hb) A1c <7.0% (NGSP) may be used as preoperative target levels [42]. When the preoperative fasting blood glucose is >180 mg/dL, we should consider starting insulin therapy [42)]. HbA1c

<7% has also been shown to decrease the rate of infectious complications in several types of surgeries [42]. However, attention should be paid to a previous report that patients without a history of DM (stress hyperglycemia) experience worse outcome and higher mortality at a glucose level the same as that for those with a known history of DM, suggesting a lack of adaptation to acute hyperglycemia and its associated inflammatory and oxidative state [43]. Maintaining stable blood glucose levels may be important for early recovery from stressful esophageal cancer surgery.

While steroids are usually used for chemotherapy-induced emesis during NAC for esophageal cancer, they may sometimes cause inadequately controlled hyperglycemia before surgery, particularly in cases with IGT or DM [44]. In addition, if NAC is successful, more meals can be eaten, resulting in more weight gained and potentially a worsened glucose tolerance when performed in combination with steroid use. Thus, changes in the levels of blood glucose, HbA1c and oral intake should be monitored during NAC. Prophylaxis of hyperglycemia throughout the perioperative period is desirable as an infection countermeasure.

8.3.4 Rehabilitation, Oral Care and Communication with Patients

Before surgery, patients should not only be educated on breathing or swallowing exercises but also given an outline of the entire surgical process so that they can imagine the procedure themselves. This support may improve respiratory practice and physical fitness before surgery and encourage voluntary rehabilitation early after such an invasive operation. Smoking cessation must be encouraged from the first visit and continued during preoperative treatment. Preoperative comprehensive rehabilitation involving physiotherapists may contribute to a reduction in the rate of postoperative respiratory complications. Indeed, it was reported that the rate of postoperative respiratory complications was reduced [20] and the hospitalized period was shortened [21] in thoracic surgery patients who had been instructed and trained for their preoperative respiratory rehabilitation. At our institution, we ask for a physiotherapist's guidance (particularly for effective discharge of sputum and abdominal breathing) whenever possible in addition to delivering respiratory training by incentive spirometory (Coach 2®), and preoperative rehabilitation is performed during hospitalization for about seven days before the operation. It may be desirable to assess the swallowing function prior to surgery by a repetitive saliva swallowing test (RSST) or modified water swallow test (MWST) [25].

Perioperative oral care has recently been expected to reduce the rate of postoperative respiratory complications in patients undergoing surgery (Table 8.1). For example, preoperative dental brushing reportedly reduced the risk of postoperative pneumonia after esophagectomy [26]. Further evidence on appropriate methods and periods of oral care are expected to be gathered in the near future.

Obtaining detailed personal information, such as the patient's lifestyle, work or hobbies, via interview may also be useful for considering the postoperative rehabilitation regimen and guidance at discharge. Communicating with patients throughout rehabilitation from the preoperative stage seems to motivate their recovery with reduced anxiety, a key concept of the ESSENSE project [18].

8.4 Intraoperative Management

Intraoperative surgical procedures and management that minimize surgical stress are essential for early recovery. Surgeons should always be conscious of the need for infection control, particularly the prevention of anastomotic leakage (SSI) and respiratory complications (RI).

8.4.1 Surgical Procedure: MIE as a Less Invasive Surgery?

MIE is expected to suppress SSI development as well as the surgical stress/invasiveness by minimizing disruption of the thoracic/abdominal walls. In addition, several reports have shown that MIE is associated with decreased blood loss [6, 10, 11]. However, Japanese nationwide NCD data demonstrated that the reoperation rate as well as the overall morbidity, particularly the incidence of anastomotic leakage, was significantly higher in the MIE group than in the OE group [6]. Therefore, while MIE is increasingly popular and appears to have at least equivalent outcomes to OE [10, 11], we have no definite data yet concerning whether or not MIE is truly "minimally invasive" or its superiority to OE for early recovery after surgery. Progress in surgical techniques and increased safety over time is anticipated in any procedure for esophagectomy. Even in OE, we have shortened the required thoracic incision and reduced the invasiveness of thoracotomy with the adequate use of endoscopic assistance or energy devices, and wound irrigation should be enforced (Table 8.1).

8.4.2 Intraoperative Management

The authors reported previously that our devised surgical procedures were effective in minimizing the surgical invasiveness and improving the postoperative clinical course in patients undergoing OE for cancer [2, 3, 45]. In particular, perioperative steroid use is recommended in esophageal cancer surgery to reduce the "surgical stress" of the patients [45]. However, the administration of steroids might conversely suppress wound healing and patients' immune defenses after "highly invasive" esophagectomy. As a result, patients with impaired immunological-competency may experience additional postoperative complications, particularly infectious complications, with the use of perioperative steroid therapy. However, it has been reported that perioperative steroid pulse therapy can maintain low serum CRP levels without severe complications, improving not only the short-term outcomes but also the long-term prognosis [46]. Our patients therefore routinely receive 250 mg of intravenous methylprednisolone at the start of thoracotomy and on POD1, followed by 125 mg on POD2.

Maintaining intraoperative blood glucose levels in the 140–180-mg/dL range is recommended, and minimizing blood glucose variability during surgery may be important [42].

Antimicrobial prophylaxis should be properly administered from the start of operation. Although short-course antimicrobial administration of cefmetazole sodium (CMZ) only on the day of surgery has been reported to be sufficient for the prevention of infectious events after 3FL [47], there is no definite evidence yet as to how long a given antibiotic drug should be administered.

8.4.3 Anesthesia and Thermoregulation

As issues of intra-operative care for postoperative early recovery, anesthesia should be optimized, fluid transfusion should be controlled properly, less-invasive and suitable operation methods should be used, and intraoperative hypothermia should be avoided [48, 49].

Current topics of anesthesia for esophagectomy have recently been reported by Durkin et al., as follows [48]: Lung protective ventilation reduces pulmonary complications in most cases of esophagectomy, requiring one-lung ventilation. The relationship between circulatory dynamics during surgery and postoperative infection is not clear. However, excess fluid administration may contribute to morbidity and be a cause of infection during the subsequent course, while restrictive approaches have not resulted in an increased risk of acute kidney injury. The significance of goal-directed fluid therapy remains unproven. Thoracic epidural analgesia may reduce the systemic inflammatory response and pulmonary complications, and may enhance postoperative pain control, while perioperative hypotension potentially caused by epidural analgesia may be associated with anastomotic leaks. Enhanced recovery pathways, including improved anesthesia protocols, have helped bring about low morbidity and mortality rates in high-risk populations undergoing esophagectomy; however, these populations are heterogeneous, and the findings are still limited by a weak evidence base [48].

Prophylaxis for anesthesia-induced hypothermia in thoracic surgery is based on previous studies including thoracoscopic esophagectomy [10] that have demonstrated benefits in postoperative outcomes. It has been reported that administering amino acids with intraoperative warming during the thoracic surgical procedure prevented hypothermia and reduced the rate of postoperative infectious complications after MIE [49]. Thermoregulation in anesthetic practice may play an important role in early recovery after MIE [49].

8.5 Postoperative Management

8.5.1 Principal Goal

Postoperative care for early recovery after esophagectomy should be focused on measures against infectious complications, which can be divided into "prophylaxis" from the preoperative stage and "early diagnosis and treatment" in the postoperative course [4–8, 12, 19]. "Prophylaxis" is mainly the prevention of respiratory infectious complications as RI [12], and "treatment" requires the early detection of and appropriate response to complications [19].

The ESSENSE project is a methodology (almost synonymous with fast-track surgery) focused on self-reliance early after surgery with a clear awareness of "patient condition" obtained by intervention; it is also an infection countermeasure [18]. As specific goals in esophageal cancer surgery according to this concept, the program aims at achieving extubation just after surgery, promoting early leaving bed and rehabilitation with sufficient analgesia, and helping prevent aspiration pneumonia as well as delivering early swallowing training.

8.5.2 Nutritional Care: Necessity and Management of Enteral Nutrition

8.5.2.1 Necessity of Enteral Nutrition Support

One of the cornerstones of the early recovery program is shortening the fasting time of patients during the perioperative period; a number of elements are therefore recommended to avoid disturbing these attempts at reducing the fasting time [13–18]. Unlike colonic surgery, even after esophagectomy which is likely to cause some trouble in postoperative oral intake, there is a tendency to aim for resumption of eating as soon as possible after operation using elements from the ERAS® program [14–17]. However, it is often impossible to do so safely, due to the high risk of aspiration. In addition, even if oral ingestion can be well-achieved, it is unlikely that the total energy individual patients require can be sufficiently ingested in the early stage after esophageal cancer surgery. Therefore, postoperative EN using jejunostomy may be recommended early after esophagectomy without expecting oral intake, at least in cases at risk of preoperative malnutrition or in high-risk cases, such as the elderly.

Several studies have shown that postoperative early EN may be valid for early recovery from esophageal surgery [12, 40, 41, 50–52]. Nevertheless, the placement of a jejunostomy during the operation may be a hurdle to increasing the use this type of catheter enteral feeding, as surgical complications due to jejunostomy can occasionally occur. In addition, previously some doctors thought that enteral feeding was always unnecessary for patients undergoing MIE, since sufficient oral intake could be resumed early and safely after performing MIE. However, esophagectomy followed by reconstruction itself is a highly invasive procedure, and even MIE can cause serious complications that affect the postoperative oral intake [6, 11, 12]. An RCT recently showed that the rate of postoperative pneumonia decreased from 30.4% to 12.5% by postoperative early EN (via jejunostomy), even in patients undergoing MIE [12]. The need for catheter enteral feeding may depend on the surgical procedure or the postoperative course at each facility.

8.5.2.2 Early Enteral Nutrition

In clinical practice, it has recently been recommended that catheter feeding be started from POD1-3 and that patients may receive a standard formula with a gradually increasing daily dose [40, 50, 51]. It may take five to seven days to reach the target intake, as described previously [40, 50, 51]. The authors routinely start catheter EN from POD1 as seamlessly as possible during the perioperative period of esophagectomy, and no standard TPN is used perioperatively (Table 8.1). Early EN using a low-fat elemental formula (ELENTAL®) after esophagectomy has been reported to be valid for postoperative recovery and potentially useful in the prophylaxis of pneumonia and chyle leak [12, 52]. The perioperative administration of EPA-enriched formula has been reported to help preserve lean body mass after esophagectomy [41]. However, in most patients undergoing esophageal cancer surgery, a standard whole-protein formula is appropriate [40, 50, 51].

8.5.3 Resumption of Oral Intake: When and How to Start Oral Intake?

We should always keep in mind, "when the gut works, use it!" However, after esophagectomy, the issues of when to start oral intake in patients, what type of diet to try first, and how to train ingestion are still controversial. One ongoing clinical trial (NUTRIENT II) is reportedly investigating two different strategies of postoperative feeding after esophagectomy: early oral feeding versus enteral feeding via jejunostomy and delayed oral feeding [53]. The primary outcome measure is functional recovery, such as the restoration of mobility to an independent level, the ability to maintain sufficient energy intake, and a lack of signs of active infection. The results of this study will clarify whether or not the early initiation of oral diet following esophageal surgery can really improve postoperative recovery. This study presages potential future benefits, including less discomfort due to jejunostomy feeding and its potential complications, and the improvement in the QOL via early start of oral intake [53].

In order to prevent aspiration pneumonia due to meals, it is considered useful to evaluate the swallowing function before starting oral intake and to conduct postoperative rehabilitation [22–25]. Our patients usually start oral ingestion after the absence of anastomotic leakage is confirmed and the swallowing function is evaluated on POD7. Individualized postoperative meals are then offered based on the assessed swallowing function and general condition (Table 8.1), which may contribute to the prevention of severe aspiration pneumonia. Specifically, the patients receive a semisolid diet or gelatin-based foods such as jelly first, followed by solid foods a few days later, in accordance with a recent report that postoperative esophageal cancer patients are more likely to aspirate liquid than solid foods, such as jelly [24]. While the daily amount of catheter EN gradually decreases with increasing oral nutrition, enteral feeding remains necessary to supplement unstable, insufficient oral intake, resulting in "early recovery of normal nutrition intake" [18].

When to stop tube feeding is another issue that remains to be resolved. The authors usually ask the patients to continue tube feeding for approximately three months after their operation. However, its continued use is often necessary to support the daily energy needs that cannot be met with oral nutrition alone, even if a long time has passed since esophagectomy.

8.5.4 Prophylaxis of and Early Recovery from Postoperative Complications

The major postoperative complications after esophagectomy are anastomotic leakage (organ space SSI) and respiratory complications (RI) [2–8, 11, 12, 19]. Because patients who develop such complications sometimes die from them, prophylaxis is extremely important. For early recovery, the principle for treating postoperative infectious complications involves proper drainage, antibiotic administration and nutritional care using EN whenever possible.

8.5.4.1 Drainage

Postoperative anastomotic leaks, particularly after intrathoracic anastomosis, and subsequent mediastinal abscess are serious complications. In such cases, naso-esophageal extraluminal drainage (NEED) and concomitant EN support have been reported to be less-invasive and effective and powerful methods of treating even major leakage and improving recovery after esophagectomy [19].

If pneumonia develops, aspiration of sputum by bronchoscopy and breathing exercises should be carried out as necessary in order to prevent atelectasis and deterioration of infection. However, in severe cases, the authors should not hesitate to perform tracheostomy for early recovery. Mini tracheostomy with Mini-Track II®, which can be inserted relatively safely, is useful for suctioning sputum in a timely manner.

8.5.4.2 Antibiotic Administration

In cases of infection, a culture of pus/sputum should be submitted more than once in order to identify pathogenic bacteria, and appropriate antibiotics should be selected based on the results. *Pseudomonas aeruginosa*, fungi such as *Candida* and methicillin-resistant *Staphylococcus aureus* (MRSA) should be kept in mind as potential causative pathogens [54], and the authors often use carbapenem-based antibiotics as empiric therapy for infections that develop after esophageal cancer surgery. *Candida* may persist in patients receiving chemoradiotherapy before surgery, and the possibility of *Candida* colonization/proliferation should be considered particularly likely in such patients with postoperative anastomotic leakage [54].

8.5.4.3 Therapeutic Nutritional Care: Enteral Nutrition Is the Basis

In patients with complications, the standard enteral formula may be replaced if necessary, according to the disease condition. A low-fat elemental formula should be used to treatment as well as to prevent chyle leak [52]. The authors often use low-potassium-containing formula (for renal failure, RENALEN LP/MP®) for patients with hyperkalemia and fat-rich formula (Pulmocare®-Ex) for those with postoperative pneumonia. These disease-specific formulae may be useful for individualized care due to the variety of postoperative courses of esophageal cancer surgery. In addition, various medicines and water can be administered via a feeding tube.

If no EN catheter has been placed after operation, patients with complications, including anastomotic leakage, should be managed with TPN until the infection is controlled. A feeding catheter may then be inserted nasally through the anastomosis, at which point EN can be started [19]. TPN should be subsequently replaced with EN to promote early recovery and cure. When TPN is required for infectious complications after esophagectomy, care must be taken to avoid the development of catheter-related bloodstream infection.

8.5.5 Postoperative Rehabilitation and Oral Care

8.5.5.1 Respiratory Rehabilitation

Although there are many types of programs available after esophageal cancer surgery, depending on the facility, the major purpose of respiratory rehabilitation after esophageal cancer surgery is to prevent dependent lung disease (DLD) caused by patient immobilization [55]. In addition, reductions in the pulmonary function due to pain, anesthesia, and sedation may become a problem. Adopting an active sitting posture and practicing standing/walking from the early postoperative stage may prevent DLD and increase the ventilation volume. Good evidence indicates that lung expansion modalities (e.g. incentive spirometry, deep breathing exercises, and continuous positive airway pressure) reduced the rate of pulmonary complications [56]. It was also reported that the prone position improved the arterial oxygenation without any deleterious effects in hypoxemic patients after esophagectomy with 3FL for cancer, due to opening of the bronchi obstructed by secretions [55].

After the critical phase, training for discharge such as exercise via walking with gradual extension of distance, bicycle ergometers, and stair climbing should be recommended, according to the patient's condition.

8.5.5.2 Swallowing Rehabilitation and Oral Care

Postoperative rehabilitation begins with indirect swallowing training without ingesting food and then proceeds to direct training using food, with adjustment for the food consistency, bite amount and eating pace for each patient. Swallowing rehabilitation is usually conducted in earnest starting approximately one week after surgery, after confirming a lack of anastomotic failure. The postoperative swallowing function is evaluated by a videofluoroscopic examination of swallowing (VF) or videoendoscopic examination of swallowing (VE) [22–25]. It has been shown that swallowing dysfunction remains a common problem even after MIE, and silent aspiration likely contributes to pneumonia after MIE with cervical anastomosis [23]. Since VF has been reported to be very useful in determining suitable food textures for postoperative esophageal cancer patients [24], swallowing training should be carefully conducted while monitoring silent aspiration with reference to the VF findings.

Swallowing rehabilitation to prevent pneumonia can be achieved by team medical care (cooperation with multiple occupations, such as dieticians, nurses, and pharmacists as well as speech therapists and physicians). As previously reported, rehabilitation including complementary measures, such as appropriate reclining posture and selection of food consistencies, may be beneficial for postoperative swallowing disorders after esophageal cancer surgery [22]. Patients who develop paralysis of the bilateral recurrent laryngeal nerves require careful management and rehabilitation to avoid developing aspiration pneumonia [22, 57].

Postoperative oral care, particularly after resumption of eating, may also be important for preventing aspiration pneumonia.

8.5.6 Mental/Psychological Support

Even after giving their informed consent, most esophageal cancer surgical patients cannot predict the magnitude of surgical stress and physical changes before actually undergoing the surgery. Therefore, psychological guidance should be provided in order to encourage recovery motivation and aim for early recovery of the function and reintegration.

Elderly patients in particular should be provided individualized support from mental (spiritual) and social as well as physical aspects immediately after esophagectomy for early recovery. To this end, assistance via multi-occupational collaboration including NST, psychiatrists and medical social workers may be necessary. Family support is also indispensable.

8.6 Conclusion

In the field of esophageal cancer surgery, enhanced recovery programs focusing on seamless enteral nutrition appear promising, and countermeasures against postoperative infectious complications may be extremely important. However, further scientific evidence will likely be accumulated in the near future. Multi-occupational team medical care including perioperative cancer rehabilitation and mental/social support may be essential, particularly in elderly patients.

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Chapter 9
ERAS for Gastric Surgery

Ryoji Fukushima

Abstract The enhanced recovery after surgery (ERAS) protocol first established in the colorectal surgery has now been extended to application to various types of surgical procedures such as gastrectomy. Many gastric surgeons consider that it is feasible and useful to apply most of the ERAS elements to gastric surgery, but one of the greatest concerns for gastric surgeons is early postoperative feeding, especially early oral feeding.

The evidence to date now shows little concern of increased morbidity by early oral feeding in gastric surgery patients. However, in contrast to colonic surgery, preoperative malnutrition is more frequent, and postoperative intake is more restricted in gastric surgery patients even though they can eat early in their postoperative course. Thus, some patients need an individualized approach because of these specific characteristics of gastric surgery that differ from those of colonic surgery. Early enteral tube feeding is a good option for those with preoperative malnutrition and those predicted to have poor oral intake after surgery. Also, patient-controlled feeding (selection of diet by patients) seems promising and should be further investigated.

Keywords Early oral feeding • Early enteral tube feeding • Patient-controlled feeding

9.1 Introduction

The enhanced recovery after surgery (ERAS) protocol, which was first introduced for the perioperative care of colorectal surgery patients, integrates a number of perioperative interventions to accelerate recovery after surgery. It aims to attenuate the surgical stress response to reduce the time required for full recovery after surgery and also reduce postoperative complications. The main components of the protocol

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are intensive pain control, early mobilization, and early oral feeding [1, 2]. Several prospective randomized studies have shown the ERAS protocol to decrease morbidity and the length of postoperative hospital stay after colorectal surgery [3]. Now, the protocol has been extended to application to various types of surgical procedures other than colorectal surgery, such as gastrectomy [4–7].

Many gastric surgeons consider that it is feasible to apply most of the ERAS elements to gastric surgery, but one of the greatest concerns for gastric surgeons is early postoperative feeding, especially early oral feeding. In this chapter, the issue of early oral feeding after gastrectomy is discussed.

9.2 Elements of ERAS That Enhance Early Oral (Enteral) Feeding After Surgery

The traditional approach to reinstitute oral intake in patients who have undergone intra-abdominal surgery has been to wait until bowel function returns to normal, i.e., resolution of postoperative ileus. In most cases, this is confirmed by the passage of flatus or stool. In fact, evidence shows that the time to recover motility is 6–12 h for the small intestine, 12–24 h for the stomach, and 48–120 h for the colon [8]. Thus, theoretically, oral food can be allowed by 12–48 h postoperatively when the stomach starts to undergo peristalsis. However, it is known that peristalsis of the resected stomach is disturbed, especially during the early postoperative period [9].

In any case, in order to feed patients early after surgery, postoperative ileus has to be minimized. The ERAS protocol involves a series of interventions to achieve this goal and thereby facilitate early recovery of oral feeding (Fig. 9.1). Avoiding the use of opioids for analgesia during and after surgery while encouraging the use of epidural analgesia is part of the ERAS strategy to minimize postoperative ileus. Sympathetic nerve stimuli that may lead to restricted bowel function can be blocked by epidural administration of local anesthetic agent.

Excessive fluid administration leads to water accumulation in the extravascular compartment, resulting in tissue edema. This affects intestinal function and delays the postoperative return of peristalsis. Moreover, overload with crystalloids significantly increases the complication rate, including anastomotic dehiscence [10]. To avoid this, restricted fluid therapy is essential during the operation, and to achieve

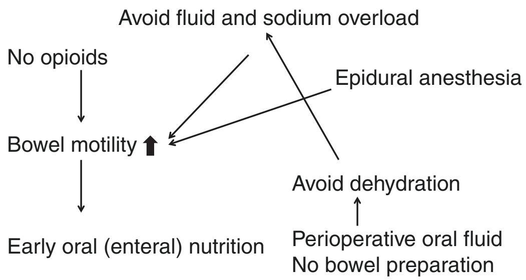


Fig. 9.1 Measures to enhance postoperative early oral (enteral) feeding

this, preoperative dehydration should be strictly avoided. In the ERAS protocol, in contrast to the traditional overnight NPO (nil per os) strategy, solid food is allowed until 6 h before the induction of anesthesia and water until 2 h before. Also, mechanical bowel preparation has the potential to produce dehydration before surgery, and this is one of the reasons for the ERAS recommendation to omit mechanical bowel preparation before surgery.

Early enteral feeding itself on the other hand may stimulate bowel motility. Allowing patients to drink desired amounts of fluids on the day of surgery was also reported to partially eliminate the need for intravenous fluid administration [11].

9.3 Early Oral Feeding After Gastrectomy

In colorectal surgery, early postoperative oral feeding is accepted by many surgeons. However, upper GI surgeons have been more reluctant to allow anything by mouth in the early postoperative period. This may be based on concern about gastric distention and anastomotic soundness. It is known that peristalsis of the resected stomach is disturbed [9]. After gastric surgery, food passes through the small remnant stomach and newly constructed anastomosis before being fully digested. The distended stomach may put tension on the anastomosis. Thus, instead of oral feeding, postoperative early enteral tube feeding has often been used when needed. The tube can be placed in a jejunal segment distal to the new anastomosis, and this can resolve the concerns of conservative surgeons. Enteral tube feeding has been shown to be beneficial in upper GI surgery patients [12]. However, it needs time to construct tube jejunostomy [13], and in addition, rare but serious complications related to tube jejunostomy feeding can occur [14].

The evidence now shows little concern of increased morbidity by early oral feeding in uncomplicated gastric surgery patients. A case-control study from Japan compared early oral feeding and traditional care after gastrectomy in 100 patients. Patients in the early group began a liquid diet within 48 h after operation, and patients in the traditional group received nil per os until the resolution of ileus. They found early oral feeding after gastrectomy to be feasible and to show no evidence of increased morbidity such as vomiting, abdominal distention, anastomotic leakage, or wound infection. Early oral feeding is also found to reduce the duration of hospital stay (16.2 vs 23.4 days) [15].

Hur et al. conducted a randomized clinical trial (RCT) to demonstrate the safety of early oral feeding after gastric cancer surgery. They randomized 54 patients to an early oral feeding group and control group. Patients in the early feeding group began a liquid diet on the second postoperative day and then were fed a soft diet from the third day until discharge. Patients in the control group began a liquid diet on the fourth day. There were no significant differences in clinico-operative characteristics between the two groups. The duration of hospitalization ($P = 0.044$) and time until flatus ($P = 0.036$) in the early group were significantly decreased. With regard to morbidity, cost of hospitalization, postoperative symptoms, and pain scale, no significant differences were found. Quality-of-life scores were significantly decreased for fatigue (P = 0.007) and nausea and vomiting (P = 0.048) immediately after operation in the early feeding group [16].

Another RCT from Iran (n = 109) compared early oral feeding (EOF) and late oral feeding (LOF) after upper GI surgery including gastrectomy and esophagectomy. They found that clinical outcome such as vomiting, postoperative hospital stay and re-hospitalization rate were better in EOF group. In the EOF group, oral feeding was initiated on the first postoperative day with 100 mL of tea supplemented with 20 g sugar, which was gradually increased in volume to 250 mL. If the initial oral feeding was well tolerated, a soft diet was promptly started. Patients in the LOF group were kept on nil per os (NPO) until the return of bowel sounds and resolution of ileus [17].

A recent RCT in Japan comparing the ERAS protocol and conventional care after gastrectomy in 148 patients concluded that the ERAS group had better short-term clinical outcomes. In this study, meals were started on postoperative day (POD) 2 in the ERAS group and POD 3 in the conventional group [6].

We have also shown the feasibility of the ERAS protocol in gastric surgery. Patients were allowed to drink water and were given an oral nutritional supplement on POD 2. On POD 3, the patients started to eat soft food, which was stepped up to regular food every 2 days (three steps). A total of 203 patients were studied, and the incidences of postoperative ileus and anastomotic leakage were 1.0 and 1.5%. These values were low compared to those in previous studies of 0–12.5% and 0–4.2% [5].

9.4 Liquid Diet for First Meal?

The tradition for postoperative feeding is to give a liquid diet as the first meal and gradually step this up to regular food. Various retrospective studies and anecdotal reports have suggested that a regular diet as the first postoperative meal is well tolerated, and the tradition of a clear liquid diet as the first meal after surgery has recently been questioned.

The first randomized study to show the safety of a regular diet as the first meal was reported by Jeffery et al. in 1996. They randomized a total of 241 patients undergoing abdominal operations to receive either routine clear liquid (N = 135) or a regular diet (N = 106) as the first oral intake. They were followed for symptoms or signs of dietary intolerance. The group receiving a regular diet was not found to have any statistically significant increase in dietary intolerance in comparison with the clear liquid group. Nutritional data collected in a subset of patients revealed a higher caloric intake in those assigned to the regular diet. However, the patients included in this study were heterogeneous, and only 27 gastrectomy patients were included in this study [18].

Pearl et al. prospectively evaluated the safety and efficacy of a regular diet as the first meal after intra-abdominal surgery in gynecologic oncology patients. Two hundred and fifty-four gynecologic oncology patients undergoing intra-abdominal surgery were enrolled in a randomized controlled trial of a clear liquid diet compared with a regular diet as the first postoperative meal on POD 1. The percentage of patients who tolerated the diet on the first attempt was comparable in both groups (94.4 vs 87.7%). The incidences of nausea, vomiting, abdominal distention, and other postoperative complications were not different between the groups. Nausea and vomiting were experienced by 19.6 and 9.3% of patients in the clear liquid group and 18.8 and 13.8% in the normal diet group [19].

There are other similar reports that a regular diet for the first postoperative meal is safe in gastrointestinal surgery. However, these reports included a variety of surgical procedures, and only a few gastrectomy patients were included [20]. Thus, it is not clear whether this result fully applies to gastrectomy patients. It is well noted that after distal gastrectomy, motility of the remnant stomach is disturbed and sometimes results in stasis of ingested foods. In these cases, passage of food after gastrectomy may mostly be attained by gravity, and a liquid diet may facilitate passage compared to solid food.

In Japan, there have been one RCT ($n = 117$) [21] and one retrospective cohort study ($n = 204$) [22] that compared a liquid diet and regular diet for the first meal after gastrectomy. They concluded that a liquid diet is not necessary and patient satisfaction is better in the latter group. However, it must be noted that in these studies, postoperative meals were started as late as 5–8 postoperative days.

9.5 Selection of Diet by Patients

Several investigators revealed that instead of a fixed dietary regimen, it may be safe and feasible to give patients food when they want to eat and what they want to eat. Lassen et al. randomly assigned 447 patients to routine nil per os and enteral tube feeding by needle-catheter jejunostomy (ETF group) or normal food at will (NF group) from the first day after major upper GI surgery. Various types of upper GI operations were included in this study, 17% of which were total gastrectomy, 18% distal gastrectomy, and 18% pancreaticoduodenectomy. They found no significant difference in 30-day mortality, incidence of postoperative complications, and reoperation rate between the groups. Time to resumption of bowel function was significantly in favor of allowing normal food at will, as were the total number of major complications, length of hospital stay, and rate of post-discharge complications. However, the amount of food taken by patients in the NF group was not measured [23].

In Japan, Hirano compared the clinical outcome of a patient-controlled dietary schedule (PC group $n = 53$) with that of a conventional dietary schedule (CR group $n = 50$) after distal gastrectomy for early gastric cancer. The PC group received a solid diet on demand, and patients in the CR group received a solid diet from POD 10. In the PC group, a liquid diet was tolerated on POD 2, and a solid diet was taken on POD 6. Postoperative hospital stay was significantly shorter in the PC group than the CR group (18.5 ± 5.9 vs 21.7 ± 8.8 days). Patients in the PC group had higher daily oral caloric intake on POD 10 than those in the CR group ($p = 0.02$). Change in body weight, incidence of complications, and variance from clinical pathways did not show significant differences between the two groups [24].

Hara et al. also tested the feasibility of patients' selection of food on POD 2 and later. Uncomplicated gastric cancer patients who underwent gastric resection were given a liquid diet on POD 1 and then asked to select their own meals (liquid, half liquid, soft, or normal), starting on POD 2. Patients selected their next day's meal every day until discharge. Seventy-five patients were used to test this protocol and compared with 25 control patients. Sixty-nine (10 total gastrectomies) out of 75 patients completed the protocol, and the patients who selected their own meals received a significantly larger amount of energy during POD 1 to 5, and their body weight loss after 1 month was significantly less than that of controls [25].

9.6 Is Early Oral Feeding After Gastrectomy Sufficient for All Patients?

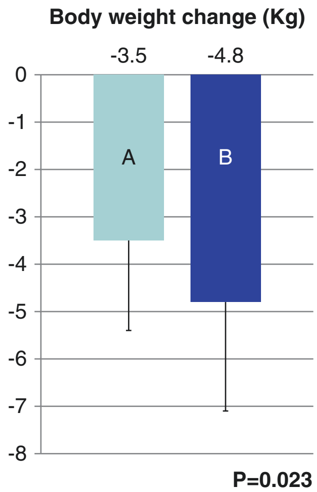
As already discussed, early oral feeding after gastric surgery may be safe and feasible. However, in contrast to colonic surgery, postoperative intake is more restricted in gastric surgery patients even though they can eat early in their postoperative course. Many papers reporting the usefulness of ERAS emphasize the possibility of early oral intake and reduced postoperative hospital stay, but the sufficiency of nutritional supply or degree of malnutrition after surgery is not reported. In our pilot study, the amount of oral food taken in distal gastrectomy patients on POD 1, 2, and 3 was 426, 595, and 569 kcal/day, respectively, which did not meet their daily energy demands. Moreover, in total gastrectomy patients, the amount of energy taken on these days was less than 300 kcal/day.

It is reported that body weight loss during the first week after surgery was significantly greater than that during the subsequent 3 weeks and loss of lean body mass accounted for a significant part of the body weight loss during the first week [26]. Body weight loss is associated with various adverse outcomes in cancer patients including those with gastric cancer. Thus, there seems room for early enteral tube feeding for gastric surgery in high-risk cancer patients such as those with preoperative severe malnutrition and those predicted to have poor oral intake after surgery. Our study demonstrated that those who received early enteral tube feeding had less postoperative weight loss at discharge than those without tube feeding (Fig. 9.2).

9.7 Conclusions

ERAS protocols for gastric surgery in general are safe, feasible, and useful. Some patients need an individualized approach because of specific characteristics of gastric surgery that differ from those of colonic surgery. Early enteral tube feeding is a

Fig. 9.2 Body weight change at discharge. Total gastrectomy patients with (A) or without (B) early enteral tube feeding



good option for those with preoperative malnutrition and those predicted to have poor oral intake after surgery. Patient-controlled feeding (selection of diet by patients) seems promising and should be further investigated.

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Chapter 10
Negative Effects of Mechanical Bowel Preparation on the Postoperative Intestinal Motility of Patients with Colorectal Cancer

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Abstract Several processes can occur as a reaction to surgery, including postoperative intestinal hypoperistalsis, which normally recovers over several hours to days. Postoperative ileus (POI), a transient impairment of bowel motility after abdominal surgery, is characterized by nausea, vomiting, inability to tolerate oral diet, abdominal distension, and delayed passage of flatus and stool. The pathophysiology of POI is multifactorial, but the detailed underlying mechanisms are unknown. This complication should be prevented; however, no single technique or agent has been found to prevent POI effectively. A multidirectional approach is therefore needed to prevent POI. Operative management following the enhanced recovery after surgery (ERAS) approach, including minimally invasive methods, optimal pain control, aggressive postoperative rehabilitation, and early oral nutrition, reportedly exerts a positive effect on the recovery speed of gastrointestinal motility after colon surgery. Although, traditionally, mechanical bowel preparation (MBP) has been thought to decrease the prevalence of surgical site infection and anastomotic leakage, no benefit of MBP has been reported in clinical trials. Some studies have associated MBP with polyethylene glycol (PEG) with poor anastomosis healing and decreased intestinal motility. We showed that MBP with PEG negatively affects motility of the small intestines after both open and laparoscopic colon surgeries. As nutrient absorption occurs in the small intestines, it is important to promote its prompt recovery. In the ERAS approach, omission of MBP is recommended and may be the most important element of ERAS, allowing for early small intestinal motility recovery.

Keywords Polyethylene glycol • Mechanical bowel preparation • Intestinal motility • Postoperative ileus

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10.1 Introduction

Early recovery after surgery includes modulation of the host response to surgical insults, early restoration of physical activity, early recovery of normal nutritional intake, and encouragement motivation for recovery with reduction of anxiety (Japanese Society for Surgical Metabolism and Nutrition). Early normal nutritional intake is achieved by preventing postoperative ileus (POI) and early recovery of gastrointestinal motility.

Postoperative intestinal hypoperistalsis is considered a normal and inevitable response to laparotomy and other surgical procedures [1]. Generally, peristalsis recovers over hours to days, and gastrointestinal motility is expected to return to normal within 2 to 3 days postoperatively. However, the recovery speed can be affected by the magnitude of surgical stress or inflammation caused by surgical manipulation and perioperative treatment. The POI is considered a prolongation of postsurgical hypoperistalsis.

The POI is generally defined as a transient impairment of bowel motility after abdominal and other types of surgeries [1, 2], and it is characterized by nausea, vomiting, inability to tolerate oral diet, abdominal distension, and delayed passage of flatus and stool. The POI can lead not only to delayed enteral feeding but also decreased mobility (e.g., delayed surgical wound healing and ambulation, atelectasis, pneumonia, and deep vein thrombosis) and patient discomfort [3]. In this section, we explain postsurgical peristalsis, POI, and the effect of preoperative mechanical bowel preparation (MBP) on gastrointestinal motility.

10.2 Early Recovery of Normal Nutritional Intake

Early recovery from postoperative intestinal hypomotility can enable early oral feeding, thereby reducing the risk of anastomotic leakage, wound infection, pneumonia, and formation of intra-abdominal abscesses [4].

Several studies have been carried out to evaluate intestinal motility in patients after surgery based on the time to flatus or first bowel movement. However, few studies have evaluated intestinal motility objectively.

10.3 Incidence and Risk Factors of POI

The frequency of POI after colorectal surgery ranges from 12.7 to 26.9% [5–9]. Preoperative risk factors for the development of POI include male sex; preexisting respiratory, cardiac, or renal diseases; greater preoperative body mass index; preoperative chemotherapy treatment; and decreased preoperative albumin [5–8]. Intraoperative risk factors include open technique, long operation time, large blood loss, and red cell transfusion [5–8].

10.4 Pathogenesis of POI

The pathophysiology of POI is multifactorial, and it involves neurogenic, inflammatory, and pharmacological mechanisms [10]. Peristalsis is dependent on parasympathetic stimulation, and it is inhibited by sympathetic stimulation. However, the detailed underlying mechanisms remain unclear [2]. The average paralytic state after major abdominal surgery lasts between 0 and 24 h in the small intestine, 24 and 48 h in the stomach, and 48 and 72 h in the colon [2]. In the POI state, recovery of the gastrointestinal motility is delayed for various reasons.

The first phase of the reaction to surgery is mediated neurally, and it is activated during and immediately after surgery. The incision of the skin induces an increased adrenergic motor neuronal activity, mediated by adrenocorticotropic hormone-releasing factor, leading to an acute intestinal paralysis [11]. The second phase begins 3–4 h after surgical manipulation, and it is mediated by inflammation. Mechanical trauma of the gastrointestinal tissue and the release of inflammatory mediators and cytokines result in POI [10]. The release of pro-inflammatory cytokines and chemokines leads to an upregulation of intracellular adhesion molecules in the endothelium. Phagocytes residing in the gut are activated, resulting in a migration of leukocytes to the muscularis externa. The release of nitric oxide and prostaglandins by these phagocytes prevents peristalsis by inhibiting smooth muscle contractility directly [11].

Bowel handling increases gastrointestinal inflammation because it induces the presence of phagocytes, neutrophils, macrophages, monocytes, dendritic cells, T cells, natural killer cells, and mast cells [12]. As the intensity of surgical manipulation increases, the accumulation of inflammatory cells increases in the intestine [12]. Thus, minimal access techniques, using laparoscopy, may aid in decreasing gastrointestinal inflammation.

Edema is known to cause stretching of the intestinal walls, stimulating an interaction between intracellular messengers. Surgery increases antidiuretic hormone, cortisol, and aldosterone secretion, which leads to sodium chloride and water retention [13]. Fluid overload following surgery and lower albumin levels can also induce gastrointestinal edema [14].

10.5 Treatment of POI

Conventionally, the initial treatment of prolonged POI consists of the placement of a nasogastric tube to relieve luminal distension while simultaneously monitoring the urine output and correcting the electrolytes if necessary by using intravenous fluids to achieve a balanced fluid state [11]. However, nasogastric suction does not always aid in the resolution of POI [15]. Early recovery of gastrointestinal motility is not achieved by early postoperative mobilization [16]. Thus far, no treatment has been shown to accelerate the recovery of POI. Therefore, prevention of POI is important.

10.6 Prevention of POI

Pre-, intra-, and postoperative interventions can prevent POI. However, no single technique or agent has been found to effectively prevent POI [2, 17]. Metoclopramide does not decrease the frequency of ileus [18]. Early oral feeding (ingestion of liquid diet on postoperative day 1) may enhance recovery of postoperative gastrointestinal motility but has not been shown to decrease the prevalence of POI [19]. It might be expected that individuals undergoing a minimally invasive or laparoscopic procedure would have a lower risk of developing POI than those undergoing an open surgical procedure. However, two major clinical trials (COLOR and COST studies) showed that laparoscopic surgery does not necessarily decrease the prevalence of POI [20]. Therefore, a multidirectional approach is needed to prevent POI.

10.7 The Effect of Enhanced Recovery After Surgery (ERAS) on the Prevention of POI After Colorectal Surgery

Fast-track surgery is a multidirectional approach to shorten the recovery of patients undergoing elective surgery. Particularly in colon surgery, this concept is recognized across the world as enhanced recovery after surgery (ERAS), which comprises 17 elements [21], and it has been reported to contribute to a decreased morbidity [21, 22]. The approach includes epidural anesthesia, minimally invasive methods, optimal pain control, aggressive postoperative rehabilitation, and early oral nutrition. The combination of these approaches reduces the stress response and organ dysfunction. However, the effect of ERAS on early recovery of motility remains unclear.

Although it is thought that ERAS can decrease the rate of POI, its impact on POI has not been thoroughly studied. Only one study with a small sample showed that ERAS can decrease the POI rate when adherence is over 85% [23]. In that study, about 10% of the patients underwent mechanical bowel preparation (MBP), which can negatively affect motility after surgery.

10.8 Disadvantages of MBP

Although MBP has been expected to decrease the prevalence of surgical site infection and anastomotic leakage, no benefit of MBP has been reported in large clinical trials [24–26]. Moreover, MBP can increase abdominal infectious complications (e.g., anastomotic leakage, intra-abdominal abscess, and wound infection) [27]. Thus, in ERAS management, MBP is usually discouraged, although it was not entirely omitted in some ERAS studies [28, 29]. Many surgeons continue to undertake MBP with polyethylene glycol (PEG) prior to colorectal surgery because they consider that PEG can substantially decrease intestinal residues and help them to carry out the surgical procedure more easily.

Previously, we conducted an observational study, which included 282 patients with colon cancer. We showed that MBP with PEG negatively affects intestinal motility after both open and laparoscopic colon surgeries [30]. In that study, we radiologically assessed the postoperative small bowel motility and colonic motility with a radiopaque marker that was ingested 2 h preoperatively. Jung et al. also reported that MBP delayed the first postoperative bowel movement in open colon surgery [31]. Further, Bucher et al. reported that PEG delayed the first postoperative bowel movement in left-sided colon surgery [27]. The first bowel movement may be affected by the motility of the small and large bowels. However, the motility of the small intestine is more important than that of the large intestine because nutrient absorption occurs mainly in the small intestine in terms of early recovery of the intestinal motility.

In our previous study, we also showed that the omission of MBP did not affect the operation time or intraoperative bleeding volume. These findings indicate that omission of PEG does not make the procedure more difficult. Further, the omission of MBP did not affect the prevalence of anastomotic leakage, POI, wound infection, intra-abdominal abscess formation, postoperative bleeding, postoperative nausea, and mortality [30].

Based on the above findings, we consider that omission of MBP can be one of the most important elements of ERAS, which can contribute to early intestinal recovery after surgery. However, no studies, including our own, have demonstrated that the omission of MBP is indeed effective to reduce the prevalence of POI.

10.9 Mechanism of MBP

The reason why MBP using PEG negatively affects postoperative intestinal motility is not clear. In rats, PEG increases bile secretion and induces mild congestion, edema, and inflammation in the small and large bowels, but not in the stomach [32]. Congestion, edema, and inflammation can negatively affect not only the wound healing of anastomoses but also intestinal motility. Moreover, even a relatively small amount of PEG (500–750 mL) causes the small intestine to dilate for many hours in humans [33]. These effects of PEG can negatively affect postoperative intestinal motility. While PEG can negatively affect intestinal motility because it increases intestinal fluid and dilates the small intestine, stimulant laxatives (e.g., sodium phosphate and senna) do not increase intestinal fluid or dilate the small intestine [34].

10.10 Conclusion

Operative management following the ERAS approach positively affects the prompt recovery of gastrointestinal motility after colon surgery. Omission of MBP can be the most important element of ERAS, which allows for early small intestinal motility recovery. However, no methods have been shown to reduce the prevalence of POI.

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Chapter 11
Enhanced Recovery After Surgery Program for Patients Undergoing Resection of Hepatocellular Carcinoma

Masaki Kaibori, Kosuke Matsui, Morihiko Ishizaki, Kentaro Inoue, Kengo Yoshii, and Masanori Kon

Abstract A recent study at our center analyzed whether an enhanced recovery after surgery (ERAS) program for patients undergoing potentially curative liver resection for hepatocellular carcinoma (HCC) influenced the feasibility, safety, and effectiveness of surgery. Clinicopathologic factors, surgical factors, and outcomes were compared in patients who underwent extended hepatectomy (resection of more than two sections) for HCC before and after the introduction of the ERAS program. Operating time and postoperative hospital stay were significantly shorter, and total volume infused during surgery significantly lower, for the ERAS than for the control group. Although retention of abdominal drainage was significantly less frequent in the ERAS group, the frequency of abdominal paracentesis in patients without intraoperative abdominal drainage was higher in this group. Oral dietary intake and ability to walk stably occurred significantly earlier in the ERAS group. Postoperative serum concentrations of albumin and cholinesterase were significantly higher in the ERAS than in the control group. These findings showed that the ERAS program for patients with mild to moderate liver dysfunction undergoing extended liver resection for HCC was feasible and effective. It allowed earlier oral dietary intake, promoted faster postoperative recovery, and reduced overall hospital stay.

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Keywords Hepatectomy • Liver cancer • Enhanced recovery after surgery

11.1 Introduction

Fast-track or enhanced recovery after surgery (ERAS) programs following surgical interventions are now within the standard of care for patients with several surgical indications [1–5]. These programs use a multimodal approach to maximize effectiveness and minimize cost, thus optimizing perioperative care pathways [6]. ERAS programs have been associated with reductions in complications, hospital stay, and hospital costs [1]. Evidence for the effectiveness of ERAS programs in patients undergoing liver surgery is limited, with just six small published series [7]; of these, two small randomized trials suggested that ERAS following hepatectomy is associated with shorter hospitalization and reduced morbidity [8, 9]. Most of the patients in these studies underwent hepatectomy for colorectal liver metastases. Few studies have analyzed the effect of ERAS in patients with diseased livers who underwent hepatectomy for hepatocellular carcinoma (HCC).

HCC is the fifth most common cancer worldwide [10]. Although most affected patients are in Asia and Africa, HCC incidence and mortality rates are increasing in North America and Europe [11, 12]. In Japan, most HCCs occur in patients with chronic hepatitis and liver cirrhosis induced by infection with the hepatitis B or C virus. Because of advances in perioperative management, anesthesia, and operative techniques, hepatectomy for HCC has become more common [13]. However, the postoperative mortality rate remains higher than in patients with cirrhosis or chronic hepatitis undergoing other types of surgery. The morbidity rate of patients with cirrhosis undergoing liver resection has been reported to range from 20 to 70%, with mortality rates of 5–21% [14–19]. However, mortality rates at high-volume centers in Japan are usually much lower, <2% [20–22], although morbidity rates remain relatively high. The postoperative course of these patients does not always proceed as expected, owing to various types of intraoperative stress, including blood loss and ischemia. These findings emphasize the importance of improving both surgical techniques and perioperative care in reducing mortality and morbidity rates of HCC patients undergoing liver resection.

Some Japanese surgeons have expressed skepticism regarding ERAS programs. Their objections fall into four general categories: (1) Surgeons believe that a well-performed operation, during which patients remain stable, can result in natural patient recovery. (2) Surgeons regard the most important aspect of an operation as surgical technique, not the recovery program. (3) Surgeons do not believe that ERAS is necessary for them and their patients. (4) Some surgeons believe that ERAS is advocated by those surgeons with less than optimal surgical technique. Nevertheless, optimal patient outcomes depend on both improved management of perioperative care as well as surgical technique. We believe that efforts to improve both surgery and care are essential.

We hypothesized that application of an ERAS program for HCC patients undergoing hepatectomy would accelerate recovery, reduce morbidity rates, and shorten hospital stay. We therefore performed a study assessing whether an ERAS program for HCC patients affected the feasibility, safety, and effectiveness of potentially curative hepatic resection.

11.2 Patients, Clinicopathologic Variables, and Surgery

Between January 2008 and December 2013, 315 patients with HCC underwent R0 resection, defined as macroscopic removal of all tumors, at our institution. Of these patients, 130 underwent resection between January 2008 and December 2010, 41 underwent resection between January 2011 and January 2012, and 144 underwent resection between February 2012 and December 2013. Eight patients died in hospital after surgery, four, one, and three, respectively, during the three time periods. Data on all patients were recorded prospectively. The study protocol was explained to all patients, who understood that those who underwent surgery between January 2008 and December 2010 would be assigned to conventional perioperative management and those who underwent surgery between February 2012 and December 2013 would be managed using the ERAS program. The study protocol was approved by the institutional ethics committee of our institution.

Patients were subclassified based on whether they underwent removal of two or more sections. The 71 patients who underwent removal of more than two sections were subclassified into an ERAS group ($n = 47$) and a control group ($n = 24$).

Before surgery, each patient underwent conventional liver function tests and measurement of the indocyanine green (ICG) retention rate 15 min after administration. Patients were screened for hepatitis by measuring serum concentrations of hepatitis B surface antigen and antibody to hepatitis C virus. Serum concentrations of α-fetoprotein and protein induced by vitamin K absence/antagonism-II were also measured in all patients. Surgical procedures were classified according to the Brisbane terminology [23]. Anatomic resection was defined as resection of the tumor together with the related portal vein branches and the corresponding hepatic territory. Anatomic resection was subclassified as hemihepatectomy (resection of half the liver), extended hemihepatectomy (hemihepatectomy plus removal of additional contiguous segments), sectionectomy (resection of two Couinaud subsegments [24]), or segmentectomy (resection of one Couinaud subsegment). All other nonanatomic procedures were classified as limited resection. The tumors treated with limited resection included both peripheral and central tumors. Patients with peripheral tumors and those with extrahepatic growth underwent partial hepatectomy because this method achieved adequate surgical margins. In contrast, patients with central tumors located near the hepatic hilum or major vessels underwent enucleation because of the difficulty and risks associated with obtaining adequate margins. In this study, resection of more than two sections was defined as extended hepatectomy. One senior pathologist reviewed each specimen for histologic confirmation of the diagnosis. Perioperative/postoperative complications and deaths were recorded to assess the morbidity and mortality associated with hepatectomy. Complications were classified by the primary investigator according to the Clavien-Dindo classification scale [25, 26]. Grade I and II complications were classified as minor morbidities, and grade III and IV complications as major morbidities. Grade V was defined as patient death.

Liver resections in both the ERAS and control groups were performed by the same liver surgeons. Right subcostal abdominal incisions were used. The transection plane was determined by intraoperative ultrasonography. The Cavitron Ultrasonic Surgical Aspiration (CUSA®; Valleylab, Boulder, CO, USA) and Aquamantys® bipolar (Medtronic, Minneapolis, MN, USA) were used for liver parenchymal dissection.

No specific measures were used to avoid prolonged preoperative and postoperative fasting, nasogastric decompression, excessive use of intravenous fluids, or prophylactic abdominal drainage. The conventional postoperative care program emphasized prolonged rest for both the patient and the gastrointestinal tract. The ERAS multimodal evidence-based recovery program protocol, which was designed originally for elective colonic surgery, was modified to cover all aspects of elective liver resection [27]. Details of the ERAS liver program are shown in Table 11.1.

Perioperative and postoperative exercises by HCC patients with hepatic impairment were shown to lead to weight loss, owing to reductions in fat mass, and improvements in insulin resistance, but had no effect on skeletal muscle mass. Intensifying perioperative and postoperative exercise may better maintain postoperative physical strength and can result in earlier resumption of daily activities. Before starting exercise therapy, patients underwent cardiopulmonary exercise testing on a bicycle ergometer using an incremental protocol (5.0, 7.5, and 10 W/min). A 12-lead electrocardiogram was continuously monitored for ST segment deviation, arrhythmias, and heart rate at rest and during the exercise and recovery periods. Blood pressure was recorded at rest and every 2 min during the exercise and recovery periods. Peak oxygen consumption per unit time (Vo_2) was obtained from breath-by-breath analysis of expired air. Peak Vo_2 was defined as the highest mean value during exercise when the subject could no longer continue pedaling at 60 rpm. The anaerobic threshold (AT), the onset of metabolic acidosis, was defined as the break point between carbon dioxide production and Vo_2 [28] or the point at which the ventilatory equivalent for oxygen and end-tidal oxygen partial pressure curves reached their respective nadirs before beginning to increase again [29]. Thus, AT was set at the time of maximum fat combustion [30] (Fig. 11.1). The respiratory compensation point was set at the point at which the ventilatory equivalent for carbon dioxide was lowest before a systemic increase and when the end-tidal carbon dioxide partial pressure reached a maximum and began to decrease [31]. Exercise was stopped when the patient requested it because of fatigue, pain, or headache or if there was a failure to maintain a speed greater than 40 rpm for more than 30 s despite encouragement.

An exercise program was tailored for each patient. Exercise was started as soon as possible after diagnosis, up to 1 month preoperatively, was resumed starting

Table 11.1 Care plan for patients undergoing liver resection in the enhanced recovery after surgery program

Before surgery
Start cirrhotic patients on BCAA within 1 month before surgery
Day before surgery
Normal oral nutrition until midnight
No preanesthetic medication
No preoperative bowel preparation
Day of surgery
Carbohydrate drinks up to 3 h before surgery (total dose 1000–1500 mL including on the day before surgery)
Mid-thoracic epidural analgesia (local anesthetic + low-dose opioid)
Short-acting i.v. anesthetic agent
Warm i.v. fluids and upper- and lower-body air-warming device
Avoidance of excessive i.v. fluids (stroke volume variation <13%)
No drainage of the peritoneal cavity
Remove nasogastric drainage immediately after surgery
Send patient to recovery ward
Postoperative day 1
Restart oral intake of water ad libitum
Send patient to surgical ward
Restart oral intake of rice gruel for evening meal
Mobilize patient at least three times per day
Continue portable epidural analgesia (local anesthetic + low-dose opioid)
Recommend NSAID for pain (loxoprofen sodium 60–240 mg/day)
Laboratory tests
Postoperative day 2
Rice gruel diet
Continue mobilization at least four times per day
Continue portable epidural analgesia (local anesthetic + low-dose opioid)
Recommend NSAID for pain (loxoprofen sodium 60–240 mg/day)
Postoperative day 3
Normal (rice) diet
Patient should drink at least 1000 mL
Stop epidural analgesia and low-dose opioids
Recommend NSAID for pain (loxoprofen sodium 60–240 mg/day)
Remove urinary catheter
Continue mobilization
Laboratory tests
Postoperative days 4–6
Normal diet
Discontinuation of intravenous fluids
Continue mobilization
Recommend NSAID for pain (loxoprofen sodium 60–240 mg/day)

(continued)

Table 11.1 (continued)

Laboratory tests (one time)
Postoperative days 7–14
Check discharge criteria
Outpatient appointment made for postoperative day 21 or 28
Discharge

BCAA branched chain amino acids, *i.v.* intravenous, *NSAID* nonsteroidal anti-inflammatory drug

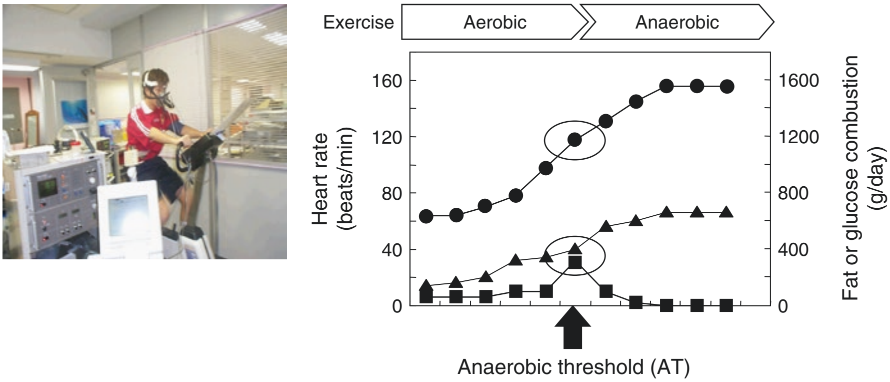


Fig. 11.1 Cardiopulmonary exercise test. The anaerobic threshold (AT) was set at the break point between carbon dioxide production and Vo_2, or the point at which the ventilatory equivalent for oxygen and end-tidal oxygen partial pressure curves reached their respective nadirs before beginning to increase again. Thus, AT was set at a maximum point of fat combustion. Filled circle, heart rate; filled triangle, glucose combustion; filled square, fat combustion

1 week postoperatively, and was continued for 6 months. The program consisted of three 60-min exercise sessions per week. Each session included 5 min of stretching exercises, 30 min of walking at an intensity based on the anaerobic threshold of each patient, 20 min of targeted stretching exercises, and 5 min of cooling down with stretching. Once or twice a month postoperatively, a medical doctor and exercise trainer confirmed the frequency and quantity of exercise performed by each patient. Patients were advised to continue exercising for 6 months after surgery [32]. Following conclusion of this randomized controlled trial, cirrhotic patients with HCC in our institution were prescribed perioperative exercise therapy, together with administration of branched chain amino acids (BCAA) (Fig. 11.2).

Patients were instructed to drink up to 1000–1500 mL of carbohydrates (OS-1®; carbohydrate 2.5 g/100 mL, glucose 1.8 g/100 mL), starting in the evening on the day prior to surgery until 3 h before surgery.

Although no formal discharge criteria were specified for patients in the control group, discharge criteria were specified in the ERAS group, including (1) normal or decreasing serum bilirubin and normal or increasing serum albumin concentrations, (2) good pain control with oral analgesia only, (3) tolerance of solid food, (4) no intravenous fluids, (5) mobile independently or at the preoperative level, and (6) willingness to go home.

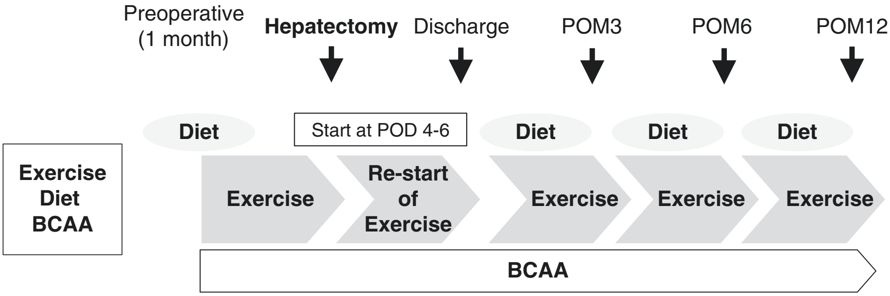


Fig. 11.2 The perioperative exercise therapy used by our institution for HCC patients undergoing hepatectomy. *POD* postoperative day, *POM* postoperative month, *BCAA* branched chain amino acids

For statistical analyses, continuous variables were reported as medians and first and third quartiles. Differences between two groups were assessed by the chi-square test or the Wilcoxon rank-sum test, as appropriate. Differences in the perioperative concentrations of albumin, cholinesterase, and C-reactive protein between two groups were assessed by two-way analysis of variance. The level of significance was set at $P < 0.05$. The Kaplan-Meier life table method was used to calculate the probability of hospitalization beyond specific time points, with differences estimated using the generalized log-rank test. All statistical analyses were performed with SPSS® for Windows 11.0J (SPSS Inc., Chicago, IL, USA).

11.3 Comparison of Results in the ERAS and Control Groups

Differences between the ERAS and control groups are shown in Table 11.2. Exercise therapy with BCAA within 1 month before surgery and the start of exercise therapy with BCAA on postoperative days 4–6 were limited for cirrhotic patients; therefore, these criteria were achieved by 41% of ERAS group patients before and 46% after surgery. Over 87% of patients in the ERAS group received normal oral nutrition until midnight on the day before surgery, did not undergo preoperative bowel preparation, and received carbohydrate drinks until 3 h before surgery. In contrast, patients in the control group started fasting after the evening meal and refrained from drinking fluids after midnight on the day before surgery. The duration of stopping fluid intake was 3.7 ± 1.4 h in the ERAS group and 11.3 ± 1.4 h in the control group ($p < 0.01$). The mean volume of carbohydrate drink ingested by patients in the ERAS group was 1068 ± 191 mL.

Intraoperatively, drainage of the peritoneal cavity was omitted for 60% of patients in the ERAS group. Nasogastric drainage was removed immediately after surgery in 137 of the 144 patients in the ERAS group, with the tubes removed the next day from the remaining seven patients because of slower awakening from anesthesia.

Table 11.2 Differences between the ERAS and control groups

ERAS group *n* = 144 Feb. 2012–Dec. 2013	Achievement of ERAS (%)	Control *n* = 130 Jan. 2008–Dec. 2010
Before surgery		
Exercise therapy with BCAA within 1 month of surgery for cirrhotic patients	41% (59/144)	ND
Day before surgery		
Normal oral nutrition (light meal) until midnight	87% (125/144)	Fasting after evening meal and absolutely no liquids after midnight
No preoperative bowel preparation	93% (134/144)	Magnesium citrate, sennoside
Day of surgery		
Carbohydrate drinks up to 3 h before surgery	98% (141/144)	ND
No drainage of the peritoneal cavity	60% (87/144)	Routine drainage of the peritoneal cavity
Remove nasogastric drainage tube immediately after surgery	95% (137/144)	
POD 1		
Restart oral intake of water ad libitum	95% (137/144)	ND
Restart oral intake of rice gruel at evening meal	68% (98/144)	ND
Patient mobilized at least three times per day	82% (118/144)	ND
		Remove nasogastric drainage on POD 1 or 2
POD 2		
Rice gruel diet	86% (124/144)	Restart oral intake of water ad libitum and oral intake of rice gruel at evening meal
Continue mobilization at least four times per day	93% (134/144)	ND
POD 3		
Normal (rice) diet	87% (125/144)	Rice gruel diet
Remove urinary catheter	90% (130/144)	ND
Discontinue intravenous fluids	67% (97/144)	ND
Continue mobilization	91% (131/144)	Patient mobilized at least three times per day
POD 4–6		
Start of exercise therapy with BCAA	46% (66/144)	ND
		Remove urinary catheter
		Discontinue intravenous fluids
		Continue mobilization at least four times per day

ERAS enhanced recovery after surgery, *BCAA* branched chain amino acids, *POD* postoperative day

Table 11.3 Preoperative characteristics of HCC patients in the ERAS and control groups who underwent removal of two or more liver segments

	ERAS (n = 47)	Control (n = 24)	p value
Sex (male/female)	37/10	22/2	0.1686
Age (years)	71 (60–81)	69 (61–77)	0.304
Hepatitis (HBV/HCV/NBC)	12/13/22	8/9/7	0.3587
ICGR15 (%)	10.3 (3.5–24.1)	10.0 (5.0–18.5)	0.964
Albumin (g/dL)	3.8 (3.0–4.4)	3.8 (3.0–4.1)	0.417
Total bilirubin (mg/dL)	0.70 (0.40–1.30)	0.70 (0.50–0.87)	0.736
AST (U/l)	36 (19–71)	47 (21–78)	0.351
Platelet count (×104/mL)	18.1 (10.4–26.4)	18.4 (12.1–25.8)	0.500
CRP (mg/dL)	0.19 (0.04–3.38)	0.29 (0.04–2.63)	0.697
AFP (ng/mL)	34 (2–11,093)	41 (5–8248)	0.251
PIVKA-II (mAU/mL)	1255 (17–70,167)	1264 (25–69,282)	0.855

Data represent the median (10th–90th percentiles) or the number (%) of patients
ERAS enhanced recovery after surgery, *HBV* hepatitis B virus, *HCV* hepatitis C virus, *NBC* non-hepatitis B or C virus, *ICGR15* indocyanine green retention rate after 15 min, *AST* aspartate aminotransferase, *CRP* C-reactive protein, *AFP* α-fetoprotein, *PIVKA-II* protein induced by vitamin K absence/antagonism-II

The postoperative times to removal of the nasogastric tube were 0.3 ± 0.1 days in the ERAS group and 1.1 ± 1.6 days in the control group ($p < 0.01$), and the mean intraoperative output volumes from the nasogastric tube were 5.5 ± 22.5 mL in the ERAS group and 20.3 ± 44.7 mL in the control group. Oral intake of rice gruel beginning at the evening meal and patient mobilization at least three times per day were achieved by 98 (68%) and 118 (82%) patients, respectively, in the ERAS group. Urinary catheters were removed and intravenous fluids discontinued on median postoperative days 5 and 6, respectively, in the control group. By postoperative day 3, however, 90% of patients in the ERAS group underwent catheter removal, and 67% discontinued intravenous fluids.

Table 11.3 summarizes the preoperative characteristics of patients in the control and ERAS groups who underwent removal of more than two segments of the liver. There were no between-group differences in sex, age, hepatitis virus status, preoperative liver function (ICG retention rate; serum albumin, total bilirubin, and alanine aminotransferase concentrations; and platelet count), and concentrations of C-reactive protein, α-fetoprotein, and protein induced by vitamin K absence/antagonism-II.

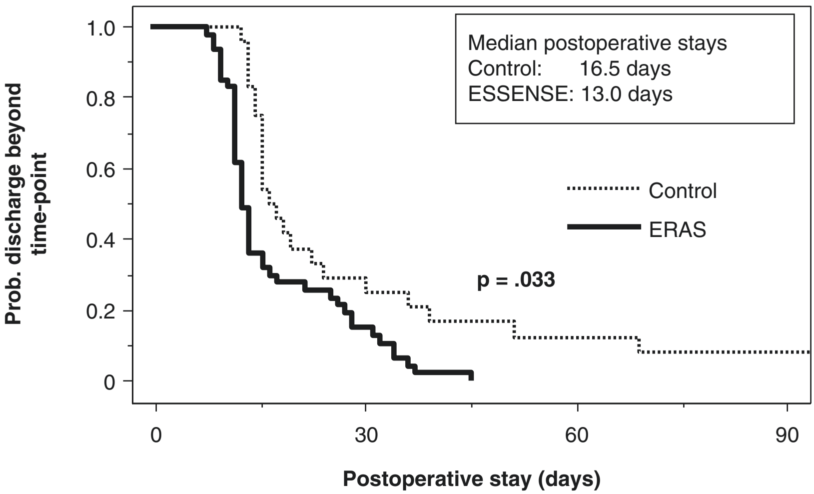
As shown in Table 11.4, the procedures used for anatomic resection, blood loss, blood transfusion, postoperative complications, and hospital death rate did not differ significantly between the control and ERAS groups. However, the percentage of patients with a severe grade on the Clavien-Dindo classification was higher in the control than in the ERAS group. Operating time and postoperative hospital stay were significantly shorter, and the total volume of blood infused during surgery significantly lower, in the ERAS than in the control group. Median postoperative hospital stay was 13.0 days in the ERAS and 16.5 days in the control group.

Table 11.4 Operative and postoperative characteristics of HCC patients in the ERAS and control groups who underwent removal of two or more liver segments

	ERAS ($n = 47$)	Control ($n = 24$)	p value
No. of sectionectomies (2/>2)	28/19	16/8	0.5604
Operative blood loss (mL)	1096 (271–3164)	1366 (560–3959)	0.464
Operating time (min)	**394 (285–548)**	506 (289–616)	**0.023**
Blood transfusion (±)	15/32	10/14	0.4158
Total volume infused during surgery operation (mL)	**6500 (3712–10,580)**	8025 (4375–12,612)	**0.031**
Tumor size (cm)	6.5 (3.4–12.4)	8.3 (3.7–14.7)	0.381
Number of tumors (solitary/multiple)	36/11	18/6	0.8815
Associated liver disease (normal/hepatitis/cirrhosis)	4/31/12	4/12/8	0.3773
Tumor stage (II/III/IV)	11/25/11	9/13/2	0.2129
Morbidity (+)	9	5	0.866
SSI	1	1	
Intra-abdominal abscess and/or bile leakage	2	1	
Intractable ascites and/or pleural effusion	6	3	
Clavien-Dindo classification (Grade II/IIIa/IIIb/IVa/IVb)	0/9/0/0/0	0/3/0/2/0	
Mortality (+)	0	0	
Retention of abdominal drainage (±)	**23/24**	19/5	**0.0142**
Abdominal paracentesis in patients with no intraoperative abdominal drainage (±)	8/16	0/5	0.129
Postoperative hospital stay (days)	**13.0 (10.0–33.8)**	16.5 (13.0–63.6)	**0.004**

Data represent the median (10th–90th percentiles) or the number (%) of patients
ERAS enhanced recovery after surgery, *SSI* surgical site infection

The probability of hospitalization beyond a given time point was significantly lower in the ERAS than in the control group (Fig. 11.3). In the control group, two patients had grade IVa complications on the Clavien-Dindo scale and were discharged from the hospital on postoperative days 111 and 147, respectively. The patient who required a postoperative hospital stay of 111 days underwent right hemihepatectomy for HCV-associated HCC and was treated postoperatively for intractable ascites, pleural effusion, and aspirational pneumonia. This patient had a preoperative serum albumin concentration of 3.2 g/dL and serum albumin concentrations immediately after surgery of 2.0–2.5 mg/dL. BCAA supplementation resulted in recovery of preoperative serum albumin concentration 3 months after surgery. The second patient underwent abdominal drain placement during surgery, with bile leakage through the drain appearing on postoperative day 2. Despite performing an intraoperative bile leakage test with saline solution, the



Number at risk		15	30	45	60	75	90
Control	24	17	6	4	3	2	2
ERAS	47	17	7	1	0	0	0

Fig. 11.3 Probability of hospitalization after resection of HCC in patients in the control (dotted line) and ERAS (unbroken line) groups. The probability of hospitalization differed significantly ($P = 0.033$). Numbers of patients at risk are shown below the graph

site of major leakage could not be detected. This patient required a postoperative hospital stay of 147 days to treat postoperative bile leakage, which was extremely difficult to cure.

Although the number of patients with retention of abdominal drainage was significantly lower in the ERAS group, the frequency of abdominal paracentesis in patients without intraoperative abdominal drainage was higher in this group. Abdominal paracentesis was caused by refractory ascites in five patients, by refractory ascites and pleural effusion in one patient, and by intra-abdominal abscesses in two patients.

A comparison of the pathological findings in the two groups showed no differences in tumor size, number of tumors per patient, associated liver diseases, and TNM stage (Table 11.4).

The percentage of patients with dietary intake on postoperative day 2 was significantly higher in the ERAS than in the control group (Fig. 11.4). Although time to first bowel movement did not differ significantly in the two groups, ability to walk stably occurred significantly earlier in the ERAS than in the control group (Fig. 11.5).

Postoperative serum concentrations of albumin and cholinesterase were significantly higher in the ERAS than in the control group (Fig. 11.6). C-reactive protein concentration was lower in the ERAS group, but the difference was not statistically significant.

Fig. 11.4 Times until dietary intake after resection of HCC in patients in the control (open circles) and ERAS (closed circles) groups. Dietary intake by postoperative day 2 was significantly more frequent ($P = 0.049$) in the ERAS than in the control group

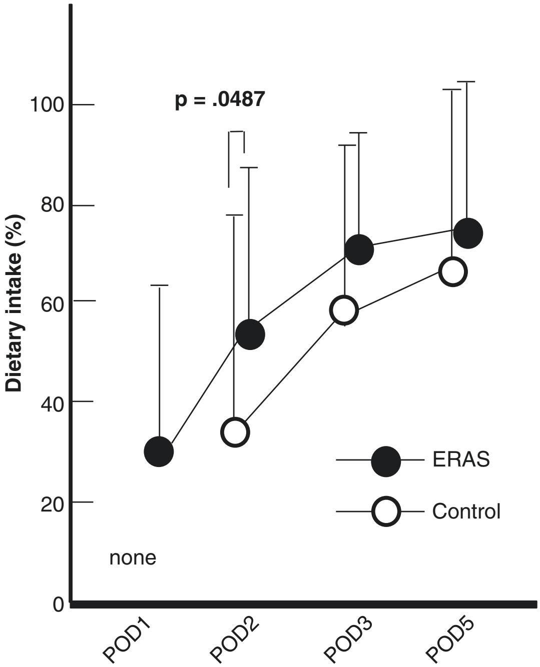
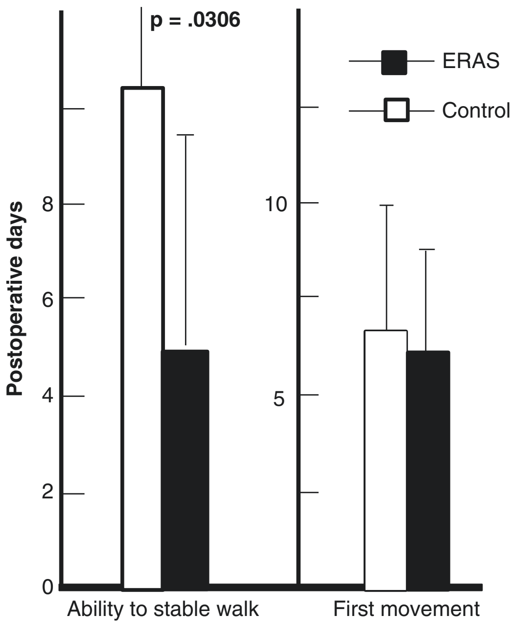


Fig. 11.5 Times to ability to walk stably and to first bowel movement after resection of HCC among patients in the control (open squares) and ERAS (closed squares) groups. Ability to walk stably occurred significantly earlier ($P = 0.031$) in the ERAS than in the control group



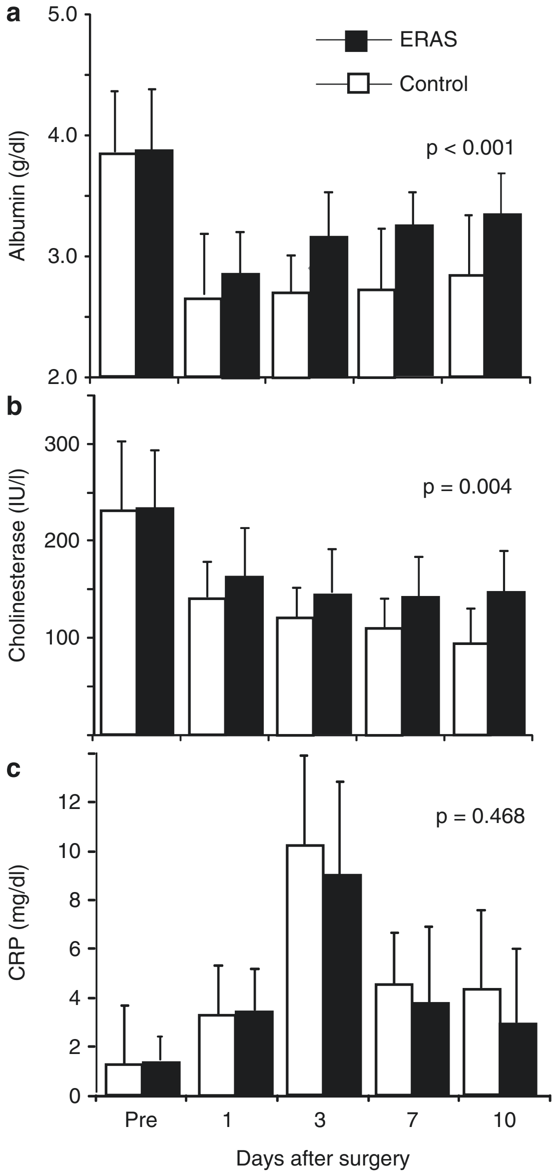


Fig. 11.6 Serum concentration of (**a**) albumin, (**b**) cholinesterase, and (**c**) C-reactive protein in the ERAS (closed squares) and control (open squares) groups after liver resection. Data are shown as the mean ± standard deviation

11.4 Clinical Application of ERAS for Patients Undergoing Resection of HCC in Japan

Application of the ERAS protocol did not have any detrimental effect on safety in HCC patients with chronic liver disease undergoing liver resection. This study showed that use of an evidence-based multimodal enhanced program following the removal of more than two liver segments for HCC accelerated postoperative recovery and resulted in a significantly shorter hospital stay. Although postoperative recovery did not differ significantly in the two patient groups overall, it differed significantly in patients who underwent extended surgery, suggesting the usefulness of ERAS was limited.

Early postoperative enteral nutrition has been found to improve clinical outcomes when compared with ‘nil by mouth’ [33]. In the present study, patients managed according to the ERAS protocol were able to drink fluids and eat normal food on the day of surgery. Early resumption of normal diet in combination with other elements of the enhanced recovery program is designed to reduce the occurrence of delayed gastrointestinal function after surgery and can even promote appetite. A restrictive perioperative intravenous fluid regimen may help reduce the occurrence of delayed gastrointestinal functioning [34]. The total volume of blood infused during the operation was significantly lower in the ERAS than in the control group. Fluid restriction may be important in hepatic surgery. In this study, postoperative dietary intake was significantly higher in the ERAS group.

It is important to treat surgical patients in an environment that encourages early mobilization [35]. In this study, mobilization was not achieved on the day of surgery in any HCC patient who underwent removal of more than two liver segments. Adequate pain control and a substantial effort by the nursing staff are required for early mobilization. Patients in the ERAS group were completely mobile after a median 5.5 days, and their median total hospital stay was 13.0 days, compared with 16.5 days in the control group. In the control group, two patients were classified as grade IVa on the Clavien-Dindo scale and were discharged from the hospital on postoperative days 111 and 147, respectively. Excluding these two patients from the control group would eliminate the significant difference between the two groups ($p = 0.052$). It is unclear whether the absence of the ERAS program was associated with the development of postoperative complications in these two patients, one of whom developed intractable ascites and the other bile leakage. Although the patient who developed intractable ascites did not receive perioperative BCAA, postoperative administration of BCAA during month 2 restored his albumin concentration to the preoperative level and reduced the volume of ascites. In contrast, none of the patients in the ERAS group administered perioperative BCAA developed postoperative intractable ascites after starting exercise therapy.

Using intraoperative ICG fluorescent cholangiography, we have attempted to eliminate the retention of abdominal drains after starting ERAS. Abdominal drains are inserted after liver surgery to monitor postoperative bleeding, reduce abdominal pressure caused by intractable ascites, and detect postoperative bile leakage and drainage. We found that intraoperative ICG fluorescent cholangiography could detect insufficiently closed bile duct stumps not detected by standard bile leak tests [36]. Thereafter, we have evaluated the usefulness of intraoperative ICG fluorescent cholangiography for our additional patients. The subjects were 132 patients who underwent hepatic resection without biliary reconstruction. Patients underwent a leakage test using ICG dye, followed by ICG fluorescent cholangiography using the photodynamic eye. Postoperative bile leakage occurred in 7/132 patients (5%) and persisted for a median 6 weeks. The incidence of postoperative bile leakage was 0%

(0/37) in patients with type A fluorescence pattern (no fluorescence type: no fluorescence detected on the cut surface of the liver, suggesting absence of bile ducts at the surgical margin), 2% (1/51) in patients with type B pattern (intact bile duct type: fluorescence showing one or more intact bile ducts on the cut surface), 6% (2/31) in patients with type C pattern (injured bile duct type: leakage of dye from one or more bile duct stumps on the cut surface), and 31% (4/13) in patients with type D pattern (unconfirmed type: leakage of dye from an unclear source on the cut surface). We have demonstrated that ICG fluorescent cholangiography may be useful for preventing bile leakage after hepatic resection, but patients with type D pattern of fluorescence should be carefully monitored for leakage for several weeks [37].

Although two patients in the ERAS group experienced postoperative intra-abdominal abscesses due to minor bile leakage, both were started on antibiotics within 2 weeks after surgery.

Japan has a universal public health insurance system, which covers 70–90% of all medical costs, and patients in Japan do not pay much for hospital admissions. Consequently, early discharge is not a priority, and some patients are reluctant to accept shorter hospital stays. Short-term outcomes have been reported in 7732 patients who underwent hepatectomy for more than one segment during 2011 in 987 different hospitals, as identified in the National Clinical Database of Japan [38]. The mean and median lengths of hospital stay after HCC surgery were 23.7 and 16.0 days, respectively.

Almost all of the patients in this study had liver dysfunction, such as chronic hepatitis or cirrhosis. We previously reported that, in patients with HCC and hepatic impairment who underwent liver resection, exercise significantly decreased body mass and fat mass, as well as insulin resistance, at 6 months postoperatively [32]. Maintenance of postoperative physical strength and earlier resumption of daily activities may be enhanced by intensifying perioperative and postoperative exercise. In this study, patients with liver dysfunction started exercise therapy, along with BCAA treatment, within 1 month before surgery, and restarted exercise therapy plus BCAA on postoperative days 4–6. Of patients who underwent removal of two or more sections, 22 (47%) of 47 in the ERAS group and 10 (42%) of 24 in the control group started exercise therapy and received BCAA. Because fasting time was shorter in the ERAS group, their increased postoperative dietary intake and perioperative exercise therapy, along with BCAA treatment, may have resulted in higher serum concentrations of albumin and cholinesterase, which are markers of nutritional status, during the early postoperative period.

It is unclear if the ERAS program reduces morbidity rates after liver resection. Randomized trials performed in the UK [8] and China [9] showed lower rates of complications in ERAS patients, but other studies have failed to show any differences. In this study, the overall rates of complications before and after surgery were similar in the ERAS and control groups. However, severe complications (Clavien-Dindo grade IV) were less common in the ERAS group.

Prophylactic drains are employed in many centers to detect early complications, such as postoperative hemorrhage and bile leakage; to remove intraperitoneal fluids; and to prevent abscess formation. However, abdominal drainage after liver resection may not reduce the incidence of re-interventions needed for postoperative complications [39–41]. Several studies have reported higher rates of infected collections with than without drainage [39, 42, 43], suggesting that drains may be detrimental to clinical outcomes by providing a route for ascending infections. Another disadvantage of drains in enhanced recovery settings is that they represent a significant impediment to achieving early mobilization. In the present study, although the number of patients without intraoperative abdominal drains was significantly higher in the ERAS than in the control group, the frequency of abdominal paracentesis was higher in the ERAS group. Abdominal paracentesis is frequently caused by refractory ascites. Postoperative abdominal paracentesis in these patients may have been avoided by the installation of abdominal drains. One patient in the control group required a postoperative hospital stay of 147 days to treat postoperative bile leakage. Insertion of an abdominal drain may prevent complications after major bile leakage. Omitting prophylactic intraoperative installation of abdominal drains in HCC patients with liver dysfunction, as part of the ERAS program, seems relatively disadvantageous (Fig. 11.7).

11.5 Conclusion

A multimodal enhanced recovery program was feasible and effective for patients with chronic liver diseases undergoing extended liver resection for HCC. Patients were able to drink and eat on the day following surgery, and most were mobile by the sixth day. Additional studies are needed to confirm the effectiveness of this protocol, as determined by patient recovery, and to determine whether to include other components of the ERAS program.

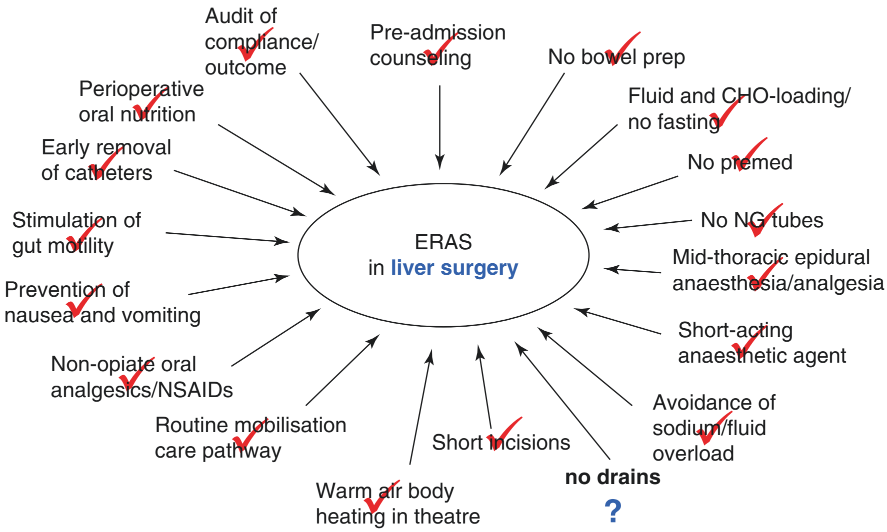


Fig. 11.7 ERAS in liver surgery. The results of excluding the prophylactic intraoperative placement of abdominal drains for HCC patients with liver dysfunction as part of the ERAS program remain unclear

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Chapter 12
Enhanced Recovery After Surgery (ERAS) for Postoperative Pediatric Surgical Disorders

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Abstract The purpose of ERAS protocol for children is less invasive operation, prevention of complication, promotion of recovery after surgery, and good mental, physical development. The most important factors of ERAS for children are avoidance of prolonged fasting, nonroutine use of tubes or drains, and early oral nutrition and mobilization. We described in detail about these important factors:

(1) Avoidance of prolonged fasting: General fasting standards were 2 h for clear fluids, 4 h for breast milk, 6 h for nonhuman milk/cow milk and solid substances, and 8 h for meat/fried or fatty foods. However, the Japanese guideline does not clearly show fasting time.
(2) Nonroutine use of tubes and drains: The non-drainage patients after large volume intraperitoneal lavage for perforated appendicitis were found to have a faster postoperative recovery. Reasons given were a control of bacterial proliferation due to physical reduction in intraperitoneal bacteria count and faster wound healing since a drainage tube is not inserted.
(3) Early oral nutrition and mobilization: Postoperative management for infants has changed from intravenous nutrition to early oral nutrition. We describe about dietary fiber as important nutrient.

Keywords ERAS • Children

12.1 ERAS Protocol for Children

The purpose of this protocol is centered on the three factors: (1) reduction of invasive operations (reaction), (2) prevention of complications in surgery, and (3) promotion of recovery after surgery, in order to achieve a reduction in the length of hospital stay, and early reintegration into society as a result. In addition, from a

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social standpoint, this protocol seeks to reduce medical fees while ensuring the safety of the patient. These three factors are important for infants as well as for adults, but for children who are in a constant state of growth and development, a long-term hospital stay is a mentally and physically unnatural environment. It is easy to predict that this strongly influences their future development. Subsequently, avoiding such demerit is also one of the purposes of the protocol.

12.2 General Factors of ERAS and Factors Needed for Children

Factors of ERA which are generally required for adults are shown in Table 12.1 [1]. However, ERAS protocol for pediatric surgical diseases has yet to be established. One reason for this is that clinical conditions vary depending on the wide range of individual diseases, and response must be made according to age and growth. As a result, the actual condition is that a consistent policy from the preoperative period has not been established. Among this, items which are especially needed for children are (1) avoidance of prolonged fasting, (2) nonroutine use of tubes and drains, and (3) early oral nutrition and mobilization.

A bibliographic consideration on these three items was carried out as follows.

12.3 Avoidance of Prolonged Fasting

Fasting for many hours before surgery is said to cause unnecessary suffering to the patient, such as a sense of thirst and hunger, and may increase the risk of complications during the perioperative period such as dehydration and hypoglycemia. In the

Table 12.1 A list of the most common components of ERAS Society recommendations for perioperative care [1]

Perioperative	Intraoperative	Postoperative
Preoperative counseling	Short-acting anesthetics	Epidural anesthesia/analgesia
Fluid and carbohydrate loading	Epidural anesthesia/analgesia	Nonroutine use of nasogastric tubes
Nonroutine bowel preparation	Nonroutine use of tubes and drains	Nausea and vomiting prophylaxis in high-risk patients
Avoid of prolonged fasting	Maintenance of normovolemia	Maintenance of normovolemia
Antibiotic and antithrombotic prophylaxis	Maintenance of normothermia	Early removal of tubes and catheters
		Early oral nutrition and mobilization
		Opioid-sparing analgesia
		Audit of compliance and outcome

Table 12.2 Preoperative fasting guideline for children [8]

	Clear fluid	Breast milk	Infant formula	Light meal, nonhuman milk
ASA	2 h	4 h	6 h	6 h: light meal without lipid
				8 h: meal with fried or fatty foods
ESA	2 h	4 h	6 h	6 h: light meal without lipid
SSAI	2 h	4 h	4 h:<6w	6 h: light meal without lipid
			6 h:>6w	
AAGBI	2 h	4 h	6 h	6 h: light meal without lipid
CAS	2 h	4 h	6 h	6 h: light meal without lipid
				8 h: meal with fried or fatty foods
ANZCA	2 h	4 h	6 h	6 h: light meal without lipid
JSA	2 h	4 h	6 h	

past few years, a shorter fasting time has been recommended by ensuring safety in the use of anesthesia by the strict observance of intake contents and intake time, and a guideline regarding preoperative fasting has been prepared by the US and EU member nations [2–7]. In Japan as well, a preoperative fasting guideline was prepared in July 2012 [8]. Recently, evidence that preoperative intake of carbohydrate (CHO) drinks reduces postoperative insulin resistance in adults has been shown by the ERAS protocol. From the bibliographic consideration of evidence regarding aspiration in children, preoperative eating and drinking, and the fasting guideline, the following conclusion was reached. Since the publication of the ASA guideline, general fasting standards were 2 h for clear fluids, 4 h for breast milk, 6 h for nonhuman milk/cow milk and solid substances, and 8 h for meat/fried or fatty foods. Safety of intake of clarified water 2 h prior has been verified by many randomized controlled trials (RCT), significantly reducing complaints of thirst and hunger [9]. On the other hand, there are few RCT on breast milk and nonhuman milk, and evidence is considered to still be inadequate [2, 9]. The Japanese guideline [8] does not clearly show fasting time, for reasons that evidence of solid food is inadequate compared to liquid food, and the definition of solid food is unclear (Table 12.2). Moreover, the target of the fasting guideline has been set as children with almost no risk of aspiration or reflux. In other words, in cases of emergency operation (especially injury), gastrointestinal stenosis/obstruction, obesity, diabetes, and when it is difficult to secure a clear airway.

12.4 Nonroutine Use of Tubes and Drains

In the ERAS protocol, drains and catheters are considered to be hindrances when getting out of bed, and the policy, “do not insert a catheter unnecessarily,” and “when a catheter is in place, remove it as soon as possible,” has been recommended.

Table 12.3 Comparison of clinical data (non-drainage versus drainage) [10]

	Non-drainage (*n* = 29)		Drainage (*n*=24)
Hospital stay (days)	10.1 ± 4.2	<	18.8 ± 12.5**
Fever (days)	2.8 ± 2.0	<	7.7 ± 5.9**
Fasting (days)	1.8 ± 1.6	<	3.5 ± 3.0*
Total complication	2 (6.9%)	<	8 (33.3%)#
Superficial wound infection	2 (6.9%)	<	6 (25.0%)
Intra-abdominal abscess	0	<	2 (8.3%)
Bowel obstruction	0		0

**$P < 0.05$ by unpaired *t*-test
*$P < 0.01$ by unpaired *t*-test
#$P = 0.015$ by Fisher test

Out of 53 cases of perforated appendicitis, 24 cases which a drainage tube was inserted after a normal amount of postoperative peritoneal lavage were targeted as the drainage group and 29 cases which a drainage tube was not inserted, and more than 10,000 ml of postoperative peritoneal lavage was performed until opacity in ascetic fluid disappeared as the non-drainage group. These two groups were compared in consideration of the following six items [10]: (1) hospital stay, (2) fever time, (3) fasting period, and as a complication, (4) superficial wound infection, (5) intra-abdominal abscess, and (6) bowel obstruction.

According to the results, the non-drainage group had a significantly shorter hospital stay, fever time, and fasting period. Moreover, although no bowel obstruction was observed, the non-drainage group experienced fewer superficial or intra-abdominal abscess formations, and a significant difference was observed (Table 12.3).

According to the above fact, the non-drainage group after large volume intraperitoneal lavage was found to have a faster postoperative recovery. Reasons given were a control of bacterial proliferation due to physical reduction in intraperitoneal bacteria count and faster wound healing since a drainage tube is not inserted [10].

12.5 Early Oral Nutrition and Mobilization

By providing postoperative oral nutrition earlier, atrophy of the bowel mucosa is minimized, and complications by postoperative infection are prevented by normalizing intestinal peristalsis and intestinal flora. In fact, this is also considered to be effective in the prevention of septic complications due to synbiotic (probiotics + prebiotics) administration. Furthermore, early postoperative oral nutrition is reported to reduce hypermetabolism level due to the body's invasion response [11].

On the other hand, regarding early oral nutrition for infants, significant reduction in postoperative complications has been reported, but does not reduce death rate or shorten time in the ICU [12]. It has also been reported that frequency of occurrence of diarrhea should be more carefully monitored in infants than in adults. Furthermore, early oral nutrition in very low birthweight infants is recommended, but attention should be given to an increased risk of necrotizing enterocolitis [13]. Therefore, at this point in time, no adequate evidence regarding early oral nutrition for infants has been obtained.

Postoperative management for infants has changed from intravenous nutrition to early oral nutrition. At this time, I would like to describe about dietary fiber which is essential for probiotics.

Regarding early oral nutrition, elemental diet is frequently used, but as a side effect, atrophy of gastrointestinal mucous membrane may be problematic, as with total parenteral nutrition (TPN) [14]. Residual jejunal type model rats with short bowels were used and the length of microvilli in the elemental diet administration group and elemental diet + water-soluble dietary fiber (pectin) administration group were compared. As a result, the length of microvilli in the jejunum and ileum in the elemental diet administration group was significantly shorter than that in the elemental diet + pectin administration group. In other words, mucosal atrophy occurs as a result of administration of only elemental diet and can be prevented by adding pectin [14].

The effects of dietary fiber in gastrointestinal tract are (1) extended gastric emptying time, (2) extended intra-intestinal migration time, (3) increase in frequency and volume of defecation, and (4) thickening of smooth muscle in the digestive tract, which have gained attention [15]. These activities are thought to occur due to short-chain fatty acids produced by fermentation of dietary fiber in the colon [16]. For this fermentation, intestinal bacteria are needed.

There are many and various clinical conditions for infants, and explaining nutrition management in a unified manner is difficult, but dietary fiber enhances growth of intestinal mucosa and is considered to be an important nutrient for the effective adaptation of the intestinal tract.

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Chapter 13
Enhanced Recovery (Fast-Track) After Cardiac and Vascular Surgery

Wataru Tatsuishi, Kiyoharu Nakano, Sayaka Kubota, Ryota Asano, Atsuhiko Sato, and Go Kataoka

Abstract Enhanced recovery after surgery (ERAS®) is an enhanced postoperative recovery program based on evidence-based medicine introduced by the European Society for Clinical Nutrition and Metabolism in 2005. Many reports have been shown that this program is useful not only in general surgery but also in cardiac and vascular surgery. The goals of this management are reducing operative stress, early restarting of meal consumption, early starting of postoperative rehabilitation, shortening the length of postoperative hospital stay, reducing medical costs, reducing patient anxiety perioperatively and encouraging the patient's volition to recover, and securing safety and satisfactory results. Although only minimally invasive surgery has been continuously developing in Japan, this management is not yet widely used and conventional management remains standard in many institutions. In this chapter, we introduce the many elements of ERAS® management for cardiac and vascular surgery divided into the preoperative, intraoperative, and postoperative periods, according to our experiences and past reports.

Keywords Enhanced recovery after surgery (ERAS®) • Cardiac surgery • Vascular surgery • Perioperative management • Patient satisfaction

13.1 Introduction

The enhanced recovery after surgery (ERAS®) protocol was reported as a multicenter analysis by the European Society for Clinical Nutrition and Metabolism (ESPEN) in 2005 [1]. It is an enhanced postoperative recovery program based on evidence-based medicine that enhances postoperative recovery and consequently improves patient prognosis. The effects of this program include shortening the

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length of postoperative hospital stay, reducing postoperative morbidity, and reducing medical costs, compared with the conventional approach.

Initially, Cotton reported a “fast-track” perioperative management for coronary artery bypass graft (CABG) surgery that was implemented to hasten recovery after an operation [2]. Recently, this fast-track method (ERAS®) has spread worldwide, and many reports have shown its effectiveness in cardiac and vascular surgery [3–5]. Furthermore, ERAS® for transcatheter aortic valve implantation (TAVI), which was introduced as a minimally invasive procedure for aortic valve stenosis, was reported recently [6].

However, many institutions of cardiovascular surgery in Japan are still using conventional management. Hence, in Japan, there is no report of ERAS® for cardiac surgery, and there are only two reports of its use for vascular surgery [7, 8]. We introduced the ERAS® management for abdominal aortic aneurysm (AAA) open surgery in 2008 and achieved excellent postoperative results. We have also used the fast-track management for cardiac surgery. On the basis of our experiences, we explain in this chapter the ERAS® management for cardiac and vascular surgery.

13.1.1 Goals of ERAS®

(1) Reducing operative stress
(2) Early restarting of meal consumption, early starting of postoperative rehabilitation, and shortening the length of postoperative hospital stay
(3) Perioperatively reducing patient anxiety and encouraging patient’s volition to recover
(4) Securing safety and satisfactory results

At our institution, ERAS® is done on the basis of the above principles.

Success of surgical treatment is based not only on the operative success. A complete surgical treatment includes preoperative examination, judgment of operative indications, informed consent, operation, postoperative management, and postoperative explanation. Hence, all aspects of perioperative management are important. ERAS® is a systematic program with various approaches to avoid postoperative fatigue due to operative invasion, consequently avoiding the physical weakening of the patient. Hence, ERAS® represents a complete surgical treatment.

Considering the first goal (reducing operative stress), as for other lesions, minimally invasive surgery has been introduced in cardiovascular surgery, for example, off-pump CABG, minimally invasive cardiac surgery, endovascular aortic repair (stent graft), and TAVI. Moreover, various devices have been developed to date. The reduction of operative invasion has attracted attention and has been accepted clinically.

However, few cardiovascular institutions in Japan consider goals 2–4 above. Probably, many surgeons consider that early recovery management has a risk of morbidity, such as hemodynamic compromise and arrhythmia, because of the high invasion potential of cardiovascular surgery. Although early mobilization is not achieved in some cases, it is possible in most cases, and many reports have shown good results of early recovery, with reduced or unchanged morbidity [3–5]. Patient

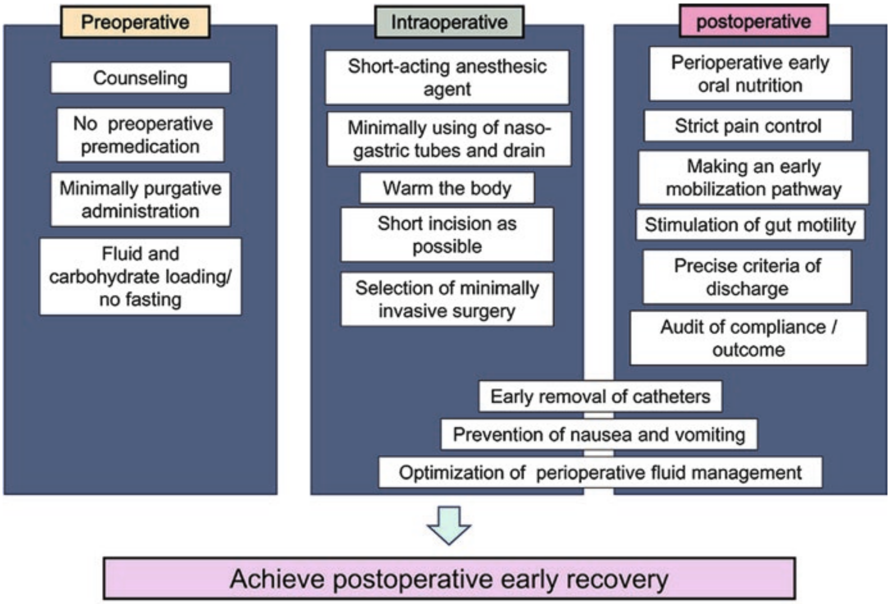

Fig. 13.1 Elements of ERAS® for abdominal aortic aneurysm open surgery at our institution divided into the preoperative, intraoperative, and postoperative periods

satisfaction could not be achieved if activities of daily living (ADL) are ultimately reduced because of delay of postoperative recovery despite the success of surgery. Therefore, we recommend the ERAS® management for cardiovascular surgery.

In Sect. 13.2, ERAS® for cardiac and vascular surgery based on our experiences, divided into preoperative, intraoperative, and postoperative managements, will be described. Although ESPEN advocated many elements of perioperative management in ERAS® [1], some elements are not always adopted and needed because of institutional capacity, the management and operation procedures of each disease, and the patient's state. Furthermore, other elements that were not advocated might be needed. At our institution, the elements were used properly depending on the situation (Fig. 13.1).

13.2 ERAS® for Cardiovascular Surgery

13.2.1 Target Disease

All diseases in cardiac and vascular surgery are indicated for ERAS® management. Cardiac surgery comprises cardiac surgery (valve surgery, CABG, etc.) and thoracic aortic surgery (because thoracic aortic surgery needs extracorporeal circulation). After cardiac surgery, restarting of early meal consumption is easy if extubation is done. Other factors include high operative invasion, need for catecholamine, and postoperative bleeding; thus, almost all patients need management in the intensive care unit (ICU). Hence, management of early discharge from the ICU and starting rehabilitation are essential for early recovery.

In vascular surgery, ERAS® is the most effective method for open (AAA) surgery. Although open surgery does not involve manipulation of the gastrointestinal tract, paralytic ileus often develops postoperatively, and ischemic enterocolitis occurs in a few cases because of embolism or vascular spasm. However, ischemic changes almost do not occur, and meal consumption can be restarted from the next morning. Another feature of patients undergoing vascular surgery is the possibility of the coexistence of whole artery diseases such as coronary artery and cerebral artery diseases. Preoperative consideration of operative procedures and coexisting diseases is important to avoid intraoperative and postoperative morbidity.

13.2.2 Preoperative Management

Preoperative assessment is important in cardiac and vascular surgery, because a safe and appropriate operation contributes to postoperative recovery. Other organ problems, age, medical history, ADL, and nutritional state should be checked. Among several preoperative examinations, enhanced computed tomography (CT) is the most important. CT enables checking the incision position and length, intraoperative operation site (calcification, atheroma, thrombus, etc.), anatomical abnormalities, and other organ abnormalities. On the basis of its findings, the strategy of the operation and the method of risk avoidance are firmly decided.

The preoperative coagulation factor levels should be checked and administration of anticoagulant and/or antiplatelet agent to avoid postoperative bleeding, which may cause recovery delay.

As for other lesions, preoperative premedication is not needed in all cases. The absence of preoperative premedication can reduce the risk of respiratory depression and has the advantage of accelerating the patient's awakening from anesthesia.

In cardiac surgery, preoperative purgative administration as a pretreatment is not needed because there is no intraperitoneal procedure and purgative administration causes dehydration. Normal meal administration is maintained until the night before surgery, and CH–O loading and oral rehydration therapy are done until 2 h before the surgery, with the exception of patients with severe heart failure. In contrast, in AAA open surgery, preoperative purgatives are administrated minimally to secure a good field of operative vision. Moreover, oral rehydration therapy and CH–O loading are done to resolve the dehydration due to purgative administration. This could avoid intraoperative overinfusion that causes intestinal edema and overvolume in the third space [9]. Another effect of oral intake is inducing parasympathetic nerve dominance. Furthermore, a normal diet, not a low-residue diet, is provided until the night before the operation.

Preoperative washing of the whole body is needed to keep the skin clean and prevent postoperative infection. If the patient is unable to walk, a bed bus is used.

One of the most important aspects of ERAS® is that the patients themselves have the will to recover during the surgical management. An informed consent (IC) form containing statements for reducing the patients' perioperative anxiety and encouraging their volition to recover is needed. The IC form should contain information not only about the surgical procedures but also about postoperative examination planning, therapy results, predicted morbidity, criteria for discharge, predicted hospital stay after surgery, and others. The most important content is that patients also need to be encouraged about early recovery through methods such as rehabilitation and meal consumption. Sufficient understanding of the IC form, including the state of the patient and the plan of therapy, should be achieved both by the medical staff and the patient's family. Moreover, preoperative teaching of motions for pain avoidance and induction of prehabilitation are also useful for the patient's relief [10, 11].

13.2.3 Intraoperative Management

Intraoperative and postoperative fluid management are essential. Either too much or too little fluid can cause several problems [12]. The objective of conventional fluid management is avoiding major problems such as acute kidney disease, myocardial ischemia, and congestive heart failure (Fig. 13.2). On the other hand, the objectives of ERAS® management are avoiding major or minor problems such as postoperative nausea and vomiting (PONV) and intestinal edema, thus requiring a stricter fluid management. Recently, the usefulness of goal-directed fluid management (GDFM), which uses factors such as systolic volume index, cardiac index, and amount of urine as the hemodynamic indices, has been reported [13]. We also have done strict fluid management by using a Swan–Ganz catheter. Moreover, a diuretic is administrated

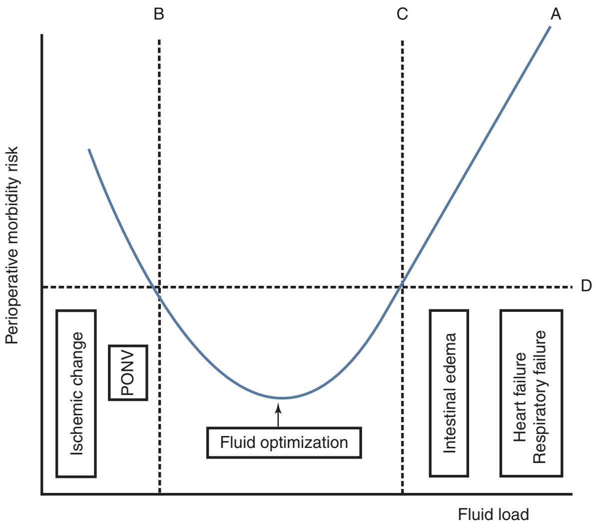

Fig. 13.2 Curve A represents the hypothesized line of risk. Broken line B represents the border between dry and normal. Broken line C represents the border between wet and normal. Broken line D represents a division between patient and groups in ERAS® and conventional management (from Ref. [12] and reorganized)

for patients with cardiac disease, causing intraoperative dehydration including tissue dehydration. Moreover, the invasion extent of cardiovascular surgery is large, causing hypoalbuminemia and movement of large fluid amounts in the third space. Consequently, hemodynamic instability easily occurs and a large fluid volume might be needed. It is difficult to recover the hypovolemic state through only preoperative oral intake. Hence, administrating sufficient fluid for patients during the operation is preferable, because postoperative hemodynamic instability adversely affects early recovery.

Furthermore, cardiovascular surgery is different from surgery of other regions in terms of the amount of bleeding. To avoid blood transfusion as much as possible, autotransfusion and intraoperative blood salvaging autotransfusion are used.

Early extubation has a good effect for early restarting of meal consumption. Considering anesthesia, remifentanil (a short-acting anesthesia) is useful to achieve early extubation after the operation. Although Borracci et al. reported that many patients undergoing cardiac surgery could receive routine extubation in the operation theater [14], the risk of reoperation owing to bleeding in cardiac surgery should be considered. Hence, we have not done extubation in the operative theater during cardiac surgery. However, in vascular surgery, bleeding after surgery is very rare; thus, all patients could receive routine extubation in the operation theater.

In abdominal aorta operation, pain control with an epidural anesthesia is useful for reducing the patient's stress and promoting early recovery. However, patients with AAA or peripheral artery disease are often administrated with antiplatelets for coronary artery disease or cerebral vascular disease; thus, care must be taken to avoid bleeding due to puncture. Except for epidural anesthesia, the usefulness of transversus abdominis plane block for abdominal surgery was reported [15]; thus, this could be considered a method for pain control.

To maintain the body temperature intraoperatively, warming infusion and heating of the operation theater are done. These could reduce the endocrine metabolism and sympathetic reactions stimulated by the operative invasion. Consequently, the amount of bleeding, postoperative infection, and cardiopulmonary problems could be reduced [16–18].

To prevent PONV and SIRS, dexamethasone (4–10 mg) administration before anesthesia induction is useful. Ephedrine–dexamethasone [19], metoclopramide–dexamethasone [20], ondansetron (4 mg) at the end of operation [21], and droperidol (1.25 mg) at the start of operation [22] were also reported as useful.

A nose–gastric tube is not inserted in cardiac surgery, in contrast to AAA open surgery in which a nose–gastric tube inserted for intraoperative air drainage and to prevent postoperative vomiting.

The surgical technique of the surgeons and nurses needs to be reliable and efficient. Therefore, we have stylized and simplified the surgical procedure (by organizing the number of instruments, sharing procedure details, etc.). Moreover, when the quality of the procedure could be maintained, minimally invasive procedures should be considered for all operations to reduce the patient's stress.

It is also important to prevent infection in ERAS® management. Preoperative wide disinfection (two times) and washing the field of operation with large amounts of physiological saline and administration of antibiotics 30 min before skin incision have been done to thoroughly prevent infection. With this management, there has been no case of mediastinitis at our institution since 2008.

13.2.4 Postoperative Management

13.2.4.1 Cardiac Surgery

Figure 13.3 shows the clinical plans of valve surgery, CABG, and thoracic aorta surgery. Postoperative management is done in the ICU. The length of ICU stay is 1 day in CABG surgery and 2 days in surgery with extracorporeal circulation. Almost all patients could be withdrawn from catecholamine management before ICU discharge. Fluid management (GDFM) was kept the same as for intraoperative management.

Early extubation is done after confirming no bleeding, good respiration, and clear consciousness. The extubation time of almost all patients in cardiac surgery is 2 h. The rate of reintubation is <1% (cardiac surgery, 0.3%; vascular surgery, 0.01%). Moreover, we investigate the state of respiration before extubation. Sufficient positive end-expiratory pressure (PEEP) and recruitment maneuver are done to open the all alveoli and achieve a PaO_2/FiO_2 (P/F) ratio of >500.

Early restarting of meal consumption is essential in ERAS®. It maintains the intestinal mucosa and intestinal immunity, prevents bacterial translocation, and reduces metabolic reaction (reduces inflammation).

In cardiac surgery, after the management for avoiding PONV is done, there is no concern about early restarting of meal consumption. However, in patients with paralysis or advanced age, care must be taken to avoid accidental ingestion. The meal is usually a normal diet; however, if the patient wants another kind of meal or if accidental ingestion occurs, the kind of meal is changed. At 2 or 3 h after extubation, the patient is allowed to drink water, and on the next morning after the operation, meal consumption is restarted.

After returning to the ward, rehabilitation is started in stages. The goal of rehabilitation is returning to the preoperative ADL and the ability of movement. For sufficient and stable rehabilitation, strict control of pain and arrhythmia is needed. Strict pain control involves preoperative teaching of motions for pain avoidance and administration of analgesics. To achieve adequate analgesia, a sufficient quantity of analgesics is needed. We have used acetaminophen (3–4 g/day); however, any analgesic providing enough pain relief is acceptable.

Postoperative atrial fibrillation (AF) is one of the most complicated and common arrhythmias after a cardiac operation. Postoperative AF is undesirable because of its many morbidities and increased mortality [23]. Anti-arrhythmia treatment consisting of pilsicainide hydrochloride hydrate (75–150 mg/day) and/or flecainide acetate (100–200 mg/day) is administrated. Additionally, heparin sodium infusion is used to achieve an activated partial thromboplastin time of twice the normal value.

rest level	V/T	free	rest in bed		walk in ward	walk free in hospital using elevator		walk free using upstairs		
	C		rest in bed	walk in ward	walk free in hospital using elevator		walk free using upstairs			
clean	V/C/T	shower	bed bath			shower				
diet	V/C/T	normal diet	stop	normal diet						
drink	V/C/T	free	stop	drink with limitation (<1000–1200ml)						
infusion	V/C/T	none	minimum infusion		none					
			antibiotics			none				
			catecholamines			none				
medication	V		none	analgesic, PPI, diuretic, warfarin, others						
	C/T		none	analgesic, PPI, others						
management	V/C/T	IC			wound check		wound check (if needed)			
			monitor				monitor (if needed)			
blood glucose	V/C/T		CVII		sliding scale					
place	V/T	ward	ICU		ward					
	C		ICU	ward						
examination	V	BE/X-P	BE/X–P/ECG	BE/X–P	BE/X–P	BE/X–P		BE/X–P		BE/X–P/TTE
	C/T							BE/CT		BE/X–P
	day	Preoperative	operative day	POD1	POD2	POD3	POD4	POD5	POD6	POD7

Fig. 13.3 Clinical plan of valve, coronary artery bypass graft (CABG), and thoracic aorta surgeries. *V* valve, *C* CABG, *T* thoracic aorta, *PPI* proton pump inhibitor, *IC* informed consent, *CVII* continuous venous insulin infusion, *ICU* intensive care unit, *BE* blood examination, *X-P* X-ray photography, *CT* computed tomography, *TTE* transthoracic echocardiography, *POD* postoperative day

Verapamil hydrochloride (1–5γ), diltiazem hydrochloride (1–5γ), or digitalis is used in cases of tachycardia (heart rate >100 beats/min). Recently, it was reported that short-term administration of amiodarone is useful and effective for paroxysmal AF without adverse effects [24].

The recent ERAS® management involves the control of postoperative blood glucose. Insufficient blood glucose control worsens the rate of surgical site infection and wound adaption. In CABG, the relationship between the postoperative blood glucose concentration and the occurrence of postoperative AF was also reported [23, 25]. The Society of Thoracic Surgeons guidelines also suggest the thorough control of blood glucose during perioperative management [25]. Blood glucose levels are often reported to be good at <180 mg/dL. Various means of blood glucose control have been reported. Control methods that can be used in the ICU and ward should be selected.

When the patients return to the ward, the Swan–Ganz catheter, bladder catheter, and/or central venous catheter are removed. Peripheral venous catheters should be removed if possible. Early catheter removal prevents infection and facilitates early rehabilitation (the presence of many catheters reduces the willingness of the patient to move). Moreover, patients tend to recognize the reduction of catheters or attached lines (such as a monitor) as signs of recovery. Consequently, it enables increasing the postoperative exercise intensity of patients from the early phase. It also eliminates atelectasis of the back side and the need for oxygen inhalation.

A shower bath is started from postoperative day 3 or 4 to wash the wound with water jet. This also enhances the patient's early mobilization, in addition to the appearance and feeling of cleanliness and the reduction of infection risk.

In the Guideline for the Prevention of Surgical Site Infection 1999 [26], the administration of prophylactic antibiotics was unified at our institution as cefazolin sodium hydrate 2 g × 2/day until the second day after the operation (the amount is reduced in patients with poor renal function.)

Figure 13.3 shows the criteria for discharge of valve, CABG, and thoracic aorta surgery. At our institution, the length of hospital stay is generally 7–12 days in patients with valve surgery and 6–10 days in patients with CABG surgery. The discharge day is decided considering the patient's age, examination results, convenience of the family, and other factors.

13.2.4.2 Vascular Surgery

Although the basic features of vascular surgery are not different from those of cardiac surgery, there are some different points.

Figure 13.4 shows the plan of AAA ERAS® management. The ICU stay is only 1 day. GDFM is also done. Especially in patients with ischemic disease, care must be taken to avoid hemodynamic instability and ischemic events.

Greater pain care is needed than for thoracic operation because of abdominal muscle damage. Abdominal pain is an obstruction to rehabilitation. We usually use loxoprofen (180 mg/day) or acetaminophen (4 g/day) on the day of the operation. In some

rest level	free	rest in bed	walk in ward	walk free in hospital using elevator	walk free using upstairs				
clean	shower	bed bath		shower					
diet	normal diet	stop	diet (patient's favorite)			normal diet			
			gum chewing						
drink	free	stop	free						
infusion	none	minimum infusion	PPN (if needed)			none			
		antibiotics			none				
medication		intestinal peristaltic reflex regulator, analgesic, PPI, others							
management	IC purgative		wound check		wound check (if needed)				
		monitor			monitor (if needed)				
blood glucose		CVII	sliding scale						
place	ward	ICU	ward						
examination	BE/X–P	BE/X–P	BE/X–P	BE/X–P	CT			(BE/X–P)	
day	Preoperative	operative day	POD1	POD2	POD3	POD4	POD5	POD6	POD7

Fig. 13.4 Clinical plan of abdominal aortic aneurysm open surgery. *PPN* peripheral parenteral nutrition; other abbreviations are same as Fig. 13.3

cases, pentazocine is also used. Moreover, loxoprofen and acetaminophen have an antipyretic effect, and they could provide relief against postoperative fatigue due to fever.

In conventional managements, the timing of restarting meal consumption is after the confirmation of flatus and bowel sound. However, postoperative adynamic ileus is recovered by protecting the intestine, postoperative medication for intestinal peristaltic reflex, walking during rehabilitation, and other methods. In ERAS® for AAA open surgery, drinking water is started 2 or 3 h after extubation, and meal administration is restarted from the next morning after surgery. As a precaution against PONV, a nose–gastric tube is kept inserted until the next morning after surgery. From the night of the operation, administrations of analgesics, antiemetics (metoclopramide), and intestinal peristaltic reflex regulators (magnesium oxide, Daikenchuto) are started. If the amount of uptake is poor, peripheral parenteral nutrition is added. In addition to glucose and amino acids, the active use of fat emulsion is effective for consuming calories and reducing the amount of fluid.

The point of care is to detect the occurrence of ischemic enteritis or intestinal necrosis. The state of stool and abdominal symptoms should be checked daily. Additionally, postoperative CT is performed earlier (3 or 4 days after surgery) to check the state of the intestine.

After discharge from the ICU, removal of all catheters and tubes is attempted. The timing of removal of the epidural catheter should be decided according to the state of pain control. If possible, patients start performing shower bath from postoperative day 2. Only on the first day of performing shower bath, the wound is covered with waterproof dressing.

The criteria for discharge are shown in Table 13.1. Although an ERAS® study reported that discharge from the hospital was possible 3 days after open AAA surgery [27], considering the Japanese medical situation, 5–7 days after operation was the

Table 13.1 The criteria of discharge

Operation	Criteria
Cardiac: valve operation	No pericardial effusion in postoperative TTE
	Good control of warfarin (PT-INR)
	Good control of arrhythmia
	No infection in wound and mediastinum
Cardiac: CABG operation	No occluded anastomosed graft by postoperative cardiac CT
	No pericardial effusion and mediastinitis by postoperative cardiac CT
	Good control of arrhythmia
	No infection in wound
Thoracic aorta operation	No abnormality around anastomosis and artificial graft by CT
	No pericardial effusion and mediastinitis by postoperative CT
Abdominal aorta operation	No infection in wound
	No abnormality around anastomosis and intestine by CT
	Sufficient meal consumption
	No infection in wound

TTE transthoracic echocardiography, *PT-INR* international normalized ratio of prothrombin time, *CABG* coronary artery bypass graft, *CT* computed tomography appropriate timing of discharge to allow sufficient checking of the wound. Moreover, patients often feel anxious about very early discharge.

ERAS® has also been used for peripheral artery disease. Although the risk of management is lower than that of abdominal aorta surgery, some risk of cardiac accidents exists. For example, electrocardiogram monitoring is done. In patients with critical limb ischemia with necrosis, various ideas for ADL recovery and intervention by various health-care providers need to be considered.

13.2.5 Results

Several reports of ERAS® in cardiac surgery have been published worldwide. The mean length of hospital stay was reported to be 4.23 ± 0.73 days in CABG [3] and 6.7 ± 5.5 days in all cardiac surgeries [4]. Almost all reports showed that ERAS® for cardiac surgery was safe and resulted in few episodes of morbidity management. Figure 13.5 shows our results of ERAS® for open AAA. We reported the results of ERAS® management for AAA open surgery [7], and showed that ERAS® could

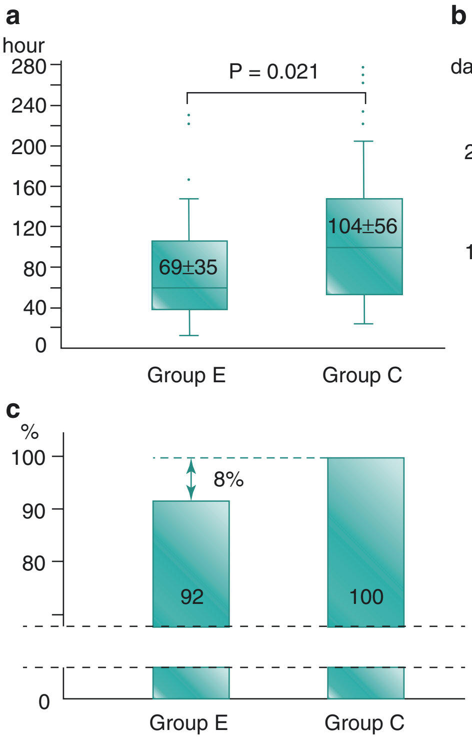

Fig. 13.5 Results of ERAS® for abdominal aortic aneurysm open surgery at our institution (from Ref. [7]). (**a**) Comparison of the timing of the resumption of meals after surgery. (**b**) Comparison of postoperative hospital stay. (**c**) Comparison of all medical costs. Group E, ERAS® management; Group C, conventional management

achieve early restarting of meal consumption, shortening of postoperative hospital stay, and reducing medical costs. In the last years, a shorter length of postoperative hospital stay was achieved (~7 days). The length of hospital stay reported from countries other than Japan was earlier; however, our plan of hospital stay is proper for the Japanese medical situation and for AAA surgery. Another report has shown the effects of reduction of postoperative inflammation by ERAS® [8].

Christensen and Kehlet reported that ERAS® management could provide relief against postoperative fatigue and enhance postoperative recovery [28]. Our results and those of Shimizu et al. support their findings.

13.2.6 Others

Although shortening the length of hospital stay is important, this is not the only important outcome. In ERAS® management, patient satisfaction is usually considered. Therefore, instead of using the same management in all cases, changes should be introduced according to the age and disease of patients.

Furthermore, improving the procedures, investigating the outcomes, finding new management practices [29], and providing feedback for the medical staff and patients should be done.

13.3 Conclusion

We provided an overview of the ERAS® management for cardiovascular surgery in this chapter. As for other lesions, ERAS® is useful to achieve early recovery and patient satisfaction. As mentioned above, minimally invasive operation was introduced in both cardiac and vascular surgery, and it contributed to preventing the lowering of patients' ADL postoperatively. However, many patients are not indicated for minimally invasive surgery because of their anatomical characteristics and/or age. Therefore, the use of ERAS® for these patients is essential to provide management that is not inferior to minimally invasive treatment. In Japan, ERAS® for cardiovascular surgery is still at its initial stages. To continue improving perioperative management in the future, accumulation of data is necessary. Therefore, ERAS® management should be widely used in cardiovascular surgery in Japan.

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Chapter 14
ERAS in the Respiratory Surgery

Takayuki Kori and Masashi Yanada

Abstract In respiratory surgery, lung lobectomy is the target of enhanced recovery after surgery protocol (ERAS), because lung lobectomy is a standard operative procedure for progressive lung cancer with a large number of operations. There is one systematic review about enhanced recovery pathways in elective lung resection. A total of 15 individual enhancer recovery program elements were described in the included studies. Some studies suggest that this intervention may reduce length of hospital stay and hospital costs. Yanada (Japanese Red Cross Society Kyoto Daini Hospital) operated a lung lobectomy and examined the safety and usability of 106 lung lobectomy cases using ERAS. The average length of drainage tube placement was 3.1 days, and the average postoperative hospitalization period was 6.9 days. Complication rate was 6.50%; mortality rate was 1.90%. In lung lobectomy, protection of lung function, hydration management to prevent pulmonary congestion, reinforcement of respiratory rehabilitation, and pain management can be considered as recommended items, compared to digestive diseases. Finally, we listed up the 15 elements that are considered useful in lobectomy.

Keywords Respiratory surgery • Lung lobectomy • Enhancer recovery

14.1 Introduction

Thoracic surgery includes manipulation of lungs, mediastinum, and chest cavity. There are only a few reports on enhanced recovery after surgery (ERAS) with this domain. Partial resection of the lung comprises minor surgical interventions enabling the patient to be discharged early. On a contrary, lung lobectomy is a standard operative procedure in progressive lung cancer that needs major surgical interventions which demands ERAS.

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Lung cancer is the leading cause of cancer death worldwide [1]. Lung resection remains the cornerstone of curative intent management of localized disease. In Japan, about 27,000 patients undergo anatomic lung resection every year [2].

14.2 Characteristic of the Lung Lobectomy

At first, I aim to describe characteristic of perioperative care of the lobe for lung excision:

1. After lung lobectomy, respiratory function falls because of decreased lung volume and damaged respiratory muscles. Therefore, preoperative respiratory function is evaluated, and postoperative respiratory function is predicted in order to judge the operative indication. Alternatively, patient's ability to maintain lung ventilation is evaluated as one-lung ventilation is used in most operations.
2. A common postoperative complication is respiratory complication. With increased sputum, there will be an increased risk of pneumonia and atelectasis. With decreased respiratory function after surgery, patient could be in serious condition if respiratory function further falls by pneumonia or atelectasis.
3. Respiratory physiotherapy is operated with an aim to recover patient's decreased respiratory function after surgery. However, postoperative low oxygenation causes spasm in the pulmonary artery and exacerbates low oxygenation even more. Therefore, an extreme care is needed to maintain the oxygenation in postoperative respiratory training.
4. In a case of lung lobectomy, lung cavity is incised which commonly causes pain during breathing and coughing. Postoperative pain not only interferes in patient's ambulation but also in deep breathing, coughing, and sputum expectoration, which may cause atelectasis and pneumonia. Therefore, a sufficient pain management is needed in postoperative care of lung lobectomy.
5. Thoracic drainage must be performed in closed-channel manner, so that negative intraperitoneal pressure is maintained. Here, air and liquid are drained, and the purpose and structure are different to those of intraperitoneal drainage. Although it is recommended not to use intraperitoneal drainage in ERAS of gastrostomy and colectomy, thoracic drainage is used in almost in all lung lobectomy cases after surgery. Accumulation of pleural fluid and air leakage causes the lung to collapse, so the use of drainage is thought to be essential.

14.3 ERAS of Lung Lobectomy

ERAS, fast-track, or clinical pathway programs are multimodal, evidence-based protocols including step-by-step management plans throughout the perioperative period. ERAS improve postoperative recovery and decrease morbidity, length of hospital stay, and cost of care [3]. However, few reports described the impact of an ERAS in outcomes of lung resection [4–8].

Postoperative complications after lung resection remain high, and complications occur at a rate of 20–50% [9–14], and postoperative complications often impair postoperative recovery, leading to increased hospital length of stay [15], delayed return to regular activities, higher costs [16, 17], poor postoperative quality of life [18], and poorer long-term outcomes [19].

There is one systematic review including six studies about enhanced recovery pathways (EPR) in elective lung resection [20]. The six studies comprised one RCT [4], one case-control study [7], two prospective cohort studies [5, 21], and two retrospective cohort studies [6, 8].

A total of 15 individual ERP elements were described in this review studies (Table 14.1). The number of elements used in each study ranged from 4 to 10 (median, 6.5). The elements most frequently cited were preoperative education ($n = 5$), prophylactic antibiotics ($n = 4$), epidural anesthesia/analgesia ($n = 4$), standardized chest tube management ($n = 5$), and early mobilization ($n = 4$) [20].

Some studies suggest that this intervention may reduce length of hospital stay (difference, 1.2–9.1 days) [5–8, 21] and treatment costs, but none of the studies showed differences in overall complications between control and ERP groups [8, 21]. The RCT reported no differences between groups (11 days in both groups) [4]. Complication rates ranged from 14 to 46%. None of the studies showed differences in overall complications between control and ERP groups—duplication of previous sentence. In the study by Maruyama and colleagues [8], costs were significantly lower in patients treated within an ERP (mean, \$13,093–\$280 vs control \$14,439–\$430; $P = 0.0002$). Zehr et al. also reported significantly lower mean costs in the ERP group (\$13,432–\$8056 vs control \$17,103–\$13,221; $P < 0.01$) [21]. In the study by Wright et al. [6], differences in hospital costs were not statistically significant (ERP \$14,792 vs control \$16,063; $P = 0.47$; variability not reported).

Table 14.1 Fifteen individual ERP elements

1. Patient education and/or counseling
2. Shorter preoperative fasting
3. Prophylactic antibiotics
4. Epidural anesthesia/analgesia
5. Use of single chest tube
6. Fissureless right upper lobectomy
7. Muscle-sparing surgery/VATS
8. Prevention of hypothermia
9. Standardized chest tube management
10. Early removal of epidural catheter
11. Early removal of urinary catheter
12. Postoperative fluid restriction/early discontinuation of IV fluids
13. Early removal of oxygen support
14. Early feeding
15. Early mobilization

14.4 Data in Japan

Yanada (Japanese Red Cross Society Kyoto Daini Hospital) operated a lung lobectomy and ERAS as shown in the Table 14.2 and examined the safety and usability of 106 lung lobectomy cases using ERAS. One hundred two cases were done VATS and four were thoracotomy. The average operation time was 210.1 min, and the average amount of bleeding was 72.1 g. The average length of drainage tube placement was 3.1 days, and the average postoperative hospitalization period was

Table 14.2 ERAS for lung resection

1. Preadmission information, education, and counseling: explain the clinical pathway to patient
2. Preoperative bowel preparation: none
3. Preoperative fasting and carbohydrate treatment: fast after dinner on the previous day. Drinking water allowed until 4 h before surgery. No carbohydrate treatment
4. Preanesthetic medication: none
5. Prophylaxis against thromboembolism: usage of elastic stockings and foot pumps from intraoperative until ambulation on the next day
6. Antimicrobial prophylaxis and skin preparation: usage of cefazolin. Administer right before skin incision. Repeat the dose 3 h into the operation and after 9 pm after returning to ward. Terminate antibiotic treatment on POD 1
7. Standard anesthetic protocol: general anesthesia (inhalation anesthetic sevoflurane or desflurane; sedative, propofol muscle relaxant rocuronium bromide and sedative remifentanil hydrochloride epidural anesthesia)
8. Thoracoscopy and modifications of surgical access: operation with VATS. A 4 cm incision on anterior axilla and two ports
9. Nasogastric intubation: intraoperative only. Remove before extubation of intubation tube
10. Preventing intraoperative hypothermia: heating of body and administration of warmed infusion by using a body temperature managing apparatus, 3 M™ Bair Hugger™ therapy
11. Perioperative fluid management: terminate infusion on POD 1
12. Drainage of the thoracic cavity after lung lobectomy: remove thoracic tube if there is no pulmonary fistula and less than 350 mL of drainage/day. Place it through POD 1 in case of lymph node dissection, and remove after POD 2
13. Urinary drainage: as a general rule, remove on POD 1 even in case of epidural anesthesia. In case of urinary retention, catheterize and decrease the dose of anesthesia temporarily. If no improvement is seen, place again
14. PONV: none
15. Prevention of postoperative ileus: none
16. Postoperative analgesia: use epidural anesthesia until removable of tube. Combine oral administration of celecoxib from POD1. Use NSAIDs as needed
17. Perioperative nutritional care: start normal meals from the morning of POD 1
18. Early mobilization: start from the morning of POD 1
19. Setting of discharge criteria: patient is discharged if drains are removed; there is no problem with the X-ray on the next day, and the patient can consume orally and get up (on POD 3 the earliest)
20. Management after discharge: do a checkup 7–10 days after discharge for a blood test and X-ray. Check again after 2 weeks, and if there is no problem, check every 3 months
21. Audit: reconsider clinical pathway arbitrarily and revise

6.9 days. Complication rate was 6.50%, mortality rate was 1.90%, and the two fatal cases were bronchial fistula and acute aggravation of interstitial pneumonia.

14.5 Recommended Items in Thoracic Domain

ERAS for patients undergoing open lobectomy decreased duration of stay and short-term morbidity, with no difference in either readmissions or emergency department visits after discharge. So, what items should be recommended for ERAS in lung lobectomy? In lung lobectomy, protection of lung function, hydration management to prevent pulmonary congestion, reinforcement of respiratory rehabilitation, and pain management can be considered as recommended items, compared to digestive diseases. I have listed up the items that are considered useful in lobectomy. However, note that this is only my personal perspective.

Preop

1. Patients' education and risk assessment

   Preadmission information, education, and counseling to patients about surgical and anesthetic procedures before the interventions may diminish fear and anxiety and enhance postoperative recovery and quicken hospital discharge [22, 23].

   Personal counseling, leaflets, or multimedia information containing explanations of the procedure along with tasks that the patient should be encouraged to fulfil may improve perioperative feeding, early postoperative mobilization, pain control, and respiratory physiotherapy and hence reduce the prevalence of complications [24–26]. Preoperative smoking and alcohol abuse are associated with an increased risk of wound complications, general infections, pulmonary complications, and neurological complications [27–29].

2. Preoperative exercise therapy

   Preoperative exercise therapy has beneficial effects on various physical fitness variables and postoperative complications in patients with lung cancer scheduled for lobectomy [30].

   The duration of the interventions ranged from 1 day to 4 weeks preoperative. And, the frequency of exercise sessions ranged from 1 time per week to ten sessions per week.

   The major exercise types are aerobic exercise (walking and cycling) and resistance exercise as part of the exercise intervention. And cardiovascular intensity ranged from 50 to 100%, as measured of the maximum workload, maximum heart rate, and VO2 peak.

   Preoperative exercise therapy might have a beneficial effect on chest draining, postoperative complications, mortality rate, length of hospital stay, physical fitness, and quality of life [31–33].

   But there were conflicting results in the effects on spirometric variables [32, 34–37]. Mean adherence to the preoperative exercise therapy program is 72–88.3% [38, 39].

3. Avoid fasting

   In thoracic surgery, we do not deal with the digestive tract, so there is no need of preoperative fasting. Similarly with elective surgeries of digestive tract, eating until the day before surgery and drinking of clear water is until 2 h before entering the operation on the operation day.

   A meta-analysis including a Cochrane review of 22 RCTs showed that fasting from midnight neither reduce gastric content nor raises the pH of gastric fluid compared with patients allowed free intake of clear fluids until 2 h before anesthesia for surgery [40, 41].

Intra-Op

In lobectomy, it is important to protect the perioperative lung function to prevent postoperative complication. Therefore, more care is needed in managing anesthesia compared to gastrointestinal surgery:

4. VATS

   Similarly with abdominal surgery, thoracoscopic surgery decreases the postoperative complication rate, compared to open surgery. Compared with thoracotomy, VATS lobectomy was associated with a lower incidence of total complications (29.1 vs 31.7%, $P = 0.0357$), major cardiopulmonary complications (15.9 vs 19.6%, $P = 0.0094$), atelectasis requiring bronchoscopy (2.4 vs 5.5%, $P < 0.0001$), initial ventilation >48 h (0.7 vs 1.4%, $P = 0.0075$), and wound infection (0.2 vs 0.6%, $P = 0.0218$) [42]. Postoperative hospital stay was 2 days shorter in the VATS lobectomy patients (mean 7.8 vs 9.8 days; $P = 0.0003$). In terms of outcome at hospital discharge, mortality in the VATS lobectomy group was 1 versus 1.9% in the thoracotomy group ($P = 0.0201$) [42].
5. Prophylactic antibiotics
6. Normothermia
7. Short-acting anesthetic and analgesic drugs
8. Thoracic epidural anesthesia/analgesia

   Similarly with other surgeries, body temperature management, anesthetic management, and pain management are needed in lung lobectomy.
9. Fluid management

   The maintenance fluid rate targeting to normovolemia without accumulating extravascular lung water is 1.5 mL/kg/h of total body weight with a balanced salt solution, which was continued until the patients were able to tolerate adequate oral intake [43]. This protocol showed no postoperative increase of extravascular lung water, maintenance of cardiac preload assessed by global end-diastolic volume index, and enhanced cardiac index. Total positive fluid balance in the first 24 h postoperatively should not exceed 20 mL/kg body weight [44].
10. Lung protective ventilation

    Lung protective strategies should be key points in the ERAS protocol to minimize and avoid respiratory complications such as atelectasis, pneumonia, and acute lung injury [45]. Best practice recommendations include short duration, optimization of lung compliance by recruitment after induction of anesthesia, positive end-expiratory pressure titration, bronchodilation, and bronchial toilet [46]. Tidal volume should be restricted, and a Vt of 4–6 mL/kg has been shown to be protective [47].

Postop

11. Early feeding

    In thoracic surgery, early oral intake is possible. However, if lymph node incision around the recurrent laryngeal nerve is included in procedure, swallowing function should be evaluated in prior to oral intake to see if there is any difficulty in swallowing.

    Amin et al. describe that diet milestone was not a predictor of duration of stay [48]. So, we do not decide that early feeding is a key item about enhanced recovery after lung lobectomy.

12. Early removal of chest tube

    The removal of chest tubes using a threshold of <300 mL of drainage in 24 h with no evidence of ongoing air leak or chylothorax decreased the hospital length of stay [48].

    Despite the earlier removal of chest tubes and resultant decrease in duration of stay, there was no change in pulmonary complications requiring an intervention or overall pulmonary complications.

    Recommendation:

    POD 0: maintained at -20 cm H_20 suction
    POD 1: remove suction
    POD 2: remove chest tube if <300 mL/24 h, nonchylous, and no air leak

13. Urinary outflow

    If no urine output is observed after 8 h of catheter removal, a bladder scan is performed, and a urinary retention protocol is followed.

    POD 1: Bladder catheter removed if adequate urine output is observed.

    Amin et al. described that the main driver of decreased duration of stay was earlier discharge of patients with no complications and that urinary catheter removal on POD 1 and removal of the last chest tube on or before POD 3 were independent predictors of decreased duration of stay [48].

14. Postoperative rehabilitation

    Postoperative aggressive ambulation can start as soon as possible [49]. Walking at 4 h after lobectomy in patients with lung cancers is a safe approach to starting pulmonary rehabilitation after surgery [50]. Postoperative pulmonary rehabilitation might have a beneficial effect on exercise tolerance, FVC% at postoperative month 3, FEV1% at postoperative months 3 and 6, and 6MWT scores at postoperative months 1, 3, and 6 [51, 52].

    Incentive spirometry did not improve overall recovery of lung function, frequency of postoperative pulmonary complications, or length of hospital stay [53].

15. Airway management

Postoperative pulmonary complications are the most frequently observed complications following lung resection [54, 55].

Mucosolvan optimizes the perioperative airway management for patients undergoing lobectomy, reducing postoperative complications and shortening time of hospital stay [56]. Aerosol (90 mg/day) of mucosolvan in combination with intravenous administration of mucosolvan (180 mg/day) for 8 consecutive days reduced postoperative complications and length of hospital stay for the patients with non-small cell lung cancer in fast track surgery.

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