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The Application Status and Prospect of ERAS in Minimally Invasive Thoracic Surgery

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Abstract

ERAS, which is the acronym for Enhanced Recovery After Surgery, is a multi-mode perioperative treatment scheme for patients undergoing surgery. Since ERAS is not a fixed pattern, ERAS protocols are not only prepared for a specific clinical disease setting but also easy to apply to all kinds of postoperative rehabilitation program. ERAS society has issued several guidelines on accelerated rehabilitation surgery for different operations, and accumulated some practical evidence concerning preoperative, Intraoperative and postoperative practice. However, ERAS in the thoracic surgery develops slowly and there is no guideline to direct enhanced recovery of thoracic surgery up to now, for this reason, a literature search and analysis of the application of ERAS in thoracic surgery is conducted to explore feasible ERAS protocols that can adjust to Thoracic Surgery and the possible development direction in the future.

Key words: ERAS or Enhanced Recovery After Surgery; Thoracic surgery; VATS or Video-Assisted Thoracoscopic Surgery;

Introduction

Surgery is an important method to treat thoracic surgery diseases. However, for the reason of great trauma in surgery procedure, patients undergoing thoracic surgery usually have obvious pain and many complications after surgery, which lead to a delayed discharge of the hospital. Despite great advances in surgical techniques and anesthesia, postoperative complications of thoracic surgery remain high, length of stay still long, hospital cost still expensive, furthermore, quality of patients' life is sacrificed [1,2]. Because of the small incision, less Intraoperative bleeding, less postoperative pain and faster recovery, VATS (Video-Assisted Thoracoscopic Surgery) has become the main operation method of thoracic surgery. Application of ERAS on the base of minimally invasive surgery is a solid integration of new technology and new conception, by doing so, enhanced recovery is achieved and postoperative complications can be distinctly reduced, so does the length of hospital stay and hospital cost. In other words, ERAS has a profound meaning for patients of thoracic surgery.

The Conception of ERAS

ERAS is a new treatment concept and rehabilitation model that subverts the traditional one. It was first proposed by a Danish surgeon called Kehlet in the year of 1997 [3]. It refers to a series of perioperative optimization measures based on evidence-based medical evidence to reduce stress response and accelerate preoperative body composition and organ function, and eventually accelerate postoperative rehabilitation of patients [4]. ERAS and minimally invasive surgery are two major medical breakthrough of the 21st century [5]. ERAS can significantly reduce the incidence of postoperative complications, improve patients' comfort, shorten hospitalization time and reduce the cost of hospitalization; therefore it has been widely used in urology, breast surgery, gastrointestinal surgery and other fields [6].

The Application of ERAS in Thoracic Surgery

The popularization of minimally invasive concept and extensive application of endoscopic technology have significantly reduced the trauma and stress respond of surgery, making ERAS feasible in thoracic surgery [7].However, the application status of ERAS in thoracic surgery is not optimistic. At present, there is no uniform ERAS guideline for thoracic surgery at home and abroad [8].China started late in the field of ERAS. This new concept of surgery was first introduced into China by academician Li Jieshou in 2007 [9]. The ERAS concept has attracted more and more attention from doctors and patients in mainland China in recent years, but only a few state-level grade hospitals are promoting and applying. Du Na from Sichuan University proposed a questionnaire survey about the application of ERAS in China, and the survey result indicated that the concept of ERAS in thoracic surgery of most China hospitals is still in the stage of theory rather than practice, and the lack of a unified and mature plan is the main reason [10].

Key elements of ERAS

Preoperative education

Surgery as a source of press will inevitably lead to the psychological and physiological responses of patients during perioperative period, causing anxiety and tension. A preoperative education can reduce the anxiety and fear of patients, accelerate postoperative rehabilitation and reduce hospitalization time, which is an independent predictor of whether ERAS have a good

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effect [11]. A good preoperative education can increase patient compliance, Jurt, et al. confirmed that patients' well compliance with ERAS protocols could significantly reduce the incidence of complications and shorten hospitalization time [12]. In a patient-led quality study, Gillis, et al. concluded that for most patients they want to get more information about what accelerated rehabilitation surgery is and what they need to do in the course of preoperative education [13]. Therefore, a good preoperative education should include: detailed information about what might happen during hospitalization, the role of patients themselves in the process of ERAS, what they need to do and some specific postoperative tasks for patients to perform [14]. Preoperative education should be conducted by the doctors and nurses in the form of oral education and be repeated again and again in the later contact with patients, because only when patients serve themselves as the leading role, fully understand the meaning of different measures and carry out them actively can the surgery get the best outcome and quick recovery effect [15].

Preoperative fasting

Forbidden to eat 12 hours and drink 6 hours before operation which aims to reduce the risk of reverse flow and pulmonary aspiration in the process of anesthesia induction aspiration, has long be recognized as the routine of preoperative preparation, but there is no clear scientific evidence [16].A whole night of fasting is extremely uncomfortable for patients, and often leads to thirst, hunger, and hypoglycemia, which not only increases the secretion of insulin antagonism hormone such as catecholamine and glucocorticoids, but also reduce the concentration of insulin in serum as well as insulin sensitivity, as a result, increase insulin resistance [17]. In addition, under the condition of long-term fasting and prohibition of drinking, the body further loses fluid through various physiological processes, resulting in relatively insufficient blood volume [18]. Regardless of the type of anesthesia, different degree of expansion of blood vessels is an inevitable side effect, causing blood pressure relatively low. In order to maintain the stability of hemodynamics anesthesiologists often speed up the infusion and transfusion volume before surgery, leading to pulmonary edema and other unwanted consequences. It has been verified by clinical evidence-based medicine, if the gastrointestinal tract is free of obstruction, the liquid food can be emptied through the stomach for 2h, and the solid food can also be emptied within 6h [19]. Several studies have confirmed that a 6h fast for solid food and intake of clear fluids until 2h before initiation of anesthesia (not more than 400 ml) can increase patients' comfort, reduce anxiety and preoperative hypotension, reduce insulin resistance, and did not increase the risk of reverse flow and aspiration [20-22]. Therefore, fasting for 6h before surgery and prohibition of drinking for 2h are acceptable, and 10% glucose can be taken orally for 200ml ~ 400ml at 2h before surgery [23].

Catheter management

Traditional view of urethral catheter management believed that indwelling catheter can evaluate the Intraoperative excess or lack of fluid by observing the urine volume, and can prevent the postoperative dysuria caused by anesthesia [24]. However, this view has many drawbacks. First, the postoperative comfort of patients is significantly reduced. Secondly, indwelling urinary catheter is not good for patients to get out of bed early. Third, urinary infection rates increased [25]. Research showed that the rate of urinary tract infection was 10% after 1 day of indwelling catheter, 15% for 2 days, and 100% over 14 days [26]. In addition, restlessness and adverse events during anesthesia awakening are often caused by indwelling catheters. Research reveals that only 10 percent had to have a catheter after surgery, while 90% of patients had increased perioperative complications due to urinary catheterization [27]. Qiu fang from Hospital of Sichuan University and other authors indicate that when operation time is less than 150 min, No indwelling catheter for patients doesn't increase the incidence of urinary retention and urinary incontinence but can reduce the rate of urinary tract infection, shorten hospitalization time and improve patients' comfort [28]. In addition, zhao jinlan pointed out that: 1. Removal of the urinary catheter before anesthesia was sober in thoracic surgery could reduce the incidence of restlessness during general anesthesia [29]. When the duration of thoracic surgery was shorter than 3h and the Intraoperative transfusion volume was not more than 1500 ml, the Intraoperative average urine volume was 500 ml. However, the normal storage capacity of bladder is about 500 ml~800 ml [30]. Therefore, for patients whose preoperative evaluation time is expected to be less than 3h, no catheterization is allowed, or urine catheterization is conducted after anesthesia but removed before anesthesia sobriety.

Intraoperative warming

Intraoperative hypothermia refers to the body temperature lower than 36°C during operation. Low operating room temperature, temperature regulating function inhibition caused by the use of anesthetics, massive Intraoperative infusion of cryogenic liquid, all above can lead to low temperature of body. Low temperature may lead to the coagulation mechanism and leukocyte function being affected in the process of rewarming, leading to increased cardiovascular burden, etc [31]. In addition, Intraoperative hypothermia may affect pharmacokinetics and anaesthesia resuscitation [32]. A study by Samsung medical center in South Korea pointed out that Intraoperative and early postoperative thermal insulation can reduce Intraoperative bleeding, reduce the incidence of postoperative infection and heart complications, and reduce the role of catabolism [33]. The use of infusion heating device, cover quilt, adjust the central air conditioner of the operating room to the appropriate temperature, the preheating of washing salt water, the use of heating mattresses can all play a good role in keeping warm.

Limited fluid resuscitation

Fluid therapy is an important element in perioperative treatment. Its' main purpose is to maintain hemodynamic

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stability and ensure adequate tissue perfusion. Traditional fluid therapy used the open replenishment strategy proposed by Shires, focusing on correcting low blood volume. However, large amount of rehydration fluid often leads to pulmonary edema, which affects patients' respiratory and circulation function [34]. In addition, Intraoperative single lung ventilation and lung tissue traction can cause pulmonary injury, which aggravates pulmonary tissue edema, and increase the risk of postoperative pulmonary infection [35]. In addition, gastrointestinal mucosa often become edematous due to a large amount of fluid infusion, which results in slow recovery of gastrointestinal function. Restrictive fluid therapy can not only satisfy the normal tissue perfusion, but also avoid the bad consequences caused by a large amount of rehydration, thus the time of gastrointestinal function recovery and hospitalization are shorten, and the incidence of pulmonary infection and other complications are decreased [36]. Research Show that using lactate ringer's balance solution to supply the fluid loss in the process of operation at the speed of 1~2 ml/(kg. h) is feasible and safe, a small amount of colloidal solution can be given if patients' blood volume is insufficient, and all intravenous infusion can be ceased when patients begin to effectively eat through mouth [37]. In recent years, more and more attention has been paid to Goal Directed Fluid Therapy (GDFT), a recent meta-analysis pointed out that the individualized target oriented fluid administration for different patients can maintain the proper circulation capacity and tissue oxygen supply and accelerate the postoperative rehabilitation [38]. Patients require continuous monitoring capacity reactivity index in the process of implementing GDFT to make sure blood pressure not less than 20% of the normal and heart rate not more than 20% of the normal, keep the central venous pressure between 4~12 mmH_2O and keep urine output above 0.5 ml/(kg. h).

The management of thoracic drainage tube

To reconstruct the negative pressure of pleural cavity is the main purpose of thoracic drainage tube. However, postoperative incision pain is often caused by the stimulation of pleural membrane and intercostal nerve's compression or injury by the chest tube. What's more, there are many inconveniences with the tube such as cough limitation, patients' unwillingness to perform rehabilitation training [39,40]. For those reasons, it has become a hot research topic in recent years to indwell less chest drainage tube, small tube and even no tube. Multiple studies confirmed that the effect of single drainage tube and double drainage tube is similar, and the incidence of postoperative complications is out of significant difference, but the pain caused by single drainage tube is apparently less, and the total volume of thoracic drainage is less [41,42]. The traditional thoracic drainage tube is usually made of PVC material with large diameter and high hardness, so the postoperative pain is obvious. At present, there are researches using no.16 gastric tube, 16F urinary tube and 19F silicone tube to replace the 28F drainage tube the results showed that the drainage effect of small diameter drainage tube and 28F drainage tube was similar, but it had obvious advantages in reducing postoperative pain and promoting wound healing [43-45]. According to the traditional concept, the thoracic drainage tube can be removed only if the thoracic drainage flow is less than 100 ml within 24 hours, and the lung on the affected side is well re-stretched and there is no air leakage. But in physiological state, 350-400 ml of chest water produced by the pleura each day can be absorbed by itself [46]. A meta-analysis showed that the thoracic drainage tube could be removed when the volume of thoracic drainage was less than 300 ml/24h, and such a standard did not increase the incidence of pulmonary atelectasis and pleural effusion [47]. Furthermore, there are also some studies in recent years reporting that the spontaneous pneumothorax, mediastinal tumor, lung wedge resection surgery have no need to dwell chest tubes if patient does not have emphysema, pleural effusion and coagulant function abnormality before operation, and pulmonary nodules is less than 2 cm, the nodule's distance to pleural is less than 3 cm, and no more than two wedge resection, there is no dense adhesion in chest and Intraoperative leak test is negative [48-50].

Multimodal pain relief

Pain is called the fifth vital sign after body temperature, pulse, respiratory and blood pressure [51]. Most patients suffer from a heavy incision pain after undergoing thoracic surgery; the pain makes breath quick and shallow, cough and expectoration inefficient, leading to complications such as hypoxemia, hypercapnia, pneumonia, atelectasis, respiratory failure and cardiac arrhythmia [52]. Despite of the small incision and deceased trauma benefited from minimally invasive surgery, most patients still experienced different degree of pain ranging from moderate to severe after surgery, which requires active analgesia [53]. Common analgesia patterns include Patient-Controlled Intravenous Analgesia (PCIA), Patient-Controlled Epidural Analgesia (PCEA), and oral opiates. Among them, PCIA is the most commonly used one, but the adverse reaction of intravenous opiates is often obvious, including slow recovery of intestinal function, respiratory inhibition, nausea and vomiting [54]. In recent years, more and more attention has been paid to multimodal analgesia. Multimodal analgesia refers to using drugs with different mechanisms and different analgesia methods to achieve balanced analgesia and reduce adverse effects on the nervous, endocrine and immune system [55]. According to Wenk and Schug, regional block (such as paravertebral block) or local anesthesia (such as intercostal nerve block) combines with general analgesia is the best choice for postoperative analgesia in thoracic surgery [56]. In addition, it is an important principle of multimodal analgesia to use Nonsteroidal Anti-Inflammatory Analgesics (NSAIDS) as the basic postoperative analgesic drugs to reduce the use of opioids [57]. Current guidelines for accelerated rehabilitation surgery in the United States and Europe recommend early use of oral NSAIDS as sequential analgesics [58].

Early oral intake

Oral intake can accelerate the recovery of gastrointestinal

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peristalsis, reduce incision infection and the incidence of pulmonary infection, protect the intestinal mucosal barrier, enhance immune function, shorten hospitalization time and reduce hospitalization costs [59]. The traditional standard of postoperative food intake is gastrointestinal exhaust. But most patients can tolerate food intake before resuming gastrointestinal motility. According to American society of enteral nutrition, the treatment of enteral nutrition should not be based on anal exhaust. Research showed that fluid in the small intestine began to be reabsorbed in the early postoperative period, and the small intestine returned to normal peristalsis 6 hours after surgery [60,61]. In addition, jiang zhiwei et al. proposed that fasting could inhibit gastrointestinal function, make gastrointestinal peristalsis slow or even disappear, and gastrointestinal peristalsis increases after eating [62]. Jin-lan Yang testified the safety of drinking water and eating within 6 hours after pulmonary surgery by a series of prospective studies [63]. There is also Research abroad reporting that after thoracoscopic pulmonary wedge resection or lobectomy, food intake can be advanced to within 1h [64]. The stepwise diet which shifts from a small amount of drinking water and a liquid diet to a normal diet and adjusts according to the patient's tolerance is relatively safer.

Early mobilization

Early mobilization is an important element of the concept of ERAS. In the past, patients were told to stay in bed for 24 hours, or even more after surgery, but long-term of lying in the bed not only increased the risk of deep vein thrombosis, but also can cause lung infection, atelectasis, increased insulin resistance, weaken muscle strength and reduce the adverse consequences such as tissue oxygenation [65,66]. Therefore, if the patient's condition permits, getting out of bed and early mobilization should begin as early as possible after the operation [67].The concept of early mobilization in the concept of ERAS is defined by Gatt as getting out of bed and walking on the day of surgery [68]. At present, there is no unified standard for the specific time of early mobilization, and there are few domestic studies on early bed movement. luo jia, etc confirmed the safety and feasibility of the patient's mobilization 6h after thoracoscopic surgery [69]. In abroad, Harada and others pointed out that 80% of patients can stay upright and walk on the day of surgery after 4 h of operation in patients undergoing non-small cell lung cancer [70,71]. Furthermore, an article published in the European journal of cardiothoracic surgery recently reported that patients of lung cancer undergoing lung resection surgery can ambulation within 1h [64]. The influential factors of postoperative early ambulation are as follow: upright standing intolerance: preoperative fluid loss as a result of long term of fasting and the use of Intraoperative anesthetic drugs reduce arterial blood pressure both lead to the reduction of brain blood supply, causing side effects such as dizziness, nausea. In addition, the loss of fluid during operation may further reduce blood perfusion in the brain when standing up, leading to delayed early mobilization [72]. Compared with the traditional concept, ERAS advocates shortening the time of fasting, and giving oral or intravenous infusion of 10% saccharide liquid 200~400 ml 2 hours before surgery to prevent the loss of excessive liquid [73]. Operation time gets shorter and intraoperative blood loss is reduced by the use of video-assisted thoracoscope surgery. What's more, early oral feeding is initiated as soon as possible after the surgery. Measures above, to some extent, can reduce the incidence of orthostatic intolerance. Pain of surgery incision: due to postoperative pain, patients are unwilling to move out of bed by instinct and self-protection. ERAS emphasizes multi-modal pain relief, so the symptom of pain is reduced and early mobilization is promoted by timely assessment the time and degree of pain and early preventive treatment. Patients' insufficient understanding of the significance of early mobilization and lack of compliance are two important factors of delayed mobilization. Strengthening preoperative health education and repeatedly informing patients of the importance of early mobilization can improve patients' compliance and enthusiasm of early mobilization.

The future of ERAS

ERAS is not a single rigid treatment model, but an approach requiring multidisciplinary teamwork and improving with the development of knowledge to help patients recover more quickly after surgery, the core of which is to reduce the psychological and physiological stress response of the body [74]. Therefore, A series of optimization measures based on evidence-based medicine were used to achieve the ultimate goal of "no pain" and "no risk" [75]. As a new concept which is contradicted to traditional treatment concept in the end of 20th century, ERAS had brought an unprecedented impact on clinical practice. After 20 years of development, the application of ERAS had been extended to the fields of orthopedics, urology and lacteal surgery, and all achieved a good clinical result. Although the present situation of the application of ERAS in the thoracic surgery is still confined to theory, the available evidence had showed ERAS using in thoracic surgery can reduce the postoperative complications, shorten the length of hospital stay, reduce hospitalization costs. With the progress of human knowledge and the continuous development of forensic medicine, the traditional perioperative concept of thoracic surgery must be replaced by the concept of ERAS.

Most thoracic surgery must be performed under double lumen tracheal intubation and one lung Ventilation. But when used for treatment, double lumen tracheal intubation and one lung Ventilation also cause some undesired complications including acute Lung injury and a series of respiratory complications [76]. During the single lung ventilation, the mechanical ventilation side of the lung is often given a high amount of moisture to maintain the oxygen saturation of the blood, easily leading to airway damage. In addition, the collapsed lung may suffer reperfusion injury during the course of pulmonary recruitment, which is mediated by the releasing of cytokine and can further lead to collateral lung injury [77]. In recent years, in order to avoid airway complications caused by endotracheal intubation, it has become a hot research topic to avoid endotracheal intubation when carrying out video-assisted thoracoscopic surgery. More and more practical

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evidence had testified the safety and feasibility of performing thoracoscopic pulmonary wedge resection, lung segment resection, lobectomy and mediastinal tumor without tracheal intubation [77]. Researchers showed that non endotracheal intubation was superior to the endotracheal intubation in terms of the incidence of complications and hospitalization time [78-80]. Therefore, non tracheal intubation is likely to be one of the important elements of ERAS in thoracic surgery in the future.

Table 1: Comparison of the perioperative cares between ERAS and traditional concept

Factors	Method in traditional care	Method in ERAS
Preoperative education	Normal notification of the process and risk of operation before surgery	Strengthened education and councel throughout the hospitalization
Preoperative fasting	Routinely fasting from midnight before the day of surgery	Fasting solids up to 6 hours prior to surgery, and clear liquids permission up to 2 hours before surgery
Catheter management	Remove the catheter after 24 hours at least	No catheter or indwell the catheter after anesthesia but remove it once the surgery is over
Intra operative warming	No warming measures	Apply different methods to keep warm
Fluid administration	Open Rehydration Strategy	Restricted fluid resuscitation
The management of thoracic drainage tube	Double drainage tube or even more, with large diameter	No chest tube or reduce the number of tube as much as possible with a small diameter
Strategies for pain relief	Single and fixed analgesia	Multimodal pain relief
The time of oral feeding	Drink water 6 hours after surgery, and initiate oral food intake at the second day	A stepwise diet from water to solid immediately after surgery
Early mobilization	At least on the second day	Get out of bed and walk as early as possible if patient's condition allow

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