



Enhanced recovery after surgery (ERAS) programs for esophagectomy

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Abstract: A perioperative treatment protocol, enhanced recovery after surgery (ERAS) focuses on accelerating patient recovery. Previous studies confirmed that ERAS decreases surgical trauma and the stress response, which improved outcomes including reduced length of hospital stay (LOS) and decreased postoperative morbidity. While ERAS protocols have been successfully implemented in a variety of surgical disciplines (colorectal, bariatric, orthopedic, and gynecologic surgery), its use in esophageal surgery is still limited. This paper analyzes the feasibility and value of the ERAS protocol for esophageal surgery. Reviewing the literature found that implementation of ERAS resulted in decreased costs, length of stay and pulmonary specific complication reduction, but not overall morbidity. The evidence lacks randomized control trials. Further, the ERAS Society published recommendations for esophageal resection. This opportunity for unification of the protocol would make the studies more comparable and leads to stronger conclusions. Surgery specific items also require further confirmation. Nonetheless, the successful introduction of the ERAS protocol into a wide variety of surgical disciplines provides optimism for ERAS's effectiveness in esophageal surgery.

Keywords: Esophageal cancer; neoplasms; esophagectomy; enhanced recovery after surgery (ERAS); thoracic surgery

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Introduction

A multidisciplinary perioperative treatment protocol aimed at acceleration of patient recovery, enhanced recovery after surgery (ERAS) was first demonstrated in practice by Kehlet and Wilmore in the early 2000s (1). Over the years, various ERAS protocols were developed. Subsequently the ERAS Society released guidelines for ERAS implementation in different surgical disciplines (2-4). Evidence supporting the benefits of ERAS has been growing rapidly in recent years. Randomized clinical trials confirmed that ERAS decreases surgical trauma and the stress response which

improved outcomes including reduced length of hospital stay (LOS) and decreased postoperative morbidity. To date, a number of systematic reviews and meta-analyses described those advantages in patients of all ages undergoing colorectal (5,6), bariatric (7), orthopedic (8) or gynecologic (9) surgery, where ERAS protocols can be recognized as successfully implemented.

As of October 2018 no official guidelines are in place for the use of the ERAS protocol in esophageal surgery. Over a dozen comparative studies addressed this subject, where the protocol varied in terms of number and types of items used (10). Both the complexity of esophagectomy and

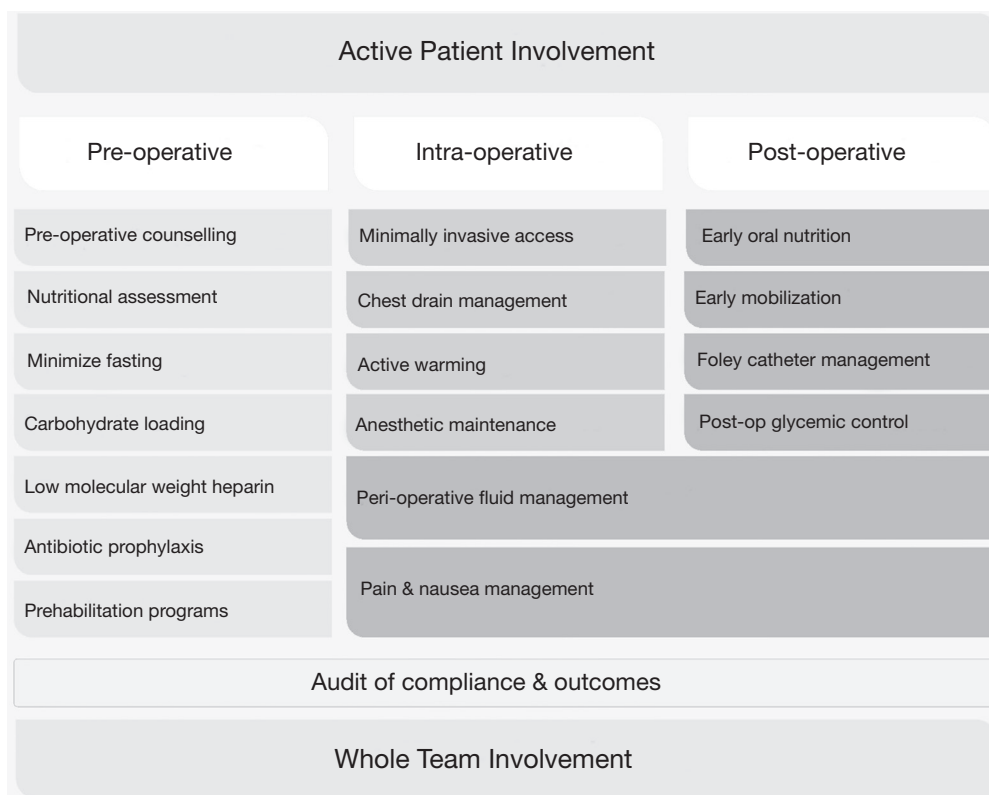


Figure 1 Key points of enhanced recovery after surgery (ERAS) protocol for esophagectomy.

the relatively late and limited introduction of minimally invasive approach to this procedure contribute to delayed postoperative recovery. A 2007 meta-analysis revealed significant reductions in non-surgical and pulmonary complications and shorter LOS in ERAS patients (11). However, conclusions from this review were less definitive due to virtually no randomized trials being included. Thus, the benefits of ERAS in esophageal surgery are still debatable (3,4,12,13). Standardization of perioperative enhanced recovery protocols is still under progress, as surgical units modify their components. It is crucial to work out a streamlined, widely applicable ERAS protocol for esophagectomy. The key points in ERAS protocol are presented on *Figure 1*.

Preoperative period

While some components of ERAS protocol are universal, others require adjustments to the type of the procedure. It is proven that proper nutritional support improves the outcomes of the treatment. Since patients with esophageal cancer are often malnourished, nutritional intervention

should be undertaken (14). Available data also shows that frailty rather than age is a major risk factor of perioperative complications (15). This evidence suggests including patient tailored physical activity in the time between diagnosis and the surgical procedure (16-18). Careful communication with the patients is of utter importance. As patients may not be aware of the ERAS protocol components, meticulous explanation is advised (19). Providing information about perioperative treatment also diminishes the patient's anxiety (20).

One of the pillars of preoperative care is to avoid fasting, which increases insulin-resistance. Insulin-resistance is a major risk factor for infections and cardiovascular complications (21). To minimize the period of fasting, intake of carbohydrate rich fluid 2–3 hours before the procedure is advised. What is important, preoperative fasting delays the time to solid food intake in the postoperative period, thus it is even more important to properly educate the surgical team (5,22).

ERAS protocol don't advice routine mechanical bowel preparation (MBP). It is said that MBP in fact increases the rate of infections and anastomotic leakage. It may

also contribute to Low Anterior Resection syndrome in colorectal surgery (23). However, in some cases exceptions should be made. For example, in very low anterior rectal resections with defunctioning ileostomy to protect the anastomosis. Similar situation can be found regarding esophagectomy with reconstruction of the gastrointestinal tract continuity with transverse colon. In that case MPB is necessary. However, we recommend combining the utilization of MPB with antibiotic administration. Such treatment reduces perioperative complications; however, its quality is low (24,25). It seems that the main cause in morbidity reduction is antibiotic preparation. Although in esophageal surgery with transverse colon reconstruction, MBP could not be avoided (26).

Low Molecular Weight Heparin should be used routinely in all patients. LMWH is as effective as non-fractionated heparin regarding occurrence of deep vein thrombosis (27). Moreover, twice a day administration seems to be even more effective and should be taken into consideration (28).

Operative procedure

Introduction of minimally invasive techniques (MIT) to oesophageal surgery raised the question of whether it should be the method of choice (29-31). Minimally invasive procedures reduce operative trauma, facilitates less postoperative pain and shorter lengths of stay (11,32,33). The biggest available meta-analysis by Yibulayin *et al.* consisting 57 studies including 15,790 patients proved the superiority of minimally invasive esophagectomy over an open approach in terms of post-operative complications and mortality (34). However, only one of included studies was a randomized control trial (RCT). The data from RCT also support minimally invasive approach. The TIME trial was a RCT involving 5 European hospitals involving 115 patients, investigating cases with resectable, intrathoracic esophageal carcinoma. The study proved, that MIT are superior regarding short-term outcomes with comparable 3-year overall and disease-free survival (35). The MIRO trial included 207 patients from 12 surgical centres. The authors compared open Ivor-Lewis esophagectomy with a hybrid approach in which abdominal step was performed laparoscopically and the thoracic part through thoracotomy. The results preferred hybrid approach in terms of overall postoperative morbidity and especially major pulmonary complications (36). Nevertheless, Rinieri *et al.* point out that the laparoscopic approach can result in a lower number of harvested lymph nodes, although it had no impact on

5-year overall and disease-free survival (37). Therefore MIT should be an approach of choice for esophageal cancer surgery.

Postoperative care

The ERAS protocol advises the avoidance of routine nasogastric tube insertion, since it decreases patients' well-being but not perioperative complications (38). A meta-analysis of seven comparative studies by Weijs *et al.* show no benefit from routine gastric decompression what extends the indications for early removal or full resignation from nasogastric tube in perioperative care (39). According to common belief, in esophageal surgery the tube may be not only inserted to decompress the stomach, but also to protect the anastomosis from excessive stretching. However, there is no evidence to support this theory. On the other hand, nasogastric or nasojejunal tube could be used as a route for early postoperative feeding, which is clearly beneficial (40,41). Moreover, enteral nutrition is better than total parenteral nutrition (40,42). Investigating early oral feeding instead of feeding by tube, Zhang *et al.* obtained good results with no increased rate of anastomotic leakage (43). Also Sun *et al.* compared early oral feeding (1 postoperative day, POD) versus late oral feeding (7 POD) and obtained satisfactory results with no increased morbidity but higher quality of life (44).

Postoperative pain impairs multiple components of the ERAS protocol. It delays patient mobilisation, decreases quality of life and increases the rate of pulmonary complications. What should be avoided is opioid-based analgesia, since it depresses the respiratory system and affects negatively on gastrointestinal function recovery (20). Thus, non-steroid anti-inflammatory drugs (NSAID) should be the method of choice. There is still discussion as to whether cyclooxygenase (COX) inhibitors damage gastrointestinal mucosa and due to that increase the anastomotic leakage ratio (45). Meta-analysis indicate that selective inhibitors of COX2 should be used, due to their lower anastomotic leakage rates (45). Alternatives such as local anaesthetic drug injection or epidural analgesia could be considered as an element of multimodal therapy. However, no difference regarding systemic and epidural analgesia was found regarding postoperative pain scores in Visser *et al.*'s meta-analysis (46).

ERAS advocates the avoidance of the routine use of drainage. Although abdominal drainage could be eliminated, this is not applicable to the thoracic cavity,

since pneumothorax requires active removal. Available data suggest that routine abdominal drainage is not necessary and thoracic drains should be removed as fast as it is possible (47). Sato *et al.* compared early chest drains removal versus late drain removal. The first alternative was found to be safe and not associated with higher rate of pulmonary complications. Moreover patients with late drain removal achieved first mobilisation faster, which is one of the most important components of ERAS protocol (48). Early mobilisation contributes to the decrease of pulmonary complications (49).

There is no need for Foley catheter keeping, as it is the major cause of urinary tract infections (20). Urinary Catheter Removal Guidelines state that the catheter should be removed within 24 hours after the surgery, which decreases not only UTI rate but also the length of stay (50). Some patients may suffer from urine retention after Foley removal. Thus careful diuresis monitoring should be performed to detect the indications for Foley reinsertion.

Rationale for ERAS introduction

Although the evidence for ERAS application in esophageal surgery is limited, ERAS has been proven to be beneficial regarding short and long term outcomes in other disciplines of surgery, confirming its versatility (51,52). ERAS was found to be safe in gastric cancer surgery, improving short term outcomes without increasing morbidity (53,54). The same situation is observed in bariatric surgery, recognized as a high-risk surgery due to multiple co-morbidities and the obesity of the patient (7). More importantly, gastric surgery has the most similarities to esophageal resections, since the anastomosis after resection is within the upper gastrointestinal tract and it should be most vulnerable for introduction of early oral nutrition. Moreover, ERAS decreases the cost of the treatment without comprising the outcomes (55,56). Recent data also show that compliance to ERAS protocol improves survival in patients undergoing colorectal surgery due to cancer (57).

ERAS implementation in esophageal surgery

Until now no clear guidelines existed on which elements of ERAS protocol should be used. Thus the evidence about its influence on postoperative results might be biased. In the Pisarska *et al.* meta-analysis of 13 trials assessing ERAS in esophageal surgery, the number of items of the

protocol varies from 8 to 16 (11). Also, implementation of ERAS resulted only in length of stay and pulmonary specific complication reduction, but not overall morbidity. It improves also the cost effectiveness of the whole treatment (58). There is also substantial lack of randomized control trials. To overcome this limitation, Liu *et al.* published a study protocol for an up-to date meta-analysis, which should bring new insight into available data. Also, recently ERAS society published recommendations for oesophageal resections (10). This is an opportunity for unification of the protocol, which would make the studies more reliable for comparison and better able from which to draw new conclusions. Nonetheless many items included in the perioperative care are still based on low and moderate level of evidence. Thus the guidelines will require further evaluation and verification.

Conclusions

ERAS significantly improves perioperative outcomes in different branches of surgery. It seems to be beneficial in esophagectomy as well. However, its utilization is still evolving. Surgery specific items require further confirmation, preferably in randomized control trials. Nonetheless, the successful introduction of ERAS into almost every type of surgical procedures (including gastrointestinal surgery, gynecology, urology, orthopaedics and even lung cancer surgery) provides optimism in the further development of this protocol in esophagectomy.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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