ERAS in esophagogastric surgery: State-of-art in the West

Silvia Salvans M.D, PhD, Luis Grande M.D,PhD, Mariagiulia Dal Cero M.D, Manuel Pera M.D, PhD

Section of GastrointestinalSurgery. Hospital del Mar. Hospital del Mar MedicalResearchInstitute (IMIM), Department of Surgery. UniversitatAutònoma de Barcelona, Barcelona, Spain

Correspondenceto:
Manuel Pera M.D, PhD. Section of Gastrointestinal Surgery. Hospital del Mar. PasseigMaritim 25-29, 08003 Barcelona, Spain. pera@psmar.cat

ORCID IDs:
Silvia Salvans orcid.org/0000-0002-9437-872X
Luis Grande orcid.org/0000-0001-9146-9004
Manuel Pera orcid.org/0000-0002-9449-1810
Mariagiulia Dal Cero orcid.org/0000-0002-0558-2244
ABSTRACT

*Enhanced recovery after surgery* programs provide a framework to standardize care processes and improve outcomes. The results of this multimodal and multidisciplinary approach have been beneficial across several surgical procedures in reducing morbidity and hospital stay without increasing readmissions.

The implementation of these programs in esophagogastric cancer surgery has been challenging due to the complexity of both procedures and the high risk of complications, with most of the evidence coming from the East. Despite the limited evidence for ERAS in esophageal surgery in Western centers, systematic reviews and meta-analysis have confirmed that ERAS programs reduce pulmonary complications and hospital stay after esophagectomy without increasing readmissions. Single-center Western studies have shown that implementing gastrectomy ERAS protocols resulted in a reduction of the use of nasogastric tube and intrabdominal drains, accelerated advancement of diet and reduced length of stay, without increasing complications.

Despite these beneficial outcomes, it has become clear that there has been wide heterogeneity and absence of standardization in the number and definition of the ERAS components. The development of ERAS consensus guidelines including procedure-specific components may reduce this variability.

Regardless of growing evidence of effectiveness, adherence to ERAS protocols in esophagogastric surgery remains challenging and had great variability with a wide adherence rate (5.6-100%) for single item.

As initial experiences have demonstrated to be beneficial, an implementation of the protocols with multidisciplinary team engagement and feedback based on periodic audits is desirable. Pre- and post-habilitation are emerging concepts that are becoming relevant for the implementation of these protocols.

248 palabras

Keywords

Enhanced recovery after surgery; Esophagectomy; Gastrectomy; Adherence; Compliance.
Declarations

The authors did not receive support from any organization for the submitted work. The authors have no relevant financial or non-financial interests to disclose.
INTRODUCTION

In 1997, Henrik Kehlet introduced a group of actions focused in reducing physiological surgical stress in the pre-, intra- and post-operative period with the intention to improve surgical outcomes[1]. This concept would be referred as Enhanced Recovery After Surgery (ERAS). These standardized and multidisciplinary team (MDT) approach programs, firstly applied in elective oncologic colorectal surgery, resulted in an accelerated convalescence with a clear improvement in post-operative outcomes including a reduction in morbidity and hospital stay[2]. The first ERAS consensus for patients undergoing colonic surgery was published in 2005 [3] and subsequent studies confirmed the benefits in reducing hospital stay and overall morbidity without increasing readmission rate compared to conventional care [4]. Moreover, economic benefits on the health care system have been described [5]. In this scenario, new guidelines were developed and applied to other surgical procedures [6].

Standardized clinical care pathways in the setting of esophagectomy were first introduced in the late 90s with the main objective to provide a targeted goal-directed recovery[7,8]. Initially, these pathways incorporated general components of the colorectal ERAS protocols that could easily be applied to gastro-esophageal surgery and progressively introduced some procedure-specific interventions for this challenging and complex operation.

Over the last decade, systematic reviews and meta-analysis have confirmed that ERAS programs reduce consistently pulmonary complications and hospital stay after esophagectomy without increasing readmissions [9, 10,11]. However, it has become clear over the years that there has been absence of standardization and wide heterogeneity in the number and definition of the ERAS components. [8]. Moreover, few data about compliance and adherence to ERAS protocols is also lacking.

In 2019, the consensus guidelines for ERAS with esophageal resection was published addressing standard recommendations and introducing 25 procedure-specific items [12]. Future studies should confirm whether adherence to these new guidelines as well as the incorporation of new evidence-based interventions into ERAS programs will yield greater improvements in post-operative outcomes. Additionally, institutional ERAS protocols have to be seen as dynamic processes that require revisions based on periodic assessments and audits in order to maintain and improve outcomes [13].

Regarding the feasibility and impact of ERAS programs in gastric cancer surgery, most of the experience describing benefits is still limited to the Asian population [14]. The consensus guidelines for ERAS in gastrectomy was released in 2014 including both general recommendations and some procedure-specific items [15]. There is, however, paucity of studies on the application of these programs in the Western population, in what some clinical differences (older age, advanced stages, neoadjuvant chemotherapy) are observed in comparison to Eastern patients [16].

The aim of this narrative review is to present an overview of the implementation and current situation of the ERAS protocols in esophageal and gastric surgery in Western countries and to outline future perspectives on optimization of these protocols.
**Esophagectomy**

Esophagectomy is a complex surgical procedure associated with a significant morbidity which can reach up to 60%, irrespective whether the outcomes originate from high-volume centers or national audits. [17, 18]. Post-operative pulmonary complications represent the most common complication (29-57%) despite major advances in surgery, anaesthesia and peri-operative care, including the development of minimally invasive approaches. [17, 19].

Any effort to reduce post-operative complications and promote early recovery is essential and the incorporation of institutional ERAS protocols may contribute to achieve more favourable outcomes [9, 10].

**Initial Experiences with ERAS**

The first study describing a well-structured clinical pathway in esophageal resection was reported by Cerfolio et al in 2004 [20]. This prospective study included 90 patients who underwent an Ivor-Lewis esophagogastrectomy for esophageal cancer between 1999 and 2003. Excellent outcomes were obtained with only 7 general measures (preadmission counselling, thoracic epidural analgesia, early extubation, early removal of drains and nasogastric tube, early enteral feeding and mobilization) resulting in a median hospital stay of 7 days without compromising morbidity (26.6%) neither 30-day mortality (4.4%). Low et al [21] also achieved very good results with a larger cohort of 340 patients applying a clinical pathway with 8 items of the ERAS protocol from 1991 to 2006. The study emphasized the importance of intra-operative fluid restriction, extubation before leaving the operating room and thoracic epidural analgesia. Overall morbidity was 45% with a low incidence of pulmonary complications (17%). Munitiz et al [22] obtained similar outcomes comparing two groups of patients undergoing open Ivor-Lewis resection with or without application of the ERAS protocol.

**Evolution and Impact of ERAS programs on post-operative outcomes**

Considering these promising initial observations, institutions encouraged to introduce clinical care pathways and ERAS programs for esophagectomy. Findlay et al in 2014 published the first systematic review including 6 retrospective studies (4 from the West) [9]. Length of stay (LOS) was shortened with favourable morbidity and mortality rates after an ERAS protocol was applied. However, the main components of ERAS protocol within esophagectomy were mostly related to non-esophageal thoracoabdominal surgery with recommendations based on either extrapolated data or lower quality studies [9]. Simultaneously, Markar et al [10] performed a new systematic review which included 8 comparative studies (7 from the West countries) and one Chinese randomized controlled trial (RCT). Similarly, a reduction of LOS and a decreased morbidity without increasing readmission rate was documented. Again, the authors attributed these excellent results to general components of the ERAS program for any major abdominal surgery such as epidural analgesia, peri-operative fluid restriction, pre-
operative assessment by a cancer nurse specialist, early mobilization, and chest physiotherapy, but no intervention could be considered specific for esophageal resection [10].

To find new specific strategies, the same group published a systematic review with meta-analysis looking for those key components of ERAS programs that lead to improved LOS. Seven factors, one intra-operative (immediate extubation) and six post-operative (performing a contrast swallow ≤ 5 days, mobilization on post-operative ≤ 1 day, removal of urinary catheter ≤ 2 days, commencing oral intake with sips of fluid ≤ 1 day, enteral diet with feeding jejunostomy or gastrostomy ≤ 1 day and epidural removal on post-operative day 4 or earlier) were associated with a significant reduction in LOS [23]. Authors suggested that these measures should form part of the core ERAS program for esophagectomy.

A recent systematic review and meta-analysis (26 articles; 5 RCT and 6 prospective trials) has assessed the collective reported experience with standardized clinical pathways before the introduction of the esophagectomy-specific ERAS consensus guidelines [11]. This meta-analysis confirmed significant improvements in pulmonary complication (34% reduction) and hospital LOS although no difference in overall morbidity, post-operative mortality or readmission rates was identified (Table 1). However, from the analysis of the studies included in this publication, it is clear that there is a great variability of protocols and only few ERAS elements such as the use of epidural analgesia, jejunostomy placement, start enteral feeds and mobilization ≤ 1 day, start soft solid diet ≤ 4 day and chest tube removal ≤ 5 day were widely utilized (> 50% of the studies) [11].

In February 2019, the ERAS Society published an international expert consensus with 39 peri-operative actions and, for the first time, 25 components covering specific issues for esophageal surgery [12]. Some of these strategies are based on moderate or high evidence level (Table 2) while other items have low level of evidence.

**Adherence to ERAS protocol and predictors of failure**

Although some authors have shown the importance of the adherence of specific factors of the ERAS protocol to achieve good results, there is increasing evidence that the greatest benefits are obtained by the aggregation of marginal gains due to the adherence of the entire pathways [24]. In this setting, it is important that all team participants should be convinced that ERAS goals are a critical component of patient-centered care to improve outcomes and reduce costs [11, 12].

In an Italian single-center study, adherence to ERAS protocol items had a success rate that ranged between 32% and 73%, with the lowest success rate obtained in the resuming of oral intake. [25]. In a recent Italian multicenter study, including 13 tertiary centers performing at least 10 procedure/year, high percentages of adherence (100%) to ERAS guidelines were observed in some items, such as presence of a multidisciplinary tumor board, possibility of dysphagia palliation, pre-operative nutritional status evaluation and nutritional support, prevention of nausea, vomiting and hypothermia, and the use of post-operative multimodal analgesia. While low adherence (<50%) was seen in cardiopulmonary exercise testing, prevention of atrial arrhythmia, use of intravenous anesthesia, avoidance of intensive care unit (ICU) transfer at the end of surgery and avoidance of nasogastric tube use [26].
Initial studies on ERAS in esophagectomy identified age and pre-operative chemo-radiation as factors associated with low adherence to protocols[20, 22]. More recently, Parise et al [27] published a clinically useful bedside score with the aim to detect patients within the first 24 post-operative hours at risk of delayed discharge (>8 days); namely, patients at risk of ERAS protocol failure or deviation. Factors associated with delayed discharge were ASA ≥3, operative time >255 minutes, “non-hybrid” esophagectomy, and failure to mobilize within 24-hours from surgery.

**Focusing on key ERAS components**

*Nutritional assessment* is one of the key components of an ERAS protocol for esophagectomy. There is an agreement about the importance of pre-operative nutritional assessment to optimize nutritional status before surgery as in other abdominal major surgery ERAS protocols [28]. Even, in high-risk cases, enteral support is indicated preferable using the gastrointestinal tract with selective use of feeding tubes [28].

*Early oral feeding* is recommended [28] but it is controversial on which post-operative day it should be started. To answer this question, a recent multi-center RCT comparing early versus delay oral intake after minimally invasive esophagectomy was published (NUTRIENT II trial) [29]. Early was defined as introduction of liquids directly on post-operative day 1 and delay start as liquid diet gradually expanded from post-operative day 5 while jejunostomy tube feeding was used before day 5. Authors concluded that direct oral feeding did not affect functional recovery and did not increase incidence or severity of post-operative complications such as pneumonia or anastomotic leak.

Minimally invasive techniques have been progressively adopted since its first introduction in 1992 [30] due to the complexity of the procedure. Nowadays, totally minimal invasive or hybrid procedures are applied in 53% of the cases [31]. The first RCT comparing a laparoscopic esophagectomy versus open procedure (TIME Trial) demonstrated a shorter hospital stay and a reduction of post-operative pulmonary infections in favour of the MIS group [19]. Furthermore, no difference in oncological outcomes at 3-years was found [32]. These results have been confirmed in a recent study that compared a hybrid MIS (laparoscopic gastric mobilization with open right thoracotomy) with open esophagectomy demonstrating a reduction in post-operative complications after hybrid MIS. [33]. Moreover, robot-assisted minimally invasive esophagectomy (RAMIE) has been shown to reduce the overall complications rate with significantly lower pulmonary and cardiac complications rate compared to open surgery [34].

*Nasogastric tube decompression* at the time of esophageal resection is currently recommended [12]. However, the timing to remove the nasogastric tube and the need for a contrast study prior to removal is controversial. Early removal of nasogastric tube policy has not been shown to increase pulmonary complications or anastomotic leakage [35]. Moreover, a recent prospective study found that early nasogastric tube removal on post-operative day 2-3 after an upper gastrointestinal contrast study showing a normal conduit emptying is feasible [36].

ERAS advocates the avoidance of the *routine use of drainages* [1, 6]. Although the use of perianastomotic drain in cervical anastomosis may be avoided [12], the avoidance of chest drain is more controversial. Thoracic drainage delay recovery due to patient discomfort and lack of mobility but it may...
have an impact on the diagnosis and outcomes of anastomotic leak [37]. There are still no studies supporting complete drain omission. The only inference that a recent systematic review and ERAS guidelines concluded is that the use (duration and number) of chest drains should be minimized [12, 37].

**Gastrectomy**

Despite improvements in surgical technique and perioperative care, radical gastrectomy is still associated with high morbidity (30-45%) and 90-day mortality (4.5-7%) rates [38, 39]. Different intervention measures, including ERAS protocols, have been used during the peri-operative period to promote the patient recovery and to reduce mortality and morbidity. However, more than 60% of all cases of gastric cancer are from Eastern countries, where the incidence has been increasing in recent years [40]. In this setting, it is not surprising that most of the available information about ERAS come from the Eastern countries [41] and that the extrapolation of these data to the Western population may be debatable, considering that the clinical profile of the patients is substantially different because of the high prevalence of advanced tumors, malnutrition and obesity [16].

In the West, initial experiences were scarce and limited to safety studies. Grantcharov and Kehlet [42] demonstrated that minimally invasive approach combined with an ERAS protocol was feasible and safe. In 2014, a Consensus guideline for ERAS in gastrectomy was published by the ERAS Society Group [15], including general recommendations (17 items) which can be applied to any gastrointestinal surgery and eight specific recommendations for gastric surgery (Table 3).

**Evolution and Impact of ERAS programs on post-operative outcomes**

After the publication of the consensus guidelines, two single studies from US compared surgical outcomes before and after the implementation of an ERAS protocol. The first one found that implementing gastrectomy ERAS protocol with many of the components recommended by the ERAS consensus guidelines reduced the use of nasogastric tube and intrabdominal drains, accelerated advancement of diet and reduced LOS, without increasing complications and readmission rates [43]. The second also demonstrated a reduction of LOS, without increasing complications [44].

Moreover, two studies analysed the economic impact of the ERAS protocols. A large single-center study from Italy confirmed its feasibility and found that its application leaded to a reduction of 2-days LOS saving 1.097€ in total cost per patient [45]. Furthermore, Luzuy-Guarnero et al. identified a significant cost reduction in most of the variables evaluated except for the disposable materials (probably related to the more frequent use of laparoscopic approach) with a significant overall reduction of 6.386€ per patient [46].
Adherence to ERAS protocol and predictors of failure

Among the few studies reporting data about adherence and compliance, a prospective observational study [47], conducted in seven Italian centers, showed a wide adherence rate (5.6-87.8%) for single items. Adherence was very low for pre-operative items, mainly related to identification of nutritional problems (5.6%). Regarding to intra-operative items, avoidance of the nasogastric tube and abdominal drains was accomplished in nearly 50% of cases. A higher adherence (>70%) was registered for post-operative items [47].

In an Italian multicenter study, the overall rates of adherence to pre-, intra- and post-operative ERAS items were 69.8%, 60.3%, and 82.5%, respectively [48]. Several ERAS domains (carbohydrate load, goal directed fluid therapy, resumption of oral diet and no use of opioids) were associated with the risk of developing overall and major complications. On the contrary, no drain policy was associated with an increased risk for complications. In a multiple logistic regression model, the authors showed that compliance of ERAS components >70% was associated with a significant reduction of overall morbidity and major complications. Finally, in a Poisson’s regression model they showed that for every 10% in ERAS compliance it could be possible a 10% reduction in LOS.

In a retrospective study from the MD Anderson group, 82.7% patients in the ERAS group met full adherence to the protocol (considering full adherence when 7 items out of 36 were accomplished). Median LOS was shorter in the patients who met full adherence, but no statistically significant differences were observed, probably because the small number of patients included in thenon-adherent group [44]. In another Italian single-center study, compliance with ERAS items was at least 70% for each item with a 2 days median discharge reduction. Adherence resulted from 73% for resumption of soft diet to 90% for early mobilization and resumption of physiotherapy [45].

In an attempt to identify perioperative factors and ERAS protocol items influencing the LOS after gastrectomy, Parise et al [49] performed a multivariate regression analysis revealing that incomplete immunonutrition, failure to extubate the patient at the end of surgery, intra-operative crystalloids >2.150 ml, blood transfusion >268 ml, surgery duration >195 min, and failure to mobilize patients within 24h from surgery were associated with delayed discharge.

Focusing on key ERAS components

Nutrition support is an essential component of management in upper gastrointestinal cancer resection and most data show worse surgical outcomes in malnourished patients [50]. In an Australian multicentre prevalence study, a poor adherence to the majority of assessed ESPEN guidelines was shown and poor nutritional adequacy was associated with increased LOS and complications [51].

Early oral feeding is safe, feasible and beneficial [52]. A systematic review and meta-analysis of RCT from Eastern countries on early versus delayed oral feeding after gastrectomy showed that early oral
feeding was associated with early discharge, shorter hospital stay and lower hospital costs without increasing the incidence of post-operative complications [53]. A single-center Western experience showed that early oral feeding (liquid diet in POD1 and soft diet ≤ POD3) was safe with an adherence reaching 73% for the resumption of soft diet [45].

Evidence from Eastern countries supports minimally invasive techniques for distal gastric resection in early [54] and locally advanced tumors [55], although doubts have been raised about the advantages of laparoscopic access in total gastrectomy for advanced tumors [56] until the results of the ongoing Klass 06 trial(NCT 03385018) will be available. In a recent Western multicenter RCT, laparoscopic gastrectomy (distal or total) did not lead to a shorter hospital stay nor to reduce the complication rate in patients mostly with advanced gastric cancer [57]. Regarding robot-assisted minimally invasive approach, preliminary results showed in national population-based cohort, a shorter hospital stay when compared to open surgery with no differences with laparoscopic approach[58].

Decompression by nasogastric or nasojejunal tube is not recommended systemically after gastrectomy. In a Chinese meta-analysis investigating post-operative outcomes in patients with or without decompression tube, no differences in complication rates were found between the two groups independently of the extension of the resection and the type of reconstruction [59]. An Italian multicentre randomized trial concluded that routine placement of a nasogastric or nasojejunal tube after Billroth II and Roux-Y partial distal gastrectomy is not necessary in elective surgery for gastric cancer[60].

Prophylactic drain in gastrectomy is still widely used although there is lack of evidence to support its use. A recent meta-analysis including 3 RCT showed that drain avoidance can reduce morbidity and LOS without affecting other major surgical outcomes [61]. Once more time, data available is limited and basically from Eastern countries. A recent multicenter study enrolling 290 patients from 8 Italian centers incorporated a no-drain policy in the ERAS protocol. Only in 9% of patients who underwent subtotal gastrectomy the drain was avoided, suggesting that there was not confidence to abandon the use of abdominal drains. Furthermore, in this study, no drain-policy was associated with an increased risk of complications [48]. A multicenter non-inferiority RCT comparing two groups of patients who underwent gastrectomy with or without perianastomotic drainage is ongoing[62].

**Barriers and Future Perspectives**

Overall, the application of ERAS protocols in esophago-gastric cancer surgery [12, 15] has resulted in better outcomes compared to traditional care. However, there is still great heterogeneity and lack of standardization between the ERAS protocols with no clear definitions of each component [11, 63]. Moreover, serious difficulties to implement ERAS programs in the clinical practice, mostly due to the resistance to traditional care changes, has been detected[26, 47]. Additionally, infrastructural resources and staff availability and turnover might lead to low adherence to the protocols. [11]. Certainly, implementation of ERAS protocols needs an initial great investment, but it is later associated with important costs reductions [46].
Successful implementation and adherence to ERAS protocols require a committed MDT and a powerful leadership to refine the protocol with the best and newest evidence-based literature [64]. Markar et al [13] showed that the knowledge and experience gained by the staff in the ERAS protocol is associated with a significant reduction in median LOS. Patients’ engagement is also fundamental to facilitate the compliance of ERAS protocols [63]. Finally, continuous data evaluation with systematic audits is crucial to improve compliance and clinical outcomes [15, 63].

With the aim to optimize functional capacity prior to surgery, the concept of prehabilitation emerged in recent years and is being considered as key component of ERAS programs. Prehabilitation comprises nutritional assessment, psychological counselling, medical optimization, and a structured exercise program involving both aerobic and strengthening activity, using the time between diagnosis and surgery [65, 66]. Recent systematic reviews have shown that the implementation of exercise intervention improves the post-operative physical fitness reducing postoperative morbidity (especially post-operative pneumonia) rates [67, 68].

Even more recently, the concept of posthabilitation has been developed. Its aim is to improve functional capacity after the surgical procedure to return earlier to baseline fitness level [69]. An ongoing RCT investigates the efficacy of a 12-week exercise rehabilitation program after upper gastrointestinal surgery supervised face-to-face by a MDT (ReStOre II) [69].

**CONCLUSIONS**

- ERAS programs are associated with shorter LOS, less incidence of pulmonary complications and a reduction in costs following esophagogastric cancer surgery.
- Studies have shown great heterogeneity and lack of definitions in the ERAS components. However, the new ERAS Group Guidelines provide a specific framework of ERAS goals to improve outcomes after esophagectomy and gastrectomy.
- MDT commitment and continuous monitoring of compliance is critical to maintain and improve ERAS protocols.
- Prehabilitation and posthabilitation are emerging concepts that might be incorporated to the ERAS programs.
ABBREVIATIONS

ERAS - Enhanced Recovery After Surgery
LOS - Length of Stay
MDT - Multidisciplinary Team
MIS - Minimally Invasive Surgery
RCT - Randomized Clinical Trial
Acknowledgements

Authors would like to thank Marta Pulido, M.D, for editorial assistance.
BIBLIOGRAPHY


<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>Nº studies</th>
<th>Considered population</th>
<th>ERAS</th>
<th>TRADITIONAL</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay</td>
<td>24</td>
<td>3626</td>
<td>9.9±2.8</td>
<td>13.4±1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-operative morbidity</td>
<td>19</td>
<td>2091</td>
<td>29.8%</td>
<td>32.5%</td>
<td>0.350</td>
</tr>
<tr>
<td>Post-operative mortality (90d)</td>
<td>17</td>
<td>2661</td>
<td>2.2%</td>
<td>2.9%</td>
<td>0.982</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>19</td>
<td>3010</td>
<td>8.3%</td>
<td>10.3%</td>
<td>0.659</td>
</tr>
<tr>
<td>Pulmonary complications</td>
<td>17</td>
<td>2509</td>
<td>17.0%</td>
<td>22.4%</td>
<td>0.011</td>
</tr>
</tbody>
</table>

*Table 1.* Post-operative outcomes reported by studies comparing results in ERAS and non-ERAS groups. Adapted from Puccetti et al. [11]
**Table 2.** Specific and general components of ERAS protocols for esophagectomy with moderate or high level of recommendation. [12]

<table>
<thead>
<tr>
<th>GENERAL</th>
<th>SPECIFIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRE-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Antithrombotic prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Avoid pre-operative fasting</td>
<td></td>
</tr>
<tr>
<td>Avoid pre-operative smoking and alcohol consumption (4 weeks)</td>
<td></td>
</tr>
<tr>
<td>Avoid oral bowel preparation (should not be used routinely)</td>
<td></td>
</tr>
<tr>
<td>Routine use of pre-operative oral pharmaconutrition cannot be supported</td>
<td></td>
</tr>
<tr>
<td>Multidisciplinary tumor board and audit</td>
<td></td>
</tr>
<tr>
<td>Continuing beta-blockers in the peri-operative period in those who are chronically on beta-blockers and prescribe beta-blockers for other high-risk patients</td>
<td></td>
</tr>
<tr>
<td><strong>INTRA-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Anesthetic maintenance (intermediate-acting anesthetic drugs; Low-tidal volume ventilation in two-lung ventilation; Titrating depth of anesthesia with bispectral index monitoring)</td>
<td>A tubulized gastric conduit is recommended as the first option</td>
</tr>
<tr>
<td>Avoid hypothermia</td>
<td>Two-field lymphadenectomy is recommended for T1b-T3/4 ADC in the middle and lower third of the esophagus. Three-field lymphadenectomy is recommended in upper third SCC.</td>
</tr>
<tr>
<td>Avoid liquid overload</td>
<td>Use nasogastric tube decompression at the time of esophageal resection</td>
</tr>
<tr>
<td>Volatile or intravenous anesthetics are equally effective</td>
<td>Routine PEEP&gt;2–5 cm H2O and recruitment maneuvers have not been fully defined</td>
</tr>
<tr>
<td></td>
<td>Thoracic epidural analgesia should be considered as first line; Paravertebral blocks are a good alternative; Regular acetaminophen dosing should be considered; Commence NSAIDS on an individualized basis</td>
</tr>
<tr>
<td><strong>POST-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Early removal of Foley catheter is worthy of consideration</td>
<td>Patient does not routinely require ICU care</td>
</tr>
<tr>
<td>Avoid liquid overload</td>
<td>Introduction of early enteral nutrition is beneficial</td>
</tr>
<tr>
<td>Blood glucose levels above 10 mmol/L (180 mg/dl) should be treated</td>
<td>Early mobilization should be encouraged as soon as possible</td>
</tr>
</tbody>
</table>

Items in bold format are recommended with high level of evidence and strong recommendation; Items in regular format are recommended with moderate level of evidence and strong recommendation.
**Table 3.** Specific and general components of ERAS protocols for gastrectomy with moderate or high level of recommendation. [15]

<table>
<thead>
<tr>
<th>GENERAL</th>
<th>SPECIFIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRE-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Antithrombotic prophylaxis</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial prophylaxis and skin preparation</td>
<td></td>
</tr>
<tr>
<td>Avoid pre-operative smoking</td>
<td></td>
</tr>
<tr>
<td>Avoid oral bowel preparation</td>
<td></td>
</tr>
<tr>
<td><strong>INTRA-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Anesthetic management (Short-acting anesthetic drugs; Low-tidal volume ventilation; Titrating depth of anesthesia with bispectral index monitoring)</td>
<td>Laparoscopic access in distal gastrectomy in early gastric cancer</td>
</tr>
<tr>
<td>Avoid hypothermia</td>
<td>Nasogastric decompression should not be used routinely</td>
</tr>
<tr>
<td>Avoid liquid overload</td>
<td>Avoid the use of abdominal drains</td>
</tr>
<tr>
<td>Monitoring volume with transoesophageal Doppler; prefer balanced crystalloids</td>
<td></td>
</tr>
<tr>
<td><strong>POST-OPERATIVE</strong></td>
<td></td>
</tr>
<tr>
<td>Remove Foley catheter safely on POD 1–2</td>
<td>Patients undergoing total gastrectomy should be offered drink and food at will from POD 1; Patients clearly malnourished or those unable to meet 60% of daily requirements by POD 6 should be given individualized nutritional support</td>
</tr>
</tbody>
</table>

Items in bold format are recommended with high level of evidence and strong recommendation; Items in regular format are recommended with moderate level of evidence and strong recommendation.