The Latest Results and Future Directions of Research for Enhanced Recovery after Surgery in the Field of Colorectal Surgery

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Enhanced recovery after surgery (ERAS) aims to promote postoperative recovery in patients by minimizing the surgical stress response through evidence-based multimodal interventions. In 2023, updated clinical practice guidelines were published in North America, potentially superseding the most recent guidelines previously announced at the ERAS Society in 2019. This review compares and reviews these two guidelines to examine the principle of ERAS and items related to colorectal surgery and to introduce the latest relevant study results published within the last 5 years. In the pre-hospitalization stage, the concept of pre-hospitalization is emphasized; this involves checking and reinforcing the patient’s nutritional status and physical functional status before surgery. In the preoperative stage, large-scale studies have prompted a change in the recommendation of mechanical bowel preparation combined with oral antibiotics in elective colorectal surgery. In the intraoperative stage, laparoscopic surgery has become a widespread and important component of ERAS, and more technologically advanced single-incision laparoscopic surgery and robotic surgery are the focus of active research. Ileus-prevention items, such as opioid-sparing multimodal pain management and euvolemic fluid therapy, are recommended in the postoperative stage. The adoption of ERAS protocols is expanding to encompass a wide range of surgical procedures, clinical scenarios, healthcare institutions, and professional medical societies. In order to maximize the effect by increasing adherence to ERAS, medical staff must fully understand the clinical basis and meaning of each item, and the protocol must be maintained and developed steadily through a team approach and audit system.

Introduction

Enhanced recovery after surgery (ERAS) constitutes a comprehensive set of evidence-based practices, collaboratively administered by a diverse healthcare team, aimed at facilitating swift postoperative recovery for patients. It has been proven to be associated with faster recovery of bowel function, reduced postoperative length of hospital stay (LOS), and a lower rate of postoperative complications compared to traditional perioperative care [1,2].

However, ERAS is relatively difficult to introduce and maintenance efforts are also required. In addition, the degree to which various items of ERAS are accepted by institutions or medical staff varies [3].

The aim of this review is to enhance readers’ understanding of ERAS and facilitate future research in this field. This will be achieved by presenting recently published papers (within the

last 5 years) on relevant topics. Additionally, we will provide a schematic comparison of the recently updated clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons (ASCRS) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) [4] with the existing ERAS Society guidelines [5].

Main Text

1. Composition of enhanced recovery after surgery items: practice guidelines from the Enhanced Recovery after Surgery Society and American Society of Colon and Rectal Surgeons

ERAS guidelines for colorectal surgery were first published in 2005 and have been updated as recently as 2019 by the ERAS Society. Meanwhile, the ASCRS and SAGES, primarily based in North America, issued their initial practice guidelines in 2017, with updates made in 2023. While these two sets of guidelines share many similar principles and protocol items, the ERAS Society guidelines are slightly more comprehensive. In contrast, the ASCRS guidelines contain less detail on individual items but incorporate the most recent research findings (Table 1).

In brief, the ASCRS guidelines advocate for the use of mechanical bowel preparation (MBP) in conjunction with oral antibiotics for colorectal resections. This differs from the ERAS Society guidelines, which suggest considering MBP (coupled with oral antibiotics) solely for rectal surgery. Furthermore, the ASCRS guidelines diverge from the ERAS Society guidelines in their approach to thoracic epidural analgesia (TEA). While the ERAS Society guidelines endorse TEA for open surgery, the ASCRS guidelines suggest considering TEA selectively, only if the surgery is open and a dedicated pain team is available. The ASCRS guidelines also underscore

| Table 1. Brief comparison of current clinical guidelines from the Enhanced Recovery after Surgery Society and the American Society of Colon and Rectal Surgery-Society of American Gastrointestinal and Endoscopic Surgeons |
|-------------------------------|--------------------------------------------------------------------------------------------------|
| **Stage**                     | **ERAS Society guidelines [5]**                                                                 |
| Preadmission                  | **ASCRS guidelines [4]**                                                                           |
| Preadmission orders           | Standardized order sets should be utilized                                                        |
| Information, education, and  | Patients should receive dedicated preoperative counseling routinely                               |
| counseling                    | A preoperative discussion regarding clinical milestones and discharge criteria should be performed. |
|                               | Stoma teaching and counseling regarding how to avoid dehydration should be provided for patients undergoing ileostomy. |
| Preoperative optimization     | Medical risk assessment                                                                            |
| Smoking cessation at least 4 | Smoking cessation at least 4 weeks prior to surgery                                                |
| weeks prior to surgery        | Preoperative nutritional assessment should be offered.                                             |
|                              | Patients at risk of malnourishment are recommended to have oral nutritional supplementation for 7−10 days. |
| Nutrition                    | Oral nutritional supplementation is recommended in malnourished patients (targeting a protein intake of 1.2−1.5 g/kg/day for 1−2 weeks). |
| Prehabilitation              | May reduce complications. Patients who are less fit may be more likely to benefit.                 |
| Anemia management            | If possible, anemia should be corrected with intravenous iron preoperatively prior to surgery, and blood transfusion should be avoided. |
|                              | May be considered for patients with multiple comorbidities or significant deconditioning.         |
|------------------------------|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| **Preoperative**             |                                                                                             |                                                                                        |
| Prevention of PONV           | A multimodal approach to PONV prophylaxis should be considered.                               | Similar (recommendations for PONV, pain, SSI prevention, and fluid management are stated in the Perioperative Interventions section). |
| Pre-anesthetic medication    | Sedative medication should be avoided if possible before surgery.                            | A multimodal, opioid-sparing, pain management plan should be implemented before the induction of anesthesia. |
| Antimicrobial prophylaxis     | Intravenous antibiotic prophylaxis should be given within 60 min before incision as a single-dose administration. |                                                                                       |
| Skin preparation             | Chlorhexidine-alcohol-based preparation                                                      | A bundle of measures (preoperative: chlorhexidine shower, bowel preparation, antimicrobial prophylaxis, chlorhexidine/alcohol skin preparation, operative: wound protector, gown and glove changes before fascial closure, antimicrobial sutures, maintaining euglycemia and normothermia) should be in place to reduce SSI perioperatively |
| Bowel preparation            | MBP alone with IV antibiotic prophylaxis may be used for rectal surgery.                    | MBP combined with preoperative oral antibiotics is typically recommended.               |
| Preoperative fasting         | The patient should be allowed to eat up until 6 h and take clear fluids up until 2 h before anesthetic induction. | Clear liquids may be continued up to 2 h before surgery.                                 |
| and carbohydrate loading     | Patients with delayed gastric emptying and emergency patients should fast overnight or 6 h before surgery. |                                                                                       |
| **Intraoperative**           |                                                                                             |                                                                                        |
| Standard anesthetic protocol | Avoidance of benzodiazepines                                                                  | Similar recommendation                                                                 |
|                             | Use of short-acting anesthetics                                                              |                                                                                        |
|                             | Cerebral function monitoring                                                                 |                                                                                        |
|                             | Monitoring of the level and complete reversal of neuromuscular block                          |                                                                                        |
| Fluid and electrolyte management | Maintain fluid homeostasis                                                                    |                                                                                       |
|                             | GDFT should be adopted, especially in high-risk patients                                     | Similar recommendation                                                                 |
| Prevention of intraoperative hypothermia | Reliable temperature monitoring should be undertaken.                                      |                                                                                        |
| Surgical access             | Minimally invasive surgery is recommended.                                                   | Similar recommendation                                                                 |
| Drain                       | Pelvic and peritoneal drains should not be used routinely.                                   | Similar recommendation                                                                 |
| Postoperative               |                                                                                             |                                                                                        |
| Nasogastric tube            | Should not be used routinely                                                                | Similar recommendation                                                                 |
|                             | If inserted during surgery, it should be removed before reversal of anesthesia.             |                                                                                        |
the importance of comprehensive preoperative education about the stoma and the potential for dehydration. They suggest that early discharge may be considered even for patients whose bowel function has not yet returned to normal. Conversely, the ERAS Society guidelines address issues such as abstaining from alcohol and smoking, correcting anemia, and thromboprophylaxis, which are not mentioned in the ASCRS guidelines. In this review, the author will sequentially present the latest research findings in accordance with the topics covered by both sets of guidelines.

Table 1. Continued

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Postoperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain control</td>
<td>Avoid opioids and apply multimodal analgesia. TEA is recommended in open colorectal surgery.</td>
<td>Similar recommendation TEA is an option for open colorectal surgery (if dedicated pain team is available)</td>
</tr>
<tr>
<td>Abdominal wall blocks</td>
<td>TAP blocks can reduce opioid consumption and improve recovery.</td>
<td>Laparoscopic-guided TAP block is safe and effective, and seems to be as effective as US-guided TAP block.</td>
</tr>
<tr>
<td>Thromboprophylaxis</td>
<td>Mechanical prophylaxis by compression stockings and/or intermittent pneumatic compression until discharge.</td>
<td>Pharmacological prophylaxis with LMWH for 28 days after surgery.</td>
</tr>
<tr>
<td>Fluid and electrolyte management</td>
<td>Net &quot;near-zero” fluid and electrolyte balance should be maintained. Balanced solutions are preferred.</td>
<td>Similar recommendation</td>
</tr>
<tr>
<td>Foley catheter</td>
<td>Recommended for 1–3 days</td>
<td>Removed within 24 h for colon–upper rectal resection Removed within 24–48 h for mid/lower rectal resection</td>
</tr>
<tr>
<td>Nutritional care</td>
<td>Early resumption of oral intake with oral supplementation from the day of surgery.</td>
<td>Patient should be offered a regular diet with 24 h.</td>
</tr>
<tr>
<td></td>
<td>Perioperative immunonutrition for malnutrition.</td>
<td>The efficacy of immunonutrition over standard high-protein oral nutritional supplements remains controversial.</td>
</tr>
<tr>
<td>Early mobilization</td>
<td>Through patient education and encouragement</td>
<td>Early and progressive patient mobilization are associated with a shorter length of stay.</td>
</tr>
<tr>
<td>Discharge criteria</td>
<td></td>
<td>Hospital discharge prior to return of bowel function may be offered for selected patients.</td>
</tr>
<tr>
<td>Audit</td>
<td>Collection of key outcome and process data used for repeated audits and feedback is essential</td>
<td></td>
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</tbody>
</table>

ERAS, Enhanced Recovery after Surgery; ASCRS, American Society of Colon and Rectal Surgeons; PONV, postoperative nausea and vomiting; SSI, surgical site infection; MBP, mechanical bowel preparation; MAP, mean arterial pressure; GDFT, goal-directed fluid therapy; TEA, transthoracic epidural analgesia; TAP, transversus abdominis plane; US, ultrasonography.
2. Pre-admission issues

1) Prehabilitation
Prehabilitation is defined as “a process in the continuum of care that occurs between the
time of diagnosis and the beginning of acute treatment and includes physical, nutritional and
psychological assessments that establish a baseline functional level, identify impairments, and
provide interventions that promote physical and psychological health to reduce the incidence
and/or severity of future impairments” [5] or simply “enhancement of the patient’s preoperative
condition” [4].

With the rise in the elderly population, there is an increasing focus on pre-habilitation.
McLennan et al. [6] presented the results of a study involving 199 patients who underwent
elective colorectal surgery and received ERAS perioperative care. The study found that patients
with a poor preoperative physical status, specifically those unable to climb two flights of stairs,
had significantly higher postoperative complications (OR, 6.64; 95% CI, 1.51–29.13, P=0.012) than
those who did not exhibit such physical limitations.

However, even though preoperative prehabilitation may enhance physical function, it remains
a topic of debate whether this improvement translates into tangible outcomes such as reducing
postoperative complications and shortening the LOS [4]. Consequently, the recommendations
of the two guidelines are confined to suggesting that prehabilitation might be beneficial for
patients with multiple comorbidities or poor physical performance.

Additionally, given that nutrition has been identified as a significant factor in postoperative
outcomes and has its own set of recommendations, the term “prehabilitation” should be narrowly
defined to focus on exercise capacity or frailty. As a result, it is crucial to pursue research efforts
that investigate preoperative evaluations, prehabilitation methods, and their respective effects.

2) Nutrition
Both guidelines suggest assessing the preoperative nutritional status and administering
oral nutritional supplementation to malnourished patients for an approximate duration of 1–2
weeks. Evidence exists that the preoperative nutritional status is linked to complications,
and enhancements in nutritional status can result in a reduction of postoperative infectious
complications [7].

Lorenzon et al. [8] conducted a study involving 1,648 patients who underwent digestive tract
surgery, of which 1,041 were colorectal cancer patients. The authors discovered a significant
interrelation among ERAS care, minimally invasive surgery (MIS), and nutritional screening. They
found that these factors significantly impacted 30-day mortality and LOS.

3. Preoperative issues

1) Bowel preparation
There are ongoing debates regarding the method and impact of bowel preparation in relation
to surgical site infection (SSI). The ASCRS guidelines typically recommend the use of MBP in
conjunction with preoperative oral antibiotics prior to elective colorectal surgery. However, the
2019 ERAS Society guidelines suggest bowel preparation only as an optional measure for rectal
surgery [4,5]. Consequently, in recent studies on ERAS in colorectal surgery, many researchers
have incorporated a “no MBP” approach into their ERAS protocols.

Further research is needed to address several issues related to bowel preparation. These
include the development of less invasive and more comfortable methods for MBP that do not significantly disturb homeostasis prior to surgery. Additionally, the selection of suitable oral antibiotics, the determination of the most beneficial bowel preparation method in MIS, and the investigation of pre- or probiotics that can aid in restoring the normal gut microbiome following bowel preparation and throughout perioperative care, all merit further investigation [9].

2) Preoperative oral carbohydrate loading

The recommendation to mitigate the detrimental effects of overnight fasting by consuming oral carbohydrates two hours prior to surgery is quite robust, and there is consensus between the two guidelines on this matter. However, there is a lack of evidence regarding this issue for patients with diabetes.

3) Surgical site infection prevention bundles

The ERAS Society guidelines incorporate a section on antimicrobial prophylaxis and skin preparation. In contrast, the ASCRS guidelines utilize a bundle concept, amalgamating various preoperative and intraoperative measures into a single comprehensive package. This discrepancy may stem from the ERAS Society guidelines’ uncertainty regarding the validity of each prophylactic item, as they evaluated the evidence for each individually. Recent evidence suggests that various SSI prevention bundles are effective in reducing SSI. Notably, the prevention effect increases with higher adherence to the various bundle items [10].

4) Postoperative nausea and vomiting

Guidelines suggest the preventive use of anti-emetic agents, combining two or more with different mechanisms, prior to surgery. An observational study involving 806 consecutive patients enrolled in the colorectal ERAS program demonstrated the varied use of these agents and the outcomes achieved through multimodal approaches [11]. In this study, the incidence of postoperative nausea and vomiting (PONV) was reported as 7%, 7%, and 10% on postoperative days 0, 1, and 2, respectively. However, the authors stressed the need for further development, as the increased rate of PONV on the second postoperative day led to an extended LOS by two nights due to poor oral intake and a delayed soft diet.

4. Intraoperative issues

1) Fluid management

The recommendations of both guidelines for perioperative fluid therapy are similar, and the summary is as follows: The first choice is typically a balanced chloride-restricted crystalloid, with the general aim being to maintain euvolemic status. For high-risk patients, or during high-risk procedures that may result in significant intravascular losses, goal-directed fluid therapy can be employed. If there are no surgical complications and the patient remains hemodynamically stable post-surgery, fluid therapy should be discontinued as soon as possible.

In this regard, recent studies [12–14] have investigated whether the risk of acute kidney injury (AKI) increases when applying the ERAS protocol (Table 2). These studies explored the association between AKI and patients undergoing colorectal surgery with ERAS perioperative care. Despite similar baseline characteristics, the incidence of AKI was consistently higher in the ERAS group compared to the non-ERAS group, resulting in an increase in complications. Additionally, the LOS was longer for AKI patients within the ERAS group.
However, in a study by Drakeford et al. [14], which analyzed 555 patients undergoing laparoscopic colorectal resection with the ERAS protocol, it was highlighted that while 13.4% of AKI cases occurred, only 2.2% of these were moderate to severe AKI (as classified by the Kidney Disease Improving Global Guidelines stage 2 and 3). The authors noted that many similar studies often neglect to provide detailed information on ERAS adherence, such as whether preoperative oral carbohydrate loading was carried out or the volume of perioperative fluid administered (including oral intake). This omission makes it challenging to accurately interpret or compare the results. However, the findings of this study revealed that even though 83.6% of the cases were mild AKI (stage I), the major complication and 1-year mortality rates were significantly higher than in patients who did not develop AKI.

Another study [15] compared 125 patients experiencing intraoperative oliguria (<0.5 mL/kg/h) during laparoscopic colorectal cancer surgery with ERAS perioperative care to another 125 patients, matched based on propensity scores. The findings indicated a significantly higher occurrence of AKI in the oliguria group, which was associated with an increased rate of surgical complications (18.4% vs. 9.6%, P=0.045). Consequently, it is crucial to adhere to the ASCRS guidelines. These guidelines emphasize the importance of avoiding a mean arterial pressure of less than 65 mmHg during the perioperative period, maintaining euvolemia, and properly addressing or preparing for the risk factors of AKI as identified in various studies.

### 2) Surgical approach

MIS is associated with fewer wound-related complications, reduced pain, and faster recovery compared to open surgery, all of which contribute to improved adherence to ERAS. Consequently, both ERAS Society guidelines advocate for the implementation of MIS where

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study design</th>
<th>Group</th>
<th>No. of patients</th>
<th>Population</th>
<th>AKI (%)</th>
<th>LOS (days) of AKI patients vs. non-AKI in ERAS group</th>
<th>LOS (days)</th>
<th>Other significant factors for AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcotte et al.</td>
<td>2018</td>
<td>Retrospective cohort</td>
<td>ERAS vs. matched pre-ERAS</td>
<td>132 vs. 132</td>
<td>Colorectal resection</td>
<td>11.4 vs. 2.3, P&lt;0.0001</td>
<td>5.5 vs 7.7, P&lt;0.0001</td>
<td>8.40 vs 5.11, P=0.0037</td>
<td>High preoperative creatinine level, open surgery, long anesthesia duration, major complications</td>
</tr>
<tr>
<td>Wiener et al.</td>
<td>2020</td>
<td>Retrospective cohort</td>
<td>ERAS vs. pre-ERAS (in the NSQIP registry)</td>
<td>572 vs. 480</td>
<td>Colorectal resection</td>
<td>13.64 vs. 7.08, OR 2.31, 95% CI 1.48−3.59, P&lt;0.01</td>
<td>7 (5−12) vs. 3 (2−6), P&lt;0.01</td>
<td>Median 4 (IQR 4−9) vs. 3 (2−5), P&lt;0.04</td>
<td>Smoking, ASA grade ≥3</td>
</tr>
<tr>
<td>Drakeford et al.</td>
<td>2022</td>
<td>Retrospective cohort</td>
<td>AKI vs. non-AKI</td>
<td>n=555</td>
<td>Colorectal surgery</td>
<td>13.4 (stage I, 11.2%, II, 2.0%, III, 0.2%)</td>
<td>Median 11 (IQR 5−17) vs. 6 (4−8), P&lt;0.001</td>
<td>Smoking, ASA grade ≥3</td>
<td>Smoking, ASA grade ≥3</td>
</tr>
<tr>
<td>Shim et al.</td>
<td>2020</td>
<td>Retrospective cohort</td>
<td>(Intraoperative) oliguria vs. matched non-oliguria</td>
<td>125 vs. 125</td>
<td>Laparoscopic colorectal cancer + ERAS</td>
<td>26.4 vs. 11.2, OR 2.708, 95% CI 1.354−5.418, P=0.005</td>
<td>Smoking, ASA grade ≥3</td>
<td>Smoking, ASA grade ≥3</td>
<td>Smoking, ASA grade ≥3</td>
</tr>
</tbody>
</table>

AKI, acute kidney injury; LOS, length of hospital stay; ERAS, enhanced recovery after surgery; NSQIP, National Surgical Quality Improvement Program; ASA, American Society of Anesthesiologists.

*Defined as <0.5 mL/kg/h.
feasible. There is an increasing interest within the MIS field to investigate whether technological advancements have resulted in variations in the effectiveness of ERAS protocols across different methods. Recent studies have examined whether single-port laparoscopic surgery and robotic surgery have a more beneficial impact on ERAS than conventional laparoscopic surgery (Table 3).

Research on robotic surgery has yielded conflicting results. In patients who underwent robotic right colonic resection with intra-corporeal anastomosis, there was no difference in postoperative complications and LOS, but the operation time was notably longer compared to those who underwent laparoscopic surgery [16]. Conversely, a large-scale population cohort study by Asklid et al. [17] and a study by Hung [18] that tracked the increasing rate of robotic surgery over time, found that robotic surgery was significantly associated with a reduced LOS. Furthermore, Hung’s study indicated that a higher rate of robotic surgery was associated with greater adherence to the ERAS protocol.

This discrepancy in study results may be due to the differences in the surgical sites examined in each study. Robotic surgery tends to offer more advantages if the lesion is closer to the anus, as it facilitates precise operations within the narrow confines of the pelvis, thereby promoting quicker recovery. Conversely, in right colonic surgery, which is performed in the abdominal cavity, robotic surgery does not present a clear advantage over laparoscopic surgery.

With advancements in laparoscopic techniques and tools, single-incision laparoscopic surgery has gained popularity due to its purported benefits over conventional laparoscopic surgery, including reduced incision size and improved patient satisfaction. Table 3 provides a summary of studies investigating the effect of new surgical techniques among the patients who underwent colorectal surgery with an enhanced recovery after surgery protocol.

**Table 3.** Studies investigating the effect of new surgical techniques among the patients who underwent colorectal surgery with an enhanced recovery after surgery protocol

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study design</th>
<th>Technique</th>
<th>No. of patients</th>
<th>Population</th>
<th>LOS</th>
<th>Complications</th>
<th>Other notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migliore et al. [16]</td>
<td>2021</td>
<td>Retrospective cohort</td>
<td>Lap. vs. Robot</td>
<td>170 vs. 46</td>
<td>Right hemicolectomy with intra-corporeal anastomosis +ERAS</td>
<td>OR 0.16, 95% CI 0.79−1.10, P=0.74</td>
<td>No difference</td>
<td>No difference in conversion, readmission, 30-day morbidity, and major morbidity. Operative time was longer in robotic surgery (P&lt;0.001)</td>
</tr>
<tr>
<td>Asklid et al. [17]</td>
<td>2022</td>
<td>Retrospective cohort (the Swedish part of the international ERAS Interactive Audit System)</td>
<td>Open vs. Lap. vs. Robot</td>
<td>3,125 (1,429 vs. 869 vs. 827)</td>
<td>Rectal tumor resection +ERAS</td>
<td>Robotic was the shortest (median 9 vs. 7 vs. 6 days)</td>
<td>No difference (40.9% vs. 31.2% vs. 35.9%)</td>
<td>Similar preoperative and intraoperative compliance to the ERAS protocol</td>
</tr>
<tr>
<td>Hung et al. [18]</td>
<td>2023</td>
<td>Retrospective cohort</td>
<td>Lap. vs. Robot</td>
<td>155 (31 cases/ quintile)</td>
<td>Colorectal resection +ERAS</td>
<td>For ≤5 days, robotic surgery: OR 5.029, 95% CI 1.321−19.421, P=0.018</td>
<td>No difference among the groups</td>
<td>The more recent the period, the higher the rate of robotic surgery, the higher median compliance rate of ERAS protocol, and the shorter LOS.</td>
</tr>
<tr>
<td>Kim et al. [19]</td>
<td>2019</td>
<td>Retrospective cohort</td>
<td>Lap./ERAS vs. SILS/Cv. Lap./Cv.</td>
<td>91 vs. 83 vs. 96</td>
<td>Colon cancer</td>
<td>ERAS was a significant factor (in multiple regression analysis, P&lt;0.001)</td>
<td>No difference among the groups</td>
<td>No difference in reoperation and readmission among the groups</td>
</tr>
</tbody>
</table>

LOS, length of hospital stay; Lap., laparoscopic surgery; ERAS, enhanced recovery after surgery; SILS, single incision laparoscopic surgery; Cv., conventional perioperative treatment.
surgery (SILS) has also been developed. Some studies have compared operative outcomes among various combinations of surgical methods and conventional or ERAS care [19,20]. Although no difference was observed in complications or readmission rates, the group that received ERAS care demonstrated a significantly shorter LOS than the other two groups receiving conventional perioperative care. This was according to a study comparing outcomes among three groups: multiport laparoscopy+ERAS care, SILS+conventional care, and multiport laparoscopy+conventional care. In the multivariable analysis, perioperative ERAS care was a significant factor in reducing LOS, while SILS was not. Another study [20] compared SILS and multiport laparoscopic surgery while implementing ERAS perioperative care in gastric cancer cases. However, only the C-reactive protein level was significantly lower in the SILS group on the third postoperative day. No differences were identified in complications, recovery time for walking/eating after surgery, and LOS.

However, even in the case of laparoscopic appendectomy, which typically has a relatively short LOS, a study found that the LOS of the SILS group was significantly shorter than that of the multiport group within the same ERAS protocol [21]. Furthermore, the application of SILS has been extended to various procedures [22]. Therefore, additional research is needed to evaluate the impact of SILS on the outcomes of ERAS perioperative care in diverse types of surgery.

5. Postoperative issues

1) Pain management

A multimodal, opioid-sparing pain management approach, which can facilitate early postoperative ambulation without adversely affecting bowel movement recovery, is one of the most crucial and highly recommended components of the ERAS protocol. Thoracic epidural analgesia (TEA), once a significant protocol, is now only considered for open surgery due to potential side effects and diminished effectiveness in laparoscopic surgery.

Recent studies have highlighted potential analgesic procedures or agents that could serve as alternatives to TEA. This is because methods previously effective in open surgery may no longer yield significant differences, given the rise of MIS and the multimodal analgesic pain management approach of ERAS.

The guidelines mention the transversus abdominis plane block. A randomized controlled trial (RCT) compared its effects with TEA using only ropivacaine without opioids. The total opioid consumption up to 48 hours post-surgery was found to be similar (29 mg vs. 40 mg, P=0.3) [23]. There was no significant difference in the time to first postoperative bowel movement, complications, or LOS among patients who underwent laparoscopic colon resection and followed the same ERAS protocol, with the exception of the regional block method used. However, the authors favored the transversus abdominis plane block, which demonstrated superior analgesia over time post-surgery, over TEA, whose efficacy has been questioned in existing studies.

An RCT [24] focusing on the quadratus lumborum block found no significant reduction in postoperative opioid use (129 mg vs. 127.2 mg in the first 24 hours, P=0.93) with this block. Furthermore, it did not accelerate recovery when compared to a placebo in the context of laparoscopic colon resection with ERAS perioperative care.

2) Other ileus-prevention items

In addition to multimodal pain management, ERAS incorporates a variety of measures to prevent postoperative ileus. These measures, commonly recommended in guidelines, include
early ambulation, prompt resumption of diet, timely withdrawal of fluids, early removal or avoidance of nasogastric tubes, early removal of urinary catheters, and minimal use of drains.

Sato et al. [25] analyzed 289 patients who had undergone surgery for colorectal cancer following the ERAS protocol. Their objective was to determine which elements of the ERAS protocol primarily influenced complications and LOS. They discovered that ceasing intravenous fluid infusion on the first postoperative day was a significant factor associated with complications and LOS. Additionally, they found that preventing intraoperative fluid overload (less than 2 L) had a substantial impact on LOS. This underscores the importance of fluid therapy within the ERAS protocol.

Regarding the timing of postoperative urinary catheter removal, the ERAS Society guidelines recommend 1–3 days after elective colorectal surgery, while the ASCRS guidelines recommend catheter removal within 24 hours for colon-upper rectal resection and within 24–48 hours after mid-lower rectal surgery. Meillat et al. [26] reported the outcomes of Foley catheter removal on the third postoperative day in 135 patients who underwent surgery under the ERAS protocol, in accordance with the ERAS Society recommendation. This study found successful removal in 88.9% of cases, with risk factors for failure including obesity, an American Society of Anesthesiologists grade greater than II, anti-aggregation platelet medication, absence of anastomosis, and extended operation time. Although the study demonstrated that early removal of the primary catheter could be safely carried out, it also revealed that 5 out of 7 patients who experienced failure developed a urinary tract infection, and 2 experienced urinary retention. This suggests a need for even more prompt removal.

Schreiber et al. [27] compared patients who underwent colorectal surgery and were administered the same ERAS protocol. These patients were divided into two groups based on the timing of Foley catheter removal. Approximately 73% of the patients in this study underwent open surgery, and TEA was applied to all patients. The conventional group, consisting of 116 patients, had the Foley catheter removed when TEA was terminated. Conversely, the catheter was removed on the first postoperative day in the early removal group. Although the early removal group experienced a higher rate of urinary retention (7.8% vs. 2.6%), the incidence of catheter-related urinary tract infections was significantly higher in the conventional treatment group (30.4% vs. 13.8%). This suggests that early removal of the catheter is a feasible option.

3) Discharge criteria

The ASCRS guidelines deal with discharge criteria, whereas the ERAS Society guidelines do not. Until now, the readiness for discharge in patients receiving colorectal ERAS perioperative care has typically been assessed based on factors such as bowel recovery, the ability to tolerate an oral diet, effective pain management, and self-mobility. However, these conditions may only be met 1–2 days post-surgery. In a study of 788 ERAS colorectal surgical patients, Biondi et al. [28] compared 146 (18.5%) who were discharged within 72 hours post-surgery to the remaining patients. They reported that over 80% adherence to ERAS was a positive factor for early discharge. Conversely, living outside the hospital area, being female, having a long operation time, drain installation, a postoperative stay in the intensive care unit, and postoperative complications were identified as negative factors.

While some research has been conducted on the practice of discharging patients before bowel recovery is achieved, a key component of the general ERAS discharge criteria, this approach has gained more traction due to the scarcity of medical resources amid the COVID-19 pandemic. This protocol, often referred to as "same day discharge" (SDD), "ambulatory colectomy" (in the
context of colectomy), or "hyper-ERAS," involves discharging patients within 24 hours post-
surgery. A systematic review [29] analyzed 38,854 patients who underwent elective colorectal
surgery patients with the ERAS protocol, of whom 1,622 (4.2%) were managed using the SDD
protocol. Of these, 1,590 (98%) successfully completed SDD. The authors concluded that,
despite variability in the type of surgery or discharge criteria, SDD reduced LOS and enhanced
patient satisfaction without increasing 30-day readmission or postoperative complications.

With advancements in surgical techniques, multimodal pain management, and video-
telecommunication technology, the LOS in ERAS is progressively being minimized. Despite this,
remains crucial to carefully select patients using a scoring system. Additionally, providing
an evidence-based, multi-dimensional team approach and close monitoring for adherence
is essential. However, there is also a need for further patient education on how to respond to
various medical situations that may potentially arise after discharge.

6. Outcomes of enhanced recovery after surgery

1) Effect of overall adherence on outcomes of enhanced recovery after surgery protocol

ERAS perioperative care typically encompasses approximately 20 distinct elements. The
number of these elements that a patient successfully completes is referred to as compliance or
adherence, which is significantly associated with surgical outcomes.

Table 4 summarizes recent studies on the outcomes of the ERAS protocol, based on
adherence. The POWER study [30] conducted a prospective collection and analysis of the
perioperative care protocol for local surgical procedures across 80 Spanish hospitals, using the
ERAS items as a basis. This study, which involved 2,084 patients, categorized participants into
quartiles according to their adherence to the standard ERAS protocol. The results showed that
the top quartile, which had the highest adherence, demonstrated significantly better outcomes
in terms of major complications (grade 3 or higher according to the Clavien-Dindo classification),
overall complications, and mortality, than the bottom quartile.

Previously, a similar trend was observed in a smaller patient cohort (n=196) with major
morbidity, anastomotic leakage, and overall LOS, when patients following the ERAS protocol
were categorized according to their adherence rate (<80%, 80%−89%, and ≥90%) [31]. This
observation raises the question of whether the ERAS protocol would yield optimal results if
adherence reaches 100%. In a study conducted by Milone et al. [32], only 8.9% of patients
achieved 100% adherence. However, even when adherence was above 75%, functional recovery
indicators such as ambulation, bowel movement, and tolerable diet were significantly higher
than in those who did not achieve this level of adherence.

Several studies have indicated that high adherence rates can positively impact not only
short-term performance, but also oncologic outcomes. It has been reported that a high
adherence rate (≥80%) significantly contributed to a favorable 3-year survival rate in patients
who underwent laparoscopic colorectal cancer surgery with ERAS perioperative care [33]. The
authors hypothesized that maintaining a low inflammatory state post-surgery through ERAS
perioperative care could have contributed to improved survival outcomes.

Conversely, a study that included 3,830 patients undergoing colorectal surgery with ERAS
perioperative care found no association between overall or postoperative adherence to the
ERAS protocol and major morbidity or anastomotic leak [34]. Another study [35] involving 1,900
patients who underwent anterior resection found that neither preoperative nor intraoperative
adherence rates were associated with anastomotic leak. Given that significant complications
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study design</th>
<th>Group</th>
<th>No. of patients</th>
<th>Population</th>
<th>Main finding</th>
<th>Other notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ripollés-Melchor et al. [30]</td>
<td>2019</td>
<td>National multicenter prospective cohort</td>
<td>Adherence rate Q1 (&gt;77.3%) vs. Q2 (&gt;63.6%, &lt;73.7%) vs. Q3 (&gt;54.5%, &lt;63.6%) vs. Q4 (&lt;54.5%)</td>
<td>521×4</td>
<td>Colorectal surgery (MIS: 59.21%)</td>
<td>Q1 compared with Q4: moderate to severe complications (OR 0.34, 95% CI 0.25–0.46, P&lt;0.001), overall complications (OR 0.33, 95% CI 0.26–0.43, P&lt;0.001), mortality (OR 0.27, 95% CI 0.07–0.97, P=0.06).</td>
<td>Adherence to 22 ERAS items</td>
</tr>
<tr>
<td>Catarci et al. [31]</td>
<td>2020</td>
<td>Prospective cohort (two centers)</td>
<td>Adherence rate &lt;80% vs. 80%−89% vs. ≥90%</td>
<td>196</td>
<td>Minimally invasive colorectal surgery</td>
<td>Overall morbidity (%/10): 5.1 vs. 3.7 vs. 2.2 vs. 0.3 vs. 0.3 (P=0.0002), anastomotic leakage (%): 14.7 vs. 2.8 vs. 0.3 (P=0.013), median overall LOS (days): 6 vs. 5 vs. 4 (P=0.05)</td>
<td>Mean adherence rate: 85.4%, a significant dose–effect curve for overall and major morbidity rates, anastomotic leakage rates and LOS</td>
</tr>
<tr>
<td>Milone et al. [32]</td>
<td>2022</td>
<td>National multicenter prospective cohort</td>
<td>Single-arm</td>
<td>1,138</td>
<td>Minimally invasive colorectal surgery</td>
<td>100% adherence: 8.9%, 75% adherence: 64.7%, Adherence of &gt;75% was associated with significantly better functional recovery (90.2±98.8 vs 95.9±33.4 h, P=0.003)</td>
<td>Definition of functional recovery: complete mobilization+stool passage+tolerance of a solid diet</td>
</tr>
<tr>
<td>Pisarska et al. [33]</td>
<td>2019</td>
<td>Prospective cohort</td>
<td>Adherence rate &lt;80% vs. ≥80%</td>
<td>109 vs. 241</td>
<td>Laparoscopic colorectal cancer resection</td>
<td>&lt;80% compliance with ERAS protocol: a significant factor associated with poor 3-year survival (HR 3.38, 95% CI 2.23–5.21, P=0.0102)</td>
<td>&lt;80% adherence was associated with a longer hospital stay (6 vs. 4 days, P&lt;0.0001), higher rate of postoperative complications (44.7% vs. 23.3%, P&lt;0.0001), poor functional recovery parameters on POD #1: tolerance of oral diet (53.4% vs. 81.5%, P&lt;0.0001) and mobilization (77.7% vs. 96.1%, P&lt;0.0001)</td>
</tr>
<tr>
<td>Catarci et al. [34]</td>
<td>2022</td>
<td>Multicenter prospective cohort</td>
<td>Single-arm</td>
<td>3,830</td>
<td>Colorectal surgery (MIS: 79.7%)</td>
<td>Overall or postoperative ERAS adherence higher or lower than the median level was not significant for major morbidity or anastomotic leak</td>
<td>Significant factors for major morbidity: perioperative transfusion (OR 7.79, 95% CI 5.46–11.10, P&lt;0.0001), standard anesthetic protocol (OR 0.68, 95% CI 0.48–0.96, P=0.028) Significant factors for anastomotic leak: male sex (OR 1.48, 95% CI 1.06–2.07, P=0.021), perioperative transfusions (OR 4.29, 95% CI 2.93–6.50, P&lt;0.0001), non-standard resections (OR 1.49, 95% CI 1.01–2.22, P=0.049)</td>
</tr>
<tr>
<td>Askild et al. [35]</td>
<td>2021</td>
<td>Retrospective cohort (the Swedish part of the international ERAS Interactive Audit System)</td>
<td>1,900</td>
<td>Anterior resection</td>
<td>Effect of mean preoperative and intraoperative compliance rate to ERAS on anastomotic leak: OR 0.99, 95% CI 0.97–101</td>
<td>Significant predictors for AL in multivariable analysis: male sex, obesity, peritoneal contamination, year of surgery 2016–2020, age, duration of primary surgery</td>
<td></td>
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</table>

MIS, minimally invasive surgery; ERAS, enhanced recovery after surgery; LOS, length of hospital stay; POD, postoperative day; AL, anastomotic leak.
after surgery may already indicate low adherence to postoperative ERAS items, it seems reasonable to exclude postoperative adherence when calculating the overall adherence rate.

The inconsistent results can be attributed to the fact that these studies are observational, each employing a different ERAS protocol (e.g., bowel preparation policy). There may have been shifts in emphasis on certain items or surgical techniques over the course of the study, and adherence may vary depending on the location of colorectal disease. Additionally, each item may have a different degree of impact on the outcome [36]. Future well-designed research taking into account the factors mentioned above is warranted.

7. Enhanced recovery after surgery in specific situations

1) Enhanced recovery after surgery for elderly patients

ERAS perioperative care requires a multidisciplinary team approach. The ability to introduce, sustain, and enhance ERAS protocols is indicative of a relatively advanced stage in a society’s healthcare system. In such developed societies, the proportion of elderly patients is bound to increase. For instance, in South Korea, one of the fastest-aging societies, a study conducted on 4,326 patients with colorectal cancer from 2006 to 2019 found that 23.9% were aged between 70 and 79, while 7.5% were 80 or older [37]. Research has indicated that aging is a significant factor contributing to ERAS failure, such as complications or increased LOS. This is because aging can often be accompanied by a decline in physical function, the presence of comorbidities, and malnourishment [38]. Furthermore, older patients exhibited a high incidence of postoperative ileus and a relatively high rate of stoma formation. These conditions can be associated with high output and may increase the likelihood of low adherence to the ERAS protocol [39].

In patients who underwent colorectal surgery with ERAS perioperative care, studies [40–42] have shown that adherence with individual items tends to be lower in elderly patients compared to younger ones, leading to an increase in LOS and overall complications. However, there was no difference in major complications (as classified by Clavien-Dindo grade 3 or higher) and no significant difference in overall adherence between the two age groups. A recent study [42] found no difference in complications or LOS between patients aged 70 or older and younger patients, despite a significantly higher rate of comorbidities in the elderly (Table 5).

Studies comparing elderly patients who underwent colorectal surgery divided into ERAS and non-ERAS groups have demonstrated the validity of implementing ERAS perioperative care in elderly patients. Tejedor et al. [43] compared the outcomes of 156 ERAS patients aged 70 or older with 156 non-ERAS patients matched based on age, sex, location (colon or rectum), and temporary stoma. They found a significantly shorter LOS and a significantly lower complication rate in the ERAS group. Notably, the rate of adherence to the ERAS protocol was only 42%. Martínez-Escribano et al. [44] compared colorectal surgery outcomes before and after the introduction of ERAS in patients over 70 years of age. They reported a significant decrease in postoperative ICU admissions and transfusions in the ERAS group, although there was no observed decrease in complications and LOS.

While the benefits of ERAS are less pronounced in the elderly compared to younger patients, there is still a distinct advantage in applying ERAS perioperative care when compared to conventional care in the same elderly population. Therefore, the implementation of ERAS should be considered in appropriately selected elderly patients.
2) Spread of enhanced recovery after surgery coverage and circumstances

In light of consistent reports on the short- and long-term effects of ERAS, it is being applied to a variety of diseases and situations beyond the realm of elective colorectal surgery, as well as in a wider range of countries. A brief assessment of this evolving status provides valuable insights into the future direction of ERAS development.

In the field of colorectal surgery, ERAS protocol adoption was reported in clinically suspected T4 colorectal cancer [45] and in Crohn's disease [46], for which surgery is relatively difficult and the complication rate is higher. An RCT [47] reported that the application of modified ERAS reduced PONV, SSI, and LOS (by about 3 days) even when open laparotomy was performed as an emergency procedure in cases of perforation peritonitis, as opposed to being elective.

In these instances, the ERAS protocol differs from that of elective surgery in that a nasogastric tube is routinely inserted prior to surgery, and a liquid diet is resumed following the first passage of flatus. However, key characteristics such as non-opioid multimodal analgesia, expedited resumption of ambulation, and swift drain removal are preserved as part of the standard ERAS protocol.

The utility of ERAS, as reported in numerous medical scenarios, extends beyond large hospitals to also include small and medium-sized hospitals [48]. Even in countries where healthcare systems are not yet fully developed, ERAS [49] is becoming more widespread [50].
3) Future directions

As discussed above, the adoption of ERAS is expanding across a range of diseases, medical scenarios, and diverse types of medical institutions and societies. Furthermore, the evolution of various medical and surgical techniques, aging, and the emergence of pandemics are generating new evidence. While the principle of ERAS is proliferating and being adapted for various situations, this not only benefits many patients and reduces social costs, but it can also complicate comparisons and analyses between studies when determining the most appropriate and effective changes.

It is necessary to establish and develop ERAS protocols tailored to specific institutions and diseases, based on international guidelines. However, it is equally important to create a network with a system capable of assessing the scientific validity of any modifications, while also selecting and managing essential items that are recorded.

Conclusion

The treatment of surgical patients necessitates a multidisciplinary approach that extends beyond surgical techniques. In response to societal changes, there is a need for treatments that can optimize the use of medical resources while ensuring the best outcomes for patients. Familiarity with the guidelines for ERAS perioperative care, as well as an understanding of the latest relevant research, can provide a solid foundation for systematically addressing these needs. To maximize the effectiveness of ERAS, it is crucial that medical staff fully comprehend the clinical basis and significance of each component. Furthermore, the protocol must be consistently upheld and progressively developed through team-based approaches and an audit system.

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Conflict of Interest
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