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The challenges of implementing the ERAS protocol (Enhanced Recovery after Surgery) in colorectal surgery: a retrospective bi-centre study in an academic and non-academic centers

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Baseline

The Enhanced Recovery After Surgery (ERAS) protocol was developed in 2005 in Edinburgh (Fearon KC et al. *Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr.* 2005 Jun;24(3):466-77). This pioneeristic study, produced an integrated multimodal approach to perioperative care resulting in an overall enhancement of recovery with decrease postoperative complications, reduce hospital stay and early discharge after colorectal surgery.

Incorrect pain management, intestinal prolonged ileus and dysfunction, motionlessness, stress induced organ dysfunction have been recognised as the primary factors for delay in postoperative recovery of patients who had undergone major surgery (Kehlet H. *The Story of Enhancing Recovery after Surgery. Anesthesiology.* 2025 Aug 1;143(2):404-409).

The term “fast track recovery” was firstly introduced by Engelman in 1994 (Engelman RM et al *Fast-track recovery of the coronary bypass patient. Ann Thorac Surg.* 1994 Dec;58(6):1742-6) to describe a newly perioperative treatment in all coronary artery bypass grafting patients coronary. Comparing two groups of patients (fast track patients vs non- fast track patients) this study involves the following principles: preoperative education; early extubation; methylprednisolone sodium succinate before bypass followed by dexamethasone for 24 hours postoperatively; prophylactic digitalization, metoclopramide HCl, docusate sodium, and ranitidine HCl; accelerated rehabilitation; early discharge; dedicated fast-track coordinator to perform daily telephone contact and a one week postoperative examination; routine one-month postoperative visit. As a results, the “fast-track” program was accompanied by significant ($p < 0.001$) decreases in intensive care unit duration from 2.4 to 1.9 days and in postoperative length of stay from 8.3 to 6.8 days between the two groups.

Laparoscopic approach in colorectal surgery taken alone has partially improved post-operative outcomes (Lacy AM et al. *Short-term outcome analysis of a randomized study comparing laparoscopic vs open colectomy for colon cancer. Surg Endosc.* 1995 Oct;9(10):1101-5) (Blackmore AE, Wong MT, Tang CL. *Evolution of laparoscopy in colorectal surgery: an evidence-based review. World J Gastroenterol.* 2014 May 7;20(17):4926-33).

The rate of postoperative recovery, especially in high risk older patients, is determined by pain, stress-induced organ dysfunction, and limitations in conventional postoperative care. In 1995, Badram attempted to provide "stress-free" colonic resection for neoplastic disease in eight elderly high-risk patients by a combination of laparoscopically assisted surgery, epidural analgesia, and early oral nutrition and mobilisation. Effective pain relief allowed early mobilisation, and hospital stay was reduced to 2 days (*Bardram L et al. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. Lancet. 1995 Mar 25;345(8952):763-4.*

A few years later, Kehlet et al confirmed a rapid recovery after open sigmoid resection using a multimodal rehabilitation programme, with emphasis in pain control with thoracic epidural anesthesia in order to control pain resulting also in postoperative ileus and improve mobility (*Kehlet H et al. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. Br J Surg. 1999 Feb;86(2):227-30.*

In those years, on the basis of data present in literature, other authors elaborated a series of measures designed to reduce surgical stress response, decrease postoperative complications, shorten recovery, and promote early discharge after major colorectal surgery (*Kehlet H et al. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg. 2008 Aug;248(2):189-98*)(*Simpson JC et al. Pain Management in Enhanced Recovery after Surgery (ERAS) Protocols. Clin Colon Rectal Surg. 2019 Mar;32(2):121-128.*

Enhanced recovery programs or "fast-track" programs have become an important focus of perioperative management after colorectal surgery (*Wind J et al. Laparoscopy and/or Fast Track Multimodal Management Versus Standard Care (LAFA) Study Group; Enhanced Recovery after Surgery (ERAS) Group. Systematic review of enhanced recovery programmes in colonic surgery. Br J Surg. 2006 Jul;93(7).*

In the following years there was an expansion of research on that topic, in order to modify the physiological and psychological responses to major surgery improving cardiopulmonary function, earlier return of bowel function and earlier resumption of normal activities (*Eskicioglu C et al. Enhanced recovery after surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. J Gastrointest Surg. 2009 Dec;13(12):2321-9*) (*Bona S et al. Introducing an enhanced recovery after*

surgery program in colorectal surgery: a single center experience. *World J Gastroenterol.* 2014 Dec 14;20(46):17578-87).

The trauma of surgery leads to metabolic, neuroendocrine, and immune responses (Desborough JP. *The stress response to trauma and surgery.* *Br J Anaesth.* 2000 Jul;85(1):109-17).

Key Components of the Response were: Damage-Associated Molecular Patterns (DAMPs) with released by injured cells, these signals alert the immune system; Neutrophils (first responders) and macrophages (phagocytosis, cytokine release) are rapidly recruited; TNF-alpha, IL-1, IL-6: Key mediators that amplify inflammation, activate immune cells, and promote fever/acute-phase protein production; IL-8 (CXCL8): A potent chemokine that specifically recruits neutrophils to the injury site; Cellular Action: neutrophils use enzymes (like MMPs) to clear dead tissue, while macrophages switch from M1 (inflammatory) to M2 (reparative) phenotypes to promote healing (Marik PE et al. *The immune response to surgery and trauma: Implications for treatment.* *J Trauma Acute Care Surg.* 2012 Oct;73(4):801-8.)(Zawadzki M et al. *Comparison of inflammatory responses following robotic and open colorectal surgery: a prospective study.* *Int J Colorectal Dis.* 2017 Mar;32(3):399-407).

Inflammatory mediators alter hepatic synthesis of acute-phase proteins, thereby adjusting the blood levels of CRP, ferritin, and albumin (Kampman SL et al. *Postoperative inflammatory response in colorectal cancer surgery: a meta-analysis.* *Int J Colorectal Dis* 38, 233 (2023)..

CRP and IL-6 have the strongest association with the magnitude of the surgical injury, but only CRP is the most clinically useful of these (Watt DG et al. *Routine clinical markers of the magnitude of the systemic inflammatory response after elective operation: a systematic review.* *Surgery.* 2015 Feb;157(2):362-8).

Core items of the ERAS protocol include preoperative counselling, preoperative nutrition, avoidance of perioperative fasting and carbohydrate loading up to 2 hours preoperatively, standardized anesthetic and analgesic regimens (epidural and non-opioid analgesia) and early mobilization (Fig. 1, Table 1) (Powers BK et al. *Enhanced Recovery Comparative Pharmacotherapy Collaborative. Enhanced recovery after surgery (ERAS®) Society abdominal and thoracic surgery recommendations:*

A systematic review and comparison of guidelines for perioperative and pharmacotherapy core items. World J Surg. 2024 Mar;48(3):509-523).

These elements are integrated throughout the patient journey and provided by various hospital departments and specialists, including surgeons, nutritionists, nursing staff, and anesthesiologists.

The ERAS literature shows substantial divergence concerning the composition of applied care bundles and the outcome parameters measured across various trials (*Nicholson A et al. Systematic review and meta-analysis of enhanced recovery programmes in surgical patients. Br J Surg. 2014 Feb;101(3):172-88*) (*Ljungqvist O et al. Enhanced Recovery After Surgery: A Review. JAMA Surg. 2017 Mar 1;152(3):292-298*).

No single element by itself will improve post-operative outcomes .

At present no consensus has been reached on the number of items that must be applied for patients to be considered fast track, but robust evidence supports the application of ERAS protocols for the clinical management of colorectal surgical patients (*Gustafsson UO et al. Guidelines for Perioperative Care in Elective Colorectal Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations: 2018. World J Surg. 2019 Mar;43(3):659-695*) (*Powers BK et al. Enhanced Recovery Comparative Pharmacotherapy Collaborative. Enhanced recovery after surgery -ERAS®- Society abdominal and thoracic surgery recommendations: A systematic review and comparison of guidelines for perioperative and pharmacotherapy core items. World J Surg. 2024 Mar;48(3):509-523*).

FIGURE 1. Core items of ERAS protocols

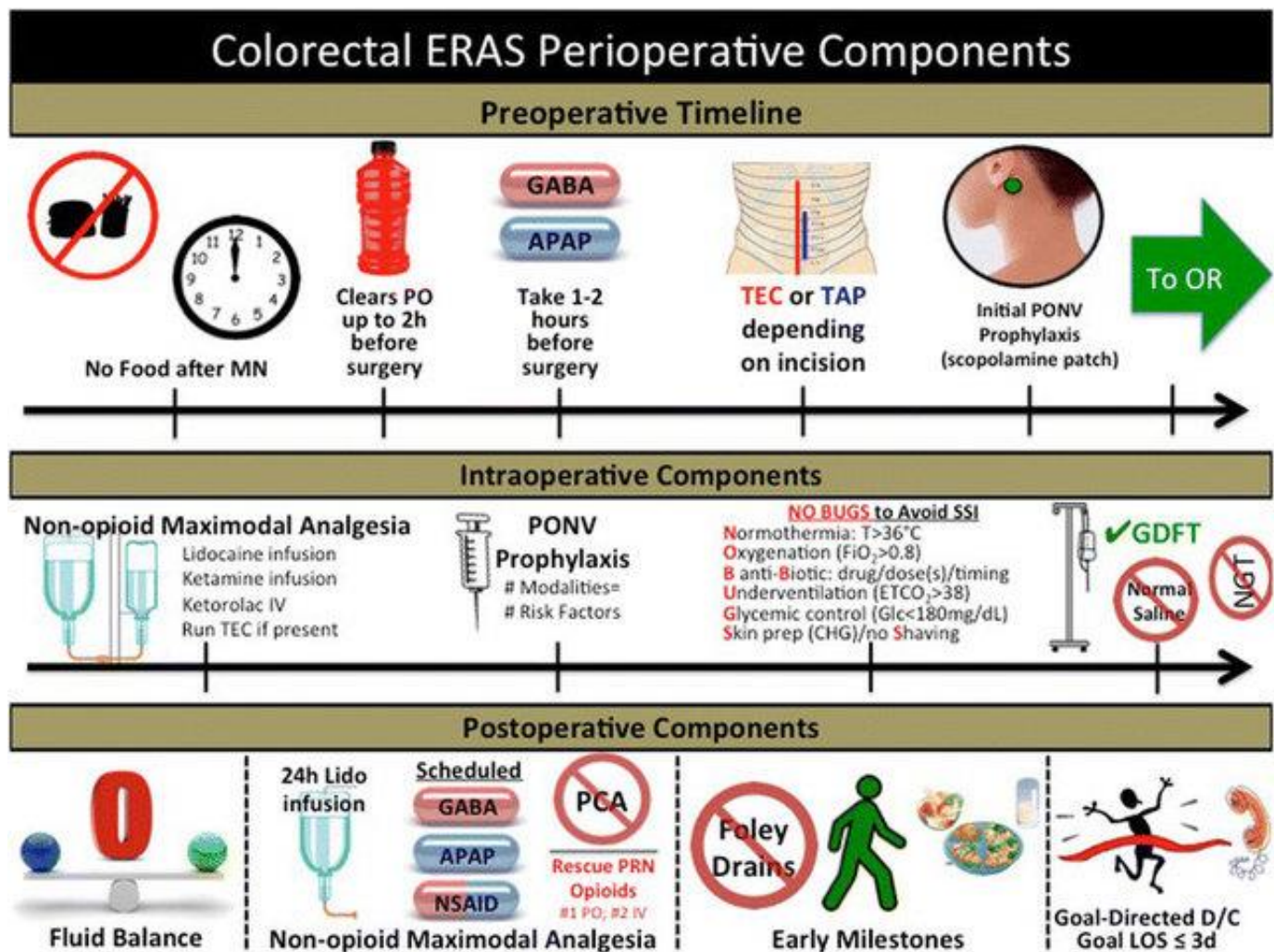


Table 1. Recommendation Enhanced Recovery After Surgery—ERAS Group Recommendations divided in “Preoperative” – “Intraoperative” and “Postoperative”



Item	Recommendation 2025	Change versus 2018
Preoperative		
1. Preadmission information	Information is strongly recommended for all patients before surgery, with moderate evidence supporting reduced anxiety but low evidence for improving quality of life or LOS	No changes
2. Preoperative optimization		
A. Identification of high-risk patients	Predictive tools are strongly recommended for identifying high-risk patients before colorectal surgery, despite very low evidence for reducing mortality and complications	Added details on specific tools
B. Management of comorbidities	Optimizing comorbidities before surgery is strongly recommended, despite low evidence for reducing mortality, complications, and length of stay	Added details on optimizing specific comorbidities
C. Alcohol cessation	Patients with high alcohol consumption are advised to stop drinking 4 weeks before surgery, though the recommendation is weak due to low evidence for reducing mortality, complications, and length of stay	Changed from strong to weak recommendation
D. Smoking cessation	Smokers should quit and undergo behavioral intervention with nicotine replacement at least 4 weeks before surgery to reduce mortality and complications, based on moderate evidence	No changes
E. Prehabilitation	No specific prehabilitation regimen can be recommended before surgery due to moderate to low evidence with conflicting results on functional capacity, complications, and length of stay	From weak recommendation to currently no recommendation for a specific regimen
F. Anemia treatment	Routine screening and correction of anemia before surgery is strongly recommended to improve long-term survival and decrease perioperative transfusions. Preoperative IV iron supplementation and high-dose erythropoietin (EPO) are weakly recommended for anemia correction	Use of EPO added in the current guidelines
3. Preoperative nutrition	Routine nutritional screening is strongly recommended for colorectal surgery patients, whereas nutritional supplementation and oral immunonutrition may be considered for malnourished patients, though evidence is that moderate and recommendations are weak	Immunonutrition added as recommendation in the current guidelines
4. PONV prophylaxis	PONV prophylaxis with medications such as aprepitant, ramosetron, granisetron, dexamethasone, and ondansetron is strongly recommended based on high-quality evidence	New optimal formulae in the current guidelines
5. Preanesthetic sedation/anxiolytics	Moderate quality of evidence showing no benefit	No change
6. Thromboprophylaxis	Patients should receive multimodal thromboembolism prevention, including mechanical and pharmacological measures. Intraoperative intermittent pneumatic compression (IPC) and extended prophylaxis for at-risk patients. Strong recommendation	Intraoperative IPC and more liberal timing of medication in the current guidelines
7. Mechanical bowel preparation (MBP)	MBP should not be used routinely in colonic surgery but may be considered in rectal surgery with diverting stomas. If MBP is used, adding oral antibiotics is recommended	Recommendation grade regarding avoidance of MBP alone have changed from strong to weak in the current guidelines
8. Fasting and carbohydrate load	Short preoperative fasting is strongly recommended in colorectal surgery to improve insulin sensitivity and reduce PONV. Preoperative carbohydrate loading may improve insulin sensitivity but offers no clinical advantages over standard short fasting protocols	Recommendation of preoperative carbohydrate loading changed from strong to weak
9. Antibiotics and skin preparation	IV antibiotics within 60 minutes before incision, repeat for prolonged surgery or blood loss. Oral antibiotics for MBP patients. Chlorhexidine-alcohol-based preparations for skin disinfection. Insufficient evidence for antiseptic showering or shaving	High-quality evidence in favor addition of oral antibiotic decontamination with MBP in the current guidelines
10. Preoperative fluids	Patients should be encouraged to stay well-hydrated with clear fluids up to 2 hours before surgery, and any fluid or electrolyte imbalances should be corrected, based on strong evidence	No changes

Intraoperative		
11. Anesthetic protocol	Use short-acting agents, cerebral monitoring, and antiadrenergic and anti-inflammatory strategies to minimize surgical stress and enhance recovery. Avoid hypotension, use protective ventilation, and ensure complete neuromuscular block reversal with TOF monitoring	No changes
12. Normothermia	Active body surface warming is strongly recommended during surgery as it reduces surgical site infections, decreases the need for blood transfusions, and improves patient satisfaction	The evidence levels for various warming methods have been incorporated into the current guidelines
13. Intraoperative fluids	A slightly positive fluid balance on the day of surgery is weakly recommended based on moderate-quality evidence	Shift from near-zero fluid balance to slightly positive fluid balance
14. Surgical approach	Minimally invasive surgery (MIS) should be routinely performed for CRC patients and combined with ERAS protocols to reduce length of stay. Strong recommendations based on high-quality evidence	Minimal invasive surgery: standard of care
15. Abdominal drainage	Routine abdominal drainage is not recommended after colonic or rectal resection, with strong support for colonic resection and weaker support for rectal resection based on moderate to low-quality evidence	Weaker evidence for avoiding rectal drain in the current guidelines
Postoperative		
16. Nasogastric tube (NGT)	Prophylactic NGT may be used during colorectal surgery but is not recommended postoperatively	Quality of evidence changed from high to moderate
17. Normoglycemia	Intraoperative and postoperative hyper- and hypoglycemia should be avoided through glycemic control, with strict monitoring in patients with elevated preoperative HbA1c	Preoperative HbA1c and specified postoperative blood glucose levels have been included
18. Postoperative fluids	Maintain a slightly positive postoperative fluid balance with weight gain limited to 1–2.5 kg, using balanced crystalloid solutions. Varying evidence quality and strength of recommendation	Shift from near-zero fluid balance to slightly positive fluid balance
19. Urinary drainage	Urinary catheters should be removed within 24 hours after uncomplicated minimal-invasive colonic surgery, within 48 hours after uncomplicated minimal-invasive rectal surgery	Specified interventions included in the recommendations
20. Prevention of ileus	A multimodal approach should be undertaken to minimize the development of postoperative ileus	Extensive evaluation included, return of chewing gum as recommendation
21. Postoperative analgesia	A multimodal analgesia strategy, including acetaminophen, TAP blocks, NSAIDs for colonic surgery, and intrathecal morphine, should be used after both open and MIS colorectal surgery	Use alternative analgesic's (versus epidurals) also in open surgery
22. Postoperative nutritional care	Early gut feeding within 24 hours after surgery, resumption of oral intake, and the use of oral nutritional supplements are recommended to improve recovery	Detailed evidence evaluation included. Immunonutrition added as a recommendation
23. Mobilization	Early postoperative mobilization should begin on the day of surgery, with at least 3 hours of mobilization per day from POD 1 to discharge, supported by strong recommendations despite limited evidence	Detailed evidence evaluation included. From POD 1 to discharge: 3 hours/d

CRC, colorectal cancer; ERAS, Enhanced Recovery After Surgery; HbA1c, hemoglobin A1c; IV, intravenous; LOS, length of stay; POD, postoperative day; PONV, postoperative nausea and vomiting; TOF, train of 4.

* Some of the previous preadmission items have been reorganized into a preoperative optimization bundle. One of these items, prehabilitation, can no longer be recommended based on current evidence. Although immunonutrition has been incorporated into the current guidelines, no specific formula can be recommended. Several items have undergone content changes, as noted under the "Change" heading. For example, because of insufficient evidence on the optimal duration of mobilization, the recommended time for postsurgery mobilization has been reduced from 6 hours per day to 3 hours per day to comply with the protocol. Recommendations from the ERAS Society for standards for the development of enhanced recovery after surgery guidelines were fully followed for 21 of 23 ERAS items. The exceptions to the grading process were the anesthetic protocol and preoperative optimization of coexisting comorbidity (2A and 2B).

ERAS Interventions: Preoperative Items

- Preadmission information, education and counseling

During the initial consultation, the patient—accompanied by a family member or designated caregiver—should participate in a collaborative session with the surgical, anesthetic, and nursing leads. The objective of this summit is to establish a clear division of responsibilities and outline a roadmap for success. Detailed preoperative education and counselling (with clear explanation of expectations during hospitalization) reduce patient anxiety, improve pain control, leading to a faster recovery and significantly earlier discharge. (Kiyohara LY et al. *Surgery information reduces anxiety in the pre-operative period. Rev Hosp Clin Fac Med Sao Paulo.* 2004 Apr;59(2):51-6. doi: 10.1590/s0041-87812004000200001) (Wilson CJ et al. *Caring for the surgically anxious patient: a review of the interventions and a guide to optimizing surgical outcomes. Am J Surg.* 2016 Jul;212(1):151-9. doi: 10.1016/j.amjsurg.2015.03.023) (Halaszynski TM et al. *Optimizing postoperative outcomes with efficient preoperative assessment and management. Crit Care Med.* 2004 Apr;32(4 Suppl):S76-86) (Nygren J et al. *Enhanced Recovery After Surgery (ERAS) Society, for Perioperative Care; European Society for Clinical Nutrition and Metabolism (ESPEN); International Association for Surgical Metabolism and Nutrition (IASMEN). Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. World J Surg.* 2013 Feb;37(2):285-305).

- Preoperative optimisation

The role of preoperative physical conditioning on surgical outcomes was investigated in several randomised controlled trials on abdominal surgery, cardiothoracic surgery and orthopaedic surgery. (Arthur HM et al. *Effect of a preoperative intervention on preoperative and postoperative outcomes in low-risk patients awaiting elective coronary artery bypass graft surgery. A randomized, controlled trial. Ann Intern Med.* 2000 Aug 15;133(4):253-62) (Oosting E et al. *Preoperative home-based physical therapy versus usual care to improve functional health of frail older adults scheduled for elective total hip arthroplasty: a pilot randomized controlled trial. Arch Phys Med Rehabil.* 2012 Apr;93(4):610-6).

Only Hulzebos et al found improvement in physiological function taking advantage of preoperative inspiratory muscle training. Reduced incidence of pulmonary complications and short postoperative hospitalization in CABG surgery (especially in frail patients) was found (Hulzebos EH et al. *Preoperative intensive inspiratory muscle training to prevent postoperative pulmonary complications in high-risk patients undergoing CABG surgery: a randomized clinical trial. JAMA. 2006 Oct 18;296(15):1851-7.*

Two randomized controlled trials reported a 50% reduction in complications but no functional capacity improvement, whereas another indicated better walking capacity at 4 and 8 weeks postoperatively (Gillis C et al. *Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. Anesthesiology. 2014;121:937e947*) (Molenaar CJL et al. *Effect of multimodal prehabilitation on reducing postoperative complications and enhancing functional capacity following colorectal cancer surgery: the PREHAB randomized clinical trial. JAMA Surg. 2023;158:572e581.*

Several factors may have impacted these findings, including the absence of precise physiological benchmarks, the focus on older patient populations, overly strenuous physical protocols, and insufficient compliance with the prescribed interventions. However, it is generally accepted that preoperative medical optimization is necessary before surgery.

Alcohol misuse is correlated with a triple increase in surgical risks, specifically involving wound dehiscence, cardiovascular issues, and excessive bleeding. Furthermore, smoking status adversely impacts recovery trajectories, with current smokers exhibiting a greater incidence of pulmonary and soft-tissue complications (Nath B et al. *Alcohol exposure as a risk factor for adverse outcomes in elective surgery. J Gastrointest Surg. 2010;14: 1732e1741*) (Rolfzen ML et al. *Association between alcohol use disorder and hospital outcomes in colectomy patients - a retrospective cohort study. J Clin Anesth. 2022;78:110674*) (

A four-week period of preoperative cessation from both alcohol and tobacco is highly advised. This duration of abstinence serves to mitigate postoperative risks by enhancing vital organ physiology. (Sorensen LT et al. *Short-term pre-operative smoking cessation intervention does not affect postoperative complications in colorectal surgery: a randomized clinical trial. Colorectal Dis. 2003;5:347e352*) (McIsaac DI et al. *Prehabilitation in adult patients undergoing surgery: an umbrella review of systematic reviews. Br J Anaesth. 2022;128:244e257.*

- Preoperative nutritional screening and nutritional support

Malnutrition was evident in up to one third of the inpatients and led to poor hospitalization outcomes and survival as well as increased costs of care. Clinical management should incorporate expert guidance from a dedicated dietician or nutritionist to address and amend preoperative nutritional deficits.

About 20% of patients undergoing colorectal surgery is malnourished. Nutritional risk index (NRI)] provided the most efficacious combination of high validity, low cost, and ease of use to examine and improve the status of malnutrition. Preoperative and postoperative weight losses were significantly different on the NRI, and the longer the length of the hospital stay, the greater was the weight loss.

(Tu MY et al. Using a nutritional screening tool to evaluate the nutritional status of patients with colorectal cancer. Nutr Cancer. 2012;64(2):323-30) (Burden ST et al. Nutritional status of preoperative colorectal cancer patients. J Hum Nutr Diet. 2010 Aug;23(4):402-7).

The detection of nutrient deficiency is vital, given that neoadjuvant protocols often compromise the patient's metabolic profile. The underlying physiological driver of cancer-associated cachexia is the mismatch between metabolic expenditure and nutritional provision. *(Lim SL et al. Malnutrition and its impact on cost of hospitalization, length of stay, readmission and 3-year mortality. Clin Nutr. 2012 Jun;31(3):345-5).*

Nutritional supplementation strategies in oncological colorectal surgery can improve pulmonary function and insulin resistance *(Lidder P et al. A randomized placebo controlled trial of preoperative carbohydrate drinks and early postoperative nutritional supplement drinks in colorectal surgery. Colorectal Dis. 2013 Jun;15(6):737-45).*

Nevertheless, there is no unequivocal evidence that nutritional support leads to a reduction in hospital stay or a decrease in anastomotic leaks *(Mathur S et al. Randomized controlled trial of preoperative oral carbohydrate treatment in major abdominal surgery. Br J Surg. 2010 Apr;97(4):485-94) (Kim JW. Topical Effect of Glutamine for Colorectal Anastomosis. Ann Coloproctol. 2015 Dec;31(6):207-8).*

Therefore is clear why the assessment and treatment of poor nutrition status is an essential component of ERAS protocols.

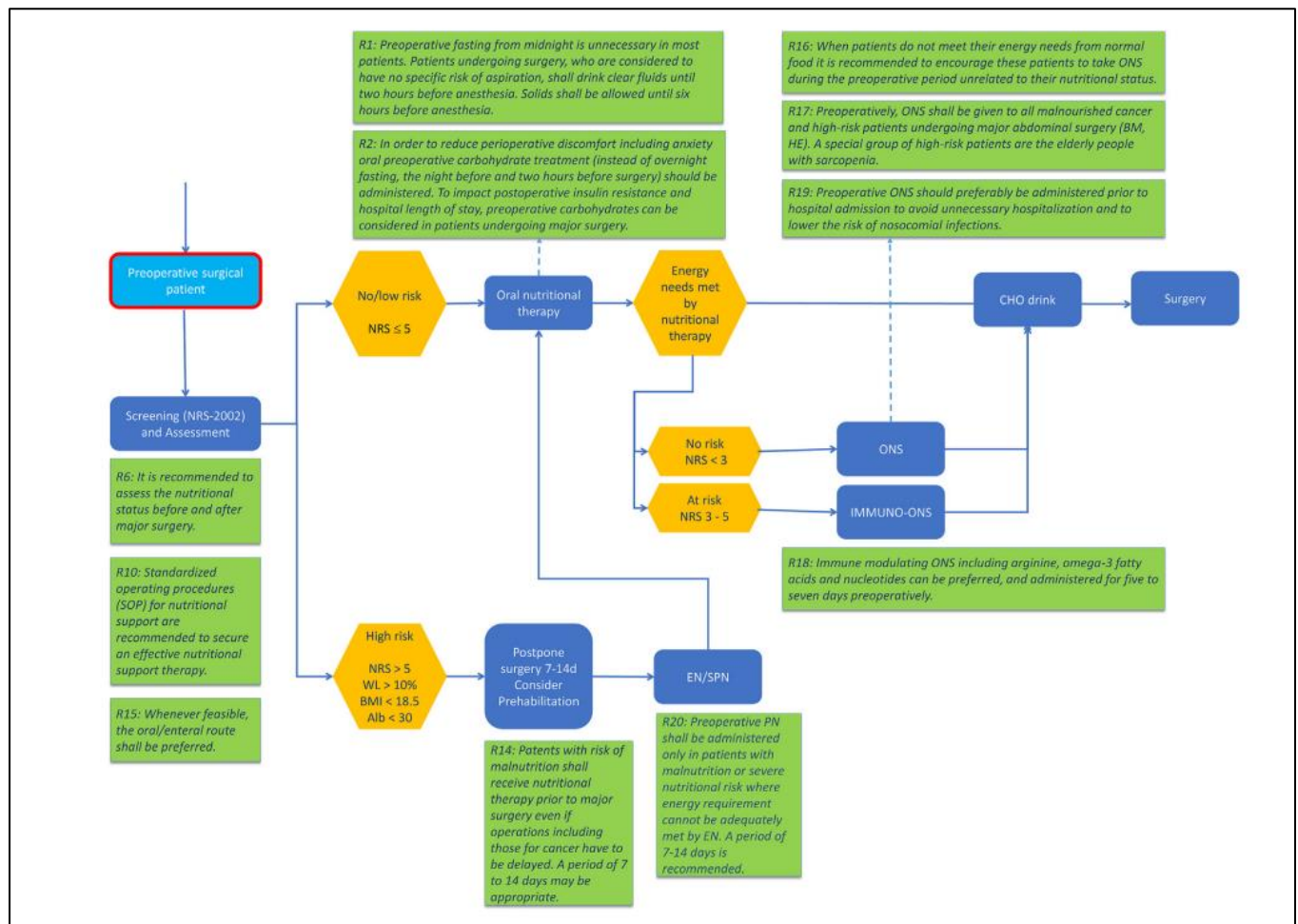
Oral or enteral nutritional aid with omega-3 fatty acids, nucleotides and arginine in the peri-operative period has demonstrated to reduce postoperative complications and length of hospital stay in gastrointestinal surgery. This support is strongly recommended by international guidelines on nutrition in surgical and critically ill patients (*Drover JW et al. Perioperative use of arginine-supplemented diets: a systematic review of the evidence. J Am Coll Surg. 2011 Mar;212(3):385-99, 399.e1*) (*Weimann A et al. ESPEN practical guideline: Clinical nutrition in surgery. Clin Nutr. 2021 Jul;40(7):4745-4761*).

Lately, significant data have indicated that nutritional support can help attenuate the physiological stress caused by surgery within a prehabilitative framework; likewise, current ESPEN guidelines on nutrition in surgery, state that patients at malnutrition risk should receive nutritional therapy prior to major surgery, preferably 7 to 14 days before. (*McClave SA et al. Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr. 2016 Feb;40(2):159-211*).

In the surgical patient sarcopenic obesity may not be underestimated, “severe” nutritional risk has been defined according to the ESPEN working group as the presence of at least one of the following criteria: Weight loss >10-15% within six months; BMI <18.5 kg/m²; SGA Grade C or NRS >5 (subjective global assessment, nutritional risk screening); Serum albumin <30 g/l (with no evidence of hepatic or renal dysfunction). These parameters reflect undernutrition as well as disease-associated catabolism. The working group agrees that hypoalbuminemia is a clear surgical risk factor however, it reflects disease-associated catabolism and disease severity rather than undernutrition (*Truong A et al. Implications of preoperative hypoalbuminemia in colorectal surgery. World J Gastrointest Surg. 2016 May 27;8(5):353-62*).

Flow scheme of preoperative nutrition (Esen 2021 guidelines) is reported in FIGURE 2.

Figure 2. Flow scheme of preoperative nutrition (Espen 2021 guidelines)



- Preoperative fasting and preoperative carbohydrate loading

The severity of insulin resistance is directly linked to the magnitude of the surgical procedure, and maintaining strict postoperative glycemic control has been shown to decrease both morbidity and mortality. Implementing effective analgesia, minimizing the duration of preoperative fasting, and utilizing preoperative carbohydrate loading can significantly mitigate insulin resistance.

Shifting the patient's metabolic profile in this manner also curtails protein catabolism and enhances muscular performance. Additionally, the administration of preoperative carbohydrates helps alleviate patient thirst, hunger, and preoperative distress (*van den Berghe G et al. Intensive insulin therapy in the critically ill patients. N Engl J Med 2001;345:1359-67*)(*Uchida I et al. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. Br J Surg 1988;75:557-62*)(*Irani JL et al. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and the Society of American Gastrointestinal and Endoscopic Surgeons. Surg Endosc. 2023 Jan;37(1):5-30. doi: 10.1007/s00464-022-09758-x*)(*Helminen H et al. Effect of preoperative intravenous carbohydrate loading on preoperative discomfort in elective surgery patients. Eur J Anaesthesiol. 2009 Feb;26(2):123-7*).

There are no evidences that support the standard practice of fasting from midnight to avoid pulmonary aspiration. Preoperative oral carbohydrate intake was associated with improved clinical recovery indicators and quality of life outcomes. In particular, it contributed to earlier return of bowel function, reduced postoperative discomfort, and significantly shorter hospital stay, indicating enhanced postoperative recovery in patients undergoing colorectal surgery. (*Urkan M et al. The effect of preoperative oral carbohydrate administration on postoperative glucometabolic response, subjective well being and quality of life in patients undergoing colorectal surgery: a randomized controlled double-blind study. BMC Surg. 2025 Aug 20;25(1):376*)

Actually, most scientific anaesthesia societies recommend intake of clear fluids until 2 hours before the induction of anaesthesia as well as a 6 hours fast for solid food (*Brady M, Kinn S, O'Rourke K, et al. Preoperative fasting for preventing perioperative complications in children. Cochrane Database Syst Rev 2005:CD005285*)(*Di Vezza F et al. Preoperative Clear Fluid Fasting Duration and Arterial Hypotension During Anesthesia Induction: A Narrative Review. J Clin Med. 2025 Oct 1;14(19):6950*).

Morbidly obese and uncomplicated type 2 diabetes mellitus patients have the same gastric emptying characteristics as healthy patients. Many study of preoperative carbohydrate loading did not find increased aspiration rates (Stenberg E et al. *Guidelines for Perioperative Care in Bariatric Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations: A 2021 Update*. *World J Surg*. 2022 Apr;46(4):729-751. doi: 10.1007/s00268-021-06394-9. Epub 2022 Jan 4. Erratum in: *World J Surg*. 2022 Apr;46(4):752) (Maltby JR et al. *Drinking 300 mL of clear fluid two hours before surgery has no effect on gastric fluid volume and pH in fasting and non-fasting obese patients*. *Can J Anaesth*. 2004;5:111- 115).

The ERAS guidelines strongly recommended preoperative oral carbohydrate treatment, also in diabetic patients along with the diabetic medication (Hausel J et al. *A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients*. *Anesth Analg* 2001;93:1344-50).

- Preoperative bowel preparation

For over thirty years, the established custom of preoperative mechanical bowel preparation (MBP) in colorectal surgery has been under debate. As early as 1972, Hughes et al. doubt on the procedure, maintaining that thorough mechanical preparation is unnecessary (Hughes ES. *Asepsis in large-bowel surgery*. *Ann R Coll Surg Engl* 1972;51:347-56).

Mechanical bowel preparation can cause dehydration and fluid and electrolyte abnormalities, particularly in elderly patients (Tan J et al. *Mechanical bowel preparation and antibiotics in elective colorectal surgery: network meta-analysis*. *BJS Open*. 2023 May 5;7(3):zrad040).

Recently, RCTs and meta-analyses confirm that bowel preparation is not beneficial in elective colonic surgery and some of these studies suggest that it increases the risk for anastomotic leak (Holte K et al. *Physiologic effects of bowel preparation*. *Dis Colon Rectum*. 2004;47:1397-1402) (Jung B et al. *Mechanical Bowel Preparation Study Group. Multicentre randomized clinical trial of mechanical bowel preparation in elective colonic resection*. *Br J Surg*. 2007;94:689-695) (Malleesh K et al. *Effect of oral antibiotic bowel preparation versus no preparation on surgical site infections in elective colorectal surgery: a randomized trial*. *Ann Coloproctol*. 2025 Oct;41(5):393-399).

Bowel preparation might be essential for certain individuals necessitating an intraoperative colonoscopy. After that, findings demonstrate that the process is strenuous and delays the recovery of bowel function (postoperative ileus). (Jung B et al. *Preoperative mechanical preparation of the colon: the patient's experience. BMC Surg.* 2007;7:5).

A Cochrane analysis included 231 low anterior resections did not find an increased leak rate in patients without bowel preparation (Willis MA et al. *Preoperative combined mechanical and oral antibiotic bowel preparation for preventing complications in elective colorectal surgery. Cochrane Database Syst Rev.* 2023 Feb 7;2(2):CD014909), while a RCT that included ultralow rectal anastomoses reported that MBP protects against anastomotic leaks requiring reoperations' mitigating severity after anastomotic leak (Platell C et al. *Randomized clinical trial of bowel preparation with a single phosphate enema or polyethylene glycol before elective colorectal surgery. Br J Surg.* 2006;93:427-433) (Zmora O et al. *Laparoscopic colectomy without mechanical bowel preparation. Int J Colorectal Dis* 2006;21:683–687).

According to ERAS standards, there is a stringent recommendation to avoid the habitual use of mechanical bowel preparation during colonic interventions

- Prophylaxis against thromboembolism

Oncology patients exhibit a four- to six-fold increased susceptibility to venous thromboembolism compared to the general public. Prophylactic strategies, including pharmacological agents (such as low-molecular-weight heparin [LMWH] or unfractionated heparin) and mechanical modalities (intermittent pneumatic compression or graduated compression stockings), are implemented either independently or as a multimodal approach.

Systematic reviews have confirmed that subcutaneous low-dose unfractionated heparin protocols effectively mitigate deep vein thrombosis, pulmonary embolism, and lethality in the colorectal surgical population. LMWH is favored due to its once-daily posology and a diminished incidence of heparin-induced thrombocytopenia.

A large-scale analysis involving 4,195 colorectal patients evidenced that pharmacological prophylaxis decreased the occurrence of symptomatic venous thromboembolism from 1.8% to 1.1%, while also lowering overall cancer-related mortality. Notably, a single daily dose of LMWH yields comparable efficacy to twice-daily regimens. Furthermore, a Cochrane meta-analysis of four RCTs established a substantial decline in symptomatic deep vein thrombosis through prolonged prophylaxis extending 28 days post-discharge malignancies (*Koch A et al. Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses. Br J Surg. 1997;84:750-759*).

In accordance with ERAS protocols, patients should use appropriate compression stockings or intermittent pneumatic compression, and undergo pharmacological prophylaxis with LMWH. Extended duration of 28 days is strongly advised for those with colorectal (*Warkentin TE et al. Heparin-induced thrombocytopenia in patients treated with low-molecular-weight heparin or unfractionated heparin. N Engl J Med. 1995;332:1330-1335*) (*McLeod RS, Geerts WH, Sniderman KW, et al; Canadian Colorectal Surgery DVT Prophylaxis Trial investigators. Subcutaneous heparin vs low-molecularweight heparin as thromboprophylaxis in patients undergoing colorectal surgery: results of the Canadian Colorectal DVT Prophylaxis Trial: a randomized, double-blind trial. Ann Surg. 2001;233:438-44*) (*Lenkov P et al. Role of Post-discharge Venous Thromboembolism Prophylaxis after Colorectal Surgery. Clin Colon Rectal Surg. 2025 Apr 17;39(1):37-50*)

- Preanaesthetic medication

Prolonged-effect sedative premedication, particularly opioids, should be omitted within the 12-hour window prior to surgery. Such agents impede early postoperative recovery by compromising the patient's capacity to mobilize and maintain oral intake, consequently preventing recovery.

When clinically indicated, rapid-acting anesthetic agents—such as fentanyl in conjunction with titrated doses of midazolam or propofol—may be utilized under close supervision. These alternatives do not interfere with the recovery timeline or the overall length of stay (*Walker KJ et al. Premedication for*

anxiety in adult day surgery. *Cochrane Database Syst Rev.* 2009 Oct 7;2009(4):CD002192) (Cavallaro P et al. Implementation of an ERAS Pathway in Colorectal Surgery. *Clin Colon Rectal Surg.* 2019 Mar;32(2):102-108. doi: 10.1055/s-0038-1676474).

- Antimicrobial prophylaxis and skin preparation

Antimicrobial prophylaxis in colorectal surgery has demonstrated a significant reduction in postoperative wound infections. The use of intravenous prophylactic antibiotics effective against both aerobes and anaerobes can minimize infectious complications in colorectal surgery, with the first dose being administered about 30-60 minutes prior to skin incision. Repeated doses during prolonged procedures may be beneficial (>3 hours) (Nelson RL et al. Antimicrobial prophylaxis for colorectal surgery. *Cochrane Database Syst Rev.* 2014;5:CD001181) (Song F et al. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. *Br J Surg.* 1998;85:1232-1241) (Bratzler DW et al. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis.* 2004;38:1706-1715) (Steinberg JP et al. Timing of antimicrobial prophylaxis and the risk of surgical site infections: results from the trial to reduce antimicrobial prophylaxis errors. *Ann Surg* 2009;250:10–16).

Surgical site infection (SSI) prevention bundles have been used to reduce infection rates in most types of surgery. Bundles tailored to colorectal surgery have been used with success (Cunha T et al. Surgical site infection prevention care bundles in colorectal surgery: a scoping review. *J Hosp Infect.* 2025 Jan;155:221-230).

A recent large study demonstrated that povidone iodine in alcohol as preoperative skin antisepsis was non inferior to chlorhexidine gluconate in alcohol in preventing SSIs after cardiac or abdominal surgery (Mei Z et al. Povidone Iodine vs Chlorhexidine Gluconate in Alcohol for Preoperative Skin Antisepsis. *JAMA.* 2025 Jan 7;333(1):88).

ERAS Interventions: Intraoperative Items

- Standard anaesthetic protocol

Anaesthesia is typically maintained using short-acting inhalational agents like sevoflurane or desflurane. Alternatively, TIVA via automated infusion pumps can be employed, offering particular advantages for patients prone to PONV (Postoperative Nausea and Vomiting). The clinician's role in optimizing postoperative recovery centers on three cornerstones: mitigating surgical stress, managing fluid balance, and providing effective analgesia. These ERAS-based priorities results in the “trimodal approach” a strategy designed to improve results in laparoscopic surgery (*Feldheiser A et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. Acta Anaesthesiol Scand. 2016 Mar;60(3):289-334*)

Supplementing general anaesthesia with a regional block serves to limit postoperative opiate consumption, promoting quicker recovery of bowel function and mobility. For open surgical cases, epidural analgesia outperforms opioid-based methods in controlling pain and reducing side effects like PONV. In minimally invasive scenarios, however, intravenous lidocaine and PCA often prove equally beneficial. Beyond pain relief, regional techniques help to reduce the surgical stress response by lowering insulin resistance (*Block BM et al. Efficacy of postoperative epidural analgesia: a meta-analysis. JAMA 2003;290:2455–2463*) (*Werawatganon T et al. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. Cochrane Database Syst Rev 2005:CD004088*) (*Jorgensen H et al. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. Cochrane Database Syst Rev 2000:CD001893*) (*Uchida I et al. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. Br J Surg 1988;75:557–562*)

During surgery, fluid delivery should be targeted against physiological measures minimizing the overload of salt and water. This is particularly important if using epidural anaesthesia to maintain

blood flow to the gut. In short, anaesthesiologists should control fluid therapy, analgesia and haemodynamic changes to reduce the metabolic stress response

- Postoperative nausea and vomiting (PONV)

Postoperative nausea and vomiting (PONV) impacts approximately one-quarter to one-third of the surgical population and it stands as a primary driver of patient discontent and prolonged hospital stays. Specific patients show higher predisposition to these symptoms, notably females, non-smokers, and individuals with a propensity for motion sickness. Furthermore, the administration of inhalational vapors, nitrous oxide, and systemic opioids markedly elevates this risk. In particular, major colorectal interventions are linked to a substantial burden of PONV, with incidence rates peaking at 70% in various clinical reports. (*Chatterjee S et al. Current concepts in the management of postoperative nausea and vomiting. Anesthesiol Res Pract*2011; 748031) (*Gan TJ et al. Society for ambulatory anesthesia guidelines for the management of postoperative nausea and vomiting. Anesth Analg* 2007;105:1615–1628).

An alternative strategy may be to administer antiemetic prophylaxis to all patients who are having inhalational anaesthesia, opiates or major abdominal surgery.

Shifting away from emetogenic stimuli like volatile agents in favor of propofol-based anaesthesia significantly decreases PONV. Integrated ERAS strategies, such as optimizing oxygen concentrations, shortening fast times, and ensuring euvoemia, also play a crucial role. Additionally, regional techniques (e.g., TAP blocks or epidurals) diminish the requirement for opioids, thereby attenuating a primary risk factor for postoperative nausea. (*Veiga-Gil et al. Postoperative nausea and vomiting: physiopathology, risk factors, prophylaxis and treatment. Rev Esp Anesthesiol Reanim.* 2017 Apr;64(4):223-232).

- Laparoscopy and modifications of surgical access

The transition from open to laparoscopic surgery in colorectal oncology was validated by four pivotal trials, which collectively demonstrated that the minimally invasive approach is oncologically safe while offering superior short-term recovery.

The Barcelona Trial: This early study was influential in showing that laparoscopic surgery for colon cancer not only provided faster recovery (shorter hospital stays and earlier bowel function) but also suggested a potential survival advantage and lower recurrence rates compared to the open approach, sparking global interest in the technique.

The COST Trial (North America): This large-scale study focused on long-term oncologic safety. It definitively proved that there was no significant difference in recurrence rates or overall survival between laparoscopic and open surgery, establishing the laparoscopic method as a legitimate alternative for colon cancer.

The CLASICC Trial (UK): This trial expanded the scope to include rectal cancer. While it confirmed that short-term benefits were consistent with previous trials, it initially highlighted higher rates of positive circumferential resection margins (CRM) in the laparoscopic rectal group, emphasizing that laparoscopic rectal surgery is technically demanding and requires a steep learning curve.

The COLOR Trial (Europe): Similar to the COST trial, the COLOR study confirmed that for colon cancer, the laparoscopic approach yields comparable long-term disease-free survival to open surgery, while significantly reducing blood loss and accelerating postoperative mobilization. The early reports of these trials described similar or even lower postoperative complication rates for laparoscopic surgery compared with open surgery. 30-day mortality rates were not significantly different.

Patients in the laparoscopic arm had significantly less blood loss, earlier return of bowel function, earlier resumption of fluid intake and regular diet, shorter use of oral and parenteral analgesics and shorter hospital stay, while operative time was longer for laparoscopy in all studies. Radicality of resection (e.g. resection margins, number of lymph nodes) did not differ significantly.

Both long- and short-term health-related quality of life are higher in laparoscopic compared with open colon cancer surgery (Vennix S et al. *Laparoscopic versus open total mesorectal excision for rectal cancer. Cochrane Database Syst Rev.* 2014) (Lacy AM et al. *Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. Lancet* 2002; 359: 2224-2229) (Clinical Outcomes of Surgical Therapy Study Group (COSST). *A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med* 2004; 350: 2050-2059) (Guillou PJ et al. *Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomized controlled trial. Lancet* 2005; 365: 1718-1726) (Veldkamp R et al. *Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol* 2005; 6: 477-484) (Wu Z et al. *Lymph node harvested in laparoscopic versus open colorectal cancer approaches: a meta-analysis. Surg Laparosc Endosc Percutan Tech* 2012; 22: 5-11) (Stucky CC et al. *Long-term follow-up and individual item analysis of quality of life assessments related to laparoscopic-assisted colectomy in the COST trial 93-46-53 (INT 0146). Ann Surg Oncol* 2011; 18: 2422-2431) (Weeks JC et al. *Short-term quality-of-life outcomes following laparoscopicassisted colectomy vs open colectomy for colon cancer: a randomized trial. JAMA* 2002; 287: 321-328) (Janson M et al. *Randomized trial of health-related quality of life after open and laparoscopic surgery for colon cancer. Surg Endosc* 2007; 21: 747-753) (Han SA et al. *Comparison of immunologic outcomes of laparoscopic vs open approaches in clinical stage III colorectal cancer. Int J Colorectal Dis.* 2010;25:631–638).

Therefore, laparoscopic surgery appears to be associated with a reduction in the postoperative systemic inflammatory response, as evidenced by circulating concentrations of C reactive protein, following colorectal surgery (Wang G et al. *Immunologic response after laparoscopic colon cancer operation within an enhanced recovery program. J Gastrointest Surg.* 2012;16:1379–1388).

The LAFA study in 2011 was conducted to evaluate whether the integration of laparoscopic or open surgery with either ERAS or conventional perioperative care represented the ideal strategy for colorectal interventions. The authors reported that length of stay was shortest in the laparoscopic/ERAS group (5 days), followed by the laparoscopic/standard group (6 days) and then by both open groups (7 days). Multivariable regression analysis identified laparoscopic surgery as the sole independent predictor for both abbreviated hospital stays and reduced postoperative morbidity. While ERAS and minimally invasive techniques appear to act synergistically, the

preponderance of clinical benefit within these pathways is attributable to the laparoscopic approach itself (Ehrlich A et al. *Comparison of laparoscopic and open colonic resection within fast-track and traditional perioperative care pathways: Clinical outcomes and in-hospital costs. Scand J Surg.* 2015 Dec;104(4):211-8).

Clinical data demonstrate that the recovery after surgery is influenced by the wound size, and the risk of developing an incisional hernia scales accordingly. Actually, a Pfannenstiel incision is associated with the lowest rate of incisional hernia and should be the incision of choice for hand assistance and specimen extraction in minimally invasive colorectal resections wherever applicable (Guo J et al. *The safety of Pfannenstiel incision for specimen extraction in laparoscopic colorectal surgery for colorectal cancer: a systematic review and meta-analysis. Wideochir Inne Tech Maloinwazyjne.* 2024 Mar;19(1):1-10)(DeSouza A et al. *Incisional hernia, midline versus low transverse incision: what is the ideal incision for specimen extraction and hand-assisted laparoscopy? Surg Endosc.* 2011 Apr;25(4):1031-6).

- Nasogastric intubation

There is no rationale for routine insertion of a nasogastric tube during elective colorectal surgery except to evacuate air that may have entered the stomach during ventilation by using a facial mask before endotracheal intubation. Over time, numerous studies have established that the routine use of nasogastric tubes in major surgery—including colorectal procedures—can lead to an escalation in pulmonary complications such as aspiration pneumonia, significant patient distress, and a prolonged delay in the resumption of bowel function (Nelson R et al. *Systematic review of prophylactic nasogastric decompression after abdominal operations. Br J Surg* 2005;92:673–680).

ERAS recommendation: Routine nasogastric decompression does not accomplish any of its intended goals and should be abandoned in favor of selective use of the nasogastric tube.

- Preventing intraoperative hypothermia

The onset of hypothermia during the perioperative phase is attributable to a combination of anesthetic agents, procedural factors, and the surgical environment. Evidence from several RCTs confirms that preserving normothermia via active warming blankets and warmed fluids lowers the risk of wound complications, blood loss, and cardiac adverse events. It is recommended that active warming measures persist into the recovery period until the patient is eutermic ($\geq 36^{\circ}\text{C}$).

(Fu Y et al. *The relationship between preoperative temperature and intraoperative hypothermia in patients undergoing robotic colorectal cancer surgery. J Robot Surg.* 2025 Nov 11;20(1):7) (Madrid et al. *Active body surface warming systems for preventing complications caused by inadvertent perioperative hypothermia in adults. Cochrane Database Syst Rev.* 2016 Apr)

- Perioperative fluid management

Intravascular volume represents a primary determinant of cardiac output and, consequently, the systemic delivery of oxygen to tissues. Acute hypovolemia may result in the hypoperfusion of vital organs and the gastrointestinal tract, potentially triggering adverse clinical events.

However, fluids overload can lead to bowel oedema and increased interstitial lung water, which can also lead to complications (Varadhan KK et al. *A meta-analysis of randomized controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. Proc Nutr Soc* 2010;69:488–498).

Vasopressors agents are recommended in blood pressure control if the patient is euvoletic.

It is apparent that fluid requirements in patients undergoing surgery by a laparotomy is different to laparoscopic surgery due to increased fluid shifts, bowel handling and an increased SIRS.

Open surgery patients is also more likely to have thoracic epidural analgesia which also changes vascular tone and venous capacitance, and further complicates fluid therapy (Jardot F et al. *Detection of hypovolemia by non-invasive hemodynamic monitoring during major surgery using Ringer's solution, 5% albumin, or 20% albumin as infusion fluid: a post-hoc analysis of a randomized clinical trial. Crit Care.* 2025 Mar 23;29(1):132).

Laparoscopic surgery, therefore, would appear to offer the potential to simplify the way fluid is administered and reduce fluid requirements, but there is evidence that cardiac output is reduced by the physiological consequences of the Trendelenburg position and pneumoperitoneum.

Recommendation: balanced crystalloids should be preferred to 0.9 % saline. In open surgery, patients should receive intraoperative fluids (colloids and crystalloids) guided by flow measurements to optimize cardiac output. Flow measurement should also be considered if: the patient is at high risk with comorbidities; if blood loss is >7 ml/kg; or in prolonged procedures. Vasopressors should be considered for intra- and postoperative management of epidural-induced hypotension provided the patient is euvolemic.

The enteral route for fluid postoperatively should be used as early as possible, and intravenous fluids should be discontinued as soon as is practicable.

These guidelines aim to prevent complications like kidney injury, metabolic derangements, and prolonged hospital stays by individualizing fluid therapy based on patient physiology, not just routine protocols (*Levy BF et al. Intraoperative oxygen delivery in infusion volume optimized patients undergoing laparoscopic colorectal surgery within an enhanced recovery programme: the effect of different analgesic modalities. Colorectal Dis 2012; 14:887–892*) (*Patel et al. Anaesthesia and intestinal anastomosis. BJA Educ. 2021 Nov;21(11):433-443. doi: 10.1016/j.bjae.2021.06.001*).

- Drainage of the peritoneal cavity

Many surgeons routinely place intraperitoneal drains after elective colorectal surgery. However, enhanced recovery after surgery guidelines recommend against their routine use owing to a lack of clear clinical benefit. In COMPASS (COMPLicAteD intra-abdominal collectionS after colorectal Surgery) study, a prospective, international, cohort study which enrolled 1805 patients from 22 countries, a drain insertion rate of 51.9 per cent (937 patients) was reported. After matching, drains were not associated with reduced rates (odds ratio (OR) 1.33, 95 per cent c.i. 0.79 to 2.23; $P = 0.287$) or earlier detection (hazard ratio (HR) 0.87, 0.33 to 2.31; $P = 0.780$) of collections. Although not associated with worse major postoperative complications (OR 1.09, 0.68 to 1.75; $P = 0.709$), drains were associated with delayed hospital discharge (HR 0.58, 0.52 to 0.66; $P < 0.001$) and an increased risk of SSIs (OR 2.47, 1.50 to 4.05; $P < 0.001$). That being said, intraperitoneal drain placement after elective colorectal surgery is not associated with earlier detection of postoperative collections, but prolongs hospital stay and increases SSI risk (*Sciuto A et al. Predictive factors for anastomotic leakage after laparoscopic colorectal surgery. World J Gastroenterol. 2018 Jun 7;24(21):2247-2260*) (*EuroSurg Collaborative. Intraperitoneal drain placement and outcomes after elective colorectal surgery: international matched, prospective, cohort study. Br J Surg. 2022 May 16;109(6):520-529*) (

- Urinary drainage

Among ERAS items, early removal of urinary catheter (UC) is considered a key issue, though adherence to this specific item still varies among centers. UC placement allows for monitoring of post-operative urinary output but relates to an increased risk of urinary tract infection (UTI), reduced mobility, and patient's discomfort. Pedrazzani et al. in a recent prospective, randomized, controlled two arm study comparing the rate of AUR after immediate versus early removal of UC in patients undergoing minimally invasive colorectal resections (MICR), demonstrated a non-inferiority of

immediate versus 24-h removal of UC would call into question the usefulness of urinary drainage in the setting of MICR (*Pedrazzani C et al. Immediate versus early (24-hours) urinary catheter removal after elective minimally invasive colonic resection: study protocol for a randomized, multicenter, non-inferiority trial. Trials. 2022 Nov 22;23(1):956*).

ERAS Interventions: Postoperative Items

1. Prevention of postoperative ileus

Preventing postoperative ileus is essential for shortening hospital stays and is a fundamental goal of ERAS pathways. Although prokinetic drugs often lack clinical effectiveness, several multimodal interventions are beneficial. Thoracic epidural blocks significantly outperform intravenous opioids in preserving gut motility. Fluid management with euvolemia is equally vital, as excessive administration impairs digestive function (bowel oedema, higher intestinal fistula and post op ileus). Evidence also suggests that avoiding nasogastric tubes and adopting minimally invasive surgery markedly accelerate the return of bowel function (*Matsui R et al. Impact of post-operative paralytic ileus on post-operative outcomes after surgery for colorectal cancer: a single-institution, retrospective study. Surg Today. 2022 Dec;52(12):1731-1740*) (*MacVicar E et al. A systematic review of the impact of post-operative oral fluid intake on ileus following elective colorectal surgery. Int J Surg. 2022 Jul;103:106651*).

Noteworthy, simple interventions like chewing gum have shown a favorable impact on reducing the clinical course of ileus. Vather et al. reported through univariate analysis that increasing age; procedure type (combined procedure, locally advanced tumours, open surgery and rectal surgery); increasing opiate consumption; elevated preoperative creatinine; post-operative haemoglobin drop, highest white cell count and lowest sodium as significant correlates (*Vather R et al. Risk factors for the*

development of prolonged post-operative ileus following elective colorectal surgery. *Int J Colorectal Dis.* 2013 Oct;28(10):1385-91) Laparoscopic-assisted colonic resection also leads to faster return of bowel function, as well as resumption of an oral diet, compared with open surgery (Murray A et al. *Clinical effectiveness and cost-effectiveness of laparoscopic surgery for colorectal cancer: systematic reviews and economic evaluation. Health Technol Assess.* 2006 Nov;10(45):1-141).

2. Postoperative analgesia

For open midline laparotomy, TEA (Thoracic Epidural Analgesia) is the optimal established analgesic technique. Administration of epidural local anaesthetics to patients undergoing laparotomy reduce gastrointestinal paralysis compared with systemic or epidural opioids, with comparable postoperative pain relief. Addition of opioid to epidural local anaesthetic may provide superior postoperative analgesia compared with epidural local anaesthetics alone. The effect of additional epidural opioid on gastrointestinal function is so far unsettled. Randomized, controlled trials comparing the effect of combinations of epidural local anaesthetic and opioid with epidural local anaesthetic alone on postoperative gastrointestinal function and pain are warranted.

Several meta-analyses have shown improved outcomes with TEA compared with opioid-based analgesia, including pain, complications, PONV and insulin resistance (Popping DM et al. *Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg* 2008;143:990–999) (Jørgensen H et al. *Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. Cochrane Database Syst Rev.* 2000;(4):CD001893).

Analgesic requirements during the first 24 hours post-surgery can often be met with oral multimodal therapy, bypassing regional blocks or high-potency opiates. Current research is focusing on replacing TEA and morphine with intrathecal (spinal) analgesia or TAP blocks, as the former supports accelerated mobilization and shorter length of stay. In the context of laparoscopic surgery, TAP

blocks targeting lower abdominal incisions—alongside systemic paracetamol—have proven effective in curtailing the reliance on opioids

Paracetamol is a vital part of multimodal analgesia. It is available in an intravenous preparation and can be given as 1 g four times daily.

NSAIDs are also an important part of multimodal analgesia. There is not sufficient evidence to stop using NSAIDs as a component of multimodal analgesia in the postoperative period. Tramadol is an alternative to NSAIDs (*Virlos I et al. Short-term outcomes with intrathecal versus epidural analgesia in laparoscopic colorectal surgery. Br J Surg 2010;97:1401–1406*) (*Zafar N et al. The evolution of analgesia in an ‘accelerated’ recovery programme for resectional laparoscopic colorectal surgery with anastomosis. Colorectal Dis 2010;12:119–124*) (*Guimard P et al. Critical care challenges after gastrointestinal surgery. Curr Opin Crit Care. 2025 Dec 1;31(6):743-749*) (*Chen Y et al. Efficacy and safety of different doses of dexmedetomidine on gastrointestinal function recovery after laparoscopic colorectal surgery. World J Gastroenterol. 2025 Aug 21*).

3. Perioperative nutritional care

In ERAS programmes, oral nutritional supplements (ONS) have been used to achieve target intakes of energy and protein during the very early postoperative phase (if started 7-10 days preoperatively) and it is associated with a reduction in the prevalence of infectious complications and anastomotic leaks (*Waitzberg DL et al. Postsurgical infections are reduced with specialized nutrition support. World J Surg. 2006 Aug;30(8):1592-604*) (*Walsh M et al. A review of perioperative immune-modulating and metabolic-modulating nutrition strategies for bowel resection surgery. JPEN J Parenter Enteral Nutr. 2024 Jul;48(5):538-545*) (*Loon MM et al. Impact of Preoperative Nutritional Support on Surgical Outcomes in Gastrointestinal Surgeries: A Systematic Review. Cureus. 2024 Mar 18;16(3):e56416*).

Specialized nutritional assessment is mandatory for elderly patients and those with chronic pathologies or alcohol dependence, who are prone to sub-therapeutic micronutrient levels. Such patients often present with nutritional intakes insufficient to meet metabolic demands, requiring

targeted supplementation both pre- and postoperatively (Gianotti L. *Nutrition and infections. Surg Infect (Larchmt)*. 2006;7 Suppl 2:S29-32).

In the postoperative phase, ERAS protocols advocate for patients to commence drinking immediately during the post-anesthetic recovery phase and incrementally reaching a spontaneous caloric intake of up to 1,500 kcal per day (Nygren J et al. *An enhanced-recovery protocol improves outcome after colorectal resection already during the first year: a single-center experience in 168 consecutive patients. Dis Colon Rectum* 2009;52:978–985) (Marimuthu K et al. *A meta-analysis of the effect of combinations of immune modulating nutrients on outcome in patients undergoing major open gastrointestinal surgery. Ann Surg* 2012;255:1060–1068).

Different combinations of diets containing components aimed to enhance immune function in surgical patients have been studied. These diets, often called ‘immunonutrition’ (IN) usually contain combinations of arginine, glutamine, omega-3 fatty acids, and nucleotides.

Current evidence indicates that this intervention is most efficacious in nutritionally compromised patients; however, there is a paucity of trials evaluating the clinical impact of these formulas within an ERAS framework where surgical stress is already optimized

4. Postoperative control of glucose

Increasing insulin resistance and glucose levels have been shown to be associated with complications and mortality after major abdominal surgery. Several treatments in the ERAS protocol affect insulin action/resistance and hence glucose levels directly or indirectly (bowel preparation prolonging preoperative fasting; preoperative carbohydrate treatment instead of overnight fasting). For ward-based patients, insulin should be used judiciously to maintain blood glucose as low as feasible with the available resources (Chabot K et al. *Prehabilitation: metabolic considerations. Curr Opin Clin Nutr Metab Care*. 2020 Jul;23(4):271-276) (Abdelmalak BB et al. *The effects of dexamethasone, light anesthesia, and tight glucose control on postoperative fatigue and quality of life after major noncardiac surgery: A randomized trial. J Clin Anesth*. 2019 Aug;55:83-91) (Krutkyte G et al. *Perioperative Fully Closed-loop Versus Usual Care Glucose Management in Adults Undergoing Major Abdominal Surgery: A Two-centre Randomized Controlled Trial. Ann Surg*. 2025 May 1;281(5):732-

740) (Akhtar S et al. *Scientific principles and clinical implications of perioperative glucose regulation and control. Anesth Analg.* 2010 Feb 1;110(2):478-97.

5. Early mobilization

Combining forced mobilisation with nutritional support results in improved muscle strength but only during the early postoperative phase. An interesting RCT study demonstrated that postoperative muscle training had little effect of long-term postoperative outcomes (Houborg KB et al. *Little effect of physical training on body composition and nutritional intake following colorectal surgery—a randomised placebocontrolled trial. Eur J Clin Nutr* 2005;59:969–977).

In contrast, sedentary postoperative behavior leads to adverse outcomes, including reduced functional capacity. The LAFA trial demonstrated that mobilization during the first three postoperative days is a significant predictor of ERAS success. The inability to mobilize on POD 1 is typically a result of suboptimal pain management, fluid overload, or prolonged catheterization. This constitutes the primary reason for protocol deviation and has been directly linked to increased hospitalization time (Convertino VA. *Cardiovascular consequences of bed rest: effect on maximal oxygen uptake. Med Sci Sports Exerc* 1997;29:191–196) (Smart NJ et al. *Deviation and failure of Enhanced Recovery After Surgery (ERAS) following laparoscopic colorectal surgery: early prediction model. Colorectal Dis.* 2012;14:e727-34) (Carli F et al. *Prehabilitation to enhance perioperative care. Anesthesiol Clin.* 2015;33:17-33).

AIM OF THE STUDY

The purpose of this study was to assess the safety and effectiveness of ERAS protocol in patients undergoing elective colorectal surgical procedure in two different facilities through our surgical department (both afferent to University G.D'Annunzio of Chieti-Pescara).

Additionally, we evaluated the prevalence and incidence of postoperative complications, the duration of hospitalization, as well as a cost analysis.

MATERIALS AND METHODS

Patients selection

Building upon our prior experience with modified ERAS protocol at the Casa Sollievo della Sofferenza Hospital - San Giovanni Rotondo- (FG, Italy), we applied fast-track perioperative care program in elective colorectal cancer surgery with the establishment of a dedicate database (*di Sebastiano P et al. A modified fast-track program for pancreatic surgery: a prospective single-center experience. Langenbecks Arch Surg. 2011 Mar;396(3):345-51*).

Since the introduction of the ERAS protocol in our surgical units in 2016, there has been a progressive increase in adherence to all guideline-recommended items. Patients meeting all the required criteria were classified as ERAS patients (Group 1), whereas those who did not were categorized as non-ERAS patients (Group 2).

A retrospective review was performed of a prospectively collected bi-institutional database of patients who underwent either open or minimally invasive surgical treatment between January 2016

and December 2024, at the Unit of General and Oncological Surgery, Casa di Cura Pierangeli (Pescara, Italy) and the Unit of General Surgery, “F. Renzetti” Hospital (Lanciano, Italy).

Both facilities were affiliated with the “G. D’Annunzio” University of Chieti-Pescara (Italy). All surgeons involved in the study are highly skilled colorectal surgeons who have performed at least 50 minimally invasive colorectal resections within the last 5 years. In order to ensure the uniformity and standardization of surgical therapy and patient management, all surgeons involved shared their training background in colorectal surgery as well as the chosen protocols.

Data were collected using patient’s charts (medical records), anaesthesia charts, pathology records. Follow up was conducted via telephone interview.

Inclusion criteria were: laparoscopic/open colorectal surgery for benign or malignant pathology; good compliance to the ERAS protocol for ERAS group. Exclusion criteria were: ASA V patients and patients who underwent an emergency colectomy due to perforation or intestinal obstruction.

The data included age, gender, diagnosis, BMI, ASA score, pre-operative blood tests, operative procedure, operative time, length of stay on the critical care unit, and total hospital length of stay. Further post-operative outcomes including 30-days readmission rates, reoperation rates, 90-days morbidity and mortality.

Operative Technique:

Regarding minimally invasive approach (laparoscopic) a traditional medial to lateral approach was routinely followed in both right-sided and left-sided resections. The splenic flexure was mobilized for all rectal resections and, when necessary, for sigmoid colectomies. A conversion to open procedure was performed in cases of intraoperative complications as bleeding or where dissection could not be completed safely laparoscopically.

The specimen was extracted by a Pfannenstiel incision through a wound protection device or an endobag. Anastomoses to the rectum were performed with circular stapler (Knight–Griffen anastomosis), ileo-colic anastomoses were mechanical and intra-corporeal. Defunctioning ileostomies were given in case of ultralow rectal resection or at-risk anastomoses. TaTME resections were carried out in selected patients with mid-low rectal cancer.

Enhanced Recovery Program Protocol

Following the evidence previously established in pancreatic surgery, a multidisciplinary institutional committee—comprising surgeons, anesthesiologists, nursing staff, and dieticians—developed a standardized clinical algorithm. This protocol included 23 standard perioperative care points in accordance with ERAS guidelines (Table 2).

Group 1 (ERAS group):

Nutritional counseling is provided and moderate aerobic physical activity is recommended, in accordance with current evidences (*Carli F et al. Prehabilitation to enhance perioperative care. Anesthesiol Clin. 2015;33:17-33*) (*A. Weimann. Proceedings from 38th ESPEN Congress, Copenhagen 2016*). Energy intake, proteins and lipids remain the same until the admission day. Only fiber consumption is reduced three days before admission, according to low fibre diets standards (*Nakazawa T et al. Oral antibiotics and a low-residue diet reduce the incidence of anastomotic leakage after left-sided colorectal surgery: a retrospective cohort study. Langenbecks Arch Surg. 2022 Sep;407(6):2471-2480*).

After admission patients are treated according to ERAS protocol: no solid food after midnight, maltodextrins and clear fluid up to 2 hours before surgery.

Antibiotic prophylaxis consists of a single dose of ampicillin/sulbactam (3g) and metronidazole (0.5g) 30 minutes preoperatively, to be readministered if the procedure lasts longer than 3 hours. Thromboembolic prophylaxis was performed with low-molecular-weight heparin and compression

stockings until discharge. Extended prophylaxis for 2 or 4 weeks was given to patients with colorectal cancers. For right and left hemicolectomies bowel preparations was achieved by to enemas. Mechanical bowel preparation was reserved exclusively for rectal cancer patients. Intraoperative fluids were restricted to 1500 mL (except in cases of blood loss >500 mL). Postoperatively, patients were transferred either to the Intensive Care Unit (ICU), based on ASA status or anaesthesiologist request, or to the standard surgical ward.

The nasogastric tube was inserted orally and removed upon emergence from anaesthesia in the operating room. Oral nutrition was resumed progressively: liquids → semi-solid diet → light diet → regular diet, starting the evening of surgery. To prevent nausea and stimulate gastrointestinal motility, metoclopramide (10 mg three times a day) was administered until discharge.

After right and left hemicolectomies, urinary catheter was removed in POD 1 (POD2 after rectal resections due to high rate of post-operative acute urinary retention).

In contrast to current ERAS guidelines, abdominal drains were routinely placed according to the intraoperative setting and patient's characteristics, and removed after the first flatus.

Postoperative pain was managed via an elastomeric pump containing: ketoprofen 960 mg, tramadol 600 mg, ranitidine 450 mg, and metoclopramide 90 mg in 300 ml of saline (infusion rate: 4 ml/h for the first 24 hours), followed by oral paracetamol (max 3g/day) until discharge. All FT patients received a Transversus Abdominis Plane (TAP) block prior to incision for analgesia.

Early mobilization is encouraged starting from the first postoperative day, consisting of a walk of at least 300 meters.

Group 2 (non-ERAS) patients received routine bowel preparation in left and rectal resection, unrestricted intraoperative and postoperative fluids, and conventional analgesia (TAP blocks was not routinely administered). The nasogastric tube was removed only after the return of bowel function

(bowel sounds, flatus, or defecation). Discharge criteria remained identical to Group 1. Care Plan for Patients in the Fast-Track (ERAS) Surgery Program are reported in Table 2.

Since January 2025, ERAS protocol has been implemented in all patients undergoing colorectal resections. From that point onward, more than 100 patients undergoing minimally invasive and open colorectal surgery successfully fulfilled all ERAS items.

Discharge was considered feasible from postoperative day 5, provided it was clinically safe and the patient consented. Discharge criteria were: adequate pain control with oral therapy (opioid-free), absence of nausea, regular passage of flatus and/or stool, no signs of infection, tolerance of solid food, mobilization equivalent to preoperative levels, patient consent for discharge.

For patients requiring a stoma, education was standardized pre- and intra-operatively. Discharge criteria included independent stoma care and proficiency in bag/plate fitting. Each patient had to demonstrate two independent changes before discharge.

Anastomotic leakage was identified through a combination of clinical symptoms (including pain, pyrexia, tachycardia, peritonitis, or the presence of feculent or purulent drainage), radiographic evidence (such as free abdominal fluid or gas collections detected via CT scan), and intraoperative findings (enteric spillage or anastomotic disruption). Intra-abdominal abscess was characterized as an infected fluid collection within the abdominal or pelvic cavity.

Surgical site infection (SSI) was defined by clinical signs of infection (erythema, purulent discharge, or tenderness) necessitating antibiotic therapy and/or wound debridement. Hemorrhage was categorized as postoperative anemia or bleeding requiring blood transfusion or surgical re-intervention. Urinary tract infections (UTI) were recorded in cases of symptomatic infection managed with antibiotics.

Regarding cardiorespiratory complications, the study identified instances of atrial fibrillation, heart failure, and pneumonia requiring pharmacological intervention (e.g., intravenous antibiotics).

Additional adverse events included venous thromboembolism, hepatic failure, delayed gastric emptying, paralytic ileus, nausea, and vomiting.

Statistical Analysis

Statistical analysis was performed using SPSS (version 13). Continuous variables were expressed as medians and compared using the Mann-Whitney U test. Categorical variables were reported as percentages and compared using the Chi-square or Fisher's exact test. Variables with $p < 0.05$ were included in a stepwise logistic regression model for multivariate analysis. To ensure the comparability of the two cohorts, a propensity score analysis (if applicable) or a stepwise multivariate logistic regression was performed to adjust for potential confounders such as age, ASA score, and surgical approach. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 802 patients undergoing elective colorectal surgery for cancer were collected. Perioperative data from 406 consecutive patients undergoing colorectal resection via the fast-track protocol (Group 1) were analysed and compared with 396 non-ERAS resections (Group 2).

Both groups were further stratified by surgical approach: in Group 1, 189 patients underwent open resection and 217 underwent laparoscopic surgery. In Group 2, 225 patients underwent open surgery and 171 underwent laparoscopic procedures. This difference in surgical approach between the two groups was statistically significant ($p = 0.004$)

As regards comorbidities of the patients enrolled in the study, no significant differences were reported for preoperative risk in ASA I-II group (according to the ASA score). Demographic data (ASA class, tumour location, resection type, and pathology) were comparable between groups (Tables 3 and 4). Median age was 69 years (range 33–93) in Group 1 and 68 years (range 36–94) in Group 2.

ASA III or IV patients were more often assigned to the non-ERAS group, as they exhibited either more frequent postoperative complications and/or reduced compliance with the full set of protocol requirements. This may be attributed to the geographical distribution of the patients, as those with higher comorbidity burdens often present to peripheral, non-academic centers. Overall, 75% of patients demonstrated full adherence to all ERAS protocol requirements.

No significant differences were found between the two groups regarding surgical technique (open vs. laparoscopic) or tumour location:

- tumour location: Colon (57%), Rectum (27%), Rectosigmoid (16%), bifocal (9 cases), local or anastomotic recurrence (1 case) in ERAS (Group 1)
- tumour location: Colon (54.2%), Rectum (30.3%), Rectosigmoid (12.9%), bifocal (6 cases), local or anastomotic recurrence (1 case) in non-ERAS (Group 2).

The median length of stay was 8 days (range 5–125) for Group 1 and 9 days (range 5–74) for Group 2 ($p < 0.05$).

Regarding postoperative outcomes, a significant difference was observed in the overall complication rates between the two cohorts. Patients in Group 1 experienced a substantially lower incidence of general complications compared to Group 2 [35/406 (8.6%) vs. 83/396 (20.9%); $p < 0.001$].

Specifically, the analysis of major surgical complications revealed that anastomotic leakage occurred in 5 patients (1.2%) in Group 1, whereas 18 patients (4.5%) were affected in Group 2. This three-fold reduction in the ERAS group was statistically significant ($p < 0.001$). No other major surgical site-

related discrepancies reached the same level of significance. Although the 30-day readmission rate was lower in Group 1 (1% vs. 2.7%), this difference did not reach statistical significance ($p = 0.071$).

The specific complications for each group are listed below:

- Group 1 Specific Complications: Anastomotic leak 2.2%, haemorrhage 2.2%, abscess 2.8%, surgical site infection (SSI) 3.2%, respiratory distress 2.2%, pulmonary complications 0.5%, and others 2.7%.
- Group 2 Specific Complications: Anastomotic leak 4.5%, haemorrhage 3.5%, abscess 4.5%, heart failure 0.7%, intestinal ischemia 0.7%, SSI 4%, respiratory distress 1.7%, pulmonary complications 1.7%. Mortality was 1.4% in Group 1 vs. 3.3% in Group 2.

Mean time of follow up was $14,6 \pm 6,6$ months for non-ERAS and $6,6 \pm 3,4$ months for ERAS group ($p < 0.0001$). The significantly shorter follow-up in the ERAS group (6.6 vs. 14.6 months) primarily reflects its recent full implementation.

A focused analysis of rectal cancer included 109 patients (Group 1) and 120 (Group 2). In the subgroup analysis of rectal cancer (defined as 0–10 cm from the anal verge), a stark difference in surgical approach was observed. Laparoscopic techniques were significantly more frequent in Group 1 compared to Group 2 [78% (85/109) vs. 22% (26/120); $p < 0.001$]. Conversely, open surgery remained the predominant approach in the second group.

Notably, Group 1 demonstrated a significantly lower incidence of several postoperative complications compared to Group 2. Specifically, pulmonary complications were observed in 0.9% of patients in Group 1 versus 4.1% in Group 2 ($p = 0.006$), while respiratory distress occurred in 0.9% and 5.0% of cases, respectively ($p < 0.001$). Furthermore, the rate of surgical site infections (SSI) was significantly reduced in the ERAS group compared to the non-ERAS cohort (0.9% vs. 3.3%; $p = 0.027$). All the data reported here are summarized in the tables 3-11

Cost-Effectiveness Analysis

Based on the official tariffs for hospital care in the Abruzzo Region (as detailed in Regional Council Resolution - DGR n. 929 and n. 930 of 20/12/2023), the estimated daily ward cost for surgical patients ranges between €600 and €800. Consequently, implementing the ERAS protocol across the entire control cohort ($n = 396$) would have yielded a projected saving of \$567\$ bed days per year, equating to a total expenditure decrease of €340,200 to €453,600.

DISCUSSION

The results of this study involving 802 patients confirm that the implementation of the Enhanced Recovery After Surgery (ERAS) protocol (Group 1) significantly improves clinical outcomes in elective colorectal cancer surgery compared to traditional perioperative care (Group 2). Despite the recent adoption of these protocols, the data demonstrate substantial benefits in terms of hospital stay reduction, safety profile, and complication rates.

A primary goal of ERAS is to accelerate functional recovery. Our data show a statistically significant reduction in the median length of stay, decreasing from 9 days in Group 2 to 8 days in Group 1 ($p < 0.05$). While a one-day difference may seem modest, it represents a standardized optimization of resources and a faster return to the domestic environment for the patient. This was achieved with a protocol compliance rate exceeding 75%, highlighting the feasibility of ERAS in a standard clinical setting. Laparoscopy, combined with ERAS, creates an optimal synergy. Minimizing incisions and tissue manipulation reduces the systemic inflammatory cascade (lower IL-6, TNF- α release), leading to faster return of bowel function. Furthermore, opioid-sparing analgesia limits intestinal depression, preventing dehydration of intestinal contents and promoting motility.

From an oncological perspective, results were equivalent to open surgery regarding resection margins and adequacy of lymphadenectomy.

The most remarkable finding is the significant reduction in postoperative morbidity.

Group 1 experienced a more than two-fold reduction in general complications (8.6% vs. 20.9%; $p < 0.001$). There was a significant three-fold reduction in anastomotic leaks (1.2% in Group 1 vs. 4.5% in Group 2; $p < 0.001$). This suggests that ERAS elements, such as optimized fluid management and the avoidance of bowel preparation or prophylactic drains, may contribute to better tissue perfusion and anastomotic healing as suggested in literature (*Greco M et al. Enhanced Recovery After Surgery (ERAS) Programs for Colorectal Resection: Meta-analysis of Randomized Controlled Trials. Annals of Surgery. 2014; 259(4): 631-641*) (*Younan SA et al. Association of perioperative immunonutrition with anastomotic leak among patients undergoing elective colorectal surgery within a robust enhanced recovery after surgery program. Surgery. 2025 May;181:1091599*) (*Guimard et al. Critical care challenges after gastrointestinal surgery. Curr Opin Crit Care. 2025 Dec 1;31(6):743-749*).

The mortality rate was notably lower in the ERAS group (1.4% vs. 3.3%), but not but does not reach statistical significance.

The study observed a significant shift toward laparoscopic surgery within the ERAS group, particularly in rectal cancer cases (78% in Group 1 vs. 22% in Group 2). This synergy between minimally-invasive surgery and ERAS protocols resulted in significant decrease in pulmonary complications (0.9% vs. 4.1%) and respiratory distress (0.9% vs. 5.0%). Surgical Site Infections (SSI) were significantly lower in the ERAS cohort (0.9% vs. 3.3%), likely due to the combination of smaller incisions and optimized perioperative metabolic care.

It should be noted that the present study presents certain biases that warrant consideration. First patients with higher comorbidities (ASA III-IV) were more frequently assigned to the non-ERAS group. This suggests a perceived lack of adherence or a "fear" of applying fast-track protocols to frailer patients.

In addition, the shorter follow-up in Group 1 (6.6 vs. 14.6 months) is a direct consequence of the recent full implementation of the protocol and the tendency in patients with several morbidity to be treated at peripheral centres (probably associated with low compliance with screening protocols and insufficient health self-management) may have influenced the baseline risk of the non-ERAS group.

Taking into account the costs, potential cost savings of implementing an ERAS protocol in colorectal surgery have been demonstrated in several publications focusing on a reduction of LOS (M. Hong et al. *Evaluating Implementation Costs of an Enhanced Recovery After Surgery (ERAS) Protocol in Colorectal Surgery, "A Systematic Review World J Surg* 47, no. 7 (2023).

Implementing an ERAS protocol requires the organization and coordination of hospital personnel around its requirements and an in-depth preoperative assessment of a patient's risk factors and treatment pathway; however, these costs are rarely presented in detail in the literature. Such costs are likely the reason for which the ERAS protocol, even if effective in obtaining better postoperative outcomes, is not as widespread in its application as it could be (Catarci M et al. *ERAS Program Adherence-Institutionalization, Major Morbidity and Anastomotic Leakage After Elective Colorectal Surgery: The iCra2 Multicenter Prospective Study, Surgical Endoscopy* 36, no. 6 (2022): 3965–3984) (Willis MA et al. *Adherence to Fast Track Measures in Colorectal Surgery-A Survey Among German and Austrian Surgeons," International Journal of Colorectal Disease* 38, 2023).

Our study highlights the significant economic advantages associated with the implementation of the ERAS protocol. By reducing the median length of stay (LOS) by 1 day in open surgery and by 2 days in laparoscopic procedures, the Fast-Track program allowed for a substantial optimization of hospital resources. Considering an average daily hospitalization cost in Italy of approximately €600–€800, the universal application of the ERAS protocol to our control group (n=396) would have resulted in an estimated saving of 567 hospital days per year, translating to a total cost reduction ranging from €340,200 to €453,600/year.

Furthermore, this narrow and superficial analysis of costs related only to the reduction in LOS underestimate the actual savings. The significantly lower overall complication rate observed in the

ERAS group (8.6% vs. 20.9%; $p < 0.001$) implies a further reduction in indirect costs, such as those related to prolonged pharmacological treatments, additional diagnostic imaging, and surgical re-interventions. Importantly, this economic efficiency was achieved without compromising patient safety, as evidenced by the comparable 30-day readmission rates between the two cohorts (1.5% vs. 2.8%; $p = 0.201$). As a final point, it is worth noting that the saving of 567 bed days/year represents more than just a financial benefit; it significantly enhances bed capacity, thereby facilitating a reduction in surgical waiting lists—a key metric in healthcare management analysis.

It should be noted that the present study has several limitations. First, this is a single-center retrospective observational study and these elements are susceptible to the inherent biases and limitations. Second, our study does not include the costs related to the preoperative diagnostic work-up and outpatient costs after discharge. Third, the cost details connected to clinical and surgical practices vary by hospitals, and for this reason, financial results found in this study may also vary between different facilities, so this does not allow for a complete study of costs. A detailed assessment of costs related to the pre-operative, intra-operative, and post-operative phases will be conducted as part of this PhD to facilitate cost containment and clinical care optimization.

Finally, clinical evidence confirms that ERAS protocols significantly reduce LOS, perioperative morbidity, and readmission rates. The integration with minimally invasive techniques further optimizes outcomes, ensuring a swifter return to baseline function.

Table 2: Care Plan for Patients in the Fast-Track (ERAS) Surgery Program

Timing	Intervention
Preoperative Day 1	Normal oral nutrition until midnight. No anesthetic premedication.
Day of Surgery	Analgesia via elastomeric pump (ketoprofen 960 mg, tramadol 600 mg, ranitidine 450 mg, metoclopramide 90 mg in saline). No nasogastric tube; if used, removed immediately after extubation. Warm intravenous fluids, upper and lower body warming devices. Goal-directed fluid therapy (CVP < 5 mmHg, max 50 ml/h). Transversus Abdominis Plane (TAP) block. Single-shot antibiotic and antithrombotic prophylaxis.
Postoperative Day 1	Return to surgical ward. Mobilization (at least 4 times per day). Resumption of oral intake with liquids and solids as tolerated. Continued analgesia with elastomeric pump. Paracetamol 1000 mg every 6 hours. Intravenous metoclopramide.
Postoperative Day 2	Discontinuation of elastomeric pump and initiation of oral NSAIDs. Mobilization (at least 4 times per day). Oral metoclopramide. Light or full diet as tolerated. Discharge if feasible.
Postoperative Day 3	Unrestricted mobilization.
Postoperative Day 4	Normal diet and discharge.

Table 3: Demographic and perioperative data

Variabile	Group 1 N=406	Group 2 N=396
Age (y - median, range)	69 (33–93)	68 (36–94)
Sex		
Male (M)	242 (59,7%)	242 (61,1%)
Female (F)	164 (40,3%)	154 (38,9%)
ASA Score		
I	139 (34%)	79
II	217 (54%)	141 (35.6%)
III	50 (12%)	161
IV	0	15
Tumour side		
Colon	230 (57%)	215 (54.2%)
Sigmoid colon	67 (16%)	51 (12.9%)
Rectum (overall)	109 (27%)	120 (30.3%)
- high	20	22
- medium	25	51
- low	10	47
Multifocal	9	10
Recurrence	1	0
Tumour Stage		
Dukes A	67	65
Dukes B	202	203
Dukes C	137	128
Dukes D	0	0

Tabella 4 Surgical procedure

	Group 1	Group 2
Open surgery	189	225
- Proctectomy with J pouch	2	0
- Subtotal colectomy	2	6
- Total colectomy	2	2
- Right Hemicolectomy	83	96
- Left Hemicolectomy	19	33
- Sigmoidectomy	10	6
- Upper anterior resection	20	19
- Lower anterior resection	19	32
- Ultra low rectal resection (intersphincteric)	5	0
- Hartmann resection	7	6
- Miles (abdominoperineal resection)	9	12
- Other resection (e.g. segmental)	11	13
Laparoscopic surgery	217	171
- Left hemicolectomy	20	42
- Splenic flexure resection	42	7
- Right hemicolectomy	50	60
- Sigmoidectomy	50	36
- Upper anterior resection	20	19
- Lower anterior resection	28	0
- Miles / Ta-TME	5	6
- Ultra low rectal resection	2	1
Sample size	406	396

Ta-Tme: transanal total mesorectal exision

Table 5. Short term outcome

	Group 1 (n=406)	Group 2 (n=396)
Morbidity	35 (8.6%)	83 (21,1%)
Mortality	5 (1.4%)	13 (3,3%)
Intrabdominal abscess	11 (2.7%)	18 (4,5%)
Anastomotic leak	9 (2.2%)	18 (4.5%)
Heart failure	0	3 (0,7%)
Haemorrhages (intrabdominal or gastroenteric)	9 (2.2%)	14 (3.5%)
Liver failure	0	0
Bowel ischaemia	0	3 (0,7%)
Pulmonary complications	2 (0,5%)	7 (1.7%)
SSI	13 (3.2%)	16 (4%)
Other	11 (2.7%)	7 (1.7%)

Table 6: Short term outcomes in laparoscopic surgery

	Group 1 (n=217)	Group 2 (n=171)
Anastomotic leak	3 (1.3%)	7 (4.1%)
Haemorrhages (intrabdominal or gastroenteric)	3 (1.3%)	9 (2.2%)
Intrabdominal abscess	4 (1.8%)	5 (1.3%)
SSI	2 (1%)	3 (1.7%)
Other	6 (2.8%)	9 (5.2%)
Mortality	0	1 (0.05%)

Table 7: Length of stay (LOS)

Open surgery	Group 1 (n=406)	Group 2 (n=396)
Discharge (days)	8 (range 5-125)	9 (range 5-74)
Readmission (n)	4 (1%)	11 (2.7%)
Laparoscopic surgery		
Discharge (days)	4 gg (2-28)	6 gg (5-21)
Readmission (n)	2 (1%)	4 (2.3%)

Tabella 8 Statistical analysis

	Group 1 (n=406)	Group 2 (n=396)	p-value
Age	69 (33–93)	68 (36–94)	0.478
Sex (M/F)	242 / 164	242 / 154	0.189
ASA score			<0.001
I	139 (34%)	79 (19.9%)	
II	217 (54%)	141 (35.6%)	
III	50 (12%)	161 (40.6%)	
IV	0	15 (3.8%)	
Complications	35 (8.6%)	83 (20,9%)	<0.001
Anastomotic leak	5 (1.2%)	18 (4.5%)	<0.001
Readmission	6 (1,5%)	11 (2.8%)	0.201
LOS (days) open	8 (5–125)	9 (5–74)	0.115
LOS (days) laparoscopic	4 d (2-28)	6 d (5-21)	0.010

Tabella 9. Complications in laparoscopic subgroup

	Group 1 (n=217)	Group 2 (n=171)	p-value
Anastomotic leak	3 (1.3%)	7 (4.1%)	0.110
Haemorrhages (intrabdominal or gastroenteric)	3 (1.3%)	9 (2.2%)	0.035
Intrabdominal abscess	4 (1.8%)	5 (1.3%)	0.224
SSI	2 (1%)	3 (1.7%)	0.358
Other	6 (2.8%)	9 (5.2%)	0.240
Mortality	0	1 (0.05%)	na

Table 10. Demographical, technical and post operative outcome in rectal resections

	Group 1 (n=109)	Group 2 (n=120)
Open surgery	24 (22%)	94 (78%)
Laparoscopic surgery	85 (78%)	26 (22%)
Sex (M/F)	75 (68,5%) / 34 (31%)	76 (63%) / 44 (37%)
Performed anastomosi	85 (78%)	93 (77,5%)
Overall complications	26 (24%)	38 (31.6%)
Mortality	1 (0.9%)	6 (5%)
Morbidity	22 (20%)	28 (23%)
Intrabdominal abscess	9 (8%)	10 (8%)
Anastomotic leak	2 (1.8%)	4 (3.3%)
Heart failure	0	1 (0.9%)
Haemorrhages (intrabdominal or gastroenteric)	1 (1%)	3 (2.5%)
Liver failure	0	0
Bowel ischaemia	2 (1.8%)	1 (0.9%)
Pulmonary complications	1 (0.9%)	5 (4.1%)
Respiratory distress	1 (0.9%)	6 (5%)
SSI	1 (0.9%)	4 (3.3%)
Other	2 (1.8%)	0
Reoperation	1 (0.9%)	2 (1.6%)

Table 11: Postoperative outcomes in rectal resection

	Group 1	Group 2	p-value
Patients	109	120	
Total anastomosis	85 (77%)	93 (77.5%)	0.930
Anastomotic leak	2 (1,8%)	4 (3.3%)	0.478