Anesthesia for Colorectal Surgery

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KEYWORDS

• Colon surgery • Rectum surgery • Optimization • Analgesia • Anesthesia
• Fluid therapy • Goal-directed therapy

KEY POINTS

- Anesthesiologists play a pivotal role in facilitating recovery of patients undergoing colorectal surgery, as many Enhanced Recovery After Surgery (ERAS) elements are under their direct control.
- Successful implementation of ERAS programs requires that anesthesiologists become more involved in perioperative care and more aware about the impact of anesthetic techniques on surgical outcomes and recovery.
- A key area for achieving a successful outcome is the strict adherence to the principle of aggregation of marginal gains.
- Anesthesia considerations for patients with colorectal cancer and those undergoing emergency colorectal surgery are discussed.

INTRODUCTION

Anesthesiologists play a pivotal role in facilitating recovery of patients undergoing colorectal surgery, as many Enhanced Recovery After Surgery (ERAS) elements are under their direct control. Successful implementation of ERAS programs requires firstly that anesthesiologists become more involved in perioperative care and more aware about the impact of anesthetic techniques on surgical outcomes and recovery. Second, there are many evidenced-based steps within ERAS protocols. Although some of these steps may have greater impact than others, a key area for achieving a successful outcome for these patients is the strict adherence to these individual steps: the principle of aggregation of marginal gains.[1] This article reviews anesthetic and analgesic care of patients undergoing elective colorectal surgery in the context of an ERAS program. Anesthesia considerations for patients with colorectal cancer and emergency colorectal surgery are also discussed.

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PREOPERATIVE PATIENT EDUCATION

Preoperative patient education is an essential component of any ERAS program. Preoperative patient education and preparation has positive effects on outcomes such as pain, psychological distress, and indices of recovery, including hospital stay, even if the intervention is relatively brief and not individualized. Patient expectation may also play a role in postoperative outcome.[2,3] As the enhanced recovery approach may differ from patients' and their caregivers' expectations, it is important to specify the active role the patient is expected to play. Specifications include explicit written information, at an appropriate literacy level, specifying daily goals for nutritional intake and ambulation in the perioperative period, discharge criteria, and expected hospital stay.

PREOPERATIVE EVALUATION, RISK STRATIFICATION, AND OPTIMIZATION

Preoperative evaluation and risk stratification are valuable only if they allow subsequent patient optimization, leading to reduced postoperative mortality and morbidity. Thirty-day mortality after colorectal surgery varies among countries and institutions,[4] and ranges between 2% and 6%.[5,6] Data from 182 hospitals participating in the American College of Surgeons National Surgery Quality Improvement Program (NSQIP) showed that in 28,863 patients undergoing colorectal surgery, overall 30-day mortality was 3.9%.[7] After emergency surgery, 30-day mortality is 3 to 4 times higher than after elective surgery.[5,8] Overall morbidity ranges between 21% and 30%,[7] and is higher after rectal surgery than after colon surgery.[9] Of interest, patients developing complications within 30 days from surgery have a 69% lower chance of surviving at 8 years.[10]

General[7,11] and organ-specific[12–16] preoperative scoring systems and assessment of functional capacity[17,18] can help to predict and stratify preoperative risk. The preoperative evaluation is also an opportunity to improve long-term health besides surgery, such as counseling patients who may benefit from long-term β-blockers, stopping smoking, or tightening glycemic control. Although a substantive discussion about cardiopulmonary risk assessment and reduction is beyond the scope of this article, current guidelines and algorithms are available for assessment and reduction of perioperative risk related to cardiac disease,[19] anemia,[20] pulmonary complications,[21] obesity,[22] obstructive sleep apnea,[23] and diabetes.[24] Preoperative evaluation and risk stratification of elderly patients is complex, and should also measure cognitive function, estimate the risk of postoperative delirium and postoperative falls, and estimate functional capacity and the patient's frailty.[25] Secondary adrenal suppression should be suspected in patients with inflammatory bowel diseases on long-term systemic steroids. Steroids should be continued at the same dose throughout the perioperative period (including the morning of surgery), with higher doses (stress dose) administered only to hypotensive patients in whom arterial hypotension is unrelated to other causes (eg hypovolemia, sepsis).[26]

Preoperative smoking cessation has been shown to improve outcomes,[27] but the optimal duration of preoperative abstinence still remains unclear. It is acknowledged that the implementation of such an approach in clinical practice is not always feasible because of limited hospital resources, lack of organization, and waiting time before the operation. Nevertheless, perioperative caregivers should take the opportunity to emphasize the importance of smoking cessation and be more proactive in helping patients to quit smoking. Preoperative alcohol cessation can improve organ dysfunction, but the effect on postoperative outcomes remains unclear.[28]

Patients undergoing colorectal surgery are commonly malnourished, as undernutrition ranges from approximately 10% to 40% depending on the nutrition risk tool used.

Poor nutritional status is associated with higher morbidity after surgery.[29] Patients with moderate and severe undernutrition benefit from preoperative nutrition, preferably using the enteral route, for 7 to 10 days before major surgery.[30] In patients with less severe malnutrition, including those with diminished oral intake resulting from their underlying disease, oral nutritional supplements are added to their normal diet. Preoperative parenteral nutrition is indicated in severely malnourished patients[31] in whom enteral nutrition is not feasible or not tolerated.[30] Combination with enteral nutrition might be beneficial in patients who need supplemental nutritional support and in whom energy needs cannot be met (<60% of caloric requirements) by the enteral route. Preoperative immune-enhancing nutrition has been shown to reduce postoperative complications after gastrointestinal surgeries, especially for infections,[32] but these results need to be confirmed in a context of a multimodal ERAS program. Moreover, adverse effects have been reported in critically ill patients.[32]

The perioperative period may be associated with rapid physical deconditioning, requiring a period of recovery during which patients are fatigued and quality-of-life and activities are curtailed. Patients with poor baseline exercise tolerance and physical conditioning are at increased risk for serious perioperative complications and prolonged disability,[17] and improving functional capacity by increasing physical activity before surgery may be protective.[33] Physical fitness can be improved in the time that patients are waiting for scheduled surgery, as modest improvements in aerobic capacity can be seen in older adults after training only 1 hour per day, 4 times a week, for 4 weeks. The strategy of augmenting physical capacity with preoperative exercise in combination with nutritional counseling and protein supplementation in anticipation of an upcoming stressor is termed prehabilitation, as opposed to rehabilitation, which begins only after the injury or surgery has occurred.[34] Several small trials have suggested that prehabilitation is effective for improving physical fitness and is safe, although evidence for improved clinical outcomes related to preoperative exercise is limited.[35] Detailed preoperative evaluation and optimization take time and are not always feasible, especially in patients undergoing emergency surgery or colorectal cancer surgery. More studies evaluating the role of optimizing preoperative conditions to a point to delay surgery in patients undergoing oncologic colorectal surgery are warranted (**Table 1**).

PREOPERATIVE FASTING AND PREOPERATIVE ORAL CARBOHYDRATE DRINKS

There is no scientific evidence to support a policy of routine NPO (nothing by mouth) after midnight.[36] Fasting from midnight increases insulin resistance,[37] depletes glycogen reserves,[38] increases patient discomfort,[39] and decreases intravascular volume, mainly in patients receiving mechanical bowel preparation (MBP).[40] In fact, functional intravascular deficit after fasting time, as indicated by guidelines[41] or after 8 hours' fasting,[42] is minimally affected in patients undergoing elective surgeries without MBP.[41,42] Current preoperative fasting guidelines for adult patients undergoing elective surgery recommend a 2-hour fast for liquids and a 6-hour fast for solids.[43] Radiologic studies have further supported the safety of allowing clear fluids up to 2 hours before the induction of anesthesia, showing complete gastric emptying within 90 minutes.[44] These recommendations do not apply to patients with delayed gastric emptying (eg, gastroparesis, gastrointestinal obstruction, upper gastrointestinal tract malignancy). Patients should receive detailed information on what they are allowed to drink and until what time. In addition, written materials should be supplied with information on minimizing fasting times to facilitate the implementation of fasting guidelines.

Table 1
Preoperative risk stratification, evaluation, and optimization

Preoperative Risk Stratification
Scoring systems that predict overall morbidity and mortality
POSSUM-CR[11]
ACS NSQIP colorectal risk calculator[7]
Walking tests[a,17]
CPET[18]
Examples of organ-specific scoring systems
Revised Cardiac Risk[12]
Cardiac Risk Calculator[15]
Modified Clinical Pulmonary Infection Score[14]
Postoperative pneumonia risk index[13]
General Surgery Acute Kidney Injury Risk Index[16]

Preoperative Risk Evaluation and Optimization

Preoperative Risk Evaluation	Preoperative Optimization
Cardiovascular function Revised Cardiac Risk[12] Cardiac Risk Calculator[15] METs[16,19]	ACC/AHA guidelines[19]
Renal function General Surgery Acute Kidney Injury Risk Index	—
Respiratory function Modified Clinical Pulmonary Infection Score[14] Postoperative pneumonia risk index[13]	American College of Physicians guidelines[21]
Diabetic patients Hb_{A1c} >6.0%[24] (even in nondiabetic patients[115])	American Association of Clinical Endocrinologists and American Diabetes Association guideline[24] Exercise Weight loss Glycemic control
Anemia Determine the cause of the anemia[20]	American Anesthesiology Society recommendations[20] Optimize preoperative Hb levels Perioperative blood management strategies
Nutritional status[30] Evaluation of Energy intake Recent weight loss or gain Body fat, muscle mass, presence or absence of fluid accumulation Grip strength' Biochemical nutritional indices Serum albumin Serum prealbumin Tools to assess nutritional risk Nutritional Risk Screening (NRS-2002) Subjective Global Assessment (SGA) Malnutrition Universal Screening Tool (MUST) Nutritional Risk Index (NRI) Severe nutritional risk[31] Weight loss 10%–15% within 6 mo or BMI <18.5 kg/m^2 Subjective Global Assessment Grade C or Serum albumin 30 g/L (with no evidence of hepatic or renal dysfunction)	Nutritional support Mild nutritional risk Nutritional supplements added to normal diet Moderate to severe nutritional risk[31] Enteral nutrition for 7–10 d (even if surgery has to be delayed) Consider combination with parenteral route if >60% of calorie requirement cannot be met Parenteral route if enteral nutrition is not feasible for 5–7 d Immune-enhancing nutrition[31,32] Prehabilitation[34]

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Table 1
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Preoperative Risk Evaluation	Preoperative Optimization
Frailty (frailty phenotype)[25] Weight loss Weakness Exhaustion Slowness Low physical activity	Prehabilitation[34]
Smoking and alcohol abuse	Smoking cessation Multidisciplinary approach Preoperative counseling + NRT The beneficial effect of smoking cessation is correlated with the length of the period of abstinence. Reduction of postoperative complications is seen after at least 3 wk of abstinence before surgery
Functional capacity METs[19] Walking test[a,17] CPET[18]	Preoperative exercise[34,35] Prehabilitation[34]
Secondary adrenal suppression	Continue administration of steroids throughout the perioperative period, including the morning of surgery, at the same dose A higher dose of steroid (stress dose) is required in hypotensive patients, in whom hypotension is unrelated to other causes (eg, hypovolemia, sepsis)[26]

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; BMI, body mass index; CPET, cardiopulmonary exercise tests; Hb, hemoglobin; METs, metabolic equivalents; NRT, nicotine replacement therapy.

[a] Six-minute or 2-minute walking test and shuttle-walking test.

Administration of oral carbohydrate (CHO) drinks with a relatively high concentration (12.5%) of complex CHO (maltodextrin), 100 g (800 mL) the evening before elective surgery, and a further 50 g (400 mL) 2 to 3 hours before induction of anesthesia, has been shown to attenuate the catabolic stress response to surgery. This effect seems particularly related to the CHO dose administered 2 to 3 hours before the induction of anesthesia.[45] As a consequence, insulin resistance is decreased, protein breakdown reduced, and muscle strength improved.[46,47] This might turn in a faster surgical recovery as indicated by the results of a recent Cochrane meta-analysis showing a 1 day reduction in hospital stay after abdominal surgery.[48] Preoperative oral CHO drinks are safe and do not increase the risk of aspiration, even in patients with uncomplicated type 2 diabetes[49] and obese patients.[50]

ANESTHETIC MANAGEMENT

Antibiotic Prophylaxis

Antibiotic prophylaxis for patients undergoing colorectal surgery should cover the aerobic and anaerobic flora of the bowel. It should begin within 30 to 60 minutes before surgical incision, be completed before surgical incision, and last no more than 24 hours. Intraoperative dosing is required for surgical procedures lasting more than 2 antibiotic half-lives or with extensive blood loss. First-choice recommended agents are cefazolin plus metronidazole, or a second-generation cephalosporin with aerobic and anaerobic activities (cefoxitin or cefotetan) for patients undergoing elective colorectal surgery. In patients with type 1 allergic reactions to β-lactamine, cefazolin and metronidazole should be replaced with gentamicin (5 mg/kg) and clindamycin (900 mg).[51] In patients with a high risk of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization or known MRSA colonization, vancomycin should be used in combination with cefazolin, as cefazolin is more effective than vancomycin in preventing surgical-site infections (SSIs) caused by methicillin-susceptible *S aureus*.[51] MBP combined with oral neomycin sulfate plus oral erythromycin base, or with oral neomycin sulfate plus oral metronidazole, and in combination with intravenous antibiotic prophylaxis has been shown to further reduce SSIs. However, the increased risk of gastrointestinal symptoms associated with this regimen can offset the former benefit.[51] Furthermore, the use of MBP causes undesirable side effects, and is no longer routinely indicated in patients undergoing colonic surgery within an ERAS program.[52] Although in many institutions surgeons and infection disease determine the choice of antibiotic based on local microbiological data and international guidelines, anesthesiologists still remain responsible for administering antibiotics before skin incision and ensuring adequate redosing when indicated.

Premedication

Patients should not routinely receive anxiolytic agents. The choice, timing, and dose of anxiolytics have to be tailored according to the patient's age, comorbidities, and medications. The type and duration of surgery need also to be considered. Long-acting anxiolytic medications can prolong immediate surgical recovery, interfering with patient mobilization and early postoperative nutrition. The use of short-acting medications to reduce anxiety associated with surgery and provide comfort during painful intervention before the induction of anesthesia, such as insertion of epidural or arterial cannulation, is recommended.[53] Benzodiazepines can cause undesirable side effects such as postoperative delirium and postoperative cognitive dysfunction that can prolong convalescence, especially in the elderly.[53] Morphine and meperidine are no longer used as premedicants, owing to their prolonged duration of action and side effects. Premedicatiing with α_2-agonists such as clonidine and dexmedetomidine has been shown to attenuate surgical stress, but side effects such as arterial hypotension and sedation that might impair early recovery must be considered.[53] Their role as premedication agents in the context of an ERAS program remains unknown.

Intraoperative Anesthetic Management

Intraoperative anesthetic management of patients undergoing colorectal surgery within an ERAS program aims to provide adequate anesthesia and analgesia, attenuate surgical stress, maintain organ perfusion and oxygenation, and facilitate early feeding and postoperative mobilization.

Anesthetic agents and cerebral monitoring

Few studies have evaluated the impact of different anesthesia techniques (intravenous anesthesia versus inhalational anesthesia) on postoperative outcomes in colorectal surgery. Contrasting results are available, and recommendations cannot be made. However, it seems intuitive to use short-acting inhalation agents such as desflurane and sevoflurane to facilitate rapid emergence from anesthesia. In patients at high risk of postoperative nausea and vomiting (PONV), total intravenous anesthesia with propofol is advised. The use of nitrous oxide (50%–70%) should be avoided, especially during laparoscopic surgery, as prolonged use of nitrous oxide can cause bowel distension and significantly increase the risk of PONV despite the administration of prophylactic antiemetic agents.[54,55] Cerebral monitoring can reduce awareness in high-risk surgical patients, and improve postanesthetic recovery.[56] Monitoring the depth of anesthesia can be particularly useful in elderly patients (>65 years old), as titrating anesthetic agents to maintain bispectral index values between 40 and 60 reduces the incidence of postoperative delirium and postoperative cognitive dysfunction.[57]

Attenuation of surgical and inflammatory stress

The attenuation of the physiologic stress response to surgery and the associated sequelae (such as insulin resistance and protein catabolism) is widely regarded as a key area within ERAS programs.[58] Many of the elements of ERAS pathways have already been very successful in this area, such as laparoscopic surgery and preoperative oral CHO loading. Intraoperative strategies attenuating surgical stress and the inflammatory response to surgery have been also shown to facilitate surgical recovery.[58] It is well established that perioperative epidural analgesia with local anesthetic attenuates the catabolic response to surgery, but poorly influences the inflammatory response.[59] Similar results have been reported after spinal anesthesia. The anti-inflammatory effect seems more related to the systemic effect of local anesthetics than to the neuraxial blockade per se, as demonstrated by the anti-inflammatory properties of intravenous lidocaine. Continuous infusion of intraoperative intravenous lidocaine has been shown to reduce postoperative pain, opioid consumption, and opioid side effects.[60] Glucocorticoids were also found to be beneficial in colorectal patients.[61–63] β-Blockers can be particularly useful to blunt the acute sympathetic response induced by pneumoperitoneum in patients undergoing laparoscopic colorectal surgery. Furthermore, they possess anticatabolic properties, as shown in burn patients in whom they attenuate catabolism.[64] Core temperature needs to be monitored and normothermia maintained throughout the perioperative period, as prevention of hypothermia attenuates circulating levels of catecholamines and reduces postoperative complications.[65,66]

Intraoperative analgesia

Several factors must be considered when choosing the type of analgesia for patients undergoing colorectal surgery. The choice depends on the surgical approach (laparotomy or laparoscopy), the site of the incision (midline, transverse, semicurve, or Pfannenstiel-like incision), the type of surgery (colon or rectum), and patient comorbidities. Perioperative analgesia should aim to provide optimal intraoperative and postoperative pain control, with minimal side effects, with the ultimate goal of facilitating early oral feeding and postoperative mobilization.

Thoracic epidural analgesia (TEA) has been shown to reduce the requirement of anesthetic, systemic opioids, and neuromuscular blockade agents, and attenuate the catabolic stress response to surgery.[59] The impact of TEA on surgical outcomes remains debatable. Although the results of the MASTER trial did not show any benefit of combining epidural analgesia with general anesthesia, a recent meta-analysis of 125 randomized controlled trials (RCTs) (N = 9044) found that epidural analgesia in combination with general anesthesia reduces 30-day mortality and morbidity by 40%, independently of the type of surgery.[67] The use of short-acting opioids such as fentanyl and remifentanil is suggested. However, opioid-inducing hyperalgesia (OIH) has been reported, especially after remifentanil infusion. The use of *N*-methyl-D-aspartate (NMDA) glutamate receptor antagonists, such as ketamine or magnesium, to prevent OIH remains controversial.[68] Intravenous lidocaine has shown to provide adequate analgesia, reduce anesthetic requirement, opioids needs and hasten recovery in open[60] and laparoscopic surgery.[69] Intrathecal morphine with local anesthetics in combination with general anesthesia has also been successfully used, especially in patients undergoing laparoscopic surgery.[70,71] Other analgesic adjuvants such as ketamine, β-blockers, and α_2-agonists are useful alternatives to spare anesthetic and opioid requirements.[53] However, their role as part of multimodal analgesic interventions to improve postoperative outcomes has not been extensively evaluated, especially in colorectal patients and in the setting of an ERAS program. Based on the PROSPECT (Procedure Specific Postoperative Pain Management) recommendations,[72] a guide to the choice of analgesia in colorectal surgery is proposed in **Fig. 1**.

Intraoperative ventilation

Intraoperative lung-protective ventilation has been shown to be beneficial even in patients undergoing abdominal surgery with normal lungs (**Table 2**).[73] Early studies failed to demonstrate reduction of systemic and local inflammatory markers in the early postoperative period (1–5 hours) in patients receiving intraoperative lung-protective ventilation with low tidal volumes (V_T = 6–8 mL/kg) and adequate positive end-expiratory pressure (PEEP) (10–12 cm H_2O), in comparison with patients receiving standard ventilation with V_T of 10 to 15 mL/kg and without PEEP (see **Table 2**). However, results from 2 recent RCTs have shown a reduction in postoperative respiratory complications and shorter hospital stay in patients receiving lung-protective ventilation with low tidal volumes (V_T = 6–8 mL/kg), adequate PEEP (6–10 cm H_2O), and lung recruitment maneuvers (see **Table 2**). Most of the studies included only patients undergoing open abdominal surgery. Similar benefits could be hypothesized, especially in patients undergoing laparoscopic colorectal surgery, in whom the effects of the pneumoperitoneum in combination with steep Trendelenburg position can significantly increase the risk of atelectasis and ventilator-induced lung injury. Further studies are warranted to confirm the role of intraoperative protective ventilation in this specific population. Oxygen therapy (fraction of inspired oxygen [Fio_2]) should be titrated to the most favorable concentration that ensures optimal tissue oxygenation based on the evaluation of oxygen saturation, arterial partial oxygen pressure (Pao_2/Fio_2 ratio), and serum lactates. The use of intraoperative high Fio_2 (Fio_2 = 0.8) to prevent SSI has shown conflicting results. However, patients undergoing colorectal surgery might particularly benefit from this intervention.[74] It must be borne in mind that hyperoxia can cause damage attributable to the production of oxygen free radicals.

Myorelaxation

Short-acting or intermediate-acting muscle relaxants are recommended in patients undergoing colorectal surgery. Cisatracurium should be used in patients with impaired liver or kidney function. Deep neuromuscular blockade (posttetanic count 1–2) facilitates surgical exposure, especially during laparoscopic procedures,[75] and could be particularly useful during laparoscopic rectal surgery. Neuromuscular function should be monitored (train-of-four [TOF], double-burst, or tetanic stimulation patterns) to avoid residual paralysis (TOF <0.9) and postoperative hypoxia.[76,77] Clinical assessment of neuromuscular function underestimates residual paralysis and increases the risk of postoperative respiratory complications, even when sugammadex is used.[78] Qualitative (visual or tactile) assessment is less sensitive than quantitative assessment (acceleromyography) in identifying patients with residual paralysis. Anticholinesterases should be administered 15 to 20 minutes before tracheal extubation and with a TOF count of 4.[77] Sugammadex has been shown to provide faster and more reliable

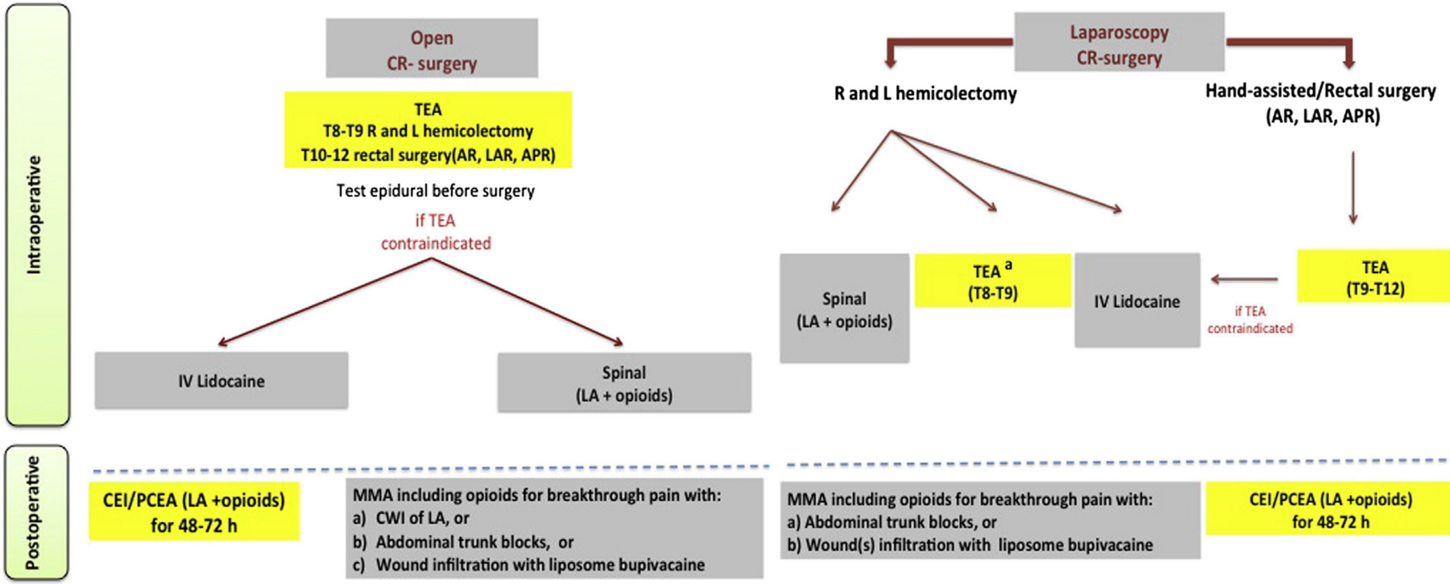

Fig. 1. A guide to the choice of analgesia in colorectal surgery. APR, abdominal perineal resection; AR, anterior resection of the rectum; CEA, continuous epidural analgesia; CR, colorectal surgery; CWI, continuous wound infusion; IV, intravenous; L, left; LA, local anesthetic; LAR, low anterior resection of the rectum; MMA, multimodal analgesia; PCEA, patient-controlled epidural analgesia; R, right; TEA, thoracic epidural analgesia. [a] In patients at high risk of pulmonary complications[122] and in those with high probability of conversion to laparotomy.

Table 2
Intraoperative ventilation and postoperative outcomes

	Protective Lung Ventilation (PV) Versus Standard Ventilation (SV)							
	Wrigge et al, 2000	**Wrigge et al, 2004**	**Choi et al, 2006**	**Determann et al, 2008**	**Weingarten et al, 2010**	**Treschan et al, 2012**	**Severgnini et al, 2013**	**Futier et al, 2013**
Study design (N)	RCT (39)	RCT (64)	RCT (40)	RCT		RCT (n = 101)	RCT (56)	RCT (400)
Population	Open, abdominal	Open, abdominal (30) and thoracic (34)	Open >5 h	Open, general surgery	Open, major abdominal	ASA >2, age >50 y Open >3 h	Open abdominal, >2 h	High-risk[a] Open (79%)/ laparoscopic (21%) >2 h
Colorectal patients, n (%)	NR	NR	0	1	NR	2	NR	87 (21)
Analgesia (%)	IV opioids	IV opioids	Epidural	Epidural	IV opioids	Epidural (83) IV opioids (17)	Epidural (67) IV/SC opioids (33)	Epidural (40%) IV opioids (60%)
Fluid managements	1.5 L of crystalloid				Not standardized	500 mL bolus of RL 2–4 mL/kg/h Crystalloid (3:1) or colloids (2:1) to replace EBL	12–15 mL/kg/h	Not standardized
Protective lung ventilation, PV (n)								
V_T (mL/kg)-IBW	6	6	6	6	6	6	7	8
PEEP (cmH_2O)	10	10	10	10	12	5	10	6–8

RM (Y/N)	No	No	No	No	Yes	No	Yes	Yes, every 30 min
Fio_2 (%)	0.3	0.3 and 1[a] (OLV)	0.4	0.4		0.5	0.4	0.46
Standard ventilation, SV (n)								
V_T (mL/kg) -IBW	15	12–15	12	12	10	12	9	10–12
PEEP (cmH_2O)	0	0	0	0	0	5	0	0
RM	No	No	No	No	No	No	No	No
Fio_2 (%)	0.3	0.3 and 1[a] (OLV)	0.4	0.4	0.5	0.5	0.4	0.47
Primary outcome	Intraoperative cytokine plasma level	Intraoperative cytokine plasma and tracheal aspirates levels	Intraoperative BAL: coagulation (TAT), MPO, IL and cytokines levels	IntraoperativeCC16	Intraoperative Pao_2/Fio_2	(TWA) FVC (TWA) FEV_1 over 5 d	mCPIS	Major pulmonary and extrapulmonary complications over 7 d
Results	No difference	No difference	TAT and MPO ↓ PV group; No differences in other cytokines	No difference	↑ PV group	No difference	↓ PV group at POD 1 and POD 3	↓ PV group (RR = 0.4, 95% CI 0.24–0.68)

Abbreviations: ASA, American Society of Anesthesiologists score; BAL, bronchoalveolar lavage; CC16, Clara cell protein; CI, confidence interval; EBL, estimated blood loss; IBW, ideal body weight; IV, intravenous; mCPIS, Modified Clinical Pulmonary Infection Score[14]; MPO, myeloperoxidase; NR, not reported; OLV, one-lung ventilation; POD, postoperative day; RCT, randomized controlled trial; RL, Ringer lactate; RM, recruitment maneuvers; RR, relative risk; SC, subcutaneous; TAT, thrombin-antithrombin; (TWA) FEV_1, time-weighted average forced expiratory volume in 1 second; (TWA) FVC, time-weighted average forced vital capacity.

[a] Postoperative pneumonia risk index greater than 2.[13]

Adapted from Coppola S, Froio S, Chiumello D. Protective lung ventilation during general anesthesia: is there any evidence? Crit Care 2014;18(2):210.

reversal than anticholinesterase agents and without muscarinic side effects, thus facilitating earlier tracheal extubation and potentially reducing postoperative respiratory complications as a result of residual muscle paralysis.[79]

Prevention of hypothermia

Intraoperative hypothermia increases the risk of postoperative complications and prolongs emergence from anesthesia. In colorectal patients, unintentional perioperative hypothermia (core temperature <35°C) has been recently associated with an increased mortality and morbidity.[65] Laparoscopic surgery does not reduce the risk of perioperative hypothermia, as hypothermia is mainly caused by anesthesia.[80] Maintenance of intraoperative normothermia with the use of active and passive warming devices together with aggressive postoperative management of shivering and residual hypothermia decreases the incidence of wound infections, blood loss, myocardial ischemia, and protein breakdown. Although not always feasible, preoperative warming strategies 20 to 30 minutes before induction of anesthesia has been shown to attenuate redistribution hypothermia, and could be indicated for patients at high risk of hypothermia, such as elderly and malnourished patients. Core temperature should be monitored and maintained higher than 36°C in the intraoperative and immediate postoperative period.[66]

Intraoperative hemodynamic management

Maintenance of optimal organ perfusion is essential in colorectal patients to prevent organ dysfunction and protect bowel anastomosis. Colonic blood flow is poorly autoregulated, and the perfusion of the colon mainly depends on mean arterial pressure, more so than cardiac output. Several considerations must be taken into account when administering intravenous fluids in the context of an ERAS program.[81] The minimization of preoperative fasting, select use of MBP, a more rational and evidence-based intravenous fluid administration, and early resumption of oral intake have significantly reduced the amount of perioperative intravenous fluids (**Table 3**).

Intraoperative fluid management of patients undergoing colorectal surgery remains controversial. However, it is well established that intravenous fluid overload or splanchnic hypoperfusion increases postoperative complications and delays the recovery of gastrointestinal function.[82] Static hemodynamic measures such as central venous pressure or pulmonary arterial wedge are inaccurate in measuring preload[83,84] and predicting fluid responsiveness.[85] Early studies showed that intravenous fluid administration and inotropic agents based on optimization of cardiac output and targeting predetermined hemodynamic goals (goal-directed therapy [GDT]) reduced postoperative complications, accelerated the recovery of bowel function, and shortened the length of hospital stay in patients undergoing colorectal surgery.[86–89] However, the last 2 RCTs found that GDT was not beneficial, as low-risk patients treated with a more restrictive fluid regimen and within an ERAS program had morbidity and surgical recovery similar to those of patients treated with GDT.[90,91] These data were also confirmed by a recent meta-analysis.[92] The value of GDT might be more evident in high-risk patients undergoing colorectal procedures with extensive blood loss (estimated blood loss >7 mL/kg).[93–97] Inotropes can be considered in patients with reduced cardiac contractility (cardiac index <2.5 L/m^2) to ensure optimal oxygen delivery. Esophageal Doppler has been mainly used to guide fluid therapy in colorectal patients. However, GDT based on pulse contour analysis and aiming to minimize stroke volume variations during the respiratory cycle of mechanically ventilated patients has also been shown to decrease morbidity and accelerate recovery, especially in high-risk patients.[93,96,98,99] Intraoperative and postoperative central venous oxygen

Table 3
Intraoperative intravenous fluid management

Intraoperative Fluid Replacement	Intravenous Fluid Administration: a Physiologic and Evidence-Based Approach (70 kg, Elective, No MBP, 2 h Fasting, 2 h Laparoscopic SR surgery, EBL = 500 mL)
Preoperative fasting	Intravascular volume is minimally reduced after overnight fasting[41,42] 30% of patients do not have an intravascular preoperative deficit[41]
MBP	Avoided in colonic surgery 1000–2000 mL if MBP is used
Preloading in patients receiving epidural or spinal analgesia	Intravenous fluids do not prevent hypotension induced by neuraxial blockade Vasopressors are the first choice to treat hypotension induced by neuraxial blockade
Intravascular volume expansion (anesthesia-related)	In normovolemic patients, intravenous fluids are not necessary and vasopressors are the first choice to treat hypotension induced by anesthesia
Maintenance	Replacement of insensible losses (iso-oncotic crystalloids, avoid 0.9% normal saline) Insensible loss during maximal bowel exposure are not higher than 1 mL/kg/h[82] Open surgery: 3–5 mL/kg/h Laparoscopic surgery: <3 mL/kg/h GDT: in high-risk patients or in patients undergoing surgery with extensive blood loss (>7 mL/kg)
Third space	Nil A primarily fluid-consuming third space has never been identified[82]
Urine/GI loss	1:1 iso-oncotic crystalloids according to clinical estimation
Blood/type 2 shifting[a]	1:1 colloid, or 3:1 iso-oncotic crystalloids (in patients with AKI) Intravascular deficit should be measured (GDT high-risk patients) GDT: in high-risk patients or in patients undergoing surgery with extensive blood loss (>7 mL/kg)
Total (mL)	1000–3200

Abbreviations: AKI, acute kidney injury; GDT, goal-directed therapy; GI, gastrointestinal; MBP, mechanical bowel preparation.

[a] Type 2 shifting refers to extravascular shift of fluids that occurs during the surgical trauma owing to an increased endothelial permeability secondary to (1) the release of inflammatory mediators and (2) the release of atrial natriuretic peptide during iatrogenic acute hypervolemia.[82]

saturation–guided fluid administration has not been shown to affect postoperative complications.[100] Intraoperative cardiac output monitoring is also useful to guide fluid therapy during hemodynamic changes induced by pneumoperitoneum and patient positioning, and avoids unnecessary fluid administration. Arterial hypotension induced by general anesthesia or epidural analgesia should be treated with vasopressors when administration of intravenous fluid fails to increase stroke volume by more than 10%,[52,94,101] as low-dose vasopressors do not impair colonic oxygenation.[102]

Crystalloid solutions should be used to replace extracellular losses, such as urine loss, insensible blood loss, and gastrointestinal loss, while in presence of objective measures of hypovolemia iso-oncotic colloid solution should be used to replace intravascular volume.[82] Crystalloid isotonic balanced solutions should be preferred and 0.9% saline solutions avoided.[103] Hyperchloremia caused by the use of 0.9% saline solutions has been associated with kidney dysfunction,[104–106] prolonged hospital stay, and increased 30-day mortality (odds ratio 1.58, 95% confidence interval 1.25–1.98).[104] Recent data have suggested that the use of hydroxyethyl starch (HES) solutions can increase the risk of death and acute kidney injury in critically ill patients,[107,108] but these results have not been confirmed in the perioperative setting.[109] Moreover, the use of large volumes of HES 130/0.4 (2605 ± 512 mL) during major urologic procedures has been shown to impair hemostasis and increase blood loss in comparison with crystalloid solutions.[110] Nevertheless, intraoperative crystalloids-based fluid regimens increase the risk of fluid overload.[110]

Acute intraoperative anemia results in increased mortality.[111] Blood loss reported during open and rectal surgery is higher than during laparoscopic and colonic surgery, respectively. Anemia thresholds triggering red blood cell transfusions cannot be currently recommended, as hemoglobin levels resulting in tissue hypoxia are patient-specific.[111] The decision to transfuse should be made on an individual basis, depending on the clinical context, serum lactate levels, central oxygen venous saturation, and patient comorbidities. Administration of red blood cell transfusion and bone marrow–stimulating agents to treat anemia failed to improve outcomes. Furthermore, it must be also considered that blood transfusions are associated with an increased risk of morbidity and mortality.[111] Optimization of preoperative hemoglobin levels and implementation of blood management programs might reduce red blood cell transfusion, minimize blood loss, and improve postoperative outcomes,[111] especially in patients at high risk of intraoperative transfusion.[112]

Prevention of postoperative nausea and vomiting

PONV prophylaxis is a key component of an ERAS program for patients undergoing colorectal surgery, as avoidance of PONV facilitates early feeding and accelerates recovery. The risk of PONV can be predicted by the Apfel score, based on the presence of the following risk factors: female, nonsmoking status, history of PONV, and opioid use.[113] Several PONV prophylaxis strategies are available, which include minimal preoperative fasting, CHO loading, adequate hydration, prophylactic administration of antiemetic agents, multimodal analgesic strategies to spare opioids and opioid side effects, use of regional analgesia techniques, total intravenous anesthesia, and avoidance of nitrous oxide. The use of high oxygen concentration has a weak effect in reducing PONV.[74] In patients with more than 2 risk factors a multimodal approach, including pharmacologic and nonpharmacologic antiemetic techniques, is required.[114] Detailed information about PONV prophylaxis can be found in the recently updated consensus guidelines for the management of PONV.[114]

Glycemic control

Perioperative hyperglycemia is associated with an increased risk of morbidity and mortality. Preoperative hemoglobin A_{1c} levels (>6.0%) can identify patients at risk of perioperative hyperglycemia and can predict postoperative complications even in nondiabetic patients.[115] Reduced preoperative fasting times, preoperative oral CHO, use of epidural anesthesia, and adequate analgesia facilitate glucose control by reducing insulin resistance. Although the optimal glucose level remains to be determined, it is recommended to maintain random blood sugar lower than 10 mmol/L.[52,94]

POSTOPERATIVE ANALGESIA

Postoperative pain after colorectal surgery is complex in nature (**Fig. 2**). A multimodal analgesic approach including opioid and nonopioid analgesics, in combination with regional analgesia techniques when indicated, is advised to provide optimal analgesia and reduce opioid side effects, aiming at facilitating early feeding and postoperative

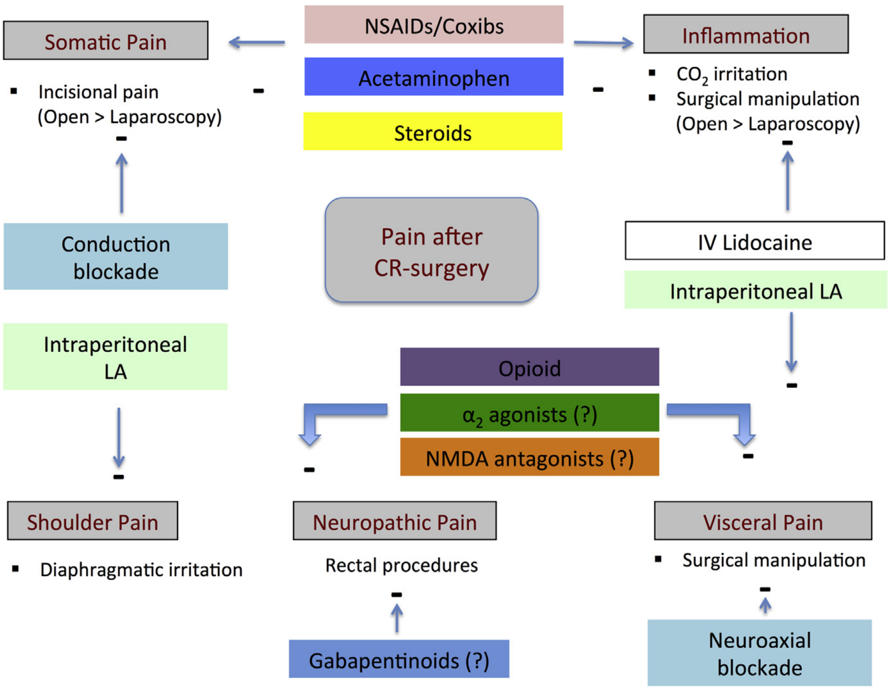

Fig. 2. Complexity of pain in colorectal surgery. The analgesic efficacy of some analgesic medications (?) remains to be proven in colorectal patients. -, inhibitory effect; CR, colorectal surgery; IV, intravenous; LA, local anesthetic; NMDA, *N*-Methyl-D-aspartate receptor; NSAIDs, nonsteroidal anti-inflammatory drugs.

mobilization. The role of preemptive analgesic strategies, such as preoperative administration of acetaminophen, cyclooxygenase-2 (COX-2) inhibitors, NMDA antagonists, and/or gabapentinoids, remains unclear, especially in the context of an ERAS program for colorectal surgery.[116] Epidural analgesia remains the only preemptive analgesic technique that consistently reduces postoperative pain, analgesic consumption, and time to rescue analgesia.[116] Perioperative opioids are still necessary, but should be used as rescue analgesia if other methods fail. An opioid-free multimodal analgesic strategy would be appealing, but more studies are warranted to establish its feasibility, efficacy, and safety. Establishing the impact of analgesia techniques on surgical outcomes remains challenging, as surgical recovery depends on many perioperative factors including patient comorbidities, type of surgery, type of perioperative care (ERAS versus traditional care), and the occurrence of postoperative complications. Common analgesic techniques used in colorectal surgery and their application in the ERAS setting are summarized in **Table 4**. Indications and contraindications are discussed in this issue in one of the article "Optimal analgesia during major open and laparoscopic abdominal surgery" by Fawcett and Baldini.

Analgesia for Open Colorectal Surgery

TEA with local anesthetic and small doses of lipophilic opioids remains the gold standard for postoperative pain after open colorectal surgery. Adding epinephrine (1.5–2.0 µg/mL) to an epidural mixture of local anesthetic improves postoperative analgesia, especially during mobilization and coughing, and reduces pruritus.[117]

Table 4
Common analgesic techniques used in colorectal surgery

Analgesia	Technique and Dose	Comments and Potential Complications
Thoracic epidural analgesia (TEA)	T8–T9 for R and L hemicolectomy T10–T12 for sigmoid-rectal surgery[a] Intraoperative: 5 mL bupivacaine 0.25%–0.5% intermittent boluses or 5 mL/h continuous infusion Postoperative (CEI or PCEA): bupivacaine 0.05%–0.125% or ropivacaine 0.2%, with fentanyl 2–3 μg/mL or hydromorphone 5–7.5 μg/mL	Arterial hypotension Bladder dysfunction Lower limb weakness Consider adding epidural epinephrine (2 μg/mL) if epidural block is patchy or weak
Spinal analgesia	10 mg 0.5% isobaric bupivacaine or 15 mg 0.5% hyperbaric bupivacaine Intrathecal morphine: <70 y 200–250 μg >70 y 150 μg	Arterial hypotension Pruritus Bladder dysfunction Respiratory depression
Intravenous lidocaine	Intraoperative and in PACU 1.5 mg/kg bolus or within 30 min before induction of anesthesia followed by 2 mg/kg/h until the end of surgery. Infusion can be extended in PACU	Local anesthetic toxicity Intravenous lidocaine infusion requires continuous cardiovascular monitoring
Continuous wound infusion of local anesthetic	In most of the studies a multihole catheter is positioned along the surgical incision between the peritoneum and the fascia (preperitoneal) Ropivacaine 0.2% 8–10 mL in the wound followed by Ropivacaine 0.2% 5–8 mL/h for 48 h	Local anesthetic toxicity The ideal anatomic location where multihole catheters are to be placed has not yet been clearly determined
TAP block US-guided or surgically performed Subcostal approach (upper abdominal surgery) Lateral approach (lower abdominal) Posterior approach (lower abdomen)	Unilateral or bilateral Single shot 15–20 mL of 0.25%–0.375% bupivacaine or levobupivacaine Intermittent boluses through multihole catheters 15–20 mL of local anesthetic every 6 h per site Continuous infusion through multihole catheters 6–8 mL/h of 0.25% bupivacaine or 0.2% ropivacaine	Few complications have been reported, especially when the TAP block is performed under direct US guidance; these include intrahepatic and intraperitoneal injections. Local anesthetic toxicity should be also considered, especially when multiples or continuous TAP blocks are performed Pain: reduced static pain score and opioid consumption

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Table 4
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Analgesia	Technique and Dose	Comments and Potential Complications
		Reduction of opioid side effects: inconclusive evidence Duration of the analgesic effect is limited (≤24 h) The analgesic effect is volume and dose dependent Dermatomal spread is limited (1.5 dermatomes) Preoperative TAP block provides better analgesia than postoperative TAP block Single-shot posterior TAP block or continuous TAP block has been used to prolong analgesia (>24 h)
Rectus sheath block US-guided	Bilateral Single shot 15–20 mL of 0.25%–0.375% bupivacaine or levobupivacaine Intermittent boluses through a multihole catheter 15–20 mL of 0.25% bupivacaine or levobupivacaine per site	Provide analgesia for the whole midline of the abdomen Shorter analgesic effect then TAP block
Liposomal bupivacaine	266 mg in 40 mL 0.9% normal saline	Use in the context of MMA phase IV studies. Limited evidence

Abbreviations: CEI, continuous epidural analgesia; MMA, multimodal analgesia; PACU, postanesthesia care unit; PCEA, patient-controlled epidural analgesia; TAP, transversus abdominis plane block; TEA, thoracic epidural analgesia; US, ultrasound.

[a] Supplementary analgesia is needed in patients undergoing abdominal perianal resection, in whom perianal pain (S1–S3 dermatomes) is not covered by TEA.

Supplementary analgesia is required in patients undergoing abdominal perianal resection, in whom perianal pain (S1–S3 dermatomes) is not controlled by TEA. Evidence supporting the use of epidural clonidine is inconclusive, and the risk of arterial hypotension and sedation is increased.[118] It remains unclear as to whether TEA improves postoperative surgical outcomes, especially in the context of an ERAS program. Compared with parenteral opioids, epidural infusion of low-dose local anesthetic and short-acting opioids has been shown to provide better postoperative static and dynamic analgesia for the first 72 hours,[119] accelerate the recovery of gastrointestinal function,[120] reduce insulin resistance,[121] and impact positively on cardiovascular and respiratory complications.[67,122] However, arterial hypotension, urinary retention, pruritus, and lower limb weakness are common side effects.[123] Arterial hypotension induced by TEA reduces splanchnic circulation,[124] and it does not respond to intravenous fluid administration.[101] Nevertheless, improvement of mean arterial pressure with small doses of vasopressors restores splanchnic perfusion[101] and does not impair colonic oxygen delivery.[102] Orthostatic hypotension associated with postoperative epidural analgesia does not impair the ability to ambulate.[125] When TEA analgesia is contraindicated, intraoperative and postoperative intravenous lidocaine infusion or spinal analgesia with intrathecal morphine can be used. Although systemic local anesthetic toxicity is rare, postoperative intravenous lidocaine infusion requires continuous cardiovascular monitoring. Abdominal trunk blocks, such as transversus abdominis plane (TAP) block[126,127] and rectus sheath block, or continuous wound infusion of local anesthetic,[128,129] can be performed at the end of surgery with the purpose of improving postoperative pain, reducing opioid side effects, and hastening recovery (see **Fig. 1**, **Table 4**).

Analgesia for Laparoscopic Colorectal Surgery

The use of TEA for patients undergoing laparoscopic colorectal surgery remains controversial. If the only purpose of using TEA is to control postoperative pain, its use seems unnecessary or sometimes disadvantageous,[130] especially in a context of an ERAS program.[131,132] Although pain scores can be statistically lower in the first 24 hours after surgery, patients not receiving TEA still report adequate analgesia (nutritional risk score <4).[133] The use of TEA remains valuable in patients at high risk of postoperative respiratory complications,[122] in those with high probability of conversion to laparotomy, and in patients with an 8- to 10-cm Pfannenstiel-like incision after laparoscopic rectal surgery, especially in the first 24 hours.[134] TEA seems to facilitate the recovery of bowel function, even after laparoscopic procedures,[135] when compared with patients receiving systemic opioids and without an ERAS program. However, faster recovery of bowel function does not necessarily translate into faster surgical recovery, as colorectal patients treated with TEA in the context of an ERAS program have a longer hospital stay[71] and medical recovery[132] than those receiving spinal analgesia or systemic opioids. Alternative and safer analgesic techniques have been shown to provide similar analgesia without delaying discharge. These approaches include intrathecal morphine with local anesthetic,[71] intravenous lidocaine,[60] the use of ultrasound-guided abdominal trunk blocks,[136] and intraperitoneal local anesthetic.[133,137] TAP block under direct laparoscopic vision has also been successfully used.[138–140] Continuous would infusion of local anesthetic has been successfully used in one feasibility study (see **Fig. 1**, **Table 4**).[141]

Coanalgesia

Nonsteroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors and acetaminophen (orally, per rectum, and intravenously) are commonly used as part of multimodal analgesic regimens as opioid-sparing strategies. Intravenous preparations are particularly valuable in the perioperative period, as oral and rectal bioavailability is unpredictable after gastrointestinal surgery. Furthermore, suppositories are not usually administered in patients with rectal anastomosis. Recent concerns have been raised about the risk of anastomotic leakage and the use of NSAIDs or COX-2 inhibitors after colorectal surgeries based on experimental, retrospective, observational, and case-series studies.[142] This effects seems to be class specific (the risk of anastomotic leakage is higher with NSAIDs than COX-2 inhibitors),[143] molecule specific (diclofenac is associated with the highest risk)[142] and time dependent.[143] Large RCTs are needed to confirm these results. Although not statistically significant, a trend toward higher risk of developing anastomotic leakage after bowel surgery was reported in a recent meta-analysis of 6 RCTs (480 patients) of patients receiving at least 1 dose of NSAIDs or COX-2 inhibitors within 48 hours of surgery (Peto odds ratio

2.16; 95% confidence interval 0.85–5.53).[144] Caution should be used in patients at high risk of anastomotic leakage. α_2-Agonists, glucocorticoids, gabapentinoids, and ketamine have been poorly studied in colorectal patients, and their use in other types of surgery has shown conflicting results. Wound infiltration with long-acting multivesicular liposome formulation of bupivacaine as part of multimodal analgesic regimens has also shown promising results.[145,146]

SPECIAL CONSIDERATIONS FOR PATIENTS UNDERGOING ONCOLOGIC COLORECTAL SURGERY

Most patients undergo colorectal surgery because of precancer or cancer lesions. In the last years, many in vitro and in vivo experimental studies and retrospective human studies have attempted to establish the impact of many perioperative factors on oncologic outcomes. Associations have been reported but causation has never been proved. Nutritional status and factual capacity of colorectal patients are negatively affected by neoadjuvant chemotherapy and cancer cachexia. In this context, prehabilitation might positively affect surgical recovery.[34] Side effects and complications associated with specific chemotherapy agents must be considered. Opioids have been shown to have an immunosuppressive effect, mainly suppressing natural killer cell activity, but the effect on cancer recurrence and metastasis remains unknown. NSAIDs might have a direct and indirect anticancer effect.[147] Intravenous lidocaine has also shown an antitumor effect at plasma concentrations observed in clinical practice.[148] By contrast, in a small sample of patients, dexamethasone has been recently associated with cancer recurrence after elective colectomy.[149] Minimizing opioid consumption, and favoring regional anesthesia techniques and nonopioid analgesics might be even more valuable in patients with cancer. Allogeneic blood transfusions have also been associated with worse oncologic outcomes.[150] At present, there is insufficient evidence to justify changing anesthesia and analgesia practice or perioperative care in the prevention of cancer recurrence or metastasis in patients with colorectal cancer.

SPECIAL CONSIDERATIONS FOR PATIENTS UNDERGOING EMERGENCY COLORECTAL SURGERY

Indications for emergency colorectal surgery include colon perforation, bowel obstruction, bowel ischemia, bleeding, and anastomotic leakage. Early optimization of hemodynamics to ensure optimal oxygen delivery and early antibiotic therapy when indicated are key elements, especially before the induction of anesthesia. Dehydration, hypovolemia, and electrolyte derangements are commonly observed in patients with bowel obstruction. Septic patients with peritonitis secondary to bowel perforation, intra-abdominal abscess, or anastomotic leakage should be treated according to international guidelines.[151] In these patients, advanced hemodynamic monitoring to guide fluid therapy is recommended,[96] and administration of inotrope and vasopressors might be required. For these reasons, the insertion of arterial and central lines before the induction of anesthesia is advised. Aspiration through nasogastric tubes (when already inserted), preoxygenation, and rapid sequence induction of anesthesia with cricoid pressure is required because of the high risk of pulmonary aspiration. If not carefully titrated, administration of induction agents can catastrophically induce hypotension, especially in septic patients with an already reduced vascular tone and increased vascular permeability. Assessment of fluid responsiveness is critical, as unnecessary administration of crystalloids to treat hemodynamically unstable patients causes interstitial edema and increases morbidity. Colloids should be avoided in septic patients.[108] Markers of systemic organ hypoperfusion such as

Table 5
ERAS elements under direct control of the anesthesiologist: key points

ERAS Elements Under Direct Control of Anesthesiologist	Key Points
Patient education	Preoperative patient education is an essential component of any ERAS program It is important to specify the active role the patient is expected to play in the perioperative period Written or visual information at an appropriate literacy level, specifying daily goals for nutritional intake and postoperative ambulation, discharge criteria, and expected hospital stay should be provided
Preoperative evaluation, risk stratification, and optimization	Optimize preoperative conditions associated with poor outcomes include patient comorbidities, nutritional status, anemia, and functional capacity Intense smoking cessation interventions including NRT and individual counseling for at least 3–4 wk before surgery to reduce postoperative complications More studies evaluating the role of optimizing preoperative conditions to a point to delay surgery in patients undergoing oncologic colorectal surgery are warranted
Preoperative fasting and preoperative oral carbohydrate (CHO) drinks	There is no scientific evidence to support policy of routine NPO after midnight Fasting from midnight increases insulin resistance and depletes glycogen reserves. These effects are magnified by the stress response induced by surgery Current preoperative fasting guidelines for adult patients undergoing elective surgery recommend a 2-h fast for liquids and a 6-h fast for solids Preoperative oral CHO drinks are safe, reduce insulin resistance, and improve patients' well-being
Antibiotic prophylaxis	Antibiotic prophylaxis for patients undergoing colorectal surgery must cover aerobic and anaerobic flora, according to international guidelines Antibiotic prophylaxis should be completed within 1 h before surgical incision. Intraoperative dosing depends on the half-life of the antibiotic used and on the surgical blood loss. It should not last more than 24 h
Premedication	Patients should not routinely receive anxiolytic agents The use of short-acting anxiolytic agents is advised to facilitate invasive procedures uncomfortable for patients (epidural, arterial lines, etc) Benzodiazepine should be avoided in patients older than 65 y
Anesthetic agents and cerebral monitoring	The use of short-acting inhalation or intravenous agents is advised TIVA with propofol should be considered in patients at high risk of PONV Avoid N_2O Monitoring depth of anesthesia reduces anesthetic requirement, minimizes anesthetic hemodynamic effects, and can be particularly useful in elderly patients to facilitate recovery
Attenuation of surgical and inflammatory stress	Attenuation of surgical stress is a key element in enhancing recovery The use of regional anesthesia techniques, glucocorticoids, intravenous lidocaine, and prevention of hypothermia has been shown to attenuate the stress response associated with surgery

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Table 5
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ERAS Elements Under Direct Control of Anesthesiologist	Key Points
Intraoperative analgesia	Regional anesthesia techniques, including TEA and spinal anesthesia, reduces anesthetic and systemic opioid requirements The analgesic and anti-inflammatory properties of intravenous lidocaine has been shown to reduce anesthetic and opioid consumption, reduce opioid side effects, and hasten recovery Ketamine, α_2-agonists, and other analgesic adjuvants have shown opioid-sparing properties, but their role in colorectal patients and in the context of an ERAS program has not been studied
Intraoperative ventilation	Intraoperative lung-protective ventilation with low tidal volumes (V_T = 6–8 mL/kg, IBW), adequate PEEP (6–10 cmH_2O), and lung recruitment maneuvers is beneficial (reduced inflammation and better outcomes) even in patients with uninjured lungs undergoing abdominal surgery Intraoperative oxygen therapy (Fio_2) should be titrated to the most favorable concentration that ensures optimal tissue oxygenation based on the evaluation of oxygen saturation, arterial partial oxygen pressure (Pao_2/Fio_2 ratio), and serum lactates The use of intraoperative high-inspired oxygen fraction (Fio_2 = 0.8) to prevent surgical-site infections has shown conflicting results. However, patients undergoing colorectal surgery might particularly benefit from this intervention
Myorelaxation	Short- or intermediate-acting muscle relaxants are recommended Adequate muscle relaxation is essential to guarantee optimal surgical conditions, especially during laparoscopic colorectal surgery Neuromuscular blockade must be monitored (TOF, double-burst, or tetanic stimulation pattern) throughout the intraoperative period. Quantitative assessment (acceleromyography) of neuromuscular function is more reliable than qualitative assessment (visual or tactile) in identifying patients with residual paralysis
Prevention of hypothermia	Core temperature must be monitored and hypothermia (core temperature <36°C) avoided
Intraoperative hemodynamic management	In colorectal patients treated within an ERAS program, minimization of preoperative fasting, avoidance of MBP, a more rational and evidence-based intravenous fluid administration, and early resumption of oral intake have significantly reduced the amount of perioperative intravenous fluids needed GDT seems beneficial in high-risk patients and in patients undergoing surgery with extensive blood loss (>7 mL/kg) Iso-oncotic crystalloid solutions should be used and 0.9% saline solutions avoided Colloid should be avoided in patents with preexisting renal diseases and in septic patients Anemia thresholds triggering blood transfusions cannot be currently recommended, as hemoglobin levels resulting in tissue hypoxia are patient-specific The decision to transfuse blood should be made on an individual basis, depending on the clinical context, serum lactate levels, central oxygen venous saturation, and patient comorbidities
PONV prophylaxis	PONV prophylaxis is an essential to facilitate early feeding Patients at high risk of PONV can be identified PONV prophylaxis guidelines must be followed

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Table 5
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ERAS Elements Under Direct Control of Anesthesiologist	Key Points
Glycemic control	Hyperglycemia is associated with worse outcomes Preoperative hemoglobin A_{1c} >6.0% can predict hyperglycemia and postoperative complications even in nondiabetic patients Maintain glycemia <10 mmol/L
Postoperative analgesia	The choice of the analgesia depends on the surgical approach (laparotomy or laparoscopy), the site of the surgical incision (midline, transverse, semicurve, or Pfannenstiel-like incision), the type of surgery (colon or rectum), and patient comorbidities TEA remains the goal standard for postoperative pain control for patients undergoing open colorectal surgery. However, TEA increases the risk of arterial hypotension Spinal analgesia with intrathecal morphine, abdominal trunk blocks, intravenous lidocaine, continuous wound infiltration of local anesthetic, and wound infiltration with liposome bupivacaine are valuable analgesic techniques, especially for laparoscopic colorectal surgery A multimodal analgesic approach is recommended with the aim of providing optimal analgesia and reducing opioid consumption and side effects, with the ultimate goal of facilitating early feeding and early postoperative mobilization

Abbreviations: GDT, goal-directed therapy; IBW, ideal body weight; MBP, mechanical bowel preparation; NPO, nothing by mouth; NRT, nicotine replacement therapy; PEEP, positive end-expiratory pressure; PONV, postoperative nausea and vomiting; TEA, thoracic epidural analgesia; TIVA, total intravenous anesthesia; TOF, train-of-four.

serum lactate, base excess, and low oxygen venous saturation might help to guide fluid therapy, but alternative explanations other than hypoperfusion should be also considered, especially in anemic patients, septic patients, and patients receiving catecholamines.[152] Titrating anesthetic depth based on cerebral monitoring helps to minimize the hemodynamic effects of the anesthetic agents. Regional anesthesia techniques are frequently contraindicated because of coagulopathy and infections. Postoperative monitoring in high-dependency units or intensive care units may be required. Early-warning scoring systems can help to identify patients who require advanced postoperative care.[153]

Key points summarizing each ERAS element for patients undergoing elective colorectal are listed in **Table 5**.

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