Anesthesia and perioperative management of colorectal surgical patients – A clinical review (Part 1)

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Abstract

Colorectal surgery is commonly performed for colorectal cancer and other pathology such as diverticular and inflammatory bowel disease. Despite significant advances, such as laparoscopic techniques and multidisciplinary recovery programs, morbidity and mortality remain high and vary among surgical centers. The use of scoring systems and assessment of functional capacity may help in identifying high-risk patients and predicting complications. An understanding of perioperative factors affecting colon blood flow and oxygenation, suppression of stress response, optimal fluid therapy, and multimodal pain management are essential. These fundamental principles are more important than any specific choice of anesthetic agents. Anesthesiologists can significantly contribute to enhance recovery and improve the quality of perioperative care.

Key words: Analgesia, anesthesia, colorectal, intestinal, perioperative

Introduction

Colorectal (CR) surgery for cancer, diverticular, or inflammatory diseases is a high-risk surgery. Other indications for CR surgery include ischemic colitis, iatrogenic perforation or injury, and volvulus. For the successful anesthetic management and a favorable perioperative outcome, an understanding of basic sciences specific for CR surgery [e.g., colon blood flow (CBF) and stress response], preoperative assessment, and fluid and pain management is required. In addition, evidence-based principles of enhanced recovery and multidisciplinary team efforts can significantly help minimizing the incidence of complications [Figure 1]. A detailed and comprehensive review of anesthetic management and perioperative care of CR surgery is lacking in literature. Major anesthesia textbooks contain either no or only minimal specific educational material relating to these patient. This review focuses on anesthesia practice, techniques, postoperative care pathways, and care including pain relief.

Colon blood flow and oxygenation

Perioperative factors affecting CBF are not well studied in humans. Preoperative medical conditions which may predispose colonic tissue to hypoxia include smoking, atherosclerosis, cardiac failure, and sickle cell anemia. During the perioperative period, CBF is affected by blood gas...
composition,\textsuperscript{11} volume status,\textsuperscript{12} intra-abdominal pressure,\textsuperscript{13} intraluminal pressure,\textsuperscript{14} type and volume of fluid therapy,\textsuperscript{15} anesthetic agents and anesthetic techniques,\textsuperscript{6,7} and critical conditions such as hemorrhage\textsuperscript{16} and sepsis.\textsuperscript{17} It would be difficult to predict changes in CBF when many of these factors coexist during surgery or the postoperative period.

Regional anesthetic techniques increase CBF by causing sympatholysis. This has been shown with both spinal\textsuperscript{18} and epidural techniques. In a canine model, high spinal anesthesia increased CBF by 22% and decreased vascular resistance by 44%, while the oxygen consumption of the colon was reduced significantly.\textsuperscript{18} In human patients, epidural block with local anesthetic has a favorable effect on colonic blood flow and oxygenation.\textsuperscript{19}

**Preoperative assessment**

Significant number of patients aged over 75 years present with rectal cancer. Kingston et al. found that the general fitness of a patient is a better predictor for outcome after surgery for CR cancer than chronological age.\textsuperscript{20}

Anemia, electrolyte imbalance, nutritional deficiency (e.g., hypoalbuminemia), and weight loss should be identified and corrected. In elective cases for noncancer surgery, a detailed evaluation and treatment of medical problems are possible. However, in patients requiring cancer or urgent surgery (e.g., for obstruction or perforation), time may be limited. During emergency surgery, the main goals are to identify deteriorating vital physiological end organ functions and their causes, e.g., sepsis and hypovolemia. History, clinical examination, a review of monitored parameters, and laboratory investigations (e.g., arterial blood gas analysis and serum electrolytes) are vital to judge the severity of problems (e.g., fluid deficit). Cardiac and respiratory diseases are commonly present among the patients undergoing major CR surgery. One third of the patients may have significant cardiac or pulmonary problems during the preoperative period.\textsuperscript{21} Cardiopulmonary exercise testing (CPET) has been suggested as an integrated objective measurement of functional reserve and is useful in predicting complications and outcome. The results of CPET have a high predictive value for patients at risk of developing cardiopulmonary complications in the postoperative period.\textsuperscript{13} In a study by Snowden, the anaerobic threshold (AT) was lower in the group with more than one complication (11.9 vs. 9.1 ml/ kg/ min; \( P=0.001 \)).\textsuperscript{14} Wilson et al. studied the predictive value of AT and ventilatory equivalent for carbon dioxide (VE/VCO\textsubscript{2}) using CPET for patients undergoing high-risk surgery. They demonstrated a VE/VCO\textsubscript{2} > 34 and an AT \( \leq 10.9 \) ml/kg/min were significant predictors of all-cause hospital and 90 days mortality. They also found that CPET was more useful in predicting the risk of death in patients with no history of ischemic heart disease or risk factors for it.\textsuperscript{15}

**Scoring systems**

Various risk indices and scoring systems have been used to stratify risk for patients undergoing gastrointestinal surgery.\textsuperscript{16} Clinical risk indices are derived from history, functional capacity, physical examination, serum markers, and variables specific to surgery such as the urgency of surgery. The Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) and Portsmouth-POSSUM (P-POSSUM) were developed in 1991 and 1996, respectively. The POSSUM-based scoring system predicts complications and outcome.\textsuperscript{17} The specialty-specific CR POSSUM (CR-POSSUM), which uses 10 measures (6 physiological and 4 operative), was developed in 2004 and is easier to use, more accurate, and has been validated.\textsuperscript{18} Ferjani et al. compared POSSUM-based scoring systems to the ACPGSI (Association of Coloproctology of Great Britain and Ireland) score. They found that the ACPGSI and the CR-POSSUM were significantly better predictors of overall 30 day mortality for CR cancer than POSSUM and P-POSSUM.\textsuperscript{20} In the US, the National Surgical Quality Improvement Programme (NSQIP) has been applied to provide risk adjusted 30-day outcome data, but its application to other health care providers is limited.

**Preoperative preparation**

To improve recovery after CR surgery, traditional clinical measures such as mechanical bowel preparation (MBP) and routine insertion of nasogastric tubes have been challenged. It does not prevent any abdominal infectious complications but may increase cardiac complications.\textsuperscript{20} It is also associated with a poor patient experience. One recent meta-analysis\textsuperscript{21} and guideline\textsuperscript{22} suggest that the routine use of MBP should be omitted in elective CR surgery. Routine insertion of nasogastric tubes is not recommended as their use is associated with a delayed return of bowel function and an increase in pulmonary complications.\textsuperscript{23}

**Antibiotic prophylaxis**

Nelson et al., in a review comprising more than 30000 patients in 182 trials, concluded that the antimicrobial prophylaxis with aerobic and anaerobic coverage reduces surgical site infection by 75%.\textsuperscript{24}

**Preoperative nutrition and carbohydrate loading**

Hypoalbuminemia, anemia, and weight loss are common in CR patients. Some patients, e.g., those with Crohn’s disease, may not tolerate an enteral diet. Enteral intake with high-energy drinks and parenteral nutrition if enteral
feeding is not tolerated should then be commenced. Poor nutritional status, particularly hypoalbuminemia, has been associated with increased postoperative complications such as infections and increased length of hospital stay. Preoperative oral carbohydrate loading has been shown to reduce preoperative patient discomfort, postoperative insulin resistance, loss of muscle mass, postoperative nausea and vomiting (PONV), and to improve muscle strength. Preoperative carbohydrates are also beneficial for enhanced recovery and reduce length of stay. A thorough nutritional assessment and nutrition management guidelines (with support from nutritional units) reduce the unnecessary use of total parenteral nutrition, time spent “nil by mouth,” and hospital stay. There are conflicting reports regarding benefits of preoperative immunonutrition on requirement of total parental nutrition or reduced infection rates.

Chewing gum
Gum chewing mimics feeding and promotes peristalsis via neural and hormonal mechanisms which increases the secretion of gastrointestinal juices and bowel motility and reduces postoperative paralytic ileus. It is a safe, effective, and economical means to reduce time to feeding and hospital stay.

Stress and immune responses
Preoperative nutritional support, presence or absence of peritonitis, intraoperative use of anesthetic agents and anesthetic technique employed, perioperative use of adjuvants such as beta-blockers or alpha-agonists, postoperative analgesia, and patient pathway (e.g., conventional or enhanced recovery program) may modify the stress response. Surgical factors which influence the stress response during CR surgery are duration of open surgery, urgency of surgery, open vs. laparoscopy techniques, and amount of blood loss and blood transfusion. An exaggerated stress response has been associated with postoperative bowel dysfunction, fatigue, delayed wound healing, infectious complications such as wound infection, anastomotic leak and cardiopulmonary complications. It may delay recovery, increase susceptibility for metastasis in cancer patients, and have long-term side effects such as the formation of adhesions. The recovery of a suppressed immune function is faster in laparoscopic surgery and this may influence recurrence in cancer surgical patients.

Modification of stress response
Several strategies to counteract the catabolic stress response have been suggested. Shortened fasting periods, use of nutritional support and glycemic control, laparoscopic surgery, and epidural analgesia have all been shown to be beneficial. Tyman et al. found no differences in inflammatory response among CR cancer surgery patients receiving either total intravenous anesthesia with propofol and remifentanil or inhalational anesthesia with sevoflurane and fentanyl, except raised IL-17 levels and hyperglycemia. With the use of intraoperative thoracic epidural anesthesia, plasma concentrations of epinephrine and cortisol were significantly lower and lymphocyte numbers and T-helper cells were significantly higher in a study by Ahler et al. Systemic lidocaine used during CR surgery also has anti-inflammatory actions and is a useful alternative to suppress the stress response in patients who are not suitable for epidural analgesia. Methyl prednisolone administered preoperatively in colon cancer patients modified the stress response and was found to improve both pulmonary function and postoperative pain, as well as to reduce length of stay regardless of the surgical technique used. During open surgery, the administration of 8 mg dexamethasone was associated with significantly lower peritoneal interleukin (IL) 6 and IL-13 concentrations on day 1 and significantly reduced early postoperative fatigue. Nonsteroidal anti-inflammatory drugs (NSAID) like parecoxib and flurbiprofen and pentoxifylline may also be useful. There is increasing evidence that a multimodal approach to perioperative care markedly reduces surgical stress and enhances recovery after major CR surgery.

Intraoperative anesthetic management
The goals of perioperative anesthetic management for CR surgical patients are minimizing stress and immune responses, maintaining systemic and colonic blood flow and oxygenation, meticulous fluid and electrolyte therapy, multimodal analgesia, and prevention of postoperative gut dysfunction. The perioperative use of B-blockers and a2-agonists may be useful, particularly for high-risk patients. However, their routine use is not recommended until large studies showing clinical benefits in this specific surgical population are available. Antiemetics should be considered to prevent PONV. Other factors can also influence the incidence of PONV. In comparison to 30% oxygen, supplemental oxygen at 80% has been found to reduce the incidence of PONV two- to five-fold after CR surgery, possibly due to decreased serotonin levels in plasma. Maintaining perioperative normothermia reduces postoperative cardiac and coagulation complications and should be standard care during colon surgery. Hypothermia causes several undesirable systemic changes, including an exaggerated stress response and suppression of the immune function in patients undergoing CR surgery. Active thermoregulation should be carried out both during open and laparoscopic CR surgery, as the reduced bowel exposure during the latter
does not compensate for the marked effects of anesthesia on temperature regulation.\cite{60} During laparoscopic surgery, systemic physiological changes due to pneumoperitoneum may cause cardiorespiratory problems. Patients should be carefully positioned and their positioning carefully maintained to prevent Trendelenburg position-related complications. Brachial plexus injury\cite{61} and lower limb compartment syndromes\cite{62,63} have been reported with laparoscopic large bowel surgery.

General anesthetic agents and technique
At present, there is no evidence to recommend specific anesthetic or analgesic agents for CR surgical patients. However, short acting agents are useful if patients are for fast track CR surgery. During prolonged laparoscopic-assisted surgery, sevoflurane-based anesthesia was associated with earlier eye opening and tracheal extubation in comparison to propofol-based anesthesia. In the latter group, the incidence of postoperative colon dysfunction (POCD) on day 2 and day 3 was higher.\cite{64} For open surgery, Jenesen et al.\cite{65} studied three different anesthetic techniques (isoflurane/nitrous oxide, propofol/air, or propofol/nitrous oxide), with fentanyl and vecuronium. There were no significant differences in overall recovery, bowel function (passage of flatus and oral intake), postoperative hospital stay, and complications. Volatile agents differ in their effects on CBF and oxygenation. Muller et al.\cite{66} studied the effects of desflurane and isoflurane on intestinal tissue oxygen pressure during open CR surgery. On completion of the anastomosis, mean tissue oxygen pressure was higher in the isoflurane group than in the desflurane group. This may be due to preservation of reactive hyperemia by isoflurane. No difference between groups could be observed with regards to splanchnic hemodynamics and global oxygenation. Intraoperative use of xenon decreased superior mesenteric artery blood flow, but had no detrimental effect on colon oxygenation.\cite{67} During CR surgery, diffusion of nitrous oxide (N\(_2\)O) into the bowel lumen may cause distention and might therefore affect surgical handling and bowel recovery. Scheilein et al.\cite{68} found an earlier return of bowel function with air in comparison to N\(_2\)O during isoflurane anesthesia. In contrast, Krough et al.\cite{69} found no differences between air and N\(_2\)O in terms of postoperative bowel function and recovery. The use of N\(_2\)O is not associated with a recurrence of CR cancer.\cite{70} Use of neostigmine has been suggested to be hazardous during the use of bowel surgery. Doses as little as 0.5 mg were associated with violent bowel contractions with intraluminal pressures increasing markedly up to 70 mm of H\(_2\)O.\cite{71} In addition, it decreased CBF up to 50% in some animals, which was attributed to a decrease in cardiac output and/or contractility. Fortunately, effects are less severe if an anticholinergic is used simultaneously.\cite{71}

Use of regional analgesia and anesthesia
Epidural analgesia is recommended for open CR surgery.\cite{72} In the case of laparoscopic surgery, an epidural may be beneficial if the patient has significant preoperative respiratory disease. It may be beneficial to insert an epidural catheter if conversion to open surgery is likely. Sole regional anesthesia, e.g., combined spinal-epidural technique, is possible for low anterior resections of the rectum.\cite{73} The use of intraoperative thoracic epidural anesthesia and analgesia has been associated with an increase in colonic blood flow\cite{16,74} and better gastrointestinal recovery. Pain control with epidural analgesia does not, however, affect the incidence of CR cancer recurrence.\cite{75} Spinal with light general anesthesia has also been found to be beneficial.\cite{76,77} Recently, Kumar et al. reported continuous spinal anesthesia using microcatheter for high-risk patients.\cite{78} A wide variety of CR surgical procedures were performed with anesthetic block height T6-T7. After establishing spinal anesthesia with heavy 0.5% bupivacaine and fentanyl, 0.5% isobaric bupivacaine was used to extend spinal anesthesia. However, the microcatheter was removed at the end of surgery.

Optimization of hemodynamics
Several studies have demonstrated that, for patients undergoing CR surgery, goal-directed hemodynamic management reduces postoperative gastrointestinal complications.\cite{79} Fluids alone or fluids and inotropes are used to achieve defined end points. Flow-, pressure-, or volume-based goals have been used.\cite{79} Interestingly, intraoperative\cite{80} or postoperative\cite{81} changes in central venous oxygen saturation (ScvO\(_2\)) have been found to predict complications. Intraoperative maintenance of ScvO\(_2\) > 73% may prevent complications.\cite{80} The perioperative use of dopexamine to improve the splanchnic circulation is controversial. Davies et al. studied high-risk patients (anaerobic threshold T of ≤11 ml/kg/min or an AT of 11–14 ml/kg/min with a history of ischemic heart disease). Low-dose dopexamine (0.5 mcg/ kg/min) was administered with goal-directed fluid therapy. It was associated with earlier enteral diet tolerance, but there were no differences in complications or length of stay.\cite{82} Stroke volume guided fluid and low-dose dopexamine therapy may improve global oxygen delivery, microvascular flow, and tissue oxygenation.

Postoperative care
Recovery after open CR surgery can be hastened by adopting perioperative evidence-based practices. This approach is described as “enhanced” or “fast track” or “accelerated” recovery after surgery.\cite{83}

Recovery – conventional or enhanced
Recovery pathways, enhanced or conventional, should be managed by multidisciplinary teams involving anesthesiologists, surgeons, nursing staff, nutritional experts, acute pain...
team, pharmacists, and physiotherapists. In comparison with conventional postoperative management, enhanced recovery pathway (ERP) is associated with a reduced postoperative morbidity (14.8% vs. 33.6%, respectively; \( P < 0.01 \)). However, it does not reduce mortality.\(^{[83]}\) ERP is recommended to reduce length of in-hospital stay.\(^{[84]}\) The aim is to reduce perioperative stress-related bowel and other organ dysfunction by incorporating a multimodal approach in perioperative care.\(^{[85]}\) ERP has not been widely implemented around the world yet,\(^{[86]}\) but even partial compliance with the components of ERP has shown to reduce hospital stays and improve patient satisfaction.\(^{[87]}\) Concerns about high readmission rates have been unfounded, and early discharge as a result of ERP does not lead to increased needs for home care, social care, or visits to general practitioners.\(^{[88]}\)

**Fluid therapy and nutrition**

Postoperative fluid therapy should take into consideration maintenance requirements, losses (insensible and sensible), and pathophysiological changes associated with major bowel surgery. There is no magic formula and an individualized approach is necessary. Restrictive fluid therapy during the postoperative period has been shown to be beneficial. There is no doubt that excessive fluid prescription to correct epidural or other systemic vasodilator-related hypotension is not justified and associated with more risks than benefits. There is no scientific basis for the traditional strategy to keep patients “nil by mouth” until flatus has been passed or bowel sounds heard, and there is no specific advantage to withhold early feeding within 24 h after CR surgery.\(^{[89]}\) Early enteral nutrition has several advantages, such as improved healing of intestinal anastomoses,\(^{[90,91]}\) preservation of gut barrier functions, a positive nitrogen balance, improved calorie intake, a reduced incidence of infectious complications,\(^{[92,93]}\) and reduced hyperglycemia and insulin resistance.\(^{[94]}\) Furthermore, septic complications and length of hospital stay were reduced in patients receiving early enteral feeding.\(^{[92,95]}\) Enteral nutrition along with epidural analgesia and forced mobilization improved nutrition uptake after CR surgery.\(^{[96]}\) Enteral nutrition is safe and more cost effective than parenteral nutrition (TPN), which requires a central line. It is also a care component of enhanced recovery.

**Pain management**

Postoperative pain relief after CR surgery has been reviewed in the literature. For open surgery, thoracic epidural analgesia is recommended. Other pain relief methods used for postoperative pain relief are patient-controlled analgesia (PCA), intrathecal (IT) analgesia, systemic lidocaine infusions, wound infusions, wound infiltration, and transversus abdominis plane (TAP) block. Opioids have significant side effects on the gastrointestinal tract, such as nausea, vomiting, inhibition of bowel motility, and constipation. Their use may delay the return of bowel function and oral intake. Peripheral opioid antagonists, such as avlimopan, have been shown to reduce the duration of paralytic ileus after colon surgery.\(^{[97]}\) In addition, NSAID and acetaminophen are commonly used to achieve multimodal analgesia. There is a concern about increased risk of anastomotic leaks with the use of cyclooxygenase 2 inhibitors.\(^{[98]}\) However, NSAIDs are widely used, and in our practice are routinely used as part of multimodal analgesia. The usefulness of other analgesics such as tramadol, gabapentin, and ketamine has not been studied for CR surgical patients, and they are not routinely recommended.

For laparoscopic CR surgery, there is no sufficient evidence for any specific postoperative analgesic method. Epidural analgesia may not offer the same benefits as in open surgery. However, epidurals may be indicated if patients have preoperative pulmonary morbidities and also if the procedure is converted to open surgery. One recent randomized controlled trial has shown an earlier return of bowel function with IT analgesia, compared to epidural analgesia.\(^{[99]}\) In contrast, Zingg et al.\(^{[100]}\) reported faster recovery of gastrointestinal function with epidural analgesia after laparoscopic surgery. Both are single centre studies involving small number of patients. There is a need for larger studies comparing analgesic regimens for laparoscopic CR surgery.

Thoracic epidural analgesia provides several benefits for open CR surgery [Table 1] and there is a strong evidence for its recommendation. Other techniques such as wound infusion with ropivacaine and systemic lidocaine infusion [Table 1] have also been reported after open surgery. These techniques may be useful if epidural is technically not feasible or contraindicated.

The choice of a specific technique or drug depends on its safety, efficacy, the patient’s comorbidities, and overall gastrointestinal, systemic, and clinical advantages and disadvantages [Table 1]. Detailed expert guidelines for pain relief after open and laparoscopic CR surgery are available on the Internet (www.postoppain.org).

**Conclusion**

CR surgery carries significant morbidity and mortality. Enhanced recovery programs, laparoscopic surgical approach, multidisciplinary team efforts, and integrated care pathways have improved the perioperative management for elective cases. There is a need for CR surgery specific education and research within our specialty. Such efforts should focus on basic and clinical sciences including CBF and oxygenation,
<table>
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<tr>
<th>Method (References)</th>
<th>Advantages/benefits</th>
<th>Disadvantages/risks</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Thoracic epidural [100-107]</td>
<td>GI: Improved intestinal blood flow, colon PO₂ and motility, better gastrointestinal recovery (short duration of ileus, time for first flatus, time for first bowel movement, time for intake of solids). Reduced incidence postoperative ileus. Non-GI: Main advantage reduction in stress response with open surgery and superior analgesia. Long-lasting effects on exercise capacity and health-related quality of life</td>
<td>GI: Role of epidural in the presence of GI sepsis not established Non-GI: As common to other surgery Effect of epidural-related hypotension on CBF, ambulation and other complications unknown.</td>
<td>No difference in length of stay (LOS), anastomotic leakages Better than any other pain relief method. More suitable for enhanced recovery after open surgery. However, may not provide same benefits for laparoscopic surgery</td>
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<tr>
<td>Patient-controlled analgesia (PCA) with opioids [108-109]</td>
<td>GI: No specific benefit Non-GI: Reduced pain scores, greater patient satisfaction (with PCA), no ceiling effect to analgesia</td>
<td>GI: Reduced GI motility, increased duration of postoperative ileus, constipation, PONV Non-GI: Inadequate pain relief and systemic side effects limit mobilization and physiotherapy</td>
<td>For laparoscopic surgery (compared to epidural) no difference found except pain control Opioid antagonists may be useful to counter GI side effects.</td>
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<tr>
<td>Wound infusion catheter [110-114]</td>
<td>GI: Reduced duration of paralytic ileus Non-GI: Reduced morphine consumption, Reduced LOS, Reduced postoperative pain scores, Better sleep quality, reduced postoperative diaphragmatic dysfunction</td>
<td>GI: Similar time for first bowel movement, flatus or mobilization, similar incidence of vomiting. Non-GI: Need special equipment May not be suitable if abdominal drains are inserted</td>
<td>Benefits not consistent in various studies. No difference in wound infection</td>
</tr>
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<td>Wound infiltration [115]</td>
<td>GI: No different to placebo Non-GI: Decreased pain scores, decreased Opioid requirement</td>
<td>GI: No different to placebo Non-GI: Short duration of action</td>
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<td>Transversalis abdominalis plane block [116]</td>
<td>GI: Early resumption of diet, no side effects of opioids Other: In compared to PCA morphine shorter hospital stay, With morphine PCA reduced opioid use</td>
<td>Technical skill needed</td>
<td>No RCT available to prove efficacy</td>
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<td>Intrathecal [99,117-121]</td>
<td>GI: In compared to epidural early return of bowel function after laparoscopic surgery Non-GI: Reduces immediate postoperative pain, reduced opioid consumption (in compare to PCA for open surgery). Shorter hospital stay and better pain control in one observational study for laparoscopic surgery</td>
<td>GI: Prolongation of postoperative ileus in one study, PONV Non-GI: Delayed awakening/sedation, limited duration of analgesia, pruritus</td>
<td>? Choice of technique for laparoscopic surgery.</td>
</tr>
<tr>
<td>Systemic lidocaine infusion [122]</td>
<td>GI: Reduced duration of postoperative ileus, PONV, time to first flatus, solid food intake and bowel movement Non-GI: Reduced anesthetic requirement during surgery, reduced postoperative pain scores/intensity, reduced opioid consumption Other: Reduced LOS, safe</td>
<td>Hypotension</td>
<td>No significant systemic toxicity or other adverse events</td>
</tr>
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<td>NSAIDs [123-125]</td>
<td>GI: Reduced duration of ileus (IV ketorolac with PCA) Non-GI: Better pain control (preincisional i.v. parecoxib), less postoperative confusion, Reduced LOS, reduced opioid consumption, Less IL-6 production (with preincisional i.v. parecoxib)</td>
<td>GI: Peptic ulceration, ?Anastomosis leak Non-GI: Other known side effects</td>
<td>IV ketorolac beneficial (improves pain control and reduced ileus) with morphine PCA for laparoscopic surgery</td>
</tr>
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**GI: Gastro-intestinal**
preoperative objective assessment, reduction of risk factors, perioperative stress, and fluid and pain management.

Acknowledgment

SP conceptualized the article. SP designed overall structure, figures and tables for part 1 and part 2. SP searched and collected literature for all sections. SP responded to reviewers’ comments and was responsible for revisions and correspondence.

SP wrote CBF and stress response sections. SP and UP wrote preoperative assessment and intraoperative management. SB and SP wrote preoperative preparation and postoperative care. JB and SP organized references and contributed for revision. Authors contributed for revision of their sections and for final revision.

References


