

Development and Implementation of a Colorectal ERAS Pathway

Developing and implementing an ERAS pathway is challenging for multiple reasons, but the rewards can be considerable.

CHRISTOPHER L. WU, MD

Professor of Anesthesiology
Director, ERAS Anesthesiology Programs
Department of Anesthesiology and Critical Care Medicine
The Johns Hopkins School of Medicine
The Armstrong Institute for Patient Safety and Quality
Johns Hopkins Medicine
Baltimore, Maryland

ANDY P. BENSON, MSN, CRNA

Chief, CRNA Division
Department of Anesthesiology and Critical Care Medicine
The Johns Hopkins School of Medicine
Johns Hopkins Medicine
Baltimore, Maryland

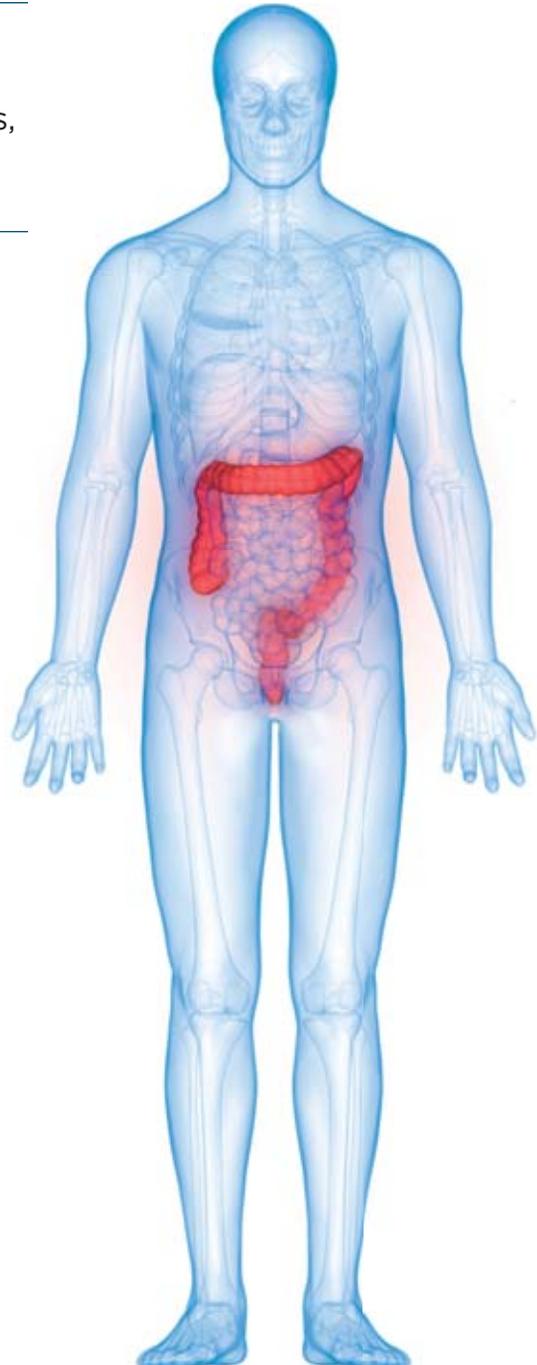
DEB B. HOBSON, RN

Department of Surgery
The Johns Hopkins University School of Medicine
The Armstrong Institute for Patient Safety and Quality
Johns Hopkins Medicine
Baltimore, Maryland

ELIZABETH C. WICK, MD

Associate Professor of Surgery
Department of Surgery
University of California, San Francisco School of Medicine
San Francisco, California

Dr Wu reported being on the advisory boards of Cara Therapeutics and Trevana. Drs Wu, Hobson, and Wick have received funding from the Agency for Healthcare Research and Quality. Dr Benson reported no relevant financial disclosures.



Introduction

Enhanced recovery after surgery (ERAS) pathways for patients can reduce variation in care and improve perioperative outcomes through the development and implementation of standardized, evidence-based perioperative pathways. The concept of “fast-track” surgery, introduced by Dr. Henrik Kehlet in the 1990s, has evolved into what we know today as ERAS programs, in which comprehensive, multidisciplinary (including surgery, anesthesiology, and nursing) perioperative care pathways, using evidence-based best practices when available, are developed and implemented to facilitate early recovery for patients undergoing surgery. Previously, ERAS pathways were used mostly in Europe, and the literature indicates that implementing ERAS pathways will result in decreases in hospital length of stay (LOS) and complications.^{1,2} Increased interest in ERAS pathways has been evident in the United States only in the past few years, partly due to the increased emphasis by payors on quality-based reimbursement and bundled payments.³⁻⁵

Initiation of an ERAS pathway may be challenging, as it is essentially an implementation of a culture change within an institution or department. The transition from a traditional siloed approach of perioperative care to a coordinated, multidisciplinary model that integrates diverse care components into an ideally seamless pathway can be difficult. At the Johns Hopkins Hospital (downtown Baltimore campus), we initially developed and implemented an evidence-based ERAS pathway for colorectal surgery and then expanded our ERAS pathways to liver resection, radical cystectomy, gynecologic oncology and pediatric surgery. We have plans to develop ERAS pathways for thoracic surgery, hyperthermic intraperitoneal chemotherapy (HIPEC), pancreatoduodenectomy, and breast surgery in the near

future. This article describes the process of how we developed our colorectal ERAS pathway, and the successes and challenges associated with its development and implementation.

Creating the Anesthesiology Portion of an ERAS Pathway

Because no two ERAS pathways are identical, there is no specific way to create an evidence-based, standardized anesthesiology regimen for any given ERAS pathway. There are general principles on which all ERAS pathways will be based, including optimization of perioperative nutrition, early mobilization, a multimodal analgesic regimen, and patient education. ERAS pathways may differ partly due to differences in available local resources and expertise. Many resources are available for the clinician interested in developing an ERAS pathway (Table 1).

For our colorectal ERAS pathway at Johns Hopkins Hospital at the downtown Baltimore campus, we were interested in not only decreasing LOS but also preserving perioperative immune function, which theoretically may reduce surgical site infections (SSIs) and cancer recurrence. Although we reviewed published pathways and guidelines, we created our colorectal pathway from scratch as our goal of preservation of immune function differed from most other pathways. An extensive PubMed literature search was conducted for each of the possible components of our colorectal pathway (Table 2). The results of each systematic literature search were carefully examined for relevant evidence, which was incorporated into a preliminary pathway.

Once a basic pathway was created, it was sent to the dedicated group of ERAS providers (anesthesiologists, CRNAs, surgeons, nurses) who reviewed the preliminary pathway and provided suggestions for changes.

Table 1. Resources for Developing an ERAS Pathway

Resource	Website	Available Items	Comments
American Society of Enhanced Recovery	aserhq.org	Sample pathways from several North American institutions; online newsletter	Implementation guide for members
ERAS Society	erassociety.org	Societal published guidelines	Other resources for purchase
Agency for Healthcare Research and Quality Safety Program for Enhanced Recovery After Surgery	ahrq.gov/professionals/quality-patient-safety/hais/tools/enhanced-recovery/index.html	Provides details for several CUSP programs that can be incorporated into ERAS pathways	Ongoing implementation project aims to help hospitals adopt the ERAS protocol using the CUSP method
American Society of Regional Anesthesia and Pain Medicine	asra.com	General educational materials on regional anesthesia and multimodal analgesia for patients and providers	Some sections only available to members

CUSP, Comprehensive Unit-based Safety Program; ERAS, enhanced recovery after surgery

Table 2. The Johns Hopkins Hospital (downtown Baltimore campus) Colorectal ERAS Pathway

Preoperative Phase
<p>1. Carbohydrate drink</p> <ul style="list-style-type: none"> Gatorade or clear liquid 2 h prior to surgery.
<p>2. Preoperative analgesics with sip of water:</p> <ul style="list-style-type: none"> Gabapentin 600 mg PO x 1 (do not give to patients on hemodialysis; 300 mg for patients with decreased renal function, age >70 y). Acetaminophen 1 g PO x 1 (do not give to patients with liver failure or elevated liver enzymes). Celecoxib 200 mg PO x 1.
<p>3. Preoperative antiemetic:</p> <ul style="list-style-type: none"> Scopolamine patch x 1 (do not give to patients with angle-closure [narrow angle] glaucoma; consider not giving to elderly patients).
<p>4. Convective warming blanket</p> <ul style="list-style-type: none"> To be started in the preanesthesia holding area.
Intraoperative Phase
<p>For All Patients:</p> <ul style="list-style-type: none"> Metronidazole 500 mg with no redosing/cefazolin 2 g (3 g for patients >120 kg) IV (clindamycin and gentamicin for penicillin allergy). Cefazolin should be redosed every 4 h. Heparin (unfractionated) 5,000 U SC at time of incision.
<p>5A. For Open Surgical Cases: Epidural anesthesia + TIVA</p> <ul style="list-style-type: none"> TIVA: propofol infusion titrated to BIS of 40-60; IV midazolam as needed. Epidural (T7-8): 2% lidocaine with 1:200,000 epinephrine as a test dose (3 mL) followed by a bolus (up to 10 mL in divided doses) to obtain T4 level. This is followed by an infusion of 2% lidocaine (no epinephrine) at 4-6 mL/h. Consider giving an appropriate bolus (4-6 mL) of 0.25% bupivacaine via epidural at end of case depending on clinical status of the patient. Muscle relaxant: Titrate to effect; will reverse at end of case. Opioids: Titrate as needed for breakthrough pain uncontrolled by epidural anesthesia.
<p>5B. For Laparoscopic Surgical Cases (or cases where epidural anesthesia is not used): TIVA + IV lidocaine</p> <ul style="list-style-type: none"> TIVA: propofol infusion titrated to BIS of 40-60; IV midazolam as needed. IV lidocaine infusion: 1.5 mg/kg bolus on induction + 1.5 mg/kg/h; stop prior to the end of surgery. TAP block for laparoscopic cases/ileostomy reversals. Muscle relaxant: Titrate to effect; will reverse at end of case. Opioids: Titrate as needed for breakthrough pain uncontrolled by IV lidocaine infusion.
<p>6. Adjuvant Analgesics:</p> <ul style="list-style-type: none"> Magnesium: 2 g/h rate to a total of 4 g (2-h infusion); start on induction. Ketorolac 30 mg IV at end of case if celecoxib not given preoperatively (decrease to 15 mg IV for age >75 y). Acetaminophen 1 g IV if oral acetaminophen not given preoperatively.
<p>7. Fluid Management (goal is euolemia):</p> <ul style="list-style-type: none"> Initial lactate Ringer's/PlasmaLyte carrier at 1-3 mL/kg/h. If hypotensive despite use of phenylephrine, additional boluses of 250-500 mL LR can be given; titrate to effect desired. May adjust carrier rate as desired for open abdomen maintenance or bolus as appropriate. May give albumin judiciously as needed. Phenylephrine infusion: Titrate to maintain appropriate blood pressure.
<p>8. Lung-Protective Ventilation Strategy; Oxygenation:</p> <ul style="list-style-type: none"> Tidal volume = 6-8 mL/kg of predicted body weight/PEEP 2-5 cm H₂O; 50% inspired FiO₂ intraoperatively.
<p>9. Antiemetics:</p> <ul style="list-style-type: none"> Ondansetron 8 mg IV 30 min prior to end of case.

Postoperative Phase

While Patient is NPO:

Patient-Controlled Epidural Analgesia:

- 0.0625% or 0.125% bupivacaine only at 4-6 mL/h + a demand dose of 2-4 mL every 10-20 min PRN (*no* fentanyl to start). Adjust as needed and continue ideally for at least 1 full day after patient tolerating oral intake including oral analgesics.

Adjuvant Analgesics (assuming no contraindications):

- Acetaminophen 1 g IV every 8 h (we are limited to 2 doses).
- Ketorolac 30 mg IV every 6 h (decrease to 15 mg IV every 6 h for age >75 y).
- Lidoderm patch: 1 patch every 24 h.

Breakthrough/PRN Analgesics:

- IV opioids PRN as needed.

When Oral Intake Resumes:

Scheduled Analgesics:

- Acetaminophen 1 g PO every 8 h.
- Ibuprofen 400 mg PO every 6 h.
- Gabapentin 100 mg PO 3 times a day.

Breakthrough/PRN Analgesics:

- Tramadol 50 mg PO every 4 h PRN (max dose 400 mg/d, or 300 mg/d age >75 y). (Avoid in patients with history of seizures and those taking SSRIs.)
- If tramadol fails, PRN opioid of choice (eg, hydromorphone 2 mg PO every 4 h prn; may also give IV PRN opioid breakthrough if PO opioid fails; no combination [with acetaminophen] products).

BIS, bispectral index; **ERAS**, enhanced recovery after surgery; **F_{IO₂}**, fraction of inspired oxygen; **NPO**, nothing by mouth; **PEEP**, positive end-expiratory pressure; **PO**, orally; **PRN**, as needed; **SC**, subcutaneously; **SSRIs**, selective serotonin reuptake inhibitors; **TAP**, transversus abdominis plane; **TIVA**, total intravenous anesthesia

Proposed changes were discussed and incorporated into a revised pathway, which was initiated for a group of several colorectal patients. Based on our initial clinical experience, further minor adjustments were made before the final pathway was rolled out in early 2014. We continue to update our pathway as new relevant literature is published.

Our Results

Upon implementation of our colorectal ERAS pathway, we saw an immediate decrease in LOS totaling approximately 2 days.⁶ This decrease has been maintained since we initiated this pathway in 2014. Our decreased LOS has also been seen in subsequent ERAS pathways (liver resection, radical cystectomy) at our institution (Table 3). In addition, we have seen a reduction in the rate of SSI, which dropped from 20.7% before ERAS (2013) to 7.3% after ERAS (2014).⁶ Our SSI rate for colorectal surgery continues in the range with our most recent data, showing an infection rate ranging from approximately 5.5% to 6.5% in the first half of 2016. In addition, we realized actual cost savings for the institution: a net savings of \$395,717 for the first year of the program compared with the cost of previous conventional perioperative care.⁷

Details of the Colorectal Pathway

The details of the colorectal ERAS pathway at Johns Hopkins Hospital are provided in this section together with the rationale and evidence behind our decisions, realizing that these selections were made in the context of our own overall goals and available resources at our institution/department. Other institutions/departments may make different choices based on their local goals and available resources and expertise.

Specifically, one of our main goals was to design a pathway to preserve perioperative immune function in an attempt to reduce perioperative infection and, theoretically, cancer recurrence. Our breakdown of the pathway into pre-/intra-/postoperative phases is for explanatory purposes only, as ideally an ERAS pathway should be thought of as a seamless continuum rather than siloed phases of care.

Preoperative Phase

During the preoperative surgical visit, the surgical team introduces the basic anesthesiology parts of the ERAS pathway, especially the use of epidural anesthesia in open cases and transversus abdominis plane (TAP) blocks in laparoscopic cases. More details of the anesthesiology portion of the colorectal ERAS pathway

are discussed in a patient booklet given at the time of the surgical preoperative visit.

1. Carbohydrate Loading: 20 oz of Gatorade is given up to 2 hours before surgery.

Rationale/evidence: Systematic reviews indicate that preoperative carbohydrate administration may be associated with an attenuation in postoperative insulin resistance, possible reduction in hospital LOS, and earlier return of bowel function.⁸⁻¹² Another systematic review indicated that there was no evidence to suggest that a shortened fluid fast resulted in an increased risk for aspiration or related morbidity, and drinking water preoperatively actually resulted in significantly lower gastric volumes.¹³ The American Society of Anesthesiologists allows clear liquids up to 2 hours and a light meal 6 hours before induction of anesthesia in healthy patients who are undergoing elective procedures.¹⁴

2. Analgesics: Gabapentin 600 mg PO x 1, acetaminophen 1 g PO x 1, celecoxib 200 mg PO x 1.

Rationale/evidence: Administration of nonopioid analgesics prior to surgery may result in preventive analgesia, improved postoperative pain, and decreased opioid use and opioid-related side effects. Several meta-analyses indicate that a single dose of preoperative gabapentin may be associated with decreased postoperative pain and opioid consumption, although this may be accompanied by an increased incidence of sedation, dizziness, and possibly blurred vision.¹⁵⁻²⁹ Initial randomized controlled trials of preoperative gabapentin used a dose of 1,200 mg, which is associated with significant sedation compared with lower doses (300-900 mg).²⁰ In addition, administering acetaminophen prior to surgery will decrease postoperative pain scores, opioid consumption, and incidence of postoperative vomiting.³⁰ Finally, nonsteroidal anti-inflammatory agents (NSAIDs) are potent analgesics and should be an integral part of most ERAS pathways. Several meta-analyses indicate a benefit of preoperative celecoxib on reducing postoperative pain, opioid use, and postoperative nausea and vomiting (PONV).^{31,32} Cyclooxygenase-2 (COX-2) inhibitors (eg, celecoxib) may be preferred prior to surgery as they have minimal effect on platelet function,³³ and a recent meta-analysis of COX-2 inhibitors revealed that these agents did not significantly increase the risk for perioperative bleeding.³⁴

3. Antiemetics: Scopolamine transdermal patch x 1 (other antiemetics to be given intraoperatively).

Rationale/evidence: Control of PONV is vital to facilitate patient oral intake and recovery, which is an important central goal of every ERAS pathway. Many of the antiemetic agents are typically administered during the intraoperative period to maximize their antiemetic effect, but some agents ideally should be administered in the pre- or early intraoperative time frame. Although dexamethasone is an effective and widely used antiemetic and exhibits analgesic properties,³⁵ we decided to omit it after discussion with our surgical colleagues who voiced some concerns about theoretical altered immune function. Systematic reviews on the perioperative use of

dexamethasone revealed no increase in SSI or delayed wound healing, but noted elevated glucose levels postoperatively.^{36,37} Instead, we chose to use transdermal scopolamine, which is initiated prior to surgery and has been shown to significantly reduce PONV.^{38,39}

In addition, the gabapentanoids given preoperatively, mostly for analgesia, may also exhibit antiemetic properties, with recent meta-analyses indicating that preoperative gabapentanoids may be associated with a reduction in PONV.^{20,40} Finally, the benzodiazepines commonly administered for sedation prior to surgery may also have antiemetic properties; recent meta-analyses have also indicated that perioperative midazolam may be associated with a reduction in PONV.^{41,42}

4. Thermoregulation: convective warming blanket to be started in the preanesthesia holding area.

Rationale/evidence: There is high-quality evidence linking maintenance of normothermia using preoperative and intraoperative warming with a decrease in SSI rates.⁴³ A collaborative guideline from the Society for Healthcare Epidemiology of America, Infectious Diseases Society of America, American Hospital Association, Association for Professionals in Infection Control and Epidemiology, and the Joint Commission recommends maintenance of normothermia (35.5°C or higher) during the perioperative period, based on Grade I evidence.⁴³ Other societies also recommend maintenance of normothermia during surgery in the perioperative period to reduce SSI.^{44,45} A meta-analysis of care bundles to reduce SSI in colorectal surgery noted that maintenance of normothermia was a component of almost all bundles in decreasing SSI.⁴⁶

Intraoperative Phase

A standardized, evidence-based intraoperative anesthetic pathway is an integral part of every surgical ERAS protocol and should incorporate core components of fluid management, multimodal analgesia with minimization of opioid use, prevention of PONV, and attenuation of the surgical stress response. Obviously, there are many possible combinations of anesthetic agents that can be used to achieve these goals, but the intraoperative anesthetic should be tailored to optimize anesthetic depth while facilitating rapid awakening after completion of the surgical procedure.

Our overall goals during this period are to preserve perioperative immune function by avoiding medications (eg, inhalation agents, opioids, possibly ketamine) or actions (eg, blood transfusions, hypothermia) that may contribute to perioperative immunosuppression. Our open colorectal cases receive epidural anesthesia (local anesthetic only, no opioids) with total intravenous anesthesia (TIVA) using propofol, whereas our laparoscopic cases receive TIVA with propofol, intravenous lidocaine infusion, and typically a TAP block postoperatively.

5A. For Open Surgical Cases: Epidural Anesthesia + TIVA

- TIVA: propofol infusion titrated to bispectral index (BIS) of 40 to 60; IV midazolam as needed.

- Epidural (at T7-8): 2% lidocaine with 1:200,000 epinephrine as a test dose (3 mL) followed by a bolus (up to 10 mL in divided doses) to obtain T4 level. This is followed by an infusion of 2% lidocaine (no epinephrine) at 4 to 6 mL per hour. Consider giving an appropriate bolus (4-6 mL) of 0.25% bupivacaine via epidural at end of case depending on the clinical status of the patient.
- Muscle relaxant: Titrate to effect; reverse at end of case.
- Breakthrough pain: If needed, use opioid first, then inhalation agent.

Rationale/evidence: Use of thoracic epidural analgesia results in superior postoperative analgesia (compared with opioids) and a decrease in some pulmonary/cardiac morbidity, and facilitates earlier return of gastrointestinal function.⁴⁸⁻⁵⁴ If used intraoperatively at appropriate doses, epidural anesthesia may attenuate the surgical stress response. We chose to avoid ketamine, inhalation agents, and opioids since these agents have been associated with immunosuppression,⁵⁵⁻⁵⁷ although they certainly can be (and are widely) used in other ERAS pathways with goals that differ from ours.

5B. For Laparoscopic Surgical Cases, or cases in which epidural anesthesia is not used: TIVA + IV lidocaine

- TIVA: propofol infusion titrated to BIS of 40 to 60; IV midazolam as needed.
- IV lidocaine infusion: 1.5 mg/kg bolus on induction + 1.5 mg/kg per hour; stop prior to the end of surgery.

TAP block for laparoscopic cases/ileostomy reversals.

- Muscle relaxant: Titrate to effect; reverse at end of case.
- Breakthrough pain: If needed, use opioid first, then inhalation agent.

Rationale/evidence: We do not use epidural anesthesia/analgesia for laparoscopic surgical procedures as the overall benefits of thoracic epidural analgesia (TEA) in improving recovery or decreasing LOS in these cases are uncertain (especially in the context of an ERAS pathway).⁵⁸⁻⁶⁰ Several meta-analyses of

perioperative IV lidocaine infusions indicate that they may result in decreased postoperative pain, reduced opioid consumption, and earlier return of bowel function.⁶¹⁻⁶⁸ The optimal dose and duration of the IV lidocaine infusion are uncertain, although the majority of randomized controlled trials (RCTs) have used a bolus of 1.5 mg/kg followed by an infusion of 1.5 mg/kg per hour⁶⁵; a meta-analysis noted that continuing an IV lidocaine infusion beyond 60 minutes after surgery provided no added analgesic or gastrointestinal benefit.⁶⁷ TAP blocks are generally performed under ultrasound guidance; several meta-analyses have indicated that use of TAP blocks is associated with lower pain scores, decreased opioid consumption, and possibly reduced opioid-related side effects.⁶⁹⁻⁷⁵

6. Adjuvant: Magnesium: 2 g per hour to a total of 4 g (2-hour infusion); start at induction

Rationale/evidence: Several meta-analyses indicate that systemic magnesium administered in the perioperative period is associated with significant decreases in postoperative pain scores and opioid consumption, without increasing adverse events.⁷⁶⁻⁷⁹ There is no consensus on the precise dosing or timing of perioperative magnesium administration.

7. Fluid Management: The goal is euvolemia. An initial lactated Ringer's/PlasmaLyte carrier is administered at 1 to 3 mL/kg per hour. A phenylephrine infusion is titrated to maintain appropriate blood pressure, assuming the patient is euvolemic. If hypotension persists despite use of phenylephrine, additional boluses of 250 to 500 mL lactated Ringer's/PlasmaLyte can be titrated to the effect desired, and albumin may be administered judiciously as needed. Goal-directed fluid therapy (GDFT) devices may be used in higher-risk patients or surgical procedures.

Rationale/evidence: The goal of perioperative fluid therapy for an ERAS pathway is to maintain euvolemia and a "near-zero" fluid balance,^{80,81} because excessive fluid administration may result in increased demands on cardiac and renal function, inhibition of gastrointestinal function, and delayed recovery.^{81,82} Intraoperative fluid requirements can be generally met with an

Table 3. Length of Stay (Johns Hopkins Downtown Baltimore Campus)

ERAS Pathway	LOS Before Implementation, d	LOS After Implementation, d	P Value
Colorectal	7.2 (mean)	5.3 (mean)	<0.00
Liver resection	6 (median)	5 (median)	0.037
Radical cystectomy	8.5 (median)	5 (median)	<0.001

Wick EC, Galante DJ, Hobson DB, et al. Organizational culture changes result in improvement in patient-centered outcomes: implementation of an integrated recovery pathway for surgical patients. *J Am Coll Surg.* 2015;221(3):669-677.

Page AJ, Gani F, Crowley KT, et al. Patient outcomes and provider perceptions following implementation of a standardized perioperative care pathway for open liver resection. *Br J Surg.* 2016;103(5):564-571.

LOS, length of stay

isotonic balanced crystalloid solution at a rate of 332 mL/kg per hour.⁸¹ Use of GDFT devices, which measure changes in stroke volume and allow the individualization of fluid therapy, may be particularly useful in higher-risk patients or surgical procedures.⁸³⁻⁸⁵ Several meta-analyses have suggested that when compared with a liberal fluid therapy regimen, a GDFT regimen is associated with a reduction in complication rates (eg, wound infection, cardiac complications, and LOS).⁸⁴⁻⁹⁴ It is not clear whether GDFT is superior to a restrictive fluid strategy.⁸⁶

8. Lung-protective ventilation strategy: Tidal volume = 6 to 8 mL/kg of predicted body weight; positive end-expiratory pressure (PEEP), 2 to 5 cm H₂O

Rationale/evidence: Several meta-analyses confirmed that anesthetized patients who received ventilation at lower tidal volumes (6-8 mL/kg) versus higher volumes (10-12 mL/kg) during surgery had a lower risk for lung injury and pulmonary infection.⁹⁵⁻⁹⁷

Oxygenation: 50% FiO₂ intraoperatively and then 100% face mask for 2 hours in recovery room

Rationale/evidence: Although several meta-analyses incorporating many different surgical procedures have provided mixed results on whether perioperative supplemental oxygen therapy will result in fewer SSIs,⁹⁸⁻¹⁰⁸ subgroup analyses from some of these meta-analyses suggest that colorectal patients are one of the groups that would benefit from perioperative supplemental oxygen therapy for decreasing SSIs.^{98,100,104,105,107} There was some concern that a high FiO₂ during surgery might reduce long-term survival in cancer patients, but a follow-up study showed no difference in new or recurrent cancers in patients given 80% or 30% oxygen during and 2 hours after abdominal surgery.^{109,110}

9. Antiemetics: Ondansetron 8 mg IV 30 minutes prior to end of case

Rationale/evidence: An important anesthesiology component of any ERAS pathway is to control PONV to facilitate oral intake and speed patient recovery. Some of these antiemetic agents can be given preoperatively (eg, scopolamine transdermal, midazolam, gabapentin), whereas others (eg, serotonin antagonists, dexamethasone) are given intra- or postoperatively. In addition, use of some techniques, such as regional anesthesia or TIVA with propofol, will reduce perioperative opioid use and PONV. A multimodal approach using multiple classes of antiemetic agents (including the 5-hydroxytryptamine [5-HT₃] receptor antagonists, corticosteroids, butyrophenones, antihistamines, anticholinergics, and neurokinin-1 receptor antagonists) for PONV prophylaxis is recommended, and ERAS pathways often incorporate multimodal preventive PONV strategies.¹¹¹

Thermoregulation: Continue use of convective warming blanket from preanesthesia area; warm all IV fluids; circuit humidified 50% low-flow oxygen (<2-3 L/min)

Rationale/evidence: As noted above, there is high-quality evidence linking maintenance of normothermia and pre- and intraoperative warming with a decrease

in SSI rates,^{43,46} and several societal guidelines recommend maintenance of normothermia (35.5°C or higher) to reduce SSI.^{44,45}

Postoperative Phase

A standardized, evidence-based postoperative multimodal analgesic regimen is an important component of any ERAS pathway because superior pain control facilitates patient mobility and recovery. The multimodal analgesic regimen is designed with multiple nonopioid analgesic agents being administered on a scheduled basis in an attempt to minimize the use of and side effects from opioids, and that can be administered as rescue analgesics on an as-needed basis after other analgesics have failed to control postoperative pain.

While the patient is NPO: we continue thoracic epidural analgesia (in open colorectal cases) using patient-controlled epidural analgesia: 0.0625% or 0.125% bupivacaine at a continuous infusion of 4 to 6 mL per hour and a bolus of 2 to 4 mL every 10 to 15 minutes, as needed. We avoid using opioids in epidural solution and will adjust the epidural solution as needed, ideally continuing for at least one full day after the patient tolerates oral intake, which will include oral analgesics. In addition, we will administer a scheduled regimen of multimodal analgesics, including IV acetaminophen, ketorolac, and transdermal lidoderm patch.

Scheduled Analgesics:

- Acetaminophen: 1 g IV every 8 hours (x 2 doses).
- Ketorolac: 30 mg IV every 6 hours (decrease to 15 mg IV every 6 h for age >75 y; max 5 days total).
- Lidoderm patch: 1 patch every 24 hours.

Breakthrough/PRN Analgesics: Hydromorphone IV 0.2 to 0.5 mg every 3 hours PRN for breakthrough pain (if needed, order IV PCA for pain not controlled with above analgesic meds).

Once the patient is able to successfully resume oral intake: a standardized scheduled regimen of multimodal analgesics is administered (assuming there are no contraindications). Tramadol is available as the first breakthrough pain analgesic, and an opioid (typically hydromorphone, both oral and IV) is available as the second breakthrough analgesic if tramadol is ineffective.

Scheduled Analgesics:

- Acetaminophen: 1 g PO every 8 hours.
- Gabapentin: 100 mg PO 3 times daily.
- Ibuprofen: 400 mg PO every 6 hours.
- Lidoderm patch: 1 patch every 24 hours.
- Breakthrough/PRN Analgesics:
- Tramadol: 50 mg PO every 4 hours.
- Hydromorphone: 2 mg PO every 4 hours.
- Hydromorphone: 0.2 to 0.5 mg IV every 4 hours.

Rationale/Evidence:

Continuous Epidural Analgesia: Epidural analgesia with a local anesthetic-based regimen (vs opioids) provides superior postoperative analgesia, facilitates earlier return of gastrointestinal function, and decreases perioperative pulmonary-cardiac morbidity in high-risk patients.⁴⁷⁻⁵⁰

Acetaminophen: Several meta-analyses demonstrate that acetaminophen provides effective postoperative analgesia and decreases opioid use.¹¹²⁻¹²¹ If the patient is NPO, scheduled IV acetaminophen, if available, can be administered as meta-analyses reveal that IV acetaminophen provides effective postoperative analgesia, decreases opioid use, and decreases PONV.^{112-114,121} If the patient is tolerating oral intake and medications, an oral (pill or liquid) formulation of acetaminophen can be administered on a scheduled basis.

Gabapentanoids: Although meta-analyses indicate that a single dose of preoperative gabapentin may be associated with decreased postoperative pain, opioid consumption, and PONV,¹⁵⁻²⁹ there are scant data on the continued postoperative and post-discharge administration of gabapentanoids. Because there are few systematic data to guide the postoperative dosing of these agents, a lower initial dose (gabapentin 100 mg PO TID) was chosen.

Lidocaine (transdermal): Although a meta-analysis of 5 relatively small RCTs¹²² suggested that the application of a transdermal lidocaine patch may not be an effective adjunct for acute and postoperative pain globally, the transdermal lidocaine patch is associated with minimal systemic absorption and side effects and may be more effective in certain populations, such as patients undergoing laparoscopic procedures.^{123,124}

NSAIDs: Meta-analyses examining the perioperative use of NSAIDs (including COX-2 inhibitors) demonstrate that these agents provide very effective analgesia¹²⁵⁻¹³⁰ and should be administered on a scheduled basis. If the patient is NPO, scheduled IV NSAIDs can be administered and converted to an oral formulation when the patient is taking PO. Although there is concern about perioperative bleeding with NSAIDs, recent meta-analyses in noncolorectal surgical procedures suggest there is no increase in postoperative bleeding with NSAIDs.^{131,132}

Another controversial issue is whether the use of NSAIDs is definitively associated with an increase in anastomotic leakage, since one meta-analysis of human and animal trials suggests a relationship¹³³ whereas another meta-analysis¹³⁴ of human RCTs did not demonstrate a difference in incidence of anastomotic dehiscence; however, the quality of the data is very poor, heterogeneous, and often biased.¹³⁵ There are many other factors that may be associated with an increased risk for colorectal anastomotic leakage (eg, diabetes mellitus, hyperglycemia or high glycosylated hemoglobin, anemia, blood loss, blood transfusions, prolonged operating time, intraoperative events, and lack of antibiotics).¹³⁶

Tramadol: Tramadol produces analgesia via opioid (very weak mu receptor activation) and nonopioid (inhibition of serotonin and norepinephrine reuptake) mechanisms of action. Although less potent than opioids or NSAIDs as analgesics, tramadol produces analgesia with a theoretically relatively lower risk for addiction,¹³⁷ less constipation, minimal cardiovascular side effects

and minimal respiratory depression,¹³⁸ and can be an effective analgesic when administered with acetaminophen.¹³⁹ Tramadol is associated with a slightly higher incidence of seizures, and should be used with caution in patients with a history of seizures and patients taking concurrent selective serotonin reuptake inhibitors, as there is a theoretical increased possibility of serotonin syndrome.¹⁴⁰

Opioids: Every ERAS pathway will attempt to limit the amount of opioids to minimize related side effects, which may delay patient recovery; however, opioids are still part of many ERAS pathways. Opioids are typically administered as a “rescue” (PRN) when all other nonopioid analgesic agents have failed to control the patient’s pain. Despite that approach, opioids should not be withheld from opioid-tolerant patients, as they will require continuation of their baseline opioid requirements to prevent withdrawal.

Challenges, Solutions, and Opportunities

There are always challenges in implementing any ERAS pathway. What essentially occurs with the initiation of an ERAS pathway is a change in culture and the way care is traditionally delivered. Many health care providers (both anesthesiologists and nonanesthesiologists) will be resistant to changing the way they have practiced. In addition, there are potential process-related issues (eg, creating new order sets, ensuring drugs will be available in Pyxis machines), some of which are unique to each institution, that will need to be addressed. Finally, a significant amount of “face time” will be needed to educate health care providers on the changes in the way that perioperative care will be delivered.

There are several possible solutions to the typical challenges encountered in implementing an ERAS pathway:

Choose a pathway that will be easiest to implement. Most commonly, colorectal ERAS pathways are one of the first to be implemented in each institution, as there are several pathways already published in the literature. The research on colorectal ERAS pathways is far more developed than for other surgical procedures; as a result, colorectal surgeons are more aware and typically more amenable to participating in an ERAS pathway. In addition, the colorectal surgical cases (eg, colectomy) are generally more straightforward and need fewer resources (eg, minimal use of ICUs). The colorectal ERAS pathway was the first one developed at the Johns Hopkins University Hospital (downtown Baltimore campus), and the success of this pathway led to demand for ERAS pathways for other surgical services.

Identify champions in each area. One of the keys to successful implementation is to identify people who will be representing anesthesiology, nursing, and surgery, as these champions will coordinate and drive the process forward. It is ideal to have a champion in each of these areas, as they will constitute the core of any ERAS pathway. There may also be champions from other

areas, including pharmacy, rehabilitation/physical therapy, the preoperative clinic, the preanesthesia/recovery room, and the ICU. For our colorectal ERAS pathway, the surgeon (EW) and nurse (DH) leaders had already worked together on an SSI Comprehensive Unit-base Safety Program (CUSP) and had developed an excellent rapport. They approached the anesthesiology department and identified an anesthesiology champion (CW) who would work with them to develop and implement an evidence-based colorectal ERAS pathway. This team approach has worked very well for us with regard to clinical implementation and research production. One benefit for the anesthesiology department is that the ERAS pathways allow us to demonstrate the added value we provide to our patients, our colleagues, and the institution.

Identify a core group of health care providers who will work with you. Not everyone in your group or department will be willing to provide care according to an ERAS pathway; however, often many others are willing (in varying degrees) to participate. When possible, limit ERAS cases to anesthesiology providers who are committed to fully participating in delivering anesthesia according to the ERAS pathway. In our department, we have a dedicated core of anesthesiology physicians, CRNAs, and rotating anesthesiology residents who provide care for our ERAS cases. We work with our schedulers to attempt to match as many ERAS surgical cases with ERAS anesthesiology providers as possible.

Consider the availability of local resources and use available evidence to develop the pathway. Even though all ERAS pathways should be based on evidence, no two ERAS pathways will be identical, partly due to differences in local resources, expertise, and goals. Within the Hopkins health care system, we have at least 4 local/regional hospitals that have a colorectal ERAS pathway, yet no two colorectal ERAS pathways are the same—again, partly due to local differences. At the Johns Hopkins Hospital (downtown Baltimore campus), we developed our colorectal ERAS pathway with one goal being preservation of perioperative immune function. We are able to utilize epidural anesthesia/analgesia for our cases, as we have additional resources in the form of residents and a stand-alone Acute Pain Service.

Obtain input while developing the pathway and modify the pathway as needed. Although usually it is the anesthesiology champion who coordinates and pulls together the evidence to create the anesthesiology portion of the ERAS pathway, it is important to obtain feedback from the whole group to ensure group ownership of the pathway. In addition, many in the group may have experiences from outside institutions or additional knowledge from the literature and will be able to provide valuable insight. For the Johns Hopkins Hospital (downtown Baltimore campus), the anesthesiology champion (CW) pulled together the evidence to

create the anesthesiology portion of the ERAS pathway, and the preliminary version then was sent out via email to the group. Several modifications were made based on the feedback. Once the initial version was finalized, we implemented the anesthesiology portion of the ERAS pathway on approximately 10 patients, which led to further very minor modifications.

One thing to note is that once an ERAS pathway is created, it should not be viewed as the final pathway. We have continued to update the pathway based on published literature and clinical experience. For instance, several articles came out on lung protective strategies⁹⁵⁻⁹⁷ after our colorectal pathway was created. This information was incorporated into a revised pathway.

Be open to feedback and provide feedback on outcomes/results. Once the front-line health care providers see that their patients are having less pain, recovering faster, and being discharged earlier (and happier for the most part), they generally will become more enthusiastic and active in facilitating the implementation of the ERAS pathway. We attempt (although not always successfully) to provide regular feedback on our metrics to our providers. We are still working on a system in which major metrics (eg, LOS, SSI rates) will be routinely available on a dashboard.

Obtain administration/C-suite support. There are often administrative costs associated with implementation of an ERAS pathway. The hospital administration may be reluctant to provide adequate resources to fully implement an ERAS pathway. If so, a limited implementation with a small cohort of patients may provide the results you need to re-engage the hospital administration for additional resources. For us, we proposed a pilot study that was extremely successful, and additional resources were allocated based on these results. Implementation of an ERAS pathway is one of the few times when anesthesiology providers can visibly demonstrate the added value we provide to our patients, our colleagues, and the institution.

Conclusion

The development and implementation of an ERAS pathway allows anesthesiology providers to be an integral part of a successful patient-centered, cost-effective, and evidence-based program. ERAS pathways are one of the more visible ways to show the added value we provide to our patients, our colleagues, and the hospital/institution, which is particularly important in the current environment where there is increasing economic pressure on hospitals and institutions to provide high-quality and high-value health care. There are always challenges in the development and implementation of an ERAS pathway; we have discussed several possible solutions to the typical challenges encountered in implementing an ERAS pathway.

References

1. Spanjersberg WR, Reurings J, van Laarhoven CJ. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev.* 2011;2:CD007635.
2. Grant MC, Yang D, Wu CL, et al. Impact of enhanced recovery after surgery and fast track surgery pathways on healthcare-associated infections: results from a systematic review and meta-analysis. *Ann Surg.* 2017;265(1):68-79.
3. Schroeder SA, Frist W; National Commission on Physician Payment Reform. Phasing out fee-for-service payment. *N Engl J Med.* 2013;368(21):2029-2032.
4. McClellan M. Reforming payments to healthcare providers: the key to slowing healthcare cost growth while improving quality? *J Econ Perspect.* 2011;25(2):69-92.
5. Thiele RH, Rea KM, Turrentine FE, et al. Standardization of care: impact of an enhanced recovery protocol on length of stay, complications, and direct costs after colorectal surgery. *J Am Coll Surg.* 2015;220(4):430-443.
6. Wick EC, Galante DJ, Hobson DB, et al. Organizational culture changes result in improvement in patient-centered outcomes: implementation of an integrated recovery pathway for surgical patients. *J Am Coll Surg.* 2015;221(3):669-677.
7. Stone AB, Grant MC, Pio Roda C, et al. Implementation costs of an enhanced recovery after surgery program in the United States: a financial model and sensitivity analysis based on experiences at a quaternary academic medical center. *J Am Coll Surg.* 2016;222(3):219-225.
8. Smith MD, McCall J, Plank L, et al. Preoperative carbohydrate treatment for enhancing recovery after elective surgery. *Cochrane Database Syst Rev.* 2014;8:CD009161.
9. Bilku DK, Dennison AR, Hall TC, et al. Role of preoperative carbohydrate loading: a systematic review. *Ann R Coll Surg Engl.* 2014;96(1):15-22.
10. Li L, Wang Z, Ying X, et al. Preoperative carbohydrate loading for elective surgery: a systematic review and meta-analysis. *Surg Today.* 2012;42(7):613-624.
11. Jones C, Badger SA, Hannon R. The role of carbohydrate drinks in pre-operative nutrition for elective colorectal surgery. *Ann R Coll Surg Engl.* 2011;93(7):504-507.
12. Awad S, Varadhan KK, Ljungqvist O, et al. A meta-analysis of randomized controlled trials on preoperative oral carbohydrate treatment in elective surgery. *Clin Nutr.* 2013;32(1):34-44.
13. Brady M, Kinn S, Stuart P. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev.* 2003;4:CD004423.
14. American Society of Anesthesiologists Committee. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. *Anesthesiology.* 2011;114(3):495-511.
15. Hurley RW, Cohen SP, Williams KA, et al. The analgesic effects of perioperative gabapentin on postoperative pain: a meta-analysis. *Reg Anesth Pain Med.* 2006;31(3):237-247.
16. Peng PW, Wijeyesundera DN, Li CC. Use of gabapentin for perioperative pain control—a meta-analysis. *Pain Res Manag.* 2007;12(2):85-92.
17. Ho KY, Gan TJ, Habib AS. Gabapentin and postoperative pain—a systematic review of randomized controlled trials. *Pain.* 2006;126(1-3):91-101.
18. Seib RK, Paul JE. Preoperative gabapentin for postoperative analgesia: a meta-analysis. *Can J Anaesth.* 2006;53(5):461-469.
19. Arumugam S, Lau CS, Chamberlain RS. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. *J Pain Res.* 2016;9:631-640.
20. Grant MC, Lee H, Page AJ, et al. The effect of preoperative gabapentin on postoperative nausea and vomiting: a meta-analysis. *Anesth Analg.* 2016;122(4):976-985.
21. Nir RR, Nahman-Averbuch H, Moont R, et al. Preoperative preemptive drug administration for acute postoperative pain: a systematic review and meta-analysis. *Eur J Pain.* 2016;20(70):1025-1043.
22. Doleman B, Heinink TP, Read DJ, et al. A systematic review and meta-regression analysis of prophylactic gabapentin for postoperative pain. *Anaesthesia.* 2015;70(10):1186-1204.
23. Achuthan S, Singh I, Varthya SB, et al. Gabapentin prophylaxis for postoperative nausea and vomiting in abdominal surgeries: a quantitative analysis of evidence from randomized controlled clinical trials. *Br J Anaesth.* 2015;114(4):588-597.
24. Zhang J, Ho KY, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth.* 2011;106(4):454-462.
25. Straube S, Derry S, Moore RA, et al. Single dose oral gabapentin for established acute postoperative pain in adults. *Cochrane Database Syst Rev.* 2010;5:CD008183.
26. Dauri M, Faria S, Gatti A, et al. Gabapentin and pregabalin for the acute post-operative pain management: a systematic-narrative review of the recent clinical evidences. *Curr Drug Targets.* 2009;10(8):716-733.
27. Eipe N, Penning J, Yazdi F, et al. Perioperative use of pregabalin for acute pain—a systematic review and meta-analysis. *Pain.* 2015;156(7):1284-1300.
28. Mishriky BM, Waldron NH, Habib AS. Impact of pregabalin on acute and persistent postoperative pain: a systematic review and meta-analysis. *Br J Anaesth.* 2015;114(1):10-31.
29. Engelman E, Cateley F. Efficacy and safety of perioperative pregabalin for post-operative pain: a meta-analysis of randomized-controlled trials. *Acta Anaesthesiol Scand.* 2011;55(8):927-943.
30. Doleman B, Read D, Lund JN, et al. Preventive acetaminophen reduces postoperative opioid consumption, vomiting, and pain scores after surgery: systematic review and meta-analysis. *Reg Anesth Pain Med.* 2015;40(6):706-712.
31. Khan JS, Margarido C, Devereaux PJ, et al. Preoperative celecoxib in noncardiac surgery: a systematic review and meta-analysis of randomised controlled trials. *Eur J Anaesthesiol.* 2016;33(3):204-214.
32. Straube S, Derry S, McQuay HJ, et al. Effect of preoperative Cox-II-selective NSAIDs (coxibs) on postoperative outcomes: a systematic review of randomized studies. *Acta Anaesthesiol Scand.* 2005;49(5):601-613.
33. Leese PT, Hubbard RC, Karim A, et al. Effects of celecoxib, a novel cyclooxygenase-2 inhibitor, on platelet function in healthy adults: a randomized, controlled trial. *J Clin Pharmacol.* 2000;40(2):124-132.
34. Teerawattananon C, Tantayakom P, Suwanawiboon B, et al. Risk of perioperative bleeding related to highly selective cyclooxygenase-2 inhibitors: a systematic review and meta-analysis. *Semin Arthritis Rheum.* 2017;46(4):520-528.
35. De Oliveira GS Jr, Almeida MD, Benzon HT, et al. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology.* 2011;115(3):575-588.
36. Toner AJ, Ganeshanathan V, Chan MT, et al. Safety of perioperative glucocorticoids in elective noncardiac surgery: a systematic review and meta-analysis. *Anesthesiology.* 2017;126(2):234-248.
37. Waldron NH, Jones CA, Gan TJ, et al. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. *Br J Anaesth.* 2013;110(2):191-200.

38. Apfel CC, Zhang K, George E, et al. Transdermal scopolamine for the prevention of postoperative nausea and vomiting: a systematic review and meta-analysis. *Clin Ther*. 2010;32(12):1987-2002.
39. Kranke P, Morin AM, Roewer N, et al. The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg*. 2002;95(1):133-143.
40. Achuthan S, Singh I, Varthya SB, et al. Gabapentin prophylaxis for postoperative nausea and vomiting in abdominal surgeries: a quantitative analysis of evidence from randomized controlled clinical trials. *Br J Anaesth*. 2015;114(4):588-597.
41. Ahn EJ, Kang H, Choi GJ, et al. The effectiveness of midazolam for preventing postoperative nausea and vomiting: a systematic review and meta-analysis. *Anesth Analg*. 2016;122(3):664-676.
42. Grant MC, Kim J, Page AJ, et al. The effect of intravenous midazolam on postoperative nausea and vomiting: a meta-analysis. *Anesth Analg*. 2016;122(3):656-663.
43. Anderson DJ, Podgorny K, Berrios-Torres SI, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol*. 2014;35(6):605-627.
44. Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: surgical site infection guidelines, 2016 update. *J Am Coll Surg*. 2017;224(1):59-74.
45. Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J Surg*. 2013;37(2):259-284.
46. Tanner J, Padley W, Assadian O, et al. Do surgical care bundles reduce the risk of surgical site infections in patients undergoing colorectal surgery? a systematic review and cohort meta-analysis of 8,515 patients. *Surgery*. 2015;158(1):66-77.
47. Block BM, Liu SS, Rowlingson AJ, et al. Efficacy of postoperative epidural analgesia: a meta-analysis. *JAMA*. 2003;290(18):2455-2463.
48. Wu CL, Cohen SR, Richman JM, et al. Efficacy of postoperative patient-controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: a meta-analysis. *Anesthesiology*. 2005;103(5):1079-1088.
49. Guay J, Nishimori M, Kopp S. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery. *Cochrane Database Syst Rev*. 2016;7:CD001893.
50. Pöpping DM, Elia N, Van Aken HK, et al. Impact of epidural analgesia on mortality and morbidity after surgery: systematic review and meta-analysis of randomized controlled trials. *Ann Surg*. 2014;259(6):1056-1067.
51. Pöpping DM, Elia N, Marret E, et al. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. *Arch Surg*. 2008;143(10):990-999.
52. Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev*. 2005;1:CD004088.
53. Marret E, Remy C, Bonnet F; Postoperative Pain Forum Group. Meta-analysis of epidural analgesia versus parenteral opioid analgesia after colorectal surgery. *Br J Surg*. 2007;94(6):665-673.
54. Jørgensen H, Wetterslev J, Møiniche S, et al. Epidural local anaesthetics versus opioid-based analgesic regimens on postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. *Cochrane Database Syst Rev*. 2000;4:CD001893.
55. Santamaria LB, Schifilliti D, La Torre D, et al. Drugs of anaesthesia and cancer. *Surg Oncol*. 2010;19(2):63-81.
56. Snyder GL, Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. *Br J Anaesth*. 2010;105(2):106-115.
57. Afsharimani B, Cabot P, Parat MO. Morphine and tumor growth and metastasis. *Canc Metastasis Rev*. 2011;30(2):225-238.
58. Borzellino G, Francis NK, Chapuis O, et al. Role of epidural analgesia within an ERAS program after laparoscopic colorectal surgery: a review and meta-analysis of randomised controlled studies. *Surg Res Pract*. 2016;2016:7543684.
59. Khan SA, Khokhar HA, Nasr AR, et al. Effect of epidural analgesia on bowel function in laparoscopic colorectal surgery: a systematic review and meta-analysis. *Surg Endosc*. 2013;27(7):2581-2591.
60. Hughes MJ, Ventham NT, McNally S, et al. Analgesia after open abdominal surgery in the setting of enhanced recovery surgery: a systematic review and meta-analysis. *JAMA Surg*. 2014;149(12):1224-1230.
61. Vigneault L, Turgeon AF, Côté D, et al. Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis of randomized controlled trials. *Can J Anaesth*. 2011;58(1):22-37.
62. Sun Y, Li T, Wang N, et al. Perioperative systemic lidocaine for postoperative analgesia and recovery after abdominal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum*. 2012;55(11):1183-1194.
63. Marret E, Rolin M, Beaussier M, et al. Meta-analysis of intravenous lidocaine and postoperative recovery after abdominal surgery. *Br J Surg*. 2008;95(11):1331-1338.
64. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. *Drugs*. 2010;70(9):1149-1163.
65. Kranke P, Jokinen J, Pace NL, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database Syst Rev*. 2015;7:CD009642.
66. Weibel S, Jokinen J, Pace NL, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *Br J Anaesth*. 2016;116(6):770-783.
67. Khan JS, Yousuf M, Victor JC, et al. An estimation for an appropriate end time for an intraoperative intravenous lidocaine infusion in bowel surgery: a comparative meta-analysis. *J Clin Anesth*. 2016;28:95-104.
68. Ventham NT, Kennedy ED, Brady RR, et al. Efficacy of intravenous lidocaine for postoperative analgesia following laparoscopic surgery: a meta-analysis. *World J Surg*. 2015;39(9):2220-2234.
69. Zhao X, Tong Y, Ren H, et al. Transversus abdominis plane block for postoperative analgesia after laparoscopic surgery: a systematic review and meta-analysis. *Int J Clin Exp Med*. 2014;7(9):2966-2975.
70. Brogi E, Kazan R, Cyr S, et al. Transversus abdominal plane block for postoperative analgesia: a systematic review and meta-analysis of randomized-controlled trials. *Can J Anaesth*. 2016;63(10):1184-1196.
71. Baeriswyl M, Kirkham KR, Kern C, et al. The analgesic efficacy of ultrasound-guided transversus abdominis plane block in adult patients: a meta-analysis. *Anesth Analg*. 2015;121(6):1640-1654.
72. De Oliveira GS Jr, Castro-Alves LJ, Nader A, et al. Transversus abdominis plane block to ameliorate postoperative pain outcomes after laparoscopic surgery: a meta-analysis of randomized controlled trials. *Anesth Analg*. 2014;118(2):454-463.
73. Johns N, O'Neill S, Ventham NT, et al. Clinical effectiveness of transversus abdominis plane (TAP) block in abdominal surgery: a systematic review and meta-analysis. *Colorectal Dis*. 2012;14(10):e635-e642.
74. Siddiqui MR, Sajid MS, Uncles DR, et al. A meta-analysis on the clinical effectiveness of transversus abdominis plane block. *J Clin Anesth*. 2011;23(1):7-14.
75. Charlton S, Cyna AM, Middleton P, et al. Perioperative transversus abdominis plane (TAP) blocks for analgesia after abdominal surgery. *Cochrane Database Syst Rev*. 2010;12:CD007705.

76. Guo BL, Lin Y, Hu W, et al. Effects of systemic magnesium on postoperative analgesia: is the current evidence strong enough? *Pain Physician*. 2015;18(5):405-418.
77. Murphy JD, Paskaradevan J, Eisler LL, et al. Analgesic efficacy of continuous intravenous magnesium infusion as an adjuvant to morphine for postoperative analgesia: a systematic review and meta-analysis. *Middle East J Anaesthesiol*. 2013;22(1):11-20.
78. De Oliveira GS Jr, Castro-Alves LJ, Khan JH, et al. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology*. 2013;119(1):178-190.
79. Albrecht E, Kirkham KR, Liu SS, et al. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. *Anaesthesia*. 2013;68(1):79-90.
80. Thiele RH, Raghunathan K, Brudney CS, et al; Perioperative Quality Initiative (POQI) I Workgroup. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on perioperative fluid management within an enhanced recovery pathway for colorectal surgery. *Perioper Med (Lond)*. 2016;5:24.
81. Feldheiser A, Aziz O, Baldini G, et al. Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice. *Acta Anaesthesiol Scand*. 2016;60(3):289-334.
82. Holte K, Sharrock NE, Kehlet H. Pathophysiology and clinical implications of perioperative fluid excess. *Br J Anaesth*. 2002;89(4):622-632.
83. Miller TE, Roche AM, Mythen M. Fluid management and goal-directed therapy as an adjunct to Enhanced Recovery After Surgery (ERAS). *Can J Anaesth*. 2015;62(2):158-168.
84. Pearse RM, Harrison DA, MacDonald N, et al; OPTIMISE Study Group. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. *JAMA*. 2014;311(21):2181-2190.
85. Cecconi M, Corredor C, Arulkumaran N, et al. Clinical review: Goal-directed therapy—what is the evidence in surgical patients? the effect on different risk groups. *Crit Care*. 2013;17(2):209.
86. Corcoran T, Rhodes JE, Clarke S, et al. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesth Analg*. 2012;114(3):640-651.
87. Som A, Maitra S, Bhattacharjee S, et al. Goal directed fluid therapy decreases postoperative morbidity but not mortality in major non-cardiac surgery: a meta-analysis and trial sequential analysis of randomized controlled trials. *J Anesth*. 2017;31(1):66-81.
88. Ripollés-Melchor J, Espinosa Á, Martínez-Hurtado E, et al. Perioperative goal-directed hemodynamic therapy in noncardiac surgery: a systematic review and meta-analysis. *J Clin Anesth*. 2016;28:105-115.
89. Ripollés J, Espinosa A, Martínez-Hurtado E, et al; EAR Group (Evidence Anesthesia Review Group). Intraoperative goal directed hemodynamic therapy in noncardiac surgery: a systematic review and meta-analysis. *Braz J Anesthesiol*. 2016;66(5):513-528.
90. Benes J, Giglio M, Brienza N, et al. The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: a meta-analysis of randomized controlled trials. *Crit Care*. 2014;18(5):584.
91. Rollins KE, Lobo DN. Intraoperative goal-directed fluid therapy in elective major abdominal surgery: a meta-analysis of randomized controlled trials. *Ann Surg*. 2016;263(3):465-476.
92. Gómez-Izquierdo JC, Feldman LS, Carli F, et al. Meta-analysis of the effect of goal-directed therapy on bowel function after abdominal surgery. *Br J Surg*. 2015;102(6):577-589.
93. Arulkumaran N, Corredor C, Hamilton MA, et al. Cardiac complications associated with goal-directed therapy in high-risk surgical patients: a meta-analysis. *Br J Anaesth*. 2014;112(4):648-659.
94. Giglio MT, Marucci M, Testini M, et al. Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: a meta-analysis of randomized controlled trials. *Br J Anaesth*. 2009;103(5):637-646.
95. Yang D, Grant MC, Stone A, et al. A meta-analysis of intraoperative ventilation strategies to prevent pulmonary complications: is low tidal volume alone sufficient to protect healthy lungs? *Ann Surg*. 2016;263(5):881-887.
96. Gu WJ, Wang F, Liu JC. Effect of lung-protective ventilation with lower tidal volumes on clinical outcomes among patients undergoing surgery: a meta-analysis of randomized controlled trials. *CMAJ*. 2015;187(3):e101-e109.
97. Guay J, Ochroch EA. Intraoperative use of low volume ventilation to decrease postoperative mortality, mechanical ventilation, lengths of stay and lung injury in patients without acute lung injury. *Cochrane Database Syst Rev*. 2015;12:CD011151.
98. Togioka B, Galvagno S, Sumida S, et al. The role of perioperative high inspired oxygen therapy in reducing surgical site infection: a meta-analysis. *Anesth Analg*. 2012;114(2):334-342.
99. Hovaguimian F, Lysakowski C, Elia N, et al. Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology*. 2013;119(2):303-316.
100. Yang W, Liu Y, Zhang Y, et al. Effect of intra-operative high inspired oxygen fraction on surgical site infection: a meta-analysis of randomized controlled trials. *J Hosp Infect*. 2016;93(4):329-338.
101. Patel SV, Coughlin SC, Malthaner RA. High-concentration oxygen and surgical site infections in abdominal surgery: a meta-analysis. *Can J Surg*. 2013;56(4):e82-e90.
102. Kao LS, Millas SG, Pedroza C, et al. Should perioperative supplemental oxygen be routinely recommended for surgery patients? a Bayesian meta-analysis. *Ann Surg*. 2012;256(6):894-901.
103. Qadan M, Akça O, Mahid SS, et al. Perioperative supplemental oxygen therapy and surgical site infection: a meta-analysis of randomized controlled trials. *Arch Surg*. 2009;144(4):359-366.
104. Al-Niaimi A, Safdar N. Supplemental perioperative oxygen for reducing surgical site infection: a meta-analysis. *J Eval Clin Pract*. 2009;15(2):360-365.
105. Wang H, Hong S, Liu Y, et al. High inspired oxygen versus low inspired oxygen for reducing surgical site infection: a meta-analysis. *Int Wound J*. 2017;14(1):46-52.
106. Wetterslev J, Meyhoff CS, Jørgensen LN, et al. The effects of high perioperative inspiratory oxygen fraction for adult surgical patients. *Cochrane Database Syst Rev*. 2015;6:CD008884.
107. Chura JC, Boyd A, Argenta PA. Surgical site infections and supplemental perioperative oxygen in colorectal surgery patients: a systematic review. *Surg Infect (Larchmt)*. 2007;8(4):455-461.
108. Brar MS, Brar SS, Dixon E. Perioperative supplemental oxygen in colorectal patients: a meta-analysis. *J Surg Res*. 2011;166(2):227-235.
109. Meyhoff CS, Jørgensen LN, Wetterslev J, et al; PROXI Trial Group. Increased long-term mortality after a high perioperative inspiratory oxygen fraction during abdominal surgery: follow-up of a randomized clinical trial. *Anesth Analg*. 2012;115(4):849-854.
110. Meyhoff CS, Jørgensen LN, Wetterslev J, et al; PROXI Trial Group. Risk of new or recurrent cancer after a high perioperative inspiratory oxygen fraction during abdominal surgery. *Br J Anaesth*. 2014;113 suppl 1:i74-i81.
111. Gan TJ, Diemunsch P, Habib AS, et al; Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg*. 2014;118(1):85-113.
112. McNicol ED, Ferguson MC, Haroutounian S, et al. Single dose intravenous paracetamol or intravenous propacetamol for postoperative pain. *Cochrane Database Syst Rev*. 2016;5:CD007126.

113. McNicol ED, Tzortzopoulou A, Cepeda MS, et al. Single-dose intravenous paracetamol or propacetamol for prevention or treatment of postoperative pain: a systematic review and meta-analysis. *Br J Anaesth*. 2011;106(6):764-775.
114. Apfel CC, Turan A, Souza K, et al. Intravenous acetaminophen reduces postoperative nausea and vomiting: a systematic review and meta-analysis. *Pain*. 2013;154(5):677-689.
115. Tzortzopoulou A, McNicol ED, Cepeda MS, et al. Single dose intravenous propacetamol or intravenous paracetamol for postoperative pain. *Cochrane Database Syst Rev*. 2011;10:CD007126.
116. De Oliveira GS Jr, Castro-Alves LJ, McCarthy RJ. Single-dose systemic acetaminophen to prevent postoperative pain: a meta-analysis of randomized controlled trials. *Clin J Pain*. 2015;31(1):86-93.
117. Maund E, McDaid C, Rice S, et al. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth*. 2011;106(3):292-297.
118. McDaid C, Maund E, Rice S, et al. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs) for the reduction of morphine-related side effects after major surgery: a systematic review. *Health Technol Assess*. 2010;14(17):1-153.
119. Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. *Br J Anaesth*. 2005;94(4):505-513.
120. Barden J, Edwards J, Moore A, et al. Single dose oral paracetamol (acetaminophen) for postoperative pain. *Cochrane Database Syst Rev*. 2004;1:CD004602.
121. Macario A, Royal MA. A literature review of randomized clinical trials of intravenous acetaminophen (paracetamol) for acute postoperative pain. *Pain Pract*. 2011;11(3):290-296.
122. Bai Y, Miller T, Tan M, et al. Lidocaine patch for acute pain management: a meta-analysis of prospective controlled trials. *Curr Med Res Opin*. 2015;31(3):575-581.
123. Kwon YS, Kim JB, Jung HJ, et al. Treatment for postoperative wound pain in gynecologic laparoscopic surgery: topical lidocaine patches. *J Laparoendosc Adv Surg Tech A*. 2012;22(7):668-673.
124. Saber AA, Elgamal MH, Rao AJ, et al. Early experience with lidocaine patch for postoperative pain control after laparoscopic ventral hernia repair. *Int J Surg*. 2009;7(1):36-38.
125. De Oliveira GS Jr, Agarwal D, Benzon HT. Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. *Anesth Analg*. 2012;114(2):424-433.
126. Straube S, Derry S, McQuay HJ, et al. Effect of preoperative Cox-II-selective NSAIDs (coxibs) on postoperative outcomes: a systematic review of randomized studies. *Acta Anaesthesiol Scand*. 2005;49(5):601-613.
127. Derry S, Moore RA. Single dose oral celecoxib for acute postoperative pain in adults. *Cochrane Database Syst Rev*. 2013;10:CD004233.
128. Derry S, Wiffen PJ, Moore RA. Single dose oral diclofenac for acute postoperative pain in adults. *Cochrane Database Syst Rev*. 2015;7:CD004768.
129. Tirunagari SK, Derry S, Moore RA, et al. Single dose oral etodolac for acute postoperative pain in adults. *Cochrane Database Syst Rev*. 2009;3:CD007357.
130. Khan JS, Margarido C, Devereaux PJ, et al. Preoperative celecoxib in noncardiac surgery: a systematic review and meta-analysis of randomised controlled trials. *Eur J Anaesthesiol*. 2016;33(3):204-214.
131. Kelley BP, Bennett KG, Chung KC, et al. Ibuprofen may not increase bleeding risk in plastic surgery: a systematic review and meta-analysis. *Plast Reconstr Surg*. 2016;137(4):1309-1316.
132. Gobble RM, Hoang HL, Kachniarz B, et al. Ketorolac does not increase perioperative bleeding: a meta-analysis of randomized controlled trials. *Plast Reconstr Surg*. 2014;133(3):741-755.
133. Bhangu A, Singh P, Fitzgerald JE, et al. Postoperative nonsteroidal anti-inflammatory drugs and risk of anastomotic leak: meta-analysis of clinical and experimental studies. *World J Surg*. 2014;38(9):2247-2257.
134. Burton TP, Mittal A, Soop M. Nonsteroidal anti-inflammatory drugs and anastomotic dehiscence in bowel surgery: systematic review and meta-analysis of randomized, controlled trials. *Dis Colon Rectum*. 2013;56(1):126-134.
135. Slim K, Joris J, Beloeil H; Groupe Francophone de Réhabilitation Améliorée après Chirurgie (GRACE). Colonic anastomoses and non-steroidal anti-inflammatory drugs. *J Visc Surg*. 2016;153(4):269-275.
136. van Rooijen SJ, Huisman D, Stuijvenberg M, et al. Intraoperative modifiable risk factors of colorectal anastomotic leakage: why surgeons and anesthesiologists should act together. *Int J Surg*. 2016;36(Pt A):183-200.
137. Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet*. 2004;43(13):879-923.
138. Shipton EA. Tramadol—present and future. *Anaesth Intensive Care*. 2000;28(4):363-374.
139. McQuay H, Edwards J. Meta-analysis of single dose oral tramadol plus acetaminophen in acute postoperative pain. *Eur J Anaesthesiol Suppl*. 2003;28:19-22.
140. Park SH, Wackernah RC, Stimmel GL. Serotonin syndrome: is it a reason to avoid the use of tramadol with antidepressants? *J Pharm Pract*. 2014;27(1):71-78.