CHAPTER

48

Perioperative Pain Management & Enhanced Outcomes

Francesco Carli, MD, MPhil and Gabriele Baldini, MD, MSc

KEY CONCEPTS

1. A well-functioning enhanced recovery program (ERP) uses evidence-based practices to decrease variation in clinical management, minimize organ dysfunction, and accelerate convalescence; it requires adjustments in multiple aspects of care, including surgical and anesthetic techniques, nursing care, physiotherapy, and nutrition support.
2. Persistent postsurgical pain—chronic pain that continues beyond the typical healing period of 1–2 months following surgery, or well past the normal period for postoperative follow-up—is increasingly acknowledged as a common and significant problem following surgery.
3. The magnitude of the surgical stress response is related to the intensity of the surgical stimulus, can be amplified by other factors, including hypothermia and psychological stress, and can be moderated by perioperative interventions, including deeper planes of general anesthesia, neural blockade, and reduction in the degree of surgical invasiveness.
4. Neuraxial blockade of nociceptive stimuli by epidural and spinal local anesthetics has been shown to blunt the metabolic and neuroendocrine stress response to surgery. In major open abdominal and thoracic procedures, thoracic epidural blockade with local anesthetic provides excellent analgesia, facilitates mobilization and physical therapy, and decreases the incidence and severity of ileus.
5. By sparing opioid use and minimizing the incidence of systemic opioid-related side effects, epidural analgesia facilitates earlier mobilization and earlier resumption of oral nutrition, expediting exercise activity and attenuating loss of body mass.
6. Continuous peripheral nerve blocks with local anesthetics block afferent nociceptive pathways and are an excellent way to reduce the incidence of opioid-related side effects and facilitate recovery.
7. Lidocaine (intravenous bolus of 100 mg or 1.5–2 mg/kg, followed by continuous intravenous infusion of 1.5–3 mg/kg/h or 2–3 mg/h) has analgesic, antihyperalgesic, and antiinflammatory properties.
8. Multimodal analgesia combines different classes of medications, having different (multimodal) pharmacological mechanisms of action and additive or synergistic effects, to control multiple perioperative pathophysiological factors that lead to postoperative pain and its sequelae.

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9. The addition of nonsteroidal antiinflammatory drugs (NSAIDs) to systemic opioids diminishes postoperative pain intensity, reduces the opioid requirement by approximately 30%, and decreases opioid-related side effects such as postoperative nausea and vomiting and sedation. However, NSAIDs may increase the risk of gastrointestinal and postoperative bleeding, decrease kidney function, and impair wound healing.
10. Opioid administration by patient-controlled analgesia provides better pain control, greater patient satisfaction, and fewer opioid side effects when compared with on-request parenteral opioid administration.
11. Single-shot and continuous peripheral nerve blockade is frequently utilized for fast-track ambulatory and inpatient orthopedic surgery, and can accelerate recovery from surgery and improve analgesia and patient satisfaction.
12. Postoperative ileus delays enteral feeding, causes patient discomfort, and is one of the most common causes of prolonged postoperative hospital stay. Nasogastric tubes should be discouraged whenever possible or used for only a very short period of time, even in gastric and hepatic surgery. Multimodal analgesia and nonopioid analgesia techniques shorten the duration of postoperative ileus.
13. Because either excessive, or excessively restricted, perioperative fluid therapy may increase the incidence and severity of postoperative ileus, a goal-directed fluid strategy should be selected to decrease postoperative morbidities and enhance recovery.

Evolution of Enhanced Recovery Programs

Despite increasing numbers of surgical patients who present with complex surgical problems and numerous medical comorbidities, major advances in surgical and anesthetic management have progressively decreased perioperative mortality and morbidity. Further improvement in perioperative outcomes, highlighted by accelerated postoperative convalescence and decreasing occurrence of perioperative complications, will depend on continued evolution of an integrated, multidisciplinary team approach to perioperative care that requires adjustments in multiple aspects of care, including surgical and anesthetic techniques, nursing care, physiotherapy, and nutrition support. The goal is to combine individual evidence-based elements of perioperative care, each of which may have modest benefits when used in isolation, into a tightly coordinated effort that has a synergistic, beneficial effect on surgical outcomes.

Such coordinated, multidisciplinary perioperative care programs are termed *enhanced recovery programs* (ERPs), *fast-track surgery*, or *enhanced recovery after surgery* (ERAS) (**Figure 48–1**). 1 A well-functioning ERP uses evidence-based practices to decrease variation in clinical management, minimize organ dysfunction, and accelerate convalescence (**Figure 48–2**). Although many publications in the surgical literature have highlighted the positive impact of such programs on surgical outcomes, reports documenting the role of anesthesia and analgesia in these programs are few. Another challenge is determining how to assess the impact of anesthetic management on outcomes in an ERP. Hospital length of stay is the most commonly used measure of success, but in many systems timing of hospital discharge is more directly related to administrative and

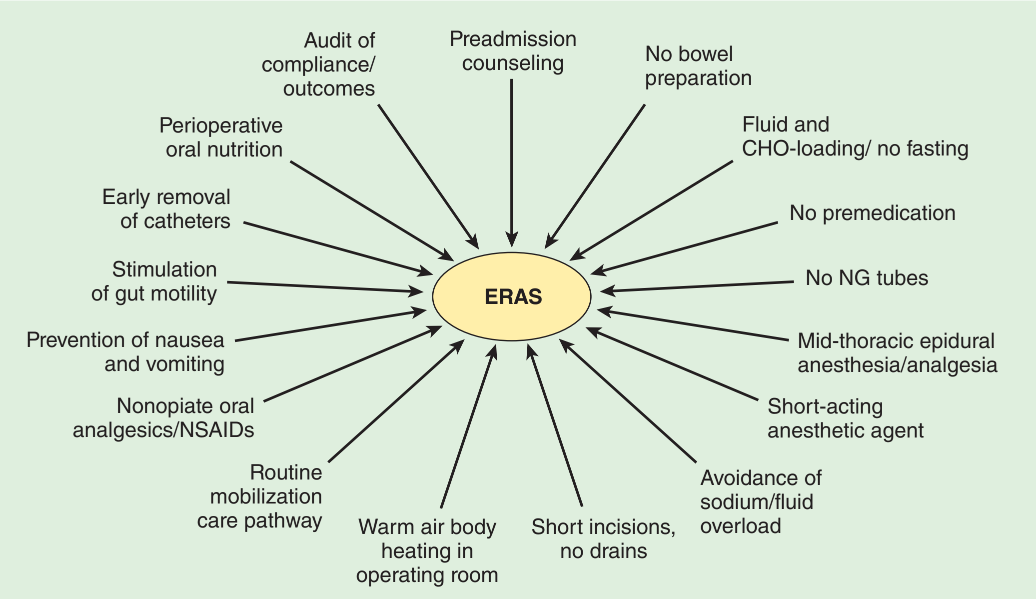

FIGURE 48–1 Perioperative elements contributing to enhanced recovery after surgery (ERAS). CHO, carbohydrate; NG, nasogastric; NSAID, nonsteroidal antiinflammatory drug. (Reproduced, with permission, from Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al: Enhanced recovery after surgery: A consensus review of clinical care for patients undergoing colonic resection. Clin Nut 2005;24:466.)

organizational issues than to discrete milestones in the patient's postoperative recovery. Little research has been undertaken to define the process of postoperative recovery, and few outcome measures are currently available to confirm that postoperative recovery has been accomplished for a given surgical disease. Other measures of successful implementation of ERPs are reduced readmission and complication rates.

It is logical to assume that more effective anesthetic interventions will reduce pain, facilitate earlier postoperative mobilization, and allow earlier resumption of oral feeding. In this context, the role of the anesthesia provider must evolve from merely providing satisfactory anesthetic conditions throughout the operation to a focus on enhancing overall perioperative care through techniques that shorten postoperative convalescence and reduce the likelihood of perioperative complications. These goals can be achieved by optimizing the patient's preoperative condition, by ablating the adverse effects of the intraoperative neuroendocrine stress response, and by providing pain and symptom control to facilitate the postoperative recovery. In endeavoring to do so, the anesthesiologist must become a perioperative physician and an active participant in the surgical team.

2 The problem of **persistent postsurgical pain**, defined as chronic pain that continues beyond the typical healing period of 1–2 months following surgery—or well past the normal period for postoperative follow-up by anesthesia providers—is increasingly acknowledged as a common and significant issue following surgery. The incidence of persistent postsurgical pain may exceed 30% after some operations, especially amputations, thoracotomy, mastectomy, and inguinal herniorrhaphy. Although the cause is unclear, several risk factors have been identified (**Figure 48–3**), and aggressive, multimodal perioperative pain control is often suggested as a fundamental preemptive strategy.

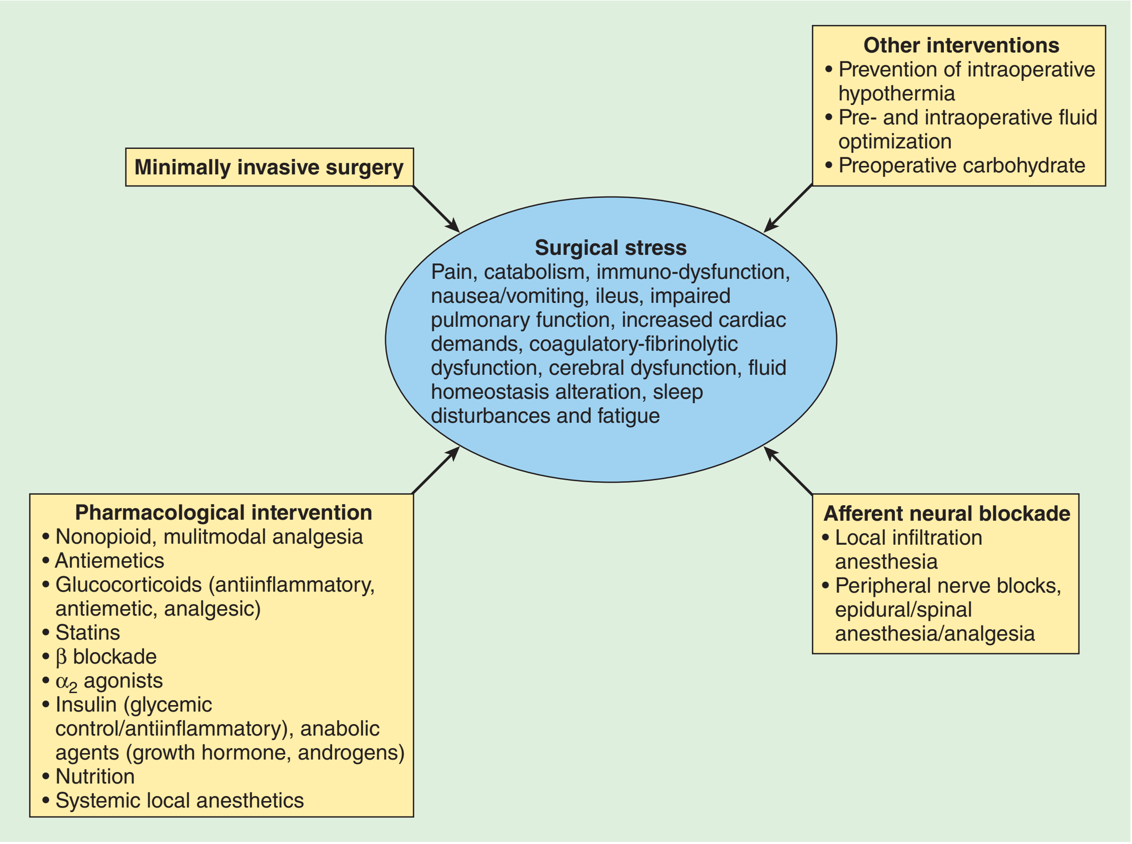

FIGURE 48–2 Multimodal interventions to attenuate the surgical stress response. (Reproduced, with permission, from Kehlet H, Wilmore DW: Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg 2008;248:189.)

Anesthetic Management–Related Factors Contributing to Enhanced Recovery

PREOPERATIVE PERIOD

Patient Education

Cooperation from the patient and family is essential if an ERP is to be effectively implemented. Preoperative teaching must use plain language and avoid medical jargon. Well-designed printed materials, such as procedure-specific booklets can be given to patients and families with the advice to keep them at the bedside and utilize them during the hospitalization.

Preoperative Risk Assessment & Optimization of Functional Status

Identification of patients at risk for intraoperative and postoperative complications, along with preoperative efforts focusing on any comorbidities, can improve surgical recovery. Preoperative assessment is discussed in detail in Chapter 18. Although international guidelines evaluating the risk for developing cardiovascular, respiratory, or metabolic complications have been extensively reviewed and published, little attention has been given to assessment and optimization of preoperative functional and physiological status. Nonetheless, some recommendations can be made. For example, routine use of β blockers, especially in

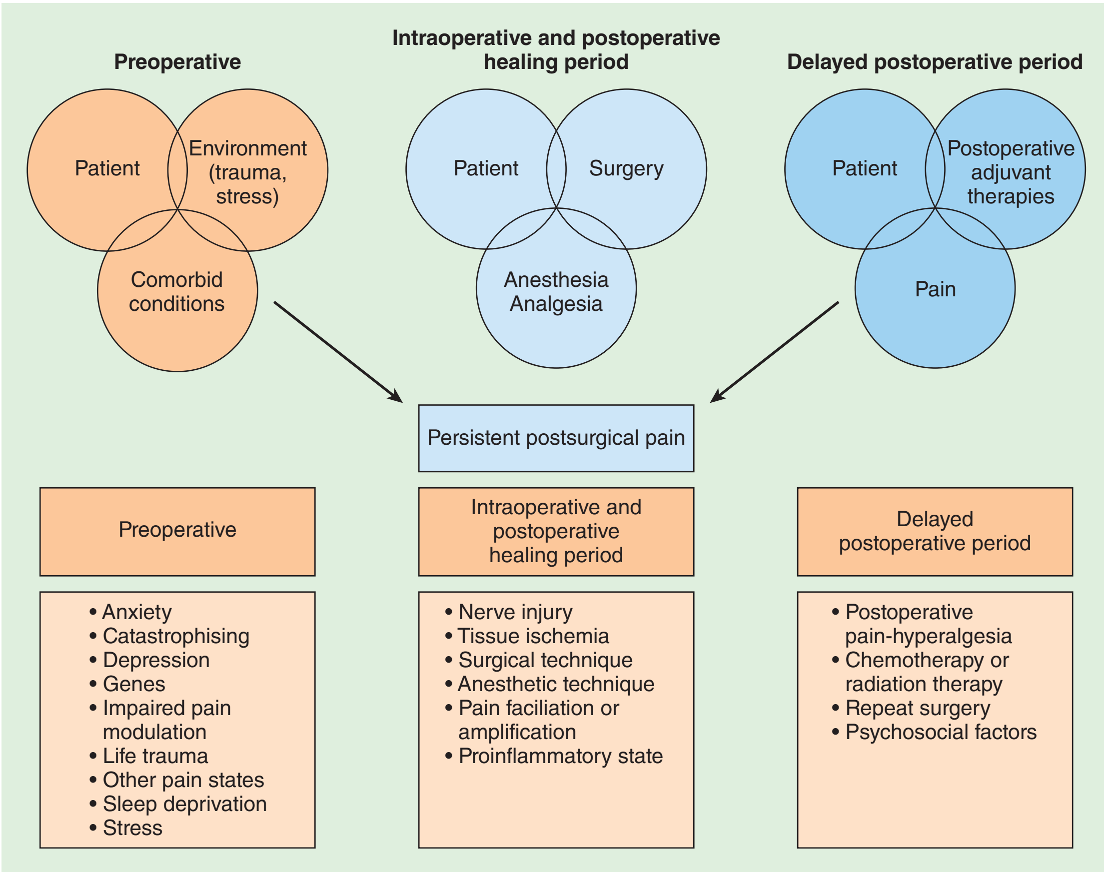

FIGURE 48–3 Risk factors for persistent postsurgical pain. (Reproduced, with permission, from Wu CL, Raja SN: Treatment of acute postoperative pain. Lancet 2011;377:2215.)

patients at low risk, has been associated with an increased risk of stroke; however, perioperative β blockers should be continued in patients already receiving this therapy. Perioperative statins appear to decrease postoperative cardiovascular complications and should not be abruptly discontinued perioperatively. Several procedure-specific scoring systems based on patient comorbidity, type of surgery, and biochemical data are being used to predict postoperative mortality and morbidity. In addition, risk-adjusted scoring systems, such as the American College of Surgeons' National Surgical Quality Improvement Program (NSQIP) and the Society of Thoracic Surgeons' National Database, can be used to compare outcomes among institutions.

Smoking & Alcohol Cessation

The preoperative period provides not only a time to evaluate surgical risk and optimize medical conditions, but also an opportunity to modify habits that can significantly affect a patient's short-term and long-term health and quality of life. Smoking, drug abuse, and excessive alcohol use are risk factors for the development of postoperative complications, and preoperative and postoperative interventions aimed at modifying these habits can improve surgical recovery. A recent meta-analysis found that preoperative smoking cessation, for any type of surgery, reduced postoperative complications by 41%, especially those related to wound healing and the lungs.

Many psychological and pharmacological strategies are available to help patients stop excessive alcohol consumption and reduce the risk of alcohol withdrawal. However, the optimal perioperative program has not been identified.

Guidelines for Food & Fluid Intake

Preoperative fasting and surgical stress induce insulin resistance. Furthermore, patients who are not allowed to drink fluids after an overnight fast and patients who receive a bowel preparation experience dehydration, which may increase discomfort and cause drowsiness and orthostatic lightheadedness. Although fasting has been advocated as a preoperative strategy to minimize the risk of pulmonary aspiration during induction of anesthesia, this benefit must be weighed against the detrimental aspects of this practice.

For instance, research suggests that avoiding preoperative fasting and ensuring adequate hydration and energy supply may moderate postoperative insulin resistance. All international fasting guidelines allow clear fluids up to 2 h prior to induction of anesthesia in patients at low risk for pulmonary aspiration (see Chapter 18). This practice has proved to be safe even in morbidly obese patients. Furthermore, recent studies have shown that preoperative administration of carbohydrate drinks (one 100-g dose administered the night before surgery and a second 50-g dose 2–3 h before induction of anesthesia) is safe; can reduce insulin resistance, hunger, fatigue, and postoperative nausea and vomiting (PONV); and positively influences immune status. Moreover, postoperative nitrogen loss and the loss of skeletal muscle mass are attenuated.

Magnetic resonance imaging studies in healthy volunteers have shown that the residual gastric volume 2 h after 400 mL of oral carbohydrate (12.5% maltodextrins) is minimal and similar to the residual volume after an overnight fast (mean volume of 21 mL). The safety of this practice has been tested in patients with uncomplicated type 2 diabetes mellitus, none of whom showed evidence of worsened risk of aspiration. Further studies of preoperative oral fluid and carbohydrate administration are needed to elaborate their role in improving short- and long-term perioperative outcomes.

INTRAOPERATIVE PERIOD

Antithrombotic Prophylaxis

Antithrombotic prophylaxis reduces perioperative venous thromboembolism and related morbidity and mortality. Both pneumatic compression devices and anticoagulant medications are now commonly used. Because neuraxial anesthesia techniques are commonly employed for many patients during major abdominal, vascular, thoracic and orthopedic surgery, appropriate timing and administration of antithrombotic agents in these cases is of critical importance in order to avoid the risk of epidural hematoma. International recommendations on the management of anticoagulated patients receiving regional anesthesia have been recently revised and published and are discussed in other chapters.

Antibiotic Prophylaxis

Appropriate selection and timing of preoperative antibiotic prophylaxis reduces the risk of surgical site infections. Antibiotics should be administered within 1 h before skin incision and, based on their plasma half-life, should be repeated during prolonged surgeries to ensure adequate tissue concentrations. Antibiotic prophylaxis of surgical site infections should be discontinued within 24 h after surgery (current guidelines permit cardiothoracic patients to receive antibiotics for 48 h following surgery).

Strategies to Minimize the Surgical Stress Response

The surgical stress response is characterized by neuroendocrine, metabolic, and inflammatory changes initiated by the surgical incision and subsequent procedures that can adversely affect organ function and perioperative outcomes, especially in elderly and physiologically compromised patients. These responses include a transient but reversible state of insulin resistance, characterized by decreased peripheral glucose uptake and increased endogenous glucose production. 3 The magnitude of the surgical stress response is related to the intensity of the surgical stimulus; can be amplified by other factors, including hypothermia and psychological stress; and can be moderated by perioperative interventions, including deeper planes of general anesthesia, neural blockade, and reduction in the degree of surgical invasiveness. Much recent effort has focused on developing surgical and anesthetic techniques that reduce the surgical stress response, with the goal of lowering the risk of stress-related organ dysfunction and perioperative complications. An overview of several techniques that have proved effective in ERP protocols follows.

A. Minimally Invasive Surgery

Laparoscopic procedures are associated with a reduced incidence of surgical complications, especially surgical site infections, compared with the same procedures performed in "open" fashion. Published data highlight the safety of minimally invasive procedures in the hands of adequately trained and experienced surgeons. Laparoscopic cholecystectomy results in shorter length of hospital stay and fewer complications compared with open cholecystectomy, and similar results have been reported for colorectal surgery. A longer term salutary impact is achieved when laparoscopic techniques are included in ERPs. A laparoscopic approach is also associated with less morbidity in elderly surgical patients.

B. Regional Anesthesia/ Analgesia Techniques

A variety of fast-track surgical procedures have taken advantage of the beneficial clinical and metabolic effects of regional anesthesia/analgesia techniques 4 (Table 48–1). Neuraxial blockade of nociceptive stimuli by epidural and spinal local anesthetics has been shown to blunt the metabolic and neuroendocrine stress response to surgery. To be effective, the blockade must be established before incision and continued postoperatively. In major open abdominal and thoracic procedures, thoracic epidural blockade with local anesthetic can be a recommended anesthetic component of a postoperative ERP, providing excellent analgesia, facilitating mobilization and physical therapy, and decreasing the incidence and severity of ileus. However, the advantages of neuraxial blockade are not as evident when minimally invasive surgical techniques are used. Lumbar epidural anesthesia/analgesia should be discouraged for abdominal surgery because it often does not provide adequate segmental analgesia for an abdominal incision. In addition, it frequently causes urinary

TABLE 48–1 Fast-track surgery programs that incorporate regional anesthesia/ analgesia techniques.[1]

Type of Surgery	Incision	Regional Anesthesia /Analgesia Techniques	Length of Stay
Colorectal resection	Laparotomy, laparoscopy	TEA, wound infusion of ropivacaine, intraperitoneal local anesthetic, intravenous lidocaine	2–4 d
Hernia repair	Open	Local infiltration, INB, TAP	2-4 h
Thoracic surgery	Thoracotomy	TEA, ICB	1–4 d
Esophageal surgery	Laparotomy	TEA	3–5 d
Open aortic surgery	Laparotomy	TEA	3–5 d
Nephrectomy	Laparotomy, laparoscopy	TEA	2–4 d
Arthroplasty (hip, knee)	Open	CPNB (femoral and sciatic), periarticular infiltration	1–3 d

[1]TEA, thoracic epidural analgesia; ICB, intercostal block; INB, ilioinguinal nerve block; TAP, transversus abdominus plane block; CPNB, continuous peripheral nerve block.

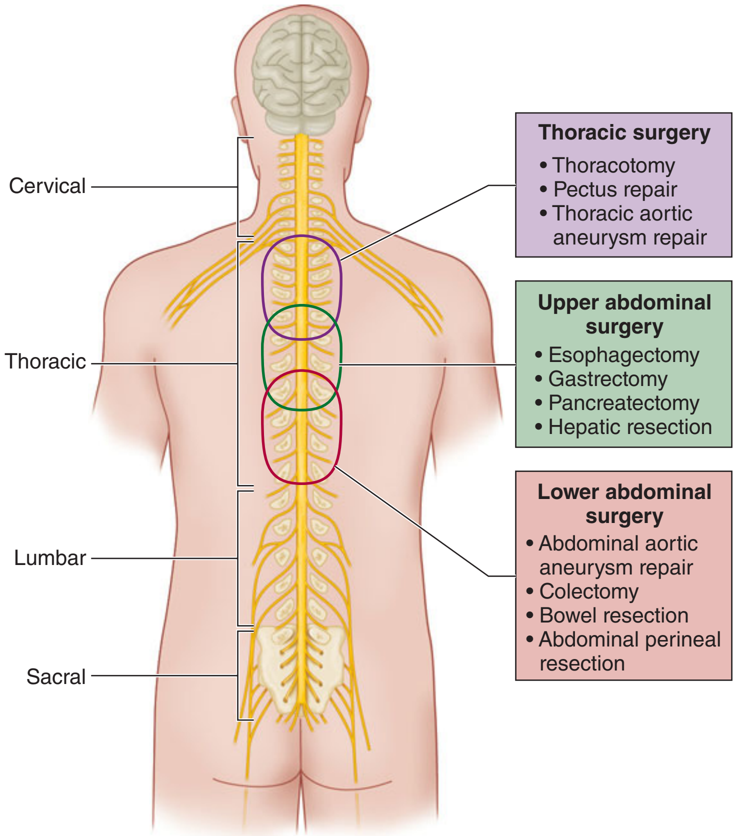

FIGURE 48–4 Optimal regions for placing an epidural catheter in the adult spine when administering epidural anesthesia/analgesia for thoracic and abdominal procedures. (Reproduced, with permission, from Manion SC, Brennan TJ: Thoracic epidural analgesia and acute pain management. Anesthesiology 2011;115:181.)

retention and lower limb sensory and motor blockade, increasing the need for urinary drainage catheters (with accompanying increased risk of urinary tract infection), delaying mobilization and recovery, and increasing the risk of falls.

Epidural blockade using a solution of local anesthetic and low-dose opioid provides better postoperative analgesia at rest and with movement than systemic opioids (Figure 48–4 and Table 48–2). By sparing opioid use and minimizing the incidence of systemic opioid-related side effects, epidural analgesia facilitates earlier mobilization and earlier resumption of oral nutrition, expediting exercise activity and attenuating loss of body mass. Neural blockade minimizes postoperative insulin resistance, attenuating the postoperative hyperglycemic response and facilitating utilization of exogenous glucose, thereby preventing postoperative loss of amino acids and conserving lean body mass.

5

If spinal anesthesia is used for fast-track (and especially ambulatory) surgery, attention must be paid to delayed recovery due to prolonged motor blockade. The use of smaller doses of intrathecal local anesthetics (lidocaine, 30–40 mg; bupivacaine, 3–7 mg; or ropivacaine, 5–10 mg) with lipophilic intrathecal opioids (fentanyl, 10–25 mcg, or sufentanil, 5–10 mcg) can prolong postoperative analgesia and minimize the motor block without delaying recovery from anesthesia. The introduction of ultrashort-acting intrathecal agents such as 2-chloroprocaine (still controversial at present) may further speed the fast-track process. Spinal opioids are associated with side effects such as nausea, pruritus, and postoperative urinary retention. Adjuvants such as clonidine are effective alternatives to intrathecal opioids, with the goal of avoiding untoward side effects that may delay hospital discharge. For example, intrathecal clonidine added to spinal local anesthetic

TABLE 48–2 Options for composition of thoracic epidural infusion analgesia solutions.[1]

Local Anesthetic	Opioid	Advantages	Disadvantages
Bupivacaine, 0.125%	None	↓ Nausea/Vomiting ↓ Pruritus ↓ Sedation ↓ Respiratory depression	↑ Hypotension ↑ Motor blockage
Bupivacaine, 0.1%	Hydromorphone, 5–10 mcg/mL or Fentanyl, 2–5 mcg/mL	↓ Both hemodynamic and opioid side effects	—
Bupivacaine, 0.05%	Hydromorphone, 5–10 mcg/mL or Fentanyl, 2–5 mcg/mL	↓ Both hemodynamic and opioid side effects	—
Bupivacaine, 0.05%	Hydromorphone, 20 mcg/mL or Fentanyl, 5–10 mcg/mL	↓ Both hemodynamic and opioid side effects	—
None	Hydromorphone, 20–40 mcg/mL	↓ Hypotension ↓ Motor blockade	↑ Nausea/Vomiting ↑ Pruritus ↑ Sedation ↑ Respiratory depression

[1]Reproduced, with permission, from Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. Anesthesiology 2011;115:181.

provides effective analgesia with less urinary retention than intrathecal morphine. Further studies are needed to define the safety and efficacy of regional anesthesia techniques in fast-track cardiac surgery (and many clinicians avoid them due to concerns about neuraxial hematomas). Although some studies have shown that spinal analgesia with intrathecal morphine decreases extubation time, decreases length of stay in the intensive care unit, reduces pulmonary complications and arrhythmias, and provides analgesia with less respiratory depression, other studies have shown no benefit to this approach.

6 Continuous peripheral nerve blocks (CPNBs) with local anesthetics block afferent nociceptive pathways and are an excellent way to reduce the incidence of opioid-related side effects and facilitate recovery (see Chapter 46). The choice of local anesthetic, dosage, and concentration should be made with the goal of avoiding prolonged motor blockade and delayed mobilization and discharge. Ropivacaine, because of its lower toxicity relative to bupivacaine, is often preferred when high volumes of local anesthetic solution are needed. CPNB after knee arthroplasty facilitates earlier discharge and rehabilitation. Efforts must be made to minimize the motor block of the quadriceps, which can be responsible for accidental falls. Administering a lumbar plexus block along with a sciatic nerve block decreases hospital length of stay, postoperative urinary retention, and ileus associated with lower extremity total joint replacement when compared with general or neuraxial anesthesia followed by intravenous opioids. The same benefits of fewer opioid side effects and accelerated discharge have been shown with regional anesthesia/analgesia for hand, shoulder, anorectal, and inguinal hernia repair surgery.

Advances in imaging techniques and peripheral catheter technology have generated interest in abdominal wall blockade, facilitating the selective localization of nerves and the direct deposition of local anesthetic in proximity to the compartments where the nerves are located. Transversus abdominis plane (TAP) block (see Chapter 46) has been used for abdominal surgery to facilitate postoperative analgesia and early return of bowel function. Rectus abdominis block can be used for midline incisions. These techniques are alternatives to epidural blockade when the latter is contraindicated.

The potential role of wound infusion of local anesthetic solution in providing analgesia for ERAS has not been determined; nevertheless, local anesthetic wound infusions are widely used to improve postoperative pain control and reduce the necessity for opioids.

C. Intravenous Lidocaine Infusion

7 Lidocaine (intravenous bolus of 100 mg or 1.5–2 mg/kg, followed by continuous intravenous infusion of 1.5–3 mg/kg/h or 2–3 mg/h) has analgesic, antihyperalgesic, and antiinflammatory properties. In patients undergoing colorectal and radical retropubic prostate surgeries, intravenous lidocaine has been shown to reduce requirements for opioids and general anesthetic agents, to provide satisfactory analgesia, to facilitate early return of bowel function, and to accelerate hospital discharge. Although lidocaine infusion potentially may replace neuraxial blockade and regional anesthesia in some circumstances, more studies are needed to confirm the advantage of this technique in the context of ERPs. The most effective dose and duration of infusion for various surgical procedures remains to be determined; even short duration of lidocaine infusion may have benefit.

D. β-Blockade Therapy

β Blockers have been used to blunt the sympathetic response during laryngoscopy and intubation and to attenuate the surgical stress-induced increase in circulating catecholamines. They also have been shown to prevent perioperative cardiovascular events in at-risk patients undergoing noncardiac surgery and to help maintain hemodynamic stability during the intraoperative period and during emergence from anesthesia. β Blockers reduce the requirement of volatile anesthetic agents and decrease minimum alveolar concentration values; they may also have an opioid-sparing effect. They possess anticatabolic properties, which may be explained by reduced energy requirements associated with decreased adrenergic stimulation. A positive protein balance has been reported in critically ill patients when β blockade is combined with parenteral nutrition. In the context of ERPs, the anesthetic- and analgesic-sparing effects of β blockers may facilitate recovery by accelerating emergence from anesthesia and by reducing anesthetic- and analgesic-related postoperative side effects, including PONV.

E. Intravenous α_2-Agonist Therapy

Both clonidine and dexmedetomidine have anesthetic and analgesic properties. Clonidine decreases postoperative pain, reduces opioid consumption and opioid-related side effects, and prolongs neuraxial and peripheral nerve local anesthetic blockade. In patients undergoing cardiovascular fast-track surgery, spinal morphine with clonidine decreases extubation time, provides effective analgesia, and improves quality of recovery. Dexmedetomidine has not been extensively studied in ERP pathways.

Use of Short-Acting Intravenous & Inhalation Agents

A. Intravenous Anesthetics

Intravenous propofol is the deep sedation and general anesthesia induction agent of choice for many surgical procedures, and may reduce the risk of PONV.

B. Inhalational Anesthetics

Compared with other volatile anesthetic agents, desflurane and sevoflurane can shorten anesthesia emergence, reduce length of stay in the postanesthesia care unit, and decrease recovery-associated costs. When compared with propofol, all inhalation agents increase the risk of PONV. Nitrous oxide, because of its anesthetic- and analgesic-sparing effects, rapid pharmacokinetic profile, and low cost, is frequently administered with other inhalation agents. However, its use may increase the risk of PONV, and nitrous oxide is frequently avoided in patients with risk factors for PONV. Moreover, the use of nitrous oxide during laparoscopic surgery may distend the bowel and impair the surgeon's view of anatomic structures (see Chapter 8).

C. Opioids

Short-acting opioids such as fentanyl, alfentanil, and remifentanil are commonly used during fast-track surgery in combination with inhalation agents or propofol, and with regional analgesia techniques. However, intraoperative administration of remifentanil to patients who will experience extensive postoperative pain has been associated with opioid-induced hyperalgesia, acute opioid tolerance, and increased analgesic requirements during the postoperative period.

D. Muscle Relaxants

The short-acting muscle relaxant succinylcholine and intermediate-acting muscle relaxants such as rocuronium, atracurium, and cisatracurium are commonly used to minimize the risk of unplanned and prolonged muscle relaxation. They are chosen to facilitate tracheal extubation while decreasing the risk of residual blockade during anesthesia recovery.

Maintenance of Normothermia

The inhibitory effect of anesthetic agents on thermoregulation, exposure to the relatively cool surgical environment, and intraoperative loss of heat through the surgical field can lead to intraoperative hypothermia in all patients undergoing surgical procedures under general or regional anesthesia. The duration and extent of the surgical procedure directly correlate with hypothermia risk. Perioperative hypothermia, by increasing sympathetic discharge and inhibiting immune cellular response, increases cardiovascular morbidity and wound infection risk. A decrease in core body temperature of 1.9°C triples the incidence of surgical wound infection. The risk of bleeding and blood transfusion requirement are also increased with hypothermia. Furthermore, by impairing the metabolism of many anesthetic agents, hypothermia significantly prolongs anesthesia recovery. These issues are discussed in Chapter 52.

Maintenance of Adequate Tissue Oxygenation

Surgical stress leads to impaired pulmonary function and peripheral vasoconstriction, resulting in arterial and local tissue hypoxemia. Perioperative hypoxia can increase cardiovascular and cerebral complications, and many strategies should be adopted during the perioperative period to prevent its development.

Maintenance of adequate perioperative oxygenation by oxygen supplementation has been associated with the improvement of some clinically relevant outcomes without increasing the risk of postoperative complications. Ensuring complete recovery of neuromuscular blockade can reduce early postoperative hypoxemia. Intraoperative and postoperative (for 2 h) inspired oxygen concentration of 80% has been associated with increased arterial and subcutaneous oxygen tension, decreased rate of wound infection, and lower incidence of PONV, but without increasing potential complications associated with high oxygen fraction, such as atelectasis and hypercapnia. However, these advantages have not been confirmed in a large, randomized, multicenter trial of patients undergoing elective and emergent laparotomy. The use of regional anesthesia techniques, by decreasing systemic vascular resistance, can also improve superficial and deep peripheral tissue perfusion and oxygenation. Finally avoidance of bedrest, and encouraging early mobilization and physiotherapy, can also improve postoperative central and peripheral tissue oxygenation.

PONV Prophylaxis

Postoperative nausea and vomiting (PONV) is a frequent complication associated with anesthetic drugs that delay early feeding and recovery from surgery. Perioperative strategies for minimizing PONV are strongly advocated for any type of surgery, and consensus guidelines for prevention and management of PONV are available in the current literature. These issues are discussed in Chapters 17 and 56.

Goal-Directed Fluid & Hemodynamic Therapy

Intraoperative and postoperative fluids are commonly infused in excess of perioperative loss. Despite numerous studies seeking to define fluid strategy (amount and type of fluid administered, crystalloid versus colloid, etc), "liberal," "standard," or "restrictive" fluid regimens have failed to consistently improve postoperative outcomes. Liberal fluid administration and sodium excess lead to fluid overload, increase postoperative morbidity, and prolong hospitalization. Fluid overload, especially of crystalloid, has been associated with anastomotic leakage, pulmonary edema, pneumonia, wound infection, postoperative ileus, and reduced tissue oxygenation. Furthermore, excess fluids commonly increase body weight by 3–6 kg and may impair postoperative mobilization. On the other hand, restrictive fluid management does not offer any substantial, clinically relevant advantage, except possibly improving pulmonary function and reducing postoperative hypoxia. However, compared with liberal fluid management, restrictive fluid management increases the release of stress-related hormones such as aldosterone, renin, and angiotensin II. The amount of perioperative extracellular fluid losses can be minimized with limited preoperative fasting, avoidance of mechanical bowel preparation, minimally invasive surgical techniques such as laparoscopic and video-assisted thoracoscopic (VAT) surgery, and early postoperative enteral nutrition.

The concept of goal-directed fluid therapy is based on the optimization of hemodynamic measures such as heart rate, blood pressure, stroke volume, pulse pressure variation, and stroke volume variation obtained by noninvasive cardiac output devices such as pulse-contour arterial waveform analysis, transesophageal echocardiography, or esophageal Doppler (see Chapter 5). The type of fluid infused is also important: isotonic crystalloid should be used to replace extracellular losses, whereas iso-oncotic colloids are needed to replace intravascular volume (Table 48–3).

TABLE 48–3 Physiologically based first-line fluid replacement for goal-directed therapy.[1]

Physiological Requirement	Replace with	Amount
Extracellular		
Insensible perspiration	Crystalloids[2]	
Closed abdomen		0.5 mL/kg/h
Open abdomen		1 mL/kg/h
Urine production	Crystalloids	Measured output[4]
Intravascular		
Blood loss	Colloids[3]	Estimated losses
Further preload deficit	Colloids	According to clinical estimation[5]

[1]Reproduced, with permission, from Chappell D, Jacob M: Influence of non-ventilatory options on postoperative outcome. Best Pract Res Clin Anaesthesiol 2010;24:267.

[2]Crystalloids should be given in an isotonic balanced form.

[3]Colloids should be given in an iso-oncotic form in balanced solutions.

[4]First-line approach in healthy kidneys.

[5]If possible use extended monitoring (eg, PICCO system, esophageal Doppler, etc).

POSTOPERATIVE PERIOD

Immediate Postoperative Care

A. Strategies to Minimize Postoperative Shivering

The primary cause of postoperative shivering is perioperative hypothermia, although other, non-thermoregulatory, mechanisms may be involved. Postoperative shivering can greatly increase oxygen consumption, catecholamine release, cardiac output, heart rate and blood pressure, and intracerebral and intraocular pressure. It increases cardiovascular morbidity, especially in elderly patients, and increases length of stay in the postanesthesia care unit. Shivering is uncommon in elderly and hypoxic patients: the efficacy of thermoregulation decreases with aging, and hypoxia can directly inhibit shivering. Many drugs, notably meperidine, clonidine, and tramadol, can be used to reduce postoperative shivering; however, prevention of hypothermia is the most efficient strategy.

B. PONV Treatment

Pharmacological treatment of PONV should be promptly initiated once medical or surgical causes of PONV have been ruled out. PONV and its treatment are reviewed in Chapter 17.

C. Multimodal Analgesia

8 The scientific rationale for multimodal analgesia is to combine different classes of medications, having different (multimodal) pharmacological mechanisms of action and additive or synergistic effects, to control multiple perioperative pathophysiological factors that lead to postoperative pain and its sequelae. Such an approach may achieve desired analgesic effects while reducing analgesic dosage and associated side effects, and often includes utilization of regional analgesic techniques such as local anesthetic wound infusion, epidural or intrathecal analgesia, or single-shot or continuous peripheral nerve blockade. Multimodal analgesia is routinely utilized in ERPs to improve postoperative outcomes. Discussion here focuses on the principal analgesic

interventions that can be used in perioperative multimodal analgesia regimens.

9 **1. NSAIDs—**The addition of nonsteroidal antiinflammatory drugs (NSAIDs) to systemic opioids diminishes postoperative pain intensity, reduces the opioid requirement by approximately 30%, and decreases opioid-related side effects such as PONV and sedation. However, NSAIDs may increase the risk of gastrointestinal and postoperative bleeding, decrease kidney function, increase the risk of anastomotic leakage after colorectal surgery, and impair wound healing.

Perioperative administration of cyclooxygenase-2 (COX-2) inhibitors likewise reduces postoperative pain and decreases both opioid consumption and opioid-related side effects, and while their use has reduced the incidence of NSAID-related platelet dysfunction and gastrointestinal bleeding, the adverse effects of COX-2 inhibitors on kidney function remain controversial. Concerns have also been raised regarding their safety for patients undergoing cardiovascular surgery; these have centered on rofecoxib and valdecoxib, specifically. Increased cardiovascular risk associated with the perioperative use of celecoxib or valdecoxib in patients with minimal cardiovascular risk factors and undergoing nonvascular surgery has not been proven. Further studies are needed to establish the analgesic efficacy and safety of COX-2 inhibitors and their clinical effect on postoperative outcomes.

2. Acetaminophen (paracetamol)—Oral, rectal, and parenteral acetaminophen is a common component of multimodal analgesia. Acetaminophen's analgesic effect is 20–30% less than that of NSAIDs, but its pharmacological profile is safer. Analgesic efficacy improves when the drug is administered together with NSAIDs, and it significantly reduces pain intensity and spares opioid consumption after orthopedic and abdominal surgery. However, acetaminophen may not reduce opioid-related side effects. Routine administration of acetaminophen in combination with regional anesthesia and analgesia techniques may allow NSAIDs and COX-2 inhibitors to be reserved for control of breakthrough pain, thus limiting the incidence of NSAID-related side effects.

3. Opioids—Despite the increasing use of new, nonopioid analgesic medications and adjuvants and of regional anesthesia and analgesia techniques intended to minimize opioid requirements and opioid-related side effects (Table 48–4), the use of systemic opioids remains a cornerstone in the management of surgical pain. Parenteral opioids are frequently prescribed in the postoperative period during the transitional phase
10 to oral analgesia. Opioid administration by patient-controlled analgesia (PCA) provides better pain control, greater patient satisfaction, and fewer opioid side effects when compared with on-request parenteral opioid administration. Oral administration of opioids, such as immediate-release and controlled-release oxycodone or hydromorphone, in combination with NSAIDs or acetaminophen, or both, is commonly used in the perioperative period. Preoperative administration of extended-release oxycodone in patients undergoing surgery of short duration provides adequate plasma concentration and analgesia following discontinuance of remifentanil infusion. Tramadol, a partial opioid agonist, has been associated with an increased incidence of PONV.

4. Epidural analgesia—In addition to providing excellent analgesia, epidural blockade blunts the stress response associated with surgery, decreases postoperative morbidity, attenuates catabolism, and accelerates postoperative functional recovery. Compared with systemic opioid analgesia, thoracic epidural analgesia provides better static and dynamic pain relief. Long-acting local anesthetics such as ropivacaine (0.2%), bupivacaine (0.1–0.125%), and levobupivacaine (0.1–0.125%) are commonly administered together with lipophilic opioids by continuous epidural infusion or by patient-controlled epidural analgesia (PCEA). Administering low doses of local anesthetic via thoracic epidural infusion avoids lower extremity motor blockade that may delay postoperative mobilization and recovery. Adding fentanyl or sufentanil to epidural local anesthetics improves the quality of postoperative analgesia without delaying recovery of bowel function.

High thoracic epidural analgesia has been introduced in patients undergoing cardiac surgery based on data from small randomized clinical trials that suggested beneficial effects on postoperative

TABLE 48–4 Analgesic adjuvants in the perioperative period.[1,2]

Adjuvant	Type of Surgery or Clinical Setting	Analgesic Efficacy as Adjuvant	Dosages Used (Boluses, CI)	Administration			Monitoring
				Route	*Timing*	*Postoperative Duration*	
Lidocaine	Tonsillectomy	–	1.5 mg/kg, *followed by* 1.5–2 mg/kg/h CI (Inra, until skin closure), *and then* 1 mg/kg/h CI (Post)	IV	Pre,[3] Intra, Peri	30 min–48 h	Signs of local anesthetic toxicity (CNS cardiovascular)
	Cardiac	+					
	Abdominal (laparotomy, laparoscopic)	+					
	Thoracotomy	+					
	Hysterectomy	+					
	Laparoscopic prostatectomy	+					
	Orthopedic	–					
Ketamine	Cardiac	+	0.5–1 mg/kg, *followed by* 2–10 mcg/kg/min CI	IV	Pre, Post (PCA[4]), Peri	4–72 h	CNS[5] (level of sedation, nystagmus hallucinations), cardiovascular
	Thoracotomy	+					
	Abdominal	+					
	Gynecological	–					
	Orthopedic	–					
	Spine	+/–					
	Chronic use of opioids	+					
	Preventing chronic pain	+/–					
	OIH	+/–					
Gabapentinoids							
Gabapentin	Cholecystectomy	–	300–1200 mg	PO	Pre,[6] Post		CNS[5] (level of sedation, somnolence, dizziness), leg edema
	Hysterectomy	+					
	Spine	+					
	Hip arthroplasty	–					
	Preventing chronic pain	+/–					
Pregabalin	Hysterectomy	+	75–300 mg	PO	Pre, Post		
	Laparoscopic cholecystectomy	–					
	Preventing chronic pain	+/–					

$MgSO_4$	Cardiac Cholecystectomy Lower limb orthopedic Gynecological Ambulatory	+ + + + +	30–50 mg/kg, *followed by* 8–15 mg/kg/h CI	IV	Pre, Intra	CNS (somnolence), neuromuscular function, respiratory depression, cardiovascular (bradycardia)
Steroids	Hip arthroplasty Breast Laparoscopic cholecystectomy	+ + +	Dexamethasone: 8–16 mg Methylprednisolone: 125 mg	IV	Pre	Glycemia, GI bleeding, wound healing
α_2-Agonist						
Clonidine	PO Abdominal Total knee arthroplasty Hysterectomy Prostatectomy	 – + + –	PO 3–5 mcg/kg	PO, IV	Pre,[7] Intra, Post (PCA[8])	CNS[5] (level of sedation), cardiovascular (hypotension, bradycardia)
	IV Cholecystectomy Abdominal Spine	 – + +	IV 150 mcg			
Dexmedetomidine	Thoracotomy Abdominal Hysterectomy Bariatric	+ + + +	Loading dose 0.5–1 mcg/kg, *followed by* 0.2–0.4 mcg/kg/h CI	IV	Pre, Intra, Post (PCA[9])	

[1]Efficacy of these agents as adjuvant analgesics has been demonstrated by a reduction of pain or opioid consumption, or both; or opioid side effects; or all three.

[2]CI, continuous infusion; Intra, Intraoperative period; Post, postoperative period; Pre, preoperative period during induction; Peri, preoperative, intraoperative, and postoperative periods; CNS, central nervous system; PCA, patient-controlled analgesia; OIH, opioid-induced hyperalgesia; GI, gastrointestinal.

[3]Bolus, or 30 min before induction of anesthesia.

[4]As a 1-mg demand dose, lockout time 7 min.

[5]Psychotomimetic side effects are dose-dependent.

[6]Single dose, 1–2.5 h before surgery.

[7]Given PO 60–90 min before surgery.

[8]As a 20-mcg demand dose, lockout time 5 min.

[9]As a 5-mcg demand dose, lockout time 5 min.

outcomes. A recent meta-analysis of more than 2700 patients who underwent cardiac surgery and received high thoracic epidural analgesia showed an overall reduction of pulmonary complications (relative risk = 0.53) and supraventricular arrhythmias (relative risk = 0.68), but no reduction in incidence of myocardial infarction, stroke, or postoperative mortality. Due to concerns about the risk of epidural hematoma and its devastating neurological consequences in patients fully heparinized during cardiopulmonary bypass, the use of high thoracic epidural analgesia is understandably limited.

11 **5. Peripheral nerve block—**Single-shot and continuous peripheral nerve blockade is frequently utilized for fast-track ambulatory and inpatient orthopedic surgery, and can accelerate recovery from surgery and improve analgesia and patient satisfaction (see Chapter 46). The opioid-sparing effect of nerve blocks minimizes the risk of opioid-related side effects. Appropriate patient selection and strict adherence to institutional clinical pathways helps ensure the success of peripheral nerve blockade as a fast-track orthopedic analgesia technique. Peripheral nerve blockade has also been used as a component of multimodal analgesia for abdominal surgery; for example, transverseus abdominis plane (TAP) block in patients undergoing total abdominal hysterectomy provides effective analgesia and decreases morphine consumption and sedation when compared with patients receiving morphine alone via PCA.

6. Local anesthetic wound infusion—The analgesic efficacy of local anesthetic wound infusion has been established for multiple surgical procedures. Inconsistent results may be due to factors that include type, concentration, and dose of local anesthetic, catheter placement technique and type of catheter, mode of local anesthetic delivery, incision location, and dislodgment of the catheter during patient mobilization.

Strategies to Facilitate Recovery on the Surgical Unit

A. Organization of Multidisciplinary Surgical Care

The multidisciplinary aspect of postoperative care should bring together the surgeon, the nurse, the anesthesiologist, the nutritionist, and the physiotherapist in an effort to customize individual patient care based on standardized, procedure-specific protocols. Comfortable chairs and walkers need to be made readily available near each patient bed to encourage patients to sit, stand, and walk. The benefits of mobilization for cardiovascular homeostasis and bowel function have been shown repeatedly. Patients should be encouraged to sit the evening following surgery, with ambulation starting the next day for a minimum of 4–6 h each day. If patients cannot get out of bed, they should be encouraged to perform physical and deep breathing exercises.

B. Optimization of Analgesia to Facilitate Functional Recovery

A well-organized, well-trained, highly motivated acute pain service (APS) and surgical nursing workforce, utilizing procedure-specific clinical protocols to optimally manage analgesia and related side effects, is critically important for fast-track surgery. The quality of pain relief and symptom control heavily influences postoperative recovery; optimal mobilization and dietary intake depend upon adequate analgesia. The anesthesiologist, in coordination with the APS, must identify and employ the optimal analgesic techniques tailored to the specific surgical procedure, and the quality of analgesia and possible presence of side effects must be closely and continuously assessed. The patient must be comfortable ambulating and performing physiotherapy, with minimal side effects such as lightheadedness, sedation, nausea and vomiting, and leg weakness.

C. Strategies to Minimize Postoperative Ileus

12 Postoperative ileus delays enteral feeding, causes patient discomfort, and is one of the most common causes of prolonged postoperative hospital stay. Because early enteral nutrition is associated with decreased postoperative morbidity, interventions and strategies aimed at decreasing postoperative ileus are required for patients in an ERP. Three main mechanisms contribute to ileus: sympathetic inhibitory reflexes, local inflammation caused by surgery, and postoperative opioid analgesia. The nasogastric tube, frequently inserted

after abdominal surgery, does not speed the recovery of bowel function and may increase pulmonary morbidity by increasing the incidence of aspiration. Therefore, nasogastric tubes should be discouraged whenever possible or used for only a very short period of time, even in gastric and hepatic surgery.

Multimodal analgesia and nonopioid analgesia techniques shorten the duration of postoperative ileus. Continuous epidural local anesthetic infusion improves the recovery of bowel function by suppressing the inhibitory sympathetic spinal cord reflexes. Thoracic epidural analgesia with local anesthetics and small doses of opioids reduces the incidence of ileus and improves postoperative pain relief. Minimally invasive surgery decreases surgical stress and inflammation, resulting in a faster return of bowel function. Any role of epidural analgesia in accelerating the recovery of bowel function after laparoscopic surgery remains controversial, at best. Laxatives, such as milk of magnesia and bisacodyl, reduce postoperative ileus duration. Prokinetic medications such as metoclopramide are ineffective. Neostigmine increases peristalsis but may also increase the incidence of PONV.

Excessive perioperative fluid administration commonly causes bowel mucosal edema and delays postoperative return of bowel function. However, results from a randomized double-blind study of liberal versus restricted fluid administration showed no differences with regard to recovery of bowel function in patients undergoing fast-track abdominal surgery. No studies have compared crystalloid versus colloid administration in terms of their effect on the return of bowel function. 13 Because either excessive, or excessively restricted, perioperative fluid therapy may increase the incidence and severity of postoperative ileus, a goal-directed fluid strategy (discussed earlier) should be selected to decrease postoperative morbidities and enhance recovery and should be utilized according to the type of surgery and patient comorbidities.

Postoperative chewing gum, by stimulating gastrointestinal reflexes, may decrease ileus duration. Although its effect has not been evaluated in ERP patients, postoperative chewing gum may be included in multimodal interventions to decrease postoperative ileus because of its safety and low cost. Peripheral opioid μ-receptor antagonists methylnaltrexone and alvimopan have been introduced to minimize the adverse effects of opioids on bowel function without antagonizing opioid analgesia. In patients receiving large-dose intravenous morphine analgesia, alvimopan decreases the duration of postoperative ileus by 16–18 h, the incidence of nasogastric tube reinsertion, postoperative morbidity, and hospital length of stay and readmission rates, especially in patients undergoing bowel resection. Nevertheless, the recovery of bowel function is slower when compared with patients receiving multimodal strategies in an ERP.

Issues in the Implementation of Enhanced Recovery Programs

The success of ERPs depends upon the capacity of multiple stakeholders to reach interdisciplinary consensus. Several aspects of perioperative care, such as use of drains, dietary and activity restrictions, fluid management, and bedrest, have been part of surgical "traditions" and must be significantly revised in ERPs. Patient involvement and patient and family expectations are critically important, but frequently overlooked, aspects of these programs. New surgical techniques, like transverse incisions or minimally invasive surgery, may require surgeons to acquire and perfect new skills. Similarly, the emphasis on thoracic epidural blockade or peripheral nerve blocks, pharmacological modulation of the neuroendocrine stress response to surgery, goal-directed fluid and hemodynamic therapy, and integral involvement of a well-organized and managed APS requires an expansion of the traditional role of anesthesia providers. Aggressive analgesia and symptom management, early ambulation and physiotherapy, early nutrition protocols, and early removal or total avoidance of urinary drainage catheters significantly change the way patients are cared for in the postanesthesia recovery unit and on the surgical unit and require a well-organized, highly trained, highly motivated nursing staff.

Although there are published studies of successful ERPs, there are no "off-the-shelf" protocols,

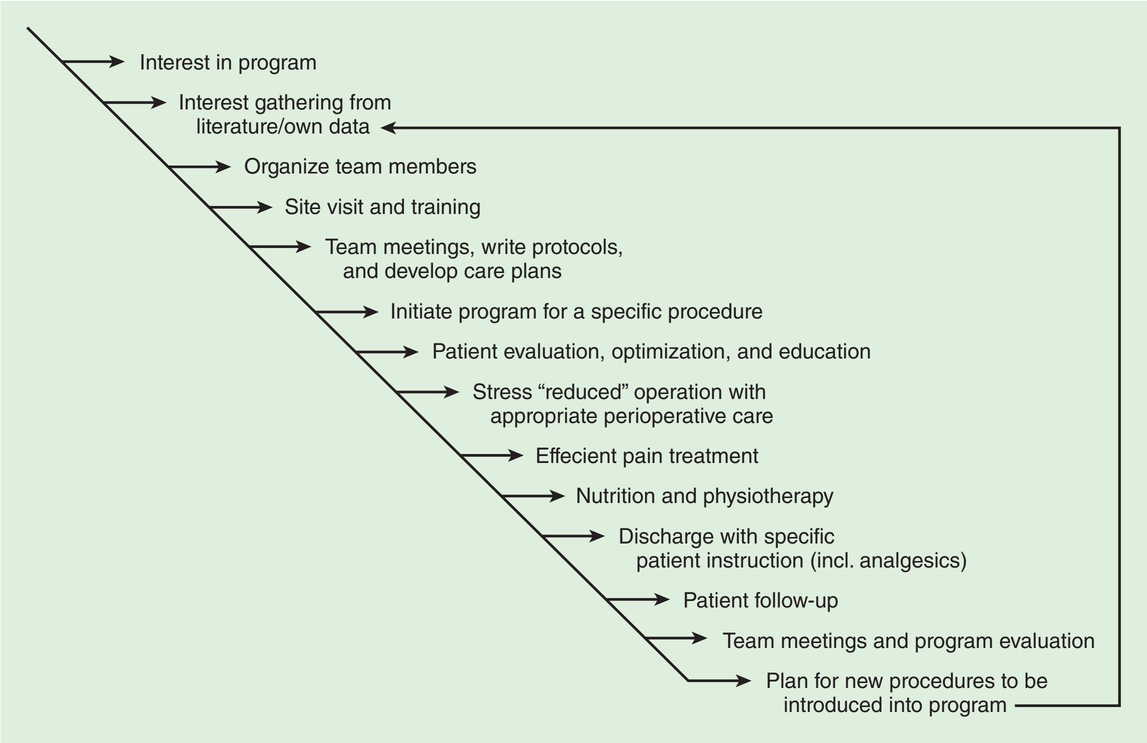

FIGURE 48–5 Stepwise process for initiating and implementing an enhanced recovery program. (Reproduced, with permission, from Kehlet et al: Ann Surg 2008;248:189.)

and local differences in expertise, experience, and resources influence the development of such protocols for each institution. Each family of similar surgical procedures requires a standardized interdisciplinary clinical protocol or pathway, with specialized input from a team with experience in caring for those patients. Such an interdisciplinary team should include representatives from surgery, anesthesiology, nursing, pharmacy, physiotherapy, nutrition, and administration, and it should be responsible not only for the clinical protocol's creation, but also for continuously monitoring its efficacy and for instituting performance improvement-related protocol modifications and provider feedback as indicated by outcomes data (Figure 48–5).

The current era is one in which optimal surgical care requires the anesthesia provider to be part of the perioperative medicine team. The anesthesiologist's skill sets are essential for the success of ERPs and have potential benefits for surgical care delivery on a global basis, from preoperative evaluation and presurgical preparation to recovery and final dismissal from care. This opportunity must be seized.

GUIDELINES

Gustafsson UO, Scott MJ, Schwenk W, et al: Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clin Nutr 2012;31:783.

Lassen K, Coolsen MM, Slim K, et al: Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clin Nutr 2012;31:817.

Nygren J, Thacker J, Carli F, et al: Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. Clin Nutr 2012;31:801.

SUGGESTED READING

Aarts M-A, Okrainec A, Glicksman A, et al: Adoption of enhanced recovery after surgery (ERAS) strategies for colorectal surgery at academic teaching hospitals and impact on total length of hospital stay. Surg Endosc 2012;26:442.

Adamina M, Kehlet H, Tomlinson GA, et al: Enhanced recovery pathways optimize health outcomes and resource utilization: A meta-analysis of randomized controlled trials in colorectal surgery. Surgery 2011;149:830.

Baldini G, F Carli: Anesthetic adjunctive drugs for fast-track surgery. Curr Drug Targets 2009;10:667.

Carli F, Kehlet H, Baldini G, et al: Evidence basis for regional anesthesia in multidisciplinary fast-track surgical care pathways. Reg Anesth Pain Med 2011;36:63.

Chappell D, Jacob M: Influence of non-ventilatory options on postoperative outcome. Best Pract Res Clin Anaesthesiol 2010;24:267.

Chappell D, Jacob M, Hofmann-Kiefer K, et al: Rational approach to perioperative fluid management. Anesthesiology 2008;109:723.

Collard V, Mistraletti G, Taqi A, et al: Intraoperative esmolol infusion in the absence of opioids spares postoperative fentanyl in patients undergoing ambulatory laparoscopic cholecystectomy. Anesth Analg 2007;105:1255.

Coulter A, Ellins J: Effectiveness of strategies for informing, educating, and involving patients. Br Med J 2007;335:24.

Dunkelgrun M, Boersma E, Schouten O, et al: Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Bisoprolol and fluvastatin for the reduction of perioperative cardiac mortality and myocardial infarction in intermediate-risk patients undergoing noncardiovascular surgery: A randomized controlled trial (DECREASE-IV). Ann Surg 2009;249:921.

Harvey KP, Adair JD, Mayyas I, et al: Can intravenous lidocaine decrease postsurgical ileus and shorten hospital stay in elective bowel surgery? A pilot study and literature review. Am J Surg 2009;198:231.

Kehlet H: Multimodal approach to postoperative recovery. Curr Opin Crit Care 2009;15:355.

Kehlet H, Wilmore DW: Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg 2008;248:189.

Kelin J: Multimodal multidisciplinary standardization of perioperative care: Still a long way to go? Curr Opin Crit Care 2008;21:187.

Liu SS, Richman JM, Thirlby RC, et al: Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: A quantitative and qualitative systematic review of randomized controlled trials. J Am Coll Surg 2006;203:914.

Ljungqvist O: Preoperative fasting. Br J Surg 2003;90:400.

Lui F, Ng KF: Adjuvant analgesics in acute pain. Expert Opin Pharmacother 2011;12:363.

Manion, SC, Brennan TJ: Thoracic epidural anesthesia and acute pain management. Anesthesiology 2011;115:181.

Neugebaure EAM, Wilkinson RC, Kehlet H, et al: PROSPECT: A practical method for formulating evidence-based expert recommendations for the management of postoperative pain. Surg Endosc 2007;21:1047.

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;143:990.

Powell AE, Davies HTO, Bannister J, et al: Challenge of improving postoperative pain management: Case studies of three acute pain services in the UK National Health Service. Br J Anaesth 2009;102:824.

Tonnesen H, Nielsen PR, Lauritzen JB, et al: Smoking and alcohol intervention before surgery: Evidence for best practice. Br J Anaesth 2009;102:297.

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;58:22.

White PF, Kehlet H, Neal JM, et al: The role of the anesthesiologist in fast-track surgery: From multimodal analgesia to perioperative medical care. Anesth Analg 2007;104:1380.

Wu CI, Raja SN: Treatment of postoperative pain. Lancet 2011;377:2215.

Yardeni IZ, Beilin B, Mayburd E, et al: The effect of perioperative intravenous lidocaine on postoperative pain and immune function. Anesth Analg 2009,109:1464.