

The Role of the Anesthesiologist in Fast-Track Surgery: From Multimodal Analgesia to Perioperative Medical Care

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BACKGROUND: Improving perioperative efficiency and throughput has become increasingly important in the modern practice of anesthesiology. Fast-track surgery represents a multidisciplinary approach to improving perioperative efficiency by facilitating recovery after both minor (i.e., outpatient) and major (inpatient) surgery procedures. In this article we focus on the expanding role of the anesthesiologist in fast-track surgery.

METHODS: A multidisciplinary group of clinical investigators met at McGill University in the Fall of 2005 to discuss current anesthetic and surgical practices directed at improving the postoperative recovery process. A subgroup of the attendees at this conference was assigned the task of reviewing the peer-reviewed literature on this topic as it related to the role of the anesthesiologist as a perioperative physician.

RESULTS: Anesthesiologists as perioperative physicians play a key role in fast-track surgery through their choice of preoperative medication, anesthetics and techniques, use of prophylactic drugs to minimize side effects (e.g., pain, nausea and vomiting, dizziness), as well as the administration of adjunctive drugs to maintain major organ system function during and after surgery.

CONCLUSION: The decisions of the anesthesiologist as a key perioperative physician are of critical importance to the surgical care team in developing a successful fast-track surgery program.

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The concept of fast-track surgery using multimodal perioperative rehabilitation programs (1) was introduced in the early 1990s to facilitate an early discharge from the hospital and more rapid resumption of normal activities of daily living after elective surgery. The increasing popularity of minimally invasive surgical

techniques has also allowed patients to undergo increasingly complex surgical procedures on an ambulatory and/or short-stay basis (2). Therefore, fast-tracking implies implementation of a perioperative patient care paradigm that reduces the time to discharge home and resumption of activities of daily living after both major (inpatient) and minor (outpatient) surgical procedures.

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The role of the anesthesiologist has evolved from that of a physician primarily concerned with providing optimal surgical conditions and minimizing pain immediately after the operation, to that of a perioperative physician responsible for ensuring that patients with coexisting medical conditions are optimally managed before, during, and after surgery (3,4). In addition to optimizing preoperative medication and providing the best possible intraoperative surgical conditions, the ability to provide for a rapid emergence from anesthesia and avoid postoperative side effects and early complications has assumed increasing importance for both outpatients and inpatients undergoing fast-track surgery. The evaluation of clinically meaningful outcomes (e.g., quality of recovery, resumption of normal activities of daily living) has increasingly become a focal point of anesthesia-related clinical research involving new drugs and techniques.

The Fast-Track Surgery Study Group is a multidisciplinary group of clinical investigators interested in critically evaluating the peer-reviewed literature related to surgical and anesthetic practices, as well as pre- and postoperative care directed at facilitating the recovery process after elective surgery. The primary aim of this article is to focus on specific aspects of perioperative care in which the anesthesiologist's contribution facilitates the recovery process. Ideally, the process begins in the preoperative period and extends into the postdischarge period. The anesthetic and analgesic techniques for facilitating the recovery process apply to all patients undergoing surgical procedures whether they are hospitalized or discharged home on the day of surgery. The complementary role of surgery and nursing care in the fast-tracking process are also discussed.

PREOPERATIVE ISSUES

Premedication

Preanesthetic medication is given primarily to provide sedation, reduce anxiety, optimize intraoperative hemodynamic stability, and decrease postoperative side effects (5). Benzodiazepines remain the most commonly used premedications because even small doses of these compounds (e.g., midazolam 20 $\mu\text{g}/\text{kg}$ IV) can improve the perioperative fast-tracking process by reducing anxiety and anxiety-related complications, as well as improving patient comfort and satisfaction (6). With respect to improving surgical outcome, both the β -blockers and α_2 -agonists are increasingly popular adjuvants to fast-track anesthetic techniques. As a result of their anesthetic and analgesic-sparing effects (7–11), these compounds can facilitate the early recovery process, improve perioperative hemodynamic stability, and reduce postoperative pain. Premedication with the α_2 -agonist clonidine or dexmedetomidine has been associated with a reduction in the use of opioid analgesics, postoperative nausea and vomiting (PONV), and intraoperative

blood loss (10–12). IV clonidine combined with epidural clonidine improves analgesia and shortens the duration of paralytic ileus after colorectal procedures (13). The inhibitory effects of these α_2 -agonists on the sympathoadrenergic and hypothalamo-pituitary stress response (14) facilitate glycemic control in type-2 diabetic patients (15) and reduce myocardial ischemia after surgery (16).

β -blockers (e.g., atenolol) suppress surgery-induced increases in circulating catecholamines, and prevent untoward perioperative cardiovascular events in elderly patients undergoing noncardiac surgery (7). Evidence suggests that β -blockers are most effective in reducing cardiac events in surgical patients with pre-existing coronary artery disease (17,18). Perioperative β -blockade improved hemodynamic stability during emergence from anesthesia and in the early postoperative period. The anesthetic and analgesic-sparing effects of β -blockers also lead to a faster emergence from anesthesia and reduce postoperative side effects (e.g., PONV). The anticatabolic properties of β -blockers may also facilitate the resumption of normal activities after major surgery procedures. In critically ill patients, β -blocker therapy combined with total parenteral nutrition can establish a positive protein balance (19).

Hydration Status

Elective surgery has traditionally been performed after an overnight fast to ensure an empty stomach and minimize the risk of aspiration during the perioperative period. However, many studies have demonstrated that avoiding fasting-induced dehydration (e.g., allowing oral intake of clear liquids up to 2–3 h before surgery and IV hydration before induction of anesthesia) is both safe and effective in reducing postoperative side effects (20–23). Liberal (versus restrictive) fluid administration during laparoscopic surgery also leads to improved patient outcomes (24,25). One study recommended that even obese patients without comorbid conditions should be allowed to drink clear liquids until 2 h before elective surgery procedures (21). Preoperative administration of glucose-containing fluids, prevents postoperative insulin resistance and attenuates the catabolic responses to surgery while replacing fluid deficits (26,27). However, the effects of glucose-containing solutions on clinical outcomes, including the length of hospital stay, incidence of PONV, muscle strength and subjective well-being remain controversial (28,29).

Perioperative hydration includes correction of preoperative dehydration due to fasting, bowel preparation, and underlying disease, replacement of blood loss, and administration of maintenance fluids (30,31). Four aspects of perioperative fluid resuscitation appear to be relevant for improving surgical outcome: 1) fluid volume, 2) fluid composition, 3) type of surgery, and 4) hemodynamic goals. With the exception of

pulmonary and major abdominal surgery, it is common practice to administer relatively large amounts of crystalloids even for procedures with minimal blood loss. For example, high intraoperative fluid therapy was associated with reduced side effects (e.g., pulmonary dysfunction, dizziness, drowsiness, thirst, and nausea/vomiting) and a shorter hospital stay after laparoscopic cholecystectomy (22,25). Although aggressive crystalloid administration during colorectal surgery improved tissue oxygenation (32), it did not decrease the risk of surgical wound infections (33). On the other hand, two studies have suggested that excess fluid hydration can increase postoperative morbidity and the length of the hospital stay after major abdominal surgery (34,35). Furthermore, perioperative water and salt restriction reduced cardiopulmonary and tissue healing complications and prevented hyperchloremic metabolic acidosis after abdominal surgery (36,37).

Goal-directed fluid administration targeting specific values for cardiac index, oxygen delivery, and oxygen consumption using synthetic colloids and inotropic drugs may further improve outcome and recovery in patients undergoing pulmonary, major abdominal and orthopedic procedures (38,39). Therefore, strategies, which avoid both hypovolemia and excessive intravascular volume postoperatively, are important in facilitating the fast-track recovery process (31).

Glycemic Control

Impaired glucose homeostasis during surgery can result in hyperglycemia (27). Recent evidence suggests that even moderate increases in blood glucose are associated with adverse outcomes, particularly in patients with cardiovascular, infectious, and neurological diseases (40,41). Intraoperative hyperglycemia is an independent risk factor for postoperative complications, including death after cardiac surgery (42–44). Morbidity and mortality correlated with mean blood glucose levels in a concentration-dependent manner in diabetic patients undergoing cardiac surgery (42,43). Van den Berghe et al. (45) also demonstrated superior surgical outcomes with strict normoglycemia in postoperative critically ill patients. Not surprisingly, improved glycemic control using a continuous perioperative insulin infusion reduces morbidity and mortality in diabetic patients undergoing cardiac surgery (46,47). Maintenance of normoglycemia also attenuates the systemic inflammatory response to cardiopulmonary bypass (48). Therefore, “tight” glycemic control clearly improves patient outcome after cardiac surgery (46–48), and other critical illnesses (49). Use of glucocorticoid steroids as part of a fast-track anesthetic technique may lead to transient postoperative hyperglycemia in at-risk surgery populations (e.g., diabetics) (50).

Temperature Control

Perioperative hypothermia can have a wide range of detrimental effects, which may include increased rates of wound infection, morbid cardiac events, blood

loss, and even prolong the hospital stay (51–54). Studies suggest that maintaining normothermia during surgery may provide significant benefits for surgical patients by reducing postoperative morbidity (55). Hypothermia can be reduced by using forced-air warming blankets, and warming irrigation and IV fluids. In addition, warmed and humidified insufflation gases may decrease postoperative pain and the need for opioid analgesics and antiemetic therapy after laparoscopic surgery (56).

FAST-TRACK ANESTHETIC TECHNIQUES

Local Anesthesia

Infiltration of local anesthetics around a surgical incision should be a component of all “balanced” fast-track anesthetic techniques (57,58). Local infiltration anesthesia alone provides adequate analgesia for superficial procedures (e.g., inguinal herniorrhaphy, breast and anorectal surgery, shoulder and knee arthroscopy), and is probably vastly under-utilized (59–61). Patient comfort can be improved if IV sedation-analgesia is used to supplement local anesthetic infiltration, particularly when the local anesthesia is not completely effective (59,62). However, use of IV adjuvants can also increase side effects (e.g., ventilatory depression, PONV) (63,64). The benefits of local wound infiltration in patients undergoing more invasive surgical procedures have not been as extensively studied. Although there is little evidence that preoperative analgesia involving local anesthetic injections at the surgical wound reduces the risk for developing persistent postoperative pain syndromes (65), it does lessen both intra- and postoperative opioid requirements as well as opioid-related side effects (66).

Many studies have demonstrated improved analgesia, greater patient satisfaction with pain management, and reduced PONV and hospital stay with infusion of local anesthetic at the surgical incision site (67). For example, patients receiving a continuous infusion of bupivacaine at the median sternotomy incision site after cardiac surgery not only experienced improved postoperative pain management, but were also able to ambulate earlier, leading to a reduced length of hospital stay (68). Infiltration of local anesthetic at portal sites and the gallbladder bed improves postoperative analgesia after laparoscopic cholecystectomy (69). Compared with neuroaxial or general anesthetic techniques, local anesthetic infiltration techniques reduce the risk of postoperative urinary retention associated with anorectal surgery (70) and inguinal herniorrhaphy (62,71). When used as the primary anesthetic technique, local anesthesia facilitates postanesthesia care unit bypass, thereby reducing recovery costs (59,62,70,72).

In summary, routine use of local anesthetics at incision sites can facilitate fast-track recovery after outpatient, and even some inpatient, surgical procedures.

Regional Anesthesia

IV regional anesthesia, peripheral nerve blocks, and "mini-dose" neuraxial blocks are the most popular regional anesthetic techniques used for fast-track surgery. Use of IV regional anesthesia for ambulatory hand surgery was associated with faster discharge and lower costs, when compared with either general anesthesia or a peripheral nerve block (72). As supplements to general anesthesia, peripheral nerve blocks (versus local infiltration) improve postoperative analgesia and reduce opioid-related side effects, thereby facilitating the fast-track recovery process (73). For example, suprascapular block improves the recovery profile after arthroscopic shoulder surgery performed under general anesthesia (74), but not after "open" surgery with an interscalene block (75). As the primary analgesic technique, peripheral nerve blocks are associated with shorter discharge times, improved analgesia, and fewer side effects compared with general anesthesia for hand (73,76), shoulder (77), anorectal (70), hernia repair (62,78), and knee surgery (79).

Although it is widely assumed that regional anesthesia offers advantages over general anesthesia with respect to speed of recovery (80), a recent metaanalysis suggested that there were no significant differences in ambulatory surgery unit time (81). However, use of continuous perineural catheters to administer local anesthetics can improve pain control and expedite hospital discharge after painful upper (82) and lower extremity (83) surgical procedures. In addition, the local analgesia can be continued at home after discharge (84). These beneficial findings were confirmed in a recent multicenter trial which used patient-controlled perineural local analgesia as an alternative to IV patient-controlled analgesia (PCA) with morphine (85). A recent metaanalysis confirmed the advantages of a peripheral catheter technique over a parenteral opioid-based analgesic technique for extremity surgery (86).

When central neuroaxis block techniques are used as a part of a fast-track regimen, it is important to select the most appropriate local anesthetic and adjuvant combination to avoid prolonged anesthetic effects that negatively impact on readiness for discharge (62). For instance, prolonging subarachnoid-induced analgesia with fentanyl rather than epinephrine avoids the prolonged time to micturition (87), and reduces the time to discharge from the hospital (88). As compared with conventional intrathecal doses of local anesthetics, use of so-called minidose lidocaine (10–30 mg), bupivacaine (3.5–7 mg), or ropivacaine (5–10 mg) spinal anesthetic techniques when combined with a potent opioid analgesic (e.g., fentanyl 10–25 μ g or sufentanil 5–10 μ g) can result in faster recovery of sensory and motor function (89,90). When compared to a monitored anesthesia care (MAC) technique for ambulatory knee surgery, a minidose spinal technique involving lidocaine and fentanyl achieved comparable recovery times after knee arthroscopy

(60). For outpatient laparoscopic gynecologic surgery, this technique has also been reported to offer significant advantages over both conventional spinal and general anesthetic techniques (90,91). However, postoperative side effects (e.g., pruritus, nausea) are increased due to the intrathecal opioid (60).

Epidural analgesia can be a valuable adjuvant to fast-track anesthesia techniques for major surgery (92). The benefits of epidural analgesia are most apparent when used as part of a multimodal analgesic regimen (93,94). Both continuous epidural infusion and epidural PCA provide better static and dynamic pain relief than IV opioid-based PCA delivery systems (95). In addition, epidural local analgesia, compared to IV-PCA, reduced postoperative pulmonary complications after thoracic or upper abdominal surgery (96), improved perioperative nutritional profiles and health-related quality of life scores, while better preserving exercise capacity after colon surgery (97–99). These factors can facilitate the achievement of postoperative milestones (e.g., earlier tracheal extubation and discharge from the intensive care unit, as well as shorter time to ambulation), but there is little evidence that epidural analgesia actually reduces mortality or hastens hospital discharge even after major surgery (95,96). Although epidural analgesia improved analgesia and reduced pulmonary complications after aortic surgery (100) and thoracoabdominal esophagectomy (101), it did not consistently reduce ileus or the length of the hospital stay in these surgical populations.

Thoracic epidural analgesia with a local anesthetic can reduce ileus and lead to a faster discharge after colonic surgery when combined with multimodal analgesic techniques (102–104). However, the advantages of epidural analgesia over simple IV-PCA are not apparent when using a fast-track postoperative care plan (104). Although epidural analgesia decreases rehabilitation time after total knee arthroplasty (105) and improved pain control, it failed to facilitate rehabilitation after hip fracture surgery (106). Given that similar analgesia can be achieved using a perineural catheter technique (e.g., continuous femoral or popliteal nerve blocks) as with epidural local analgesia without the attendant risk of epidural-related complications (e.g., hematoma formation, abscesses, hemodynamic instability), peripheral nerve blocks would appear to be preferable for lower extremity surgery.

The use of epidural analgesia for minimally invasive surgery (e.g., laparoscopic colectomy, nephrectomy, prostatectomy) is highly questionable. Epidural anesthesia and analgesia for laparoscopic colectomy only facilitated recovery of bowel function when a traditional, nonaccelerated perioperative care program was used (107). Future advances in fast-track surgery techniques and perioperative use of peripheral μ -opioid antagonists (108) will likely further lessen the future role of epidural analgesia (109). Although epidural analgesia *per se* minimally impacts fast-track surgery, as a component of multimodal

management strategy it can provide superior analgesia and physiologic advantages that facilitate attainment of clinical pathway goals after major surgery (95,96). For example, intrathecal opioids as part of a multimodal analgesia technique are increasingly used as part of fast-track cardiac anesthesia techniques (110–112). Although there were no differences in the rates of mortality or myocardial infarction after coronary artery bypass grafting with central neuroaxial analgesia when using local anesthetics, there were associated improvements in time to tracheal extubation, decreased pulmonary complications and cardiac dysrhythmias, and reduced postoperative pain and opioid analgesic requirements (113). When the need for systemic opioids are reduced, cardiac surgery patients are able to be extubated earlier and experience a reduced length of stay in the intensive care unit (111), as well as a faster recovery of bowel and bladder function (68).

Monitored Anesthesia Care

Compared with general endotracheal and central neuroaxis anesthetic techniques for superficial (non-cavitary) surgical procedures, MAC-based techniques involving the use of local anesthesia via infiltration or peripheral nerve block in combination with and IV sedative-analgesic drugs can facilitate a fast-track recovery (62,63,70). The *simplest* local anesthetic technique, which provides adequate analgesia, is recommended to minimize the risk of side effects and complications (114).

Use of a MAC technique for inguinal hernia repair, anorectal, and hand surgery was associated with a decreased incidence and severity of postoperative pain, reduced need for opioid-containing analgesics, less PONV, constipation, ileus, urinary retention, and other opioid-related side effects (62,70,72). MAC techniques commonly involve the use of local anesthetic infiltration and/or peripheral nerve blocks using a mixture of lidocaine (2%) and bupivacaine (0.5%) or ropivacaine (0.5%) in combination with small doses of midazolam (1–3 mg IV) and a variable-rate propofol infusion (25–100 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) (115). Increasingly, dexmedetomidine (0.5–1 $\mu\text{g}/\text{kg}$) (116) and ketamine (75–150 $\mu\text{g}/\text{kg}$) (117) are being used as alternatives to opioid analgesics like fentanyl (0.5–1 $\mu\text{g}/\text{kg}$) (118) or remifentanyl (0.25–0.5 $\mu\text{g}/\text{kg}$ boluses or 0.025–0.05 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ infusion) (119), as part of a MAC anesthetic technique to reduce the ventilatory depression produced when combining a potent opioid analgesic with midazolam and propofol (119). Respiratory depression due to over sedation and a lack of vigilance is the leading cause of serious patient injuries during MAC (64).

In summary, use of MAC techniques can facilitate a fast-track recovery after surgery, since patients routinely bypass the postanesthesia care unit, and can be discharged home earlier due to the low incidence of

postoperative side effects. However, careful intraoperative vigilance to avoid respiratory complications is mandatory to insure patient safety.

General Anesthesia

Despite the obvious advantages of local, regional and MAC anesthetic techniques, many patients (and surgeons) still prefer general anesthesia because they remain unaware of events during the operation. Propofol, 1.5–2.5 mg/kg, is clearly the IV induction drug of choice for fast-track anesthesia (120). The less-soluble volatile anesthetics, desflurane (3%–6%) and sevoflurane (0.75%–1.5%), appear to offer advantages over propofol and isoflurane for maintenance of general anesthesia with respect to facilitating the early recovery process (121–124). Nitrous oxide (50%–70%) remains a popular adjuvant during the maintenance period because of its anesthetic and analgesic-sparing effects, low cost, and favorable pharmacokinetic profile (125). However, remifentanyl infusion (0.05–0.20 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) is an increasingly popular alternative to nitrous oxide as an adjuvant to the less-soluble volatile anesthetics (126,127).

The β -blocking drugs (e.g., esmolol, labetalol) can be used as an alternative to short-acting opioid analgesics for controlling the transient, acute autonomic responses during surgery (128–130). Whenever possible, a laryngeal mask airway should be used as an alternative to a tracheal tube (131). If tracheal intubation is required, short (e.g., succinylcholine, mivacurium) (132) or intermediate-acting (e.g., cisatracurium, vecuronium, rocuronium) neuromuscular blocking drugs should be used (133). A novel cyclodextrin compound, sugammadex (134), is capable of facilitating a faster reversal of steroid-based, nondepolarizing neuromuscular blockers than either a combination of edrophonium-atropine or neostigmine-glycopyrrolate without anticholinergic side effects (135). Use of this reversal drug may also lead to earlier tracheal extubation after surgery and reduce postoperative respiratory complications resulting from residual muscle paralysis (134).

Use of volatile anesthetics (versus propofol) for maintenance of anesthesia will increase PONV in the early postoperative period (136). For patients receiving volatile anesthetics, the most cost-effective antiemetic prophylaxis technique consists of a combination of low-dose droperidol (0.625–1.25 mg IV) and dexamethasone (4–8 mg IV) (137,138) or methylprednisolone (125 mg IV) (139). If the patient is at increased risk for developing PONV, a 5-HT₃ antagonist should also be added as part of a multimodal antiemetic regimen (140). The neurokinin-1 antagonists may play an increasingly important role in the management of emetic symptoms in the future. Finally, use of non-opioid analgesics [e.g., nonsteroidal antiinflammatory drugs (NSAIDs), cyclooxygenase-2 (COX-2) inhibitors, acetaminophen, α_2 -agonists, glucocorticoids, ketamine,

and local anesthetics] as part of a multimodal analgesic regimen will minimize postoperative pain and opioid-related side effects (66,141).

In summary, use of short-acting anesthetic agents and prophylactic drugs, which minimize postoperative side effects, and avoiding surgical misadventures, will enhance the ability to fast-track patients after both ambulatory (142) and major inpatient surgery procedures (110–113). Not surprisingly, combining the use of short-acting anesthetic techniques with an educational program has been reported to significantly increase fast-tracking in ambulatory centers (143). Although a majority of both adults and children can be fast-tracked after ambulatory surgery under general anesthesia, minimizing patient discomfort and anxiety is critically important in establishing a successful fast-track surgery program after all types of elective surgery (129,142–144). Finally, improving the titration of both IV and inhaled anesthetics by using cerebral monitoring devices may also facilitate the fast-tracking process (145–148). However, in spontaneously breathing (nonparalyzed) patients, the value of cerebral monitoring in facilitating the recovery process is questionable (149).

POSTOPERATIVE ISSUES

Pain Management

Observational studies have confirmed that poorly controlled pain and associated PONV can delay discharge after ambulatory surgery (150). Improving postoperative pain control accelerates normalization of quality of life and functionality that may otherwise persist for weeks after an elective operation (151–153). According to a recent systematic review by Liu and Wu (154) there is “insufficient evidence to conclude that analgesic techniques influence postoperative mortality or morbidity” due to the current low incidences of complications. However, excessive reliance upon opioids for perioperative analgesia contributes to acute opioid tolerance and hyperalgesia (155), as well as dose-related side effects (e.g., hypoventilation, sedation, nausea and vomiting, urinary retention, ileus) that delay hospital discharge and add to the cost of surgical care (66,156). Although opioid infusions are frequently used both IV and epidurally, they do not improve postoperative pain management due to the rapid development of tolerance (157), and increased risk of ventilatory depression. Even if acute pain control has little or no beneficial economic or physiological effects, efforts to improve pain management are being mandated by accrediting agencies, and excessive reliance on opioid analgesics will lead to increased morbidity and mortality (158).

Multimodal (or “balanced”) analgesia involves the use of more than one modality of pain control to obtain additive (or even synergistic) beneficial analgesic effects while reducing opioid-related side effects (159). Early fast-track studies demonstrated that these

multimodal analgesic techniques can improve recovery and patient outcome after ambulatory procedures (160,161). This approach is currently the standard practice in fast-track clinical care plans (1,162) because reliance on a single non-opioid analgesic modality such as NSAIDs may not suffice to control severe pain, and reliance exclusively on opioids produces many undesirable side effects (141). Use of partial opioid agonists (e.g., tramadol) is associated with increased side effects and patient dissatisfaction compared with that of both opioid and non-opioid analgesics (163).

The clinically relevant benefits of multimodal analgesia remain controversial (154). Unfortunately, many individual studies are under-powered, the reporting of adverse effects of analgesic drugs has been inconsistent, and meta-analyses (or systematic literature reviews) have often pooled data inappropriately from studies involving diverse types of operations which lacked common internal controls, and estimated aggregate effects often used insensitive measures such as number-needed-to-treat (164–166). Furthermore, the definition of “multimodal” is not uniform in the anesthesia and surgery literature. In some contexts, multimodal analgesia refers to systemic administration of analgesic drugs with different mechanisms of action (142), while in other it refers to concurrent application of analgesic pharmacotherapy and regional analgesia (167). Despite these weaknesses in the published literature, recent meta-analyses have confirmed the opioid dose-sparing effect of NSAIDs (including the COX-2 inhibitors) and decreases in the opioid-related side effects of PONV and sedation (166,168,169). Improvements in late outcome variables may be possible with short-term use of these drugs in the postoperative period (170). However, these positive findings do not necessarily extend to discernible benefits on opioid-induced pruritus, urinary retention, and respiratory depression (168,169), nor are these benefits evident with the reduced opioid-sparing effect of acetaminophen (171).

Studies suggest that an opioid-sparing effect can be achieved postoperatively using a pharmacologically diverse variety of non-opioid adjuvants (i.e., ketamine, clonidine, dexmedetomidine, adenosine, gabapentin, pregabalin, glucocorticoids, esmolol, neostigmine, magnesium) (66). The current evidence from the peer-reviewed literature in support of these non-opioid adjuvants is summarized in Table 1. The recent attention given to opioid-related side effects as impediments to achieving a high degree of patient satisfaction and early discharge home after surgery has increased interest in local and regional anesthetic techniques (63), and led to the development of longer-acting local anesthetics (e.g., suspensions, liposomes, microspheres) (214–217) and continuous delivery methods (e.g., peripheral nerve and wound infusion techniques) (67,82–84,86). Although continuous local anesthetic techniques have become increasingly popular due to the availability of disposable delivery systems,

Table 1. Clinical Evidence for Addition of Selected Second Drugs to an Opioid or a Nonsteroidal Antiinflammatory Drug (NSAID) Cyclooxygenase-2 (COX-2) Inhibitors and Other Non-Opioid Compounds as Part of a Multimodal Analgesic Technique

Drug group	Second drug	Evidence for benefit of combination	Comments	Selected references
Opioid	+NSAID (including COX-2 inhibitors)	A	Meta-analyses describe robust effects on enhancement of analgesia and/or opioid dose-sparing, and corresponding reduction in opioid side effects	Ashburn et al. (167) Cepeda et al. (166) Curatolo et al. (172) Elia et al. (169) Gilron et al. (173) Marret et al. (168)
	+Local anesthetics	A	Multiple meta-analyses describe opioid dose-sparing and reduction of opioid side effects for many operative sites and analgesic routes and techniques.	Sarantopoulos et al. (174) Moiniche et al. (175) Richman et al. (86) Walker et al. (176)
	+ β -Adrenergic blockers	A	Limited evidence indicates opioid-sparing (including tramadol-sparing) independent from well-recognized reduction of postoperative cardiac events	Chia et al. (9) White et al. (130) Zaugg et al. (7)
	+Acetaminophen	B	Meta-analysis describes opioid-sparing but no clear effect upon opioid side effects	Curatolo et al. (172) Edwards et al. (177) Elia et al. (169) Remy et al. (171) Romsing et al. (178) Zhang et al. (179)
	+Adrenergics, α -2 agonists (includes epinephrine, clonidine, dexmedetomidine)	B	Limited evidence indicates potential for opioid dose-sparing but no evident effect upon opioid side effects	Armand et al. (180) Curatolo et al. (172) Segal et al. (10) Walker et al. (176)
	+Antiepileptic drugs (includes gabapentin)	B	Growing clinical literature indicates clear-cut effect on opioid dose-sparing, but not reduction of opioid side effects for gabapentin	Dierking et al. (181) Fassoulaki et al. (182) Fassoulaki et al. (183) Turan et al. (184) Turan et al. (185)
	+Glucocorticoids	B	Positive although limited data on opioid dose reduction and improvements in postoperative nausea/vomiting	Aasboe et al. (186) Holte and Kehlet (187) Moiniche et al. (188) Romundstad et al. (189)
	+NMDA antagonist (includes ketamine, dextromethorphan, magnesium)	B	Sufficient evidentiary base indicates opioid dose-sparing with few adverse effects during low doses of ketamine; much weaker effect, if any, for dextromethorphan; positive but very limited data for memantine, magnesium	Aida et al. (190) Bolcal et al. (191) Duedahl et al. (192) McCartney et al. (193) Seyhan et al. (194)
	+Antidepressants (includes tricyclics, SSRIs)	C	Small evidence base indicates potential of tricyclics, not SSRIs, for opioid dose-sparing but no evident effect upon opioid side effects	Lynch et al. (195)
	+Cholinomimetics (includes neostigmine, physostigmine)	C	Limited positive, exploratory data on systemic and neuraxial physostigmine indicates opioid reduction but additional cholinergic side effects	Beilin et al. (196) Chia et al. (197) Ho et al. (198) Poyhia et al. (199) Lin et al. (200)
	+Antihistamines (includes hydroxyzine, diphenhydramine)	C	Insufficient data to show an opioid-sparing or opioid side effect-reducing effect; clinical series show anticholinergic side effects and reduction of nausea	
	+Nitroglycerine	C	Limited data	Lauretti et al. (201) Sen et al. (202)
	+Calcium channel blockers	C	Limited data	White et al. (130) Atanassoff et al. (203) Choe et al. (204)
NSAID (including COX-2 inhibitors)	+Local anesthetics	A	Positive data indicate clear analgesic benefit and indirectly, avoidance or sparing of opioids in operations otherwise requiring opioid therapy	Ashburn et al. (167) Coloma et al. (205) Ma et al. (206) White et al. (170)
	+Acetaminophen	B	Limited data indicate an analgesic benefit but no clear clinical benefit otherwise	Hyllested et al. (207) Romsing et al. (178) Issioui et al. (208) Issioui et al. (209) Watcha et al. (210)
	+Tramadol	C	Limited data	Lauretti et al. (211)
	+Dextroethorphan	C	Limited data	Yeh et al. (212) Yeh et al. (213)

Citations include randomized controlled trials (RCTs) and, where available, syntheses of multiple RCTs in published systematic reviews and/or metaanalyses. Evidence rated as "A" is sufficiently strong that the addition of the drug be considered for each patient, unless specifically contraindicated. Evidence rated as "B" is favorable but insufficient to warrant consideration of the drug for every patient. Evidence rated as "C" is negative, inconclusive or highly preliminary. SSRI = selective serotonin reuptake inhibitor; NMDA = *N*-methyl-D-aspartate.

the encouraging results from these early pilot studies must be balanced against the cost of the equipment and the resources need to manage these systems outside the hospital (38,217).

An evaluation of multimodal analgesic therapy by Curatolo and Svetcic (172) in 2002 yielded 55 clinical trials and 47 randomized controlled trials relevant to the treatment of acute postoperative pain. These investigators concluded that adding a NSAID (or ketamine) to morphine was advantageous, and that the combination of acetaminophen and a NSAID is superior to either drug alone. Unfortunately, most multimodal analgesia studies have focused on the combination of an opioid with a single non-opioid drug. Ideally, multiple non-opioids (e.g., NSAIDs, acetaminophen, COX-2 inhibitors and gabapentin) could be combined to achieve more optimal pain relief and, perhaps ultimately, an opioid-free environment (66,141). Therefore, multimodal analgesia represents a *key element* for successful fast-track surgery by minimizing postoperative pain, opioid-related organ dysfunction and facilitating the recovery process from anesthesia. Newer fast-tracking criteria recognize the importance of controlling pain and opioid-related side effects (e.g., PONV) (218).

Nausea and Vomiting

Despite the introduction of many new antiemetic therapies, the incidence of PONV remains high, occurring in up to 30% of all surgical cases (including both cardiac and neurosurgery) due to patient, anesthesia and surgery-related factors (219). The major risk factors for PONV include female gender, nonsmoker status, history of PONV or motion sickness, intraoperative use of volatile anesthetics and high-dose opioid techniques, as well as postoperative opioid analgesic use (220). In adults, a multidrug antiemetic prophylaxis strategy is recommended for patients who present with two or more risk factors (221). In addition to the administration of antiemetic drugs, multimodal strategies to reduce the risk of PONV include use of propofol and local anesthetic-based analgesic techniques, adequate hydration, as well as *minimizing* perioperative opioid use (222). Use of cardiovascular drugs (e.g., β -blockers, α_2 -agonists) to control transient acute autonomic responses to noxious surgical stimuli and non-opioid analgesics to reduce postoperative pain will minimize emetic symptoms (66,129,130). Nonpharmacological techniques (e.g., acupuncture, acupressure, and transcutaneous electrical nerve stimulation) can be useful adjuvants to standard antiemetic drugs when used after surgery (223–225). Therefore, replacing intravascular fluid deficits, minimizing use of volatile anesthetics and nitrous oxide, opioid analgesics and reversal drugs, and using propofol, multimodal antiemetic prophylaxis and non-opioid analgesic techniques are all important factors in preventing PONV (141). In the future, practitioners should also consider

incorporating alternative medical therapies into their treatment plans (226).

Ileus and Constipation

Postoperative ileus can cause discomfort and delay oral food intake, thereby prolonging convalescence and the length of the hospital stay (227). The key elements in a multimodal fast-track strategy for preventing postoperative ileus include use of minimally invasive surgical techniques, use of a peripherally acting μ -opioid receptor antagonist, avoidance of a nasogastric (NG) tube, early oral feeding and ambulation, and opioid-sparing analgesic regimens (228). One of the most important factors in accelerating the return of bowel function after major abdominal surgery is the use of continuous thoracic epidural local analgesia (227,229). The positive effect of epidural analgesia on bowel function appears to be related to segmental visceral afferent and efferent blockade. Therefore, thoracic epidural infusion of a local anesthetic solution should reduce the duration of ileus after major abdominal surgery (99).

Multimodal rehabilitation paradigms, which combine epidural analgesia with early oral feeding and mobilization, have been found to decrease the duration of ileus (227). In addition, there is evidence that reduced perioperative sodium administration and avoidance of fluid excess is associated with earlier return of bowel function after abdominal surgery (230), and a decrease in the length of the hospital stay (231). The results of recent clinical trials indicate that use of a peripheral μ -opioid receptor antagonist (i.e., alvimopan, methylnaltrexone) can facilitate the recovery of postoperative bowel activity and may reduce the time to hospital discharge after major surgical procedures (108,232,233). Importantly, minimizing the use of opioid-containing oral analgesics after discharge reduces both constipation and PONV (234).

Nutritional Supplementation

The objective of nutritional management of surgical patients is to accelerate wound healing and increase resistance to infection while preventing loss of functional and structural proteins (97). Administration of hypercaloric amounts of glucose in combination with amino acids is the only nutritional modality that has been shown to produce a positive effect on protein balance (i.e., anabolism). Clinical studies support the concept that enteral nutrition is preferable to parenteral nutrition, and that early (versus late) oral feeding is advantageous with respect to improved surgical outcomes (235–237). Parenteral nutrition is a useful strategy only in surgical patients who are unable to resume oral feeding. Hyperalimentation requiring central venous cannulation should be avoided because it causes hyperglycemia, which can increase postoperative morbidity (238). The choice of perioperative analgesia (e.g., epidural local analgesia versus IV PCA

with opioid analgesics) can also affect the perioperative feeding strategy (98). Epidural analgesia facilitates glucose use and improves insulin sensitivity, thereby diminishing the amount of energy required to attenuate the catabolic losses after major intracavitary surgery (97,239,240). In addition, epidural local analgesia facilitates recovery of ileus and allows earlier resumption of oral nutrition.

INTERACTIONS WITH SURGEONS AND NURSES IN FACILITATING THE RECOVERY PROCESS

Since the principles of fast-track surgery by definition include a multidisciplinary approach, the “total care” principle involves anesthesiologists as members of the perioperative care team with surgical, nursing, and rehabilitation personnel. The benefits of the anesthesiologist’s fast-track anesthetic techniques can only be fully realized when they are incorporated into a comprehensive perioperative patient care plan (162). Compared to traditional postoperative care after colon surgery, patients cared for by surgeons experienced in using fast-tracking protocols had shorter hospital stays (4.5 d vs 7–10 d) (229,241). However, no differences were found in the postoperative activity levels, suggesting that reductions in the length of stay were related to factors other than changes in the patient’s level of physical activity after surgery (242).

Technical and Procedural Aspects of Surgical Care

There have been recent advances in minimally invasive surgery in almost all surgical specialties. As a result of this paradigm shift, there have been beneficial effects on perioperative organ function including improvements in nociceptive control (i.e., reduced pain) and pulmonary function (i.e., less atelectasis), decreased cardiac demands, and reduced endocrine-metabolic responses, muscle catabolism, and inflammatory responses. Laparoscopic (versus open) colectomy and nephrectomy was associated with longer operating times, but significantly reduced the length of the hospital stay and the time to resume normal activities of daily living (243,244). In a metaanalysis of published studies involving laparoscopic (versus open) procedures, Abraham et al. (244) reported that resections for colorectal cancer required 33% more time in the operating room (OR). However, the time to pass flatus was reduced by 34%, and the time to tolerate dietary intake was decreased by 24%. Postoperative pain scores and the need for opioid analgesics were reduced by 34%–63% during the first 3 days after surgery. The greatest benefits of minimally invasive surgery are for operations where the alternative is a large incision (e.g., esophageal reflux surgery, bariatric surgery, splenectomy, thoracic, vascular procedures, arthroscopy, adrenalectomy, and nephrectomy). However, the differences are less pronounced with other types of surgery (e.g., colonic resection, appendectomy, cholecystectomy, inguinal herniorrhaphy).

Importantly, the maximal benefits of minimally invasive surgery (e.g., laparoscopic techniques) can only be achieved when perioperative care principles are adjusted to the principles of fast-track surgery in order to take advantage of the reduced disturbance in perioperative pathophysiology (245). The differences between minimal invasive surgery *per se* and “open” surgery combined with a fast-track recovery strategy become small, or may even favor open procedures in some situations (e.g., colonic resection). Therefore, there is still a need for prospective, randomized, patient and observer-blinded studies to define the role of minimally invasive surgery for many common surgical procedures.

Only two blinded studies with planned early recovery programs have been published, and these studies demonstrated no clinically important differences between open and laparoscopic colonic resection (246) or appendectomy (247). A similar criticism can be made about many of the published series comparing recovery after a so-called fast-track multimodal rehabilitation program to “conventional recovery care.” Most of these series are nonrandomized and involve the use of historical control groups. Many of these comparative studies have emphasized the ability to achieve a shorter hospital stay, reduced postoperative fatigue, and earlier resumption of normal activities without an increase need for additional support after discharge with fast-track multimodal rehabilitation programs (248,249). However, concerns have been raised regarding the possibility of a higher readmission rate (250), and the need for more effective communication and education regarding postdischarge care (251).

In implementing fast-track surgical programs, several surgical aspects of care (e.g., type of incision, use of drains, NG tubes, urinary catheters, bowel preparation) must be revised based on current evidence (1,162). For example, several randomized studies have demonstrated less pain and pulmonary dysfunction with transverse (versus vertical) incisions (252,253). A possible explanation for this improved outcome relates to the larger number of dermatomal levels being disrupted by vertical incisions. In order to facilitate early functional recovery, traditional care principles that hinder early mobilization and feeding must be changed. For elective mid-to-lower abdominal procedures, the routine use of NG tubes should be avoided (254), since their use can prolong paralytic ileus, hinder oral intake, cause oropharyngeal discomfort, and predispose the patient to pulmonary morbidity (e.g., aspiration pneumonitis). Similarly, prolonged routine use of surgical drains should be avoided because randomized clinical trials have demonstrated that they are not necessary and can have detrimental effects on recovery after hepatic, colonic, and rectal resections with primary anastomoses, as well as appendectomy (255). The traditional bowel preparation (e.g., polyethylene glycol-electrolyte solution) prior to abdominal procedures may actually increase the risk

of infectious morbidity (256,257). The same situation may also apply to the use of urinary catheters (1). In addition, the surgical care principles must be adjusted based on recent evidence regarding optimal fluid management (31) and adequate early oral nutrition (258).

Finally, surgical patients undergoing major surgery who are unfit and who have comorbid illnesses experience more postoperative complications and a longer convalescence period (99). The process of enabling surgical patients to withstand the adverse effects of surgery-induced inactivity by increasing their exercise capacity through preoperative conditioning (i.e., physical training) is termed "prehabilitation" (259). This consists of a program of aerobic and resistance exercises over a period of 3–4 wk before elective surgery. Preliminary studies suggest that a prehabilitation program can increase preoperative exercise capacity by 15%–20%, even in lower risk patients undergoing cardiac surgery (260). A recent study by Hulzebos et al. (261) found that preoperative inspiratory muscle training reduced the incidence of postoperative pulmonary complications and the duration of hospital stay after coronary artery bypass graft surgery. A perioperative exercise program was also found to be effective in improving early recovery of physical function after total hip arthroplasty in the elderly (262). Simple walking tests (using pedometers, accelerometers, and treadmills to monitor daily activity) may be useful predictors of postoperative recovery (263).

Changing the Postsurgical Nursing Culture

A common experience at centers implementing fast-track surgery has been the challenge of changing long-standing surgical nursing care principles (264,265), and this is a major component of the total care package (266). An intensified nurse-based preoperative patient education program is a crucial adjunct to improved fast-track anesthetic surgical care (143). These programs need to focus on what is expected from the patient as an active participant in the recovery and rehabilitation process (267). The provision of daily nurse care (i.e., clinical pathway) charts remains an important element in the fast-track recovery process. It is essential to secure daily tasks, and to establish programs to facilitate education of new personnel as every aspect of care must be carefully explained. Therefore, multidisciplinary meetings before and after implementing fast-track surgery are crucial to the overall success of the program. These meetings should include a presentation of results and patient follow-up in order to facilitate an understanding of the goals and results of fast-track surgery compared with traditional recovery care.

CONCLUSIONS

As perioperative physicians, anesthesiologists play an important role in the implementation of fast-track surgery programs (Table 2). Understanding the im-

Table 2. Key Elements of the Perioperative Anesthetic Management for Facilitating a Fast-Track Recovery After Elective Surgery

<i>I. Preoperative period</i>	
Stabilizing coexisting diseases (e.g., hypertension, diabetes) and encourage prehabilitation exercise program and smoking cessation	
Optimizing patient comfort by minimizing anxiety and discomfort	
Insure adequate rehydration by replacing fluid deficits	
Appropriate use of prophylactic therapies to prevent postoperative complications (e.g., nausea, vomiting, pain, ileus)	
<i>II. Intraoperative period</i>	
Utilize anesthetic techniques which optimize surgical conditions, while insuring a rapid recovery with minimal side effects	
Administer local analgesia via peripheral nerve blocks, wound infiltration, and/or instillation	
Apply multimodal analgesia and antiemetic prophylaxis (including use of glucocorticoid steroids)	
Minimize use of nasogastric tubes and avoid excessive fluid administration	
<i>III. Postoperative period</i>	
Allow patients who meet discharge criteria to be fast-tracked (i.e., discharged earlier from recovery units)	
Insure adequate pain control in the postdischarge period utilizing non-opioid analgesics to minimize need for opioid-containing analgesics	
Encourage early ambulation and resumption of normal activities of daily living	

Table 3. Future Strategies for Anesthesiologist to Advance Fast-Track Surgery

1. Participate in identification of preoperative risk factors and improvement in organ function by optimizing intra- and postoperative hemodynamic stability (268)
2. Development of multimodal non-opioid analgesic and antiemetic regimens based on the type of surgery and the patient's risk assessment (66,140,141)
3. Pharmacological modifications of the autonomic "stress" responses during and after surgery (269)
4. Optimizing perioperative fluid regimens based on the duration of preoperative fasting and the type of surgery (e.g., intracavitary, blood loss) (30,31)
5. Postoperative rounds by anesthesiologists caring for high-risk surgical patients (270)
6. Establishment of "outreach" services for ancillary healthcare personnel involved in facilitating the rehabilitation process (271)
7. Multidisciplinary approaches to routine perioperative care which would ideally include specific procedure-based clinical pathways (162,272)
8. Preventing acute postoperative pain from becoming a chronic problem by optimizing the analgesic therapy both before and after discharge from the surgical facility (65)

portance of coexisting diseases and taking appropriate steps to minimize postoperative complications through appropriate use of preoperative medications, selecting the optimal anesthetic and analgesic techniques, and maintaining normal organ system function will lead to improved patient care at a reduced cost (268). As more information becomes available, it should be possible to

make recommendations for each of these steps on a procedure-specific basis, as has been achieved for postoperative pain management (www.postoppain.org).

Future advances in fast-track surgery will require interdisciplinary collaborations involving anesthetic, surgery and nursing care (Table 3) (269). However, anesthesiologists are the ones who make the important decisions regarding premedication, fluid management, anesthetic and adjuvant drugs, treatment of side effects, and pain management in the early postoperative period. Interventions to modify surgical stress responses are also performed by anesthesiologists and include perioperative use of β -blockers, glucocorticoid steroids, administration of fluids, as well as control of stress-induced hyperglycemia by administering insulin (30,66,269). The effective control of stress responses will likely prove to be advantageous with respect to improving patient outcome. Furthermore, an expansion of the anesthesiologists' interventions beyond the operating and recovery rooms may also be necessary. Preliminary data suggest that positive outcome effects may be achieved when anesthesiologists participate in ward rounds in the later postoperative period (270), or if an outreach service is established for early recognition of organ dysfunction (271).

Perioperative anesthetic care should, therefore, be considered as a multidisciplinary strategy to improve the management and outcome of patients undergoing surgery, rather than a subspecialty limited to one medical profession (272). As a member of the multidisciplinary team, the decisions of the anesthesiologist have a direct impact on the ability to achieve a fast-track recovery after surgery (4,162). It has recently been reported that an anesthesiologist-led management team improved OR efficiency (resulting in a 48% reduction in gap time between cases in the same OR) when defined scheduling policies were supported by surgeons, nurses, and hospital administrators (273). In addition, the implementation of a multidisciplinary approach to minimizing common postoperative side effects can lead to a reduced recovery room and hospital stay, as well as better pain control and patient satisfaction after surgery (274,275). However, more prospectively randomized, controlled studies involving multidisciplinary approaches to facilitating a fast-track recovery are needed.

The role of the anesthesiologists would ideally expand beyond the time of hospitalization since effective pain control after discharge is critically important for achieving successful convalescence (4,13,66,141). Anesthesiologists may contribute by encouraging the optimal use of multimodal analgesia, as well as in implementing novel techniques, which can improve pain control and minimize side effects (e.g., PONV, ileus) after the patient has been discharged home (2,84,226,233). The time is right for anesthesiologists to take a more active role as perioperative physicians in implementing fast-track surgery programs.

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