

# Postoperative Pain Control

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## Abstract

The effective relief of pain is of the utmost importance to anyone treating patients undergoing surgery. Pain relief has significant physiological benefits; hence, monitoring of pain relief is increasingly becoming an important postoperative quality measure. The goal for postoperative pain management is to reduce or eliminate pain and discomfort with a minimum of side effects. Various agents (opioid vs. nonopioid), routes (oral, intravenous, neuraxial, regional) and modes (patient controlled vs. “as needed”) for the treatment of postoperative pain exist. Although traditionally the mainstay of postoperative analgesia is opioid based, increasingly more evidence exists to support a multimodal approach with the intent to reduce opioid side effects (such as nausea and ileus) and improve pain scores. Enhanced recovery protocols to reduce length of stay in colorectal surgery are becoming more prevalent and include multimodal opioid sparing regimens as a critical component. Familiarity with the efficacy of available agents and routes of administration is important to tailor the postoperative regimen to the needs of the individual patient.

## Keywords

- ▶ postoperative
- ▶ analgesia
- ▶ opioids
- ▶ nonsteroidal
- ▶ transversus abdominis

**Objectives:** On completion of this article, the readers should be able to summarize the current evidence supporting the various approaches for the management of postoperative pain.

According to the American Society of Anesthesiologist practice guidelines for acute pain management in the perioperative setting, acute pain is defined as pain present in a surgical patient after a procedure.<sup>1</sup> The World Health Organization and International Association for the Study of Pain have recognized pain relief as a human right.<sup>2</sup> Poorly managed postoperative pain can lead to complications and prolonged rehabilitation.<sup>3</sup> Uncontrolled acute pain is associated with the development of chronic pain with reduction in quality of life.<sup>4</sup> Appropriate pain relief leads to shortened hospital stays, reduced hospital costs, and increased patient satisfaction. As a result, the management of postoperative pain is an increasingly monitored quality measure. The Hospital Consumer Assessment of Health Providers and Systems (HCAHPS) scores measures patient satisfaction with in-hospital pain management and may have implications in regards to reimbursements.

The failure to provide good postoperative analgesia is multifactorial. Insufficient education, fear of complications associated with analgesic drugs, poor pain assessment and inadequate staffing are among the causes. This review will focus on the management of acute postoperative pain. The goal of postoperative pain management is to relieve pain while keeping side effects to a minimum. This is often best accomplished with a multimodal approach. Recent trends in minimally invasive surgery and enhanced recovery protocols have addressed pain management in terms of these goals.

## Assessment

Preoperative patient evaluation and planning is vital to successful postoperative pain management. Recommended preoperative evaluation includes a directed pain history, a directed physical exam and a pain control plan; however, the literature is insufficient in regards to efficacy.<sup>1</sup> Likewise patient preparation should include adjustments of preoperative medications to avoid withdrawals effect, treatment to reduce preoperative pain/anxiety, and preoperative initiation of treatment as part of a multimodal pain management plan.

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There is some support that preoperative pain levels may predict levels of postsurgical pain.<sup>5,6</sup> Certain preoperative variables such as age, anxiety levels, and depression may have an effect on levels of postoperative pain.<sup>7</sup> Higher postoperative pain levels can be associated with lower quality of care.<sup>8</sup> Although preoperative patient and family education are recommended, the literature is equivocal regarding its impact on postoperative pain, anxiety, and time to discharge.<sup>9,10</sup>

Pain needs to be quantified to be treated effectively. The gold standard is the patient's self-assessment done routinely after surgery to measure the efficacy of pain management. Several scoring tools are available but a 10-point pain assessment scale, where 1 is no pain and 10 is the worst possible pain imaginable, has been nationally accepted. The key to adequate pain control is to reassess the patient and determine if he or she is satisfied with the outcome. A satisfaction score should be obtained together with a pain score so as to minimize the chances that inadequately treated pain goes unnoticed. Responsive analgesia management with good patient communication is the key to a successful program.

### Pre-emptive Analgesia

Analgesia administered before the painful stimulus occurs may prevent or substantially reduce subsequent pain or analgesic requirements. This hypothesis has prompted numerous clinical studies, but few robust studies have clearly demonstrated its efficacy. Effective pre-emptive analgesic techniques use multiple pharmacological agents to reduce nociceptor activation by blocking or decreasing receptor activation, and inhibiting the production or activity of pain neurotransmitters. Pre-emptive analgesia can be administered via local wound infiltration, epidural or systemic administration prior to surgical incision. A meta-analysis of randomized trials reported patients receiving pre-emptive local anesthetic wound infiltration and nonsteroidal anti-inflammatory administration experience a decrease in analgesic consumption, but no decrease in postoperative pain scores. Pre-emptive epidural analgesia did show a decrease in pain scores as well as analgesic consumption.<sup>11</sup> Pre-emptive local anesthetic injection around small laparoscopic port incision sites was not effective in terms of managing postoperative visceral pain.<sup>12,13</sup> Overall, pre-emptive analgesia may offer some short-term benefits, particularly in ambulatory surgery patients.

### Opioid Analgesia

Despite years of advances in pain management, the mainstay of postoperative pain therapy in many settings is still opioids. Opioids bind to receptors in the central nervous system and peripheral tissues and modulate the effect of the nociceptors. They can be administered via oral, transdermal, parenteral, neuraxial, and rectal routes. The most commonly used intravenous opioids for postoperative pain are morphine, hydromorphone (dilaudid), and fentanyl. Morphine is the standard choice for opiates and is widely used. It has a rapid onset of action with peak effect occurring in 1 to 2 hours. Fentanyl and

hydromorphone are synthetic derivatives of morphine and are more potent, have a shorter onset of action, and shorter half-lives compared with morphine.

All opioids have significant side effects that limit their use. The most important side effect is respiratory depression that could result in hypoxia and respiratory arrest. Hence, regular monitoring of respiration and oxygen saturation is essential in patients on opioids postoperatively. In addition, nausea, vomiting, pruritus, and reduction in bowel motility leading to ileus and constipation are also common side effects of these medications.<sup>14,15</sup> Longer-term use of opioids can lead to dependence and addiction. Once the patient is able to tolerate oral intake, oral opioids can be initiated and continued after discharge from the hospital. With the development of enhanced recovery protocols, particularly in colorectal surgery, primarily opioid-based regimens are being challenged by other agents and approaches to postoperative pain management.<sup>16,17</sup>

### Intravenous Patient-Controlled Analgesia

The concept of continuous intravenous and subsequently of patient-controlled analgesia (PCA) came into practice in the 1970s.<sup>18,19</sup> Morphine, hydromorphone, and fentanyl can be administered through the PCA pump. This method of analgesia requires special equipment and gives patient better autonomy and control over the amount of medication used. However, both patients, as well as staff setting up the equipment, require training for proper use. A meta-analysis of 15 randomized controlled trials comparing IV PCA and intramuscular-administered opioid showed that patients preferred IV PCA and obtained better pain control with no increase in side effects.<sup>20</sup> A subsequent Cochrane Review comparing IV opioid PCA with conventional IV "as needed" opioid administration reported that IV PCA had more analgesic effect and was preferred by patients based on satisfaction scores. However, the amount of opioid used, pain scores, length of hospital stay, and incidence of opioid-related side effects were similar between the groups, concluding that PCA is an efficacious alternative to conventional systemic analgesia when managing postoperative pain.<sup>21</sup>

### Epidural and Spinal Analgesia

Epidural and spinal analgesia act as neuraxial regional blocks and are used extensively in thoracic, abdominal, and pelvic surgery. In epidural analgesia, a catheter is inserted into the epidural space in the thoracic or lumbar spine and continuous infusion of local anesthetic agent along with opioids results in postoperative analgesia. A Cochrane database review of nine randomized controlled trials comparing IV PCA and continuous epidural analgesia (CEA) showed the latter to achieve better pain control in the first 72 hours after abdominal surgery.<sup>22</sup> There was no difference in length of hospital stay and adverse events between the two routes. Patients with CEA had a higher incidence of pruritus related to opioids. Subsequent meta-analysis of randomized controlled trials comparing the two modes of opioid delivery in colorectal surgery showed that CEA significantly reduced postop pain

and ileus, but was associated with pruritus, hypotension, and urinary retention.<sup>23</sup> A combination of local anesthetic and opioid can be administered via a patient controlled epidural pump, which lowers the dose requirements for each individual drug as well as the frequency of side effects.<sup>24</sup>

Insertion of epidural catheters is technically challenging, and failure of adequate analgesia is seen in 27% of patients after lumbar and 32% after thoracic epidural,<sup>25</sup> despite adequate catheter placement. In patients with successful analgesia from CEA, hypotension can be a problem requiring administration of additional IV fluids.

Intrathecal administration of opioid and local anesthetic (0.5% bupivacaine) at induction of anesthesia results in good postoperative analgesia for up to 24 hours. Administration of intrathecal analgesia takes the same time as epidural analgesia during anesthetic process before surgery, but does not need the skilled postoperative care required for epidural.

A recent observational study showed that single-dose intrathecal opioid followed by IV PCA resulted in better pain control than CEA in patients undergoing colorectal surgery.<sup>26</sup> In addition, time to mobility and consequently hospital stay was shorter in the intrathecal analgesia group. A subsequent randomized controlled trial comparing CEA, intrathecal analgesia, and IV PCA in laparoscopic colorectal surgery showed that duration of nausea, return of bowel function, and total hospital stay were higher in the CEA group than the other two groups. The pain scores were significantly higher in the IV PCA group than the other two groups.<sup>27</sup> This positive effect of intrathecal analgesia in laparoscopic colorectal surgery was further confirmed in a subsequent randomized study.<sup>28</sup>

## Nonopioid Analgesia

Opioid-sparing techniques using different analgesic mechanisms of action is recognized as an important component strategy for postoperative pain management. Nonsteroidal anti-inflammatory agents (NSAIDs) are useful in reducing the amount of opiates requested and administered to the patient thus reducing opioid side effects.<sup>29</sup> They are useful in mild to moderate levels of pain. NSAIDs act by inhibiting the enzyme cyclooxygenase (COX) thereby blocking the production of prostaglandins resulting in an anti-inflammatory response. NSAIDs are classified by their selectivity of the COX isoenzymes. There is a risk of bleeding with these agents, so use of NSAIDs is dependent on the individual patient's risk factors. Nonselective agents such as ibuprofen do have an increased side effect profile (bleeding, antiplatelet effect); however, general consensus in the literature is that COX-1 inhibitors are preferred over selective COX-2 inhibitors such as celecoxib, given the recent evidence of cardiovascular risks associated with COX-2 agents.<sup>29-31</sup>

Ketorolac is an injectable nonsteroidal anti-inflammatory drug with analgesic properties. It predominantly affects COX-1 and can be used as pre-emptive analgesia and as an adjunct to other agents.<sup>31</sup> Ketorolac reduces narcotic consumption by 25 to 45% and is a common adjunct in colorectal surgery postoperative protocols.<sup>31-33</sup> The usual dose is 30 mg given

intravenously. In a prospective randomized clinical trial in postoperative colorectal surgery patients, the addition of ketorolac to morphine PCA had an opioid-sparing effect with a resultant decrease in postoperative ileus.<sup>34</sup>

Acetaminophen is a centrally acting analgesic, but lacks peripheral anti-inflammatory effects. Oral acetaminophen is widely used for acute pain relief. Acetaminophen is a common ingredient in many combination oral pain medications, so it is vital to counsel the patient not to exceed the 4000 mg daily maximum dose due to the risk of hepatotoxicity. Systematic reviews of randomized controlled trials (RCTs) confirm the efficacy of oral acetaminophen for acute pain.<sup>35</sup> However, acetaminophen has a slow onset of analgesia; until recently the nonavailability of the oral route immediately after surgery limited its value in treating immediate postoperative pain. Paracetamol is a stable IV form of acetaminophen and is now commercially available. Paracetamol's major advantages over NSAIDs are its lack of interference with platelet function and safe administration in patients with a history of peptic ulcers or asthma. Opioid-sparing effects have been associated with paracetamol administered intravenously.<sup>36</sup> A mixed trial comparison found a decrease in 24-hour morphine consumption when paracetamol, NSAIDs, or COX-2 inhibitors are given in addition to PCA morphine after surgery with a reduction in morphine-related adverse effects. However, the study did not find any clear differences between the three nonopioid agents.<sup>36</sup> A systematic review identified 21 studies comparing paracetamol alone or in combination with other NSAIDs and reported increased efficacy with the combination of two agents than with either alone.<sup>37</sup>

## Peripheral Nerve Blocks

The transversus abdominis plane (TAP) block is a peripheral nerve block that results in anesthesia of the abdominal wall.<sup>38</sup> The technique was first described in 2001 as a refined abdominal field block with a single shot into the plane between the internal oblique and transabdominal muscles.<sup>39</sup> This plane represents an anatomical potential space with nerves leaving the plane to innervate the abdominal muscles and skin. Local anesthetic is injected into this plane either uni- or bilaterally. The site of injection can be modified according to the anticipated site of incision. The technique can be blind, laparoscopically, or ultrasound guided. Furthermore, the TAP block is thought by its proponents to have a lower risk of complications and greater acceptability to patients than epidural analgesia. There are several heterogeneous studies looking at TAP rectus sheath blocks on pain relief after abdominal surgery with insufficient data on method of localization, timing, doses, and volumes of local anesthetics. TAP blocks are clearly subject to operator variability and skill.

A Cochrane Review that included eight studies with 358 participants with moderate risk of bias showed that TAP block patients had significantly less postoperative requirement for morphine at 24 and 48 hours compared with no TAP or saline placebo. There was no significant impact on nausea, vomiting, or sedation scores. Recent studies have looked at the use of TAP in colorectal surgery. In an enhanced recovery protocol,

TAP plus IV paracetamol in laparoscopic colorectal surgery resulted in earlier resumption of diet and discharge from hospital compared with morphine PCA.<sup>17</sup> One study from 2012 compared TAP plus PCA versus subcutaneous local infiltration plus PCA in open right hemicolectomies.<sup>40</sup> This study showed reduced PCA morphine use at 24 hours and decreased sedation in the TAP arm. Similarly, Conaghan et al reported decreased IV opioid use in laparoscopic colorectal resections with TAP + PCA versus PCA alone.<sup>41</sup> Although there is limited evidence to suggest improvement in pain scores and opioid consumption after abdominal surgery, further studies are needed to evaluate the role of TAP blocks compared with other modalities of pain management such as epidural anesthesia.

### Local Infiltration

Colon and rectal surgeons have used infiltration of local anesthetics throughout the history of the specialty. Many cases such as anorectal procedures can be accomplished with local anesthetics and IV sedation.<sup>42</sup> A limitation of the anesthetics previously available (Xylocaine and bupivacaine) was their short duration (minutes to a few hours). Recently a new formulation of liposomal bupivacaine (Exparel®, Pacira Pharmaceuticals, Parsippany, NJ) has received approval from the U.S. Food and Drug Administration and can provide analgesia for up to 72 hours. It was approved for injection into the surgical site to produce postsurgical analgesia. The two pivotal studies leading to approval were in hemorrhoidectomy and bunionectomy patients.<sup>43</sup> The drug is provided in a 20-cc vial that contains 266 mg of liposomal bupivacaine. It can be diluted up to 14 times if desired. Since its release, this drug has seen increasing adoption, but the reported experience has been limited to date.<sup>44</sup> A series of four consecutive patients undergoing loop ileostomy closure were successfully managed with multimodality postoperative pain management (including liposomal bupivacaine, IV paracetamol, and ibuprofen) as 23-hour procedures. Utilization of local infiltration as part of a multimodality approach appears to have great potential.

### Special Circumstances

#### Obese Patients

Postoperative pain management is challenging given this population's susceptibility to sleep apnea and respiratory depression that may be exacerbated by administration of parenteral opioids. For morbidly obese patients, it can be beneficial to provide postoperative analgesia via the epidural route. Patient-controlled analgesia is an alternative in the absence of epidural analgesia; however, the patients need to be closely monitored during the postoperative period with particular attention to sedation and pulse oximetry. The general consensus for pain management has been to use multimodal analgesic approach with a preference for regional techniques and avoidance of sedatives.<sup>45</sup> A study by Batistich et al in 2004 showed that need for morphine by IV PCA in morbidly obese patients after bariatric surgery was signifi-

cantly lower than previously described for both open laparotomy or laparoscopic surgery when regional blocks and systemic nonopioid analgesia were used as adjuncts.<sup>46</sup>

#### Chronic Pain Patients

Patients on opioid treatment for chronic pain present a challenge as their postoperative analgesic needs will typically exceed their baseline daily doses. Their requirement of analgesia is considerably higher than the typical patient and is due to tolerance of opioids and hyperalgesia.<sup>47</sup> Postoperatively, a multimodal approach to analgesia must be utilized including regional, local infiltration, and nonopioid systemic analgesia. A continuous PCA basal infusion or administration of long-acting opiates via a transdermal route may provide more effective pain control as routine dosing schedules are likely to not be sufficient. Appropriate discussion with patients in the preoperative period with drawing up of a mutually agreeable pain contract and addressing hyperalgesia may result in better postoperative pain control.

### Conclusions

Each patient is unique in his or her perception of pain allowing for many combinations in the treatment of pain. The introduction of enhanced recovery programs for colorectal surgery have changed both physician and patient expectations in terms of perioperative pain management making the reduction of opiate intake a factor in meeting these expectations. In conclusion, multimodal pain management therapy should be used whenever possible. Unless contraindicated patients should receive around the clock regimen of NSAIDs or acetaminophen. Pre-emptive analgesia with such agents as well as regional blocks may be beneficial in ambulatory cases. Patient-controlled analgesia with morphine or hydromorphone is appropriate for patients undergoing abdominal procedures under general analgesia. If not

**Table 1** Sample multimodality pain management

Preoperative
Acetaminophen (paracetamol) 1,000 mg IV in preop
Ketorolac 800 mg IV in preop
Intraoperative
Liposomal bupivacaine 266 mg wound infiltration
Postoperative
Acetaminophen (paracetamol) 1,000 mg IV every 6 h until patient taking oral meds
Ibuprofen 800 mg IV every 8 h until patient taking oral meds
PCA (morphine or Dilaudid) for severe pain (scale 6–10) until patient taking oral meds
Oxycodone 10 mg PO every 4 h for moderate pain when taking oral medication

Abbreviations: IV, intravenously; PCA, patient-controlled anesthesia; PO, by mouth.

contraindicated, addition of NSAIDs may lower the narcotic requirement and improve the quality of analgesia. An example of a multimodality approach is presented in ►Table 1. An epidural or intrathecal approach postoperatively is appropriate for patients undergoing abdominal procedures requiring extensive incisions, and those who are morbidly obese or are on chronic pain medications. There is only limited evidence to suggest that the use of perioperative TAP block reduces opioid consumption and pain scores after abdominal surgery when compared with no intervention or placebo. Further studies comparing TAP to other standard methods of postoperative analgesia are needed.

## References

- American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology* 2012;116(2):248–273
- Brennan F, Carr DB, Cousins M. Pain management: a fundamental human right. *Anesth Analg* 2007;105(1):205–221
- Kehlet H, Holte K. Effect of postoperative analgesia on surgical outcome. *Br J Anaesth* 2001;87(1):62–72
- Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006;367(9522):1618–1625
- Kalkman CJ, Visser K, Moen J, Bonsel GJ, Grobbee DE, Moons KG. Preoperative prediction of severe postoperative pain. *Pain* 2003;105(3):415–423
- Abrishami A, Chan J, Chung F, Wong J. Preoperative pain sensitivity and its correlation with postoperative pain and analgesic consumption: a qualitative systematic review. *Anesthesiology* 2011;114(2):445–457
- Caumo W, Schmidt AP, Schneider CN, et al. Preoperative predictors of moderate to intense acute postoperative pain in patients undergoing abdominal surgery. *Acta Anaesthesiol Scand* 2002;46(10):1265–1271
- Gunningberg L, Idvall E. The quality of postoperative pain management from the perspectives of patients, nurses and patient records. *J Nurs Manag* 2007;15(7):756–766
- Shuldham CM, Fleming S, Goodman H. The impact of pre-operative education on recovery following coronary artery bypass surgery. A randomized controlled clinical trial. *Eur Heart J* 2002;23(8):666–674
- Walker JA. What is the effect of preoperative information on patient satisfaction? *Br J Nurs* 2007;16(1):27–32
- Ong CK, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. *Anesth Analg* 2005;100(3):757–773 table of contents.
- Ghezzi F, Cromi A, Bergamini V, et al. Preemptive port site local anesthesia in gynecologic laparoscopy: a randomized, controlled trial. *J Minim Invasive Gynecol* 2005;12(3):210–215
- Leung CC, Chan YM, Ngai SW, Ng KF, Tsui SL. Effect of pre-incision skin infiltration on post-hysterectomy pain—a double-blind randomized controlled trial. *Anaesth Intensive Care* 2000;28(5):510–516
- Barletta JF, Asgeirsson T, Senagore AJ. Influence of intravenous opioid dose on postoperative ileus. *Ann Pharmacother* 2011;45(7-8):916–923
- Goettsch WG, Sukel MP, van der Peet DL, van Riemsdijk MM, Herings RM. In-hospital use of opioids increases rate of coded postoperative paralytic ileus. *Pharmacoepidemiol Drug Saf* 2007;16(6):668–674
- Levy BF, Tilney HS, Dowson HM, Rockall TA. A systematic review of postoperative analgesia following laparoscopic colorectal surgery. *Colorectal Dis* 2010;12(1):5–15
- Zafar N, Davies R, Greenslade GL, Dixon AR. The evolution of analgesia in an 'accelerated' recovery programme for resectional laparoscopic colorectal surgery with anastomosis. *Colorectal Dis* 2010;12(2):119–124
- Keeri-Szanto M, Remington B. Drug levels on continuous intravenous infusion. *Lancet* 1971;2(7724):601
- Evans JM, Rosen M, MacCarthy J, Hogg MI. Apparatus for patient-controlled administration of intravenous narcotics during labour. *Lancet* 1976;1(7949):17–18
- Ballantyne JC, Carr DB, Chalmers TC, Dear KB, Angelillo IF, Mottler F. Postoperative patient-controlled analgesia: meta-analyses of initial randomized control trials. *J Clin Anesth* 1993;5(3):182–193
- Hudcova J, McNicol E, Quah C, Lau J, Carr DB. Patient controlled opioid analgesia versus conventional opioid analgesia for postoperative pain. *Cochrane Database Syst Rev* 2006;(4):CD003348
- Werawatganon T, Charuluxanun S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. *Cochrane Database Syst Rev* 2005;(1):CD004088
- Marret E, Remy C, Bonnet F, Postoperative Pain Forum G, Postoperative Pain Forum Group. Meta-analysis of epidural analgesia versus parenteral opioid analgesia after colorectal surgery. *Br J Surg* 2007;94(6):665–673
- Mann C, Pouzeratte Y, Boccarda G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology* 2000;92(2):433–441
- Hermanides J, Hollmann MW, Stevens MF, Lirk P. Failed epidural: causes and management. *Br J Anaesth* 2012;109(2):144–154
- Virlos I, Clements D, Beynon J, Ratnalikar V, Khot U. Short-term outcomes with intrathecal versus epidural analgesia in laparoscopic colorectal surgery. *Br J Surg* 2010;97(9):1401–1406
- Levy BF, Scott MJ, Fawcett W, Fry C, Rockall TA. Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery. *Br J Surg* 2011;98(8):1068–1078
- Wongyingsinn M, Baldini G, Stein B, Charlebois P, Liberman S, Carli F. Spinal analgesia for laparoscopic colonic resection using an enhanced recovery after surgery programme: better analgesia, but no benefits on postoperative recovery: a randomized controlled trial. *Br J Anaesth* 2012;108(5):850–856
- Lowder JL, Shackelford DP, Holbert D, Beste TM. A randomized, controlled trial to compare ketorolac tromethamine versus placebo after cesarean section to reduce pain and narcotic usage. *Am J Obstet Gynecol* 2003;189(6):1559–1562, discussion 1562
- Dajani EZ, Islam K. Cardiovascular and gastrointestinal toxicity of selective cyclo-oxygenase-2 inhibitors in man. *J Physiol Pharmacol* 2008;59(Suppl 2):117–133
- De Oliveira GS Jr, Agarwal D, Benzon HT. Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. *Anesth Analg* 2012;114(2):424–433
- Pavy TJ, Paech MJ, Evans SF. The effect of intravenous ketorolac on opioid requirement and pain after cesarean delivery. *Anesth Analg* 2001;92(4):1010–1014
- Chen JY, Wu GJ, Mok MS, et al. Effect of adding ketorolac to intravenous morphine patient-controlled analgesia on bowel function in colorectal surgery patients—a prospective, randomized, double-blind study. *Acta Anaesthesiol Scand* 2005;49(4):546–551
- Chen JY, Ko TL, Wen YR, et al. Opioid-sparing effects of ketorolac and its correlation with the recovery of postoperative bowel function in colorectal surgery patients: a prospective randomized double-blinded study. *Clin J Pain* 2009;25(6):485–489

- 35 Toms L, McQuay HJ, Derry S, Moore RA. Single dose oral paracetamol (acetaminophen) for postoperative pain in adults. *Cochrane Database Syst Rev* 2008;(4):CD004602
- 36 Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: a systematic review. *Br J Anaesth* 2011;106(3):292–297
- 37 Ong CK, Seymour RA, Lirk P, Merry AF. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperative pain. *Anesth Analg* 2010;110(4):1170–1179
- 38 Charlton S, Cyna AM, Middleton P, Griffiths JD. Perioperative transversus abdominis plane (TAP) blocks for analgesia after abdominal surgery. *Cochrane Database Syst Rev* 2010;(12):CD007705
- 39 Rafi AN. Abdominal field block: a new approach via the lumbar triangle. *Anaesthesia* 2001;56(10):1024–1026
- 40 Brady RR, Ventham NT, Roberts DM, Graham C, Daniel T. Open transversus abdominis plane block and analgesic requirements in patients following right hemicolectomy. *Ann R Coll Surg Engl* 2012;94(5):327–330
- 41 Conaghan P, Maxwell-Armstrong C, Bedforth N, et al. Efficacy of transversus abdominis plane blocks in laparoscopic colorectal resections. *Surg Endosc* 2010;24(10):2480–2484
- 42 Scott NB. Wound infiltration for surgery. *Anaesthesia* 2010;65 (Suppl 1):67–75
- 43 Haas E, Onel E, Miller H, Ragupathi M, White PF. A double-blind, randomized, active-controlled study for post-hemorrhoidectomy pain management with liposome bupivacaine, a novel local analgesic formulation. *Am Surg* 2012;78(5):574–581
- 44 Cohen SM. Extended pain relief trial utilizing infiltration of Exparel (®), a long-acting multivesicular liposome formulation of bupivacaine: a Phase IV health economic trial in adult patients undergoing open colectomy. *J Pain Res* 2012;5:567–572
- 45 Schug SA, Raymann A. Postoperative pain management of the obese patient. *Best Pract Res Clin Anaesthesiol* 2011;25(1): 73–81
- 46 Batistich S, Kendall A, Somers S. Analgesic requirements in morbidly obese patients. *Anaesthesia* 2004;59(5):510–511
- 47 Richebé P, Beaulieu P. Perioperative pain management in the patient treated with opioids: continuing professional development. *Can J Anaesth* 2009;56(12):969–981