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Use of a Continuous Local Anesthetic Infusion for Pain Management after Median Sternotomy

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Background: **The use of large doses of opioid analgesics to treat pain after cardiac surgery can prolong the time to tracheal extubation and interfere with recovery of bowel and bladder function in the postoperative period. Therefore, the authors investigated the efficacy of a continuous infusion of bupivacaine 0.25% or 0.5%, at the median sternotomy site, for 48 h after cardiac surgery in reducing the opioid analgesic requirement and improving the recovery process.**

Methods: **In this prospective, randomized, placebo-controlled, double-blind clinical trial, 36 consenting patients undergoing open-heart surgery with a standardized general anesthetic technique had two indwelling infusion catheters placed at the median sternotomy incision site at the end of surgery. The patients were randomly assigned to receive normal saline (control), bupivacaine 0.25% or bupivacaine 0.5% *via* an elastomeric infusion pump at a constant rate of 4 ml/h for 48 h. Patients evaluated their chest pain using an 11-point verbal rating scale, with 0 = no pain to 10 = worst pain imaginable. In addition, the postoperative opioid analgesic requirements and opioid-related adverse effects were recorded. Patient satisfaction with their pain management was assessed at specific intervals during the postoperative period using a 100-point verbal rating scale, with 1 = highly dissatisfied to 100 = highly satisfied. Finally, serum bupivacaine concentrations were measured 24 and 48 h after surgery.**

Results: **Compared with the control group, there was a statistically significant reduction in verbal rating scale pain scores and patient-controlled analgesia morphine use in the bupivacaine-0.5% group. Patient satisfaction with their pain management was also improved in the bupivacaine-0.5% (*vs.* control) group. However, there were no significant differences in patient-controlled analgesia morphine use between the bupivacaine-0.25% and control groups. Although the duration of the intensive care unit stay (30 *vs.* 34 h, respectively) was not significantly decreased, the time to ambulation (1 ± 0.5 *vs.* 2 ± 1 days, respectively) and the duration of hospital stay (4.2 *vs.* 5.7 days, respectively) were lower in the bupivacaine-0.5% group than in the control group. Mean ± SD serum bupivacaine concentrations at 48 h in the bupivacaine-0.25% and bupivacaine-0.5% groups were 0.5 ± 0.5 and 1.3 ± 0.7 μg/ml, respectively.**

Conclusion: **A continuous infusion of bupivacaine 0.5% at 4 ml/h is effective for decreasing pain and the need for opioid analgesic medication as well as for improving patient satisfaction with their pain management after cardiac surgery. Patients in the bupivacaine-0.5% group were able to ambulate earlier, leading to a reduced length of hospital stay.**

PAIN after cardiac surgery is most often related to the median sternotomy.[1] Intensity of sternotomy pain has been found to be significantly higher on the first two postoperative days. Developing strategies for optimizing the analgesic management after cardiac surgery has assumed increased importance with the introduction of fast-track discharge protocols requiring early tracheal extubation.[2–4] In addition, postoperative pain is one of the primary concerns of patients admitted to the intensive care unit (ICU).[2,5–7]

The most often used analgesic methods for alleviating pain after cardiac surgery are intravenous opioid analgesics *via* patient- or nurse-controlled delivery systems.[2,4] However, the use of parenteral opioid-based analgesic techniques can delay tracheal extubation as a result of their ability to produce drowsiness and respiratory depression. Opioid analgesics also produce adverse effects on the gastrointestinal tract (*e.g.*, nausea, vomiting, and ileus) and bladder function (*e.g.*, urinary retention). To reduce the adverse systemic effects of opioid analgesics, the use of central neuraxial techniques involving small doses of opioids has become increasingly popular.[8–11] In addition, adjunctive use of nonopioid analgesics that are devoid of respiratory depression has been suggested to facilitate the fast-tracking process after cardiac surgery.[5] However, a recent study evaluating the use of propacetamol (acetaminophen) to supplement opioid analgesia failed to demonstrate any clinically significant benefits.[12]

Hynninen *et al.*[13] reported that the use of nonsteroidal antiinflammatory drugs as adjuvants to the opioid analgesics in the early postoperative period can produce opioid-sparing effects after cardiothoracic surgery. However, nonsteroidal antiinflammatory drugs can also produce adverse effects that complicate the recovery process after cardiac surgery (*e.g.*, bleeding and renal dysfunction). A recent study by Ilfeld *et al.*[14] found that a local anesthetic infusion at the popliteal sciatic nerve decreased pain and opioid use and improved patient outcome after podiatric surgery. However, controlled studies evaluating the opioid-sparing effects of local anesthetic infusions at the surgical site have yielded conflicting results.[15,16]

Therefore, we designed this clinical study to examine the hypothesis that the infusion of a local anesthetic solution at the median sternotomy site would produce

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improved pain control and an opioid-sparing effect after cardiac surgery. A secondary objective of the study was to determine if the opioid-sparing effects of the local anesthetic infusion would facilitate the recovery process and improve patient outcome with respect to satisfaction with their pain management.

Materials and Methods

Patient Demographics and Anesthetic Techniques

After obtaining approval from the Institutional Review Board at the University of Texas Southwestern Medical Center and St. Paul Medical Center in Dallas, 45 consenting patients who were scheduled to have an open-heart operation were enrolled in this randomized, placebo-controlled, double-blind study. The patients were assigned to receive one of three solutions: saline (control), bupivacaine 0.25%, and bupivacaine 0.5% at a fixed infusion rate of 4 ml/h during the first 48 h after cardiac surgery. Patient exclusion criteria included known allergy to local anesthetics, paragenes, or para-aminobenzoic acid, clinically significant kidney or liver disease, neurologic dysfunction, chronic use of systemic lidocaine or other antiarrhythmic drugs, insulin-dependent diabetes mellitus, or active bacterial infection.

All patients received intravenous midazolam (2–5 mg) for sedation in the preoperative holding area during placement of the standard invasive monitors. Monitors included those for five-lead electrocardiography, radial intraarterial blood pressure, central venous pressure, pulse oximetry, and capnography and a three-channel Holter monitor (for 24 h). Anesthesia was induced using intravenous sufentanil (0.3–1.0 μg/kg) and intravenous etomidate (0.2–0.3 mg/kg), and tracheal intubation was facilitated with intravenous rocuronium (1 mg/kg). Maintenance of anesthesia consisted of a sufentanil infusion (0.3–1.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$) with desflurane (3–6% end-tidal concentration). At the end of surgery, desflurane and sufentanil were discontinued, and a propofol infusion was initiated at 25–50 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Continuous Local Anesthetic Infusion Technique

The cardiac surgeon placed catheters at either end of the sternotomy incision site during closure of the chest wound. The first catheter was placed in the subfascial plane above the sternum, and the second catheter was positioned above the fascia in the subcutaneous tissue at the median sternotomy incision site. Both catheters were attached to an elastomeric infusion pump (ON-Q® Pain Relief System; I-Flow Corporation, Lake Forest, CA) at the end of surgery before leaving the operating room. This infusion pump consists of a disposable 270-ml elastomeric reservoir that delivers a continuous infusion at a fixed rate of 2 ml/h through each of the two 5-in-long soaker catheters. A one-way valve prevents any backflow into the drug reservoir, which contained saline, bupivacaine 0.25%, or bupivacaine 0.5% solution. An operating room pharmacist who was not involved in the study filled the reservoir with the study medication.

Follow-up Assessments

Postoperative evaluations were performed by a blinded observer 4, 8, 12, 24, 48, and 72 h after tracheal extubation, including assessments of the level of sedation (using the Ramsay scale),[17] severity of pain using an 11-point verbal rating scale, where 0 = no pain and 10 = worst pain imaginable, the amount of opioid analgesic medication administered (*i.e.*, patient-controlled analgesia morphine use), and patient satisfaction with their postoperative pain management using a 100-point verbal rating scale, where 1 = highly dissatisfied to 100 = highly satisfied. Patients were also questioned regarding the occurrence of pruritis, nausea, and vomiting at each of the previously described time intervals. Urinary retention was defined as the need for reinsertion of a bladder catheter because of an inability to void within 8 h after its removal. The time intervals from arrival in the ICU to tracheal extubation, first bowel sound, first bowel movement, ambulation with assistance, tolerating normal dietary intake, and discharge from the ICU and the hospital were also assessed by the nursing staff according to the institution's standardized protocol for all patients undergoing cardiac surgery. A sample of the mediastinal drainage fluid was obtained 4 h after surgery, and blood samples were obtained 24 and 48 h after surgery for analysis of the bupivacaine concentrations.

Statistical Analysis

An *a priori* power analysis suggested that minimum group sizes of 10 would have 80% power to detect a difference between the groups if the local anesthetic solutions decreased the pain scores or patient-controlled analgesia opioid use by 75% compared with saline (based on a study involving the use of continuous local anesthetic infusions after major orthopedic surgery procedures[14]), assuming a significance level of 0.05 and an SD of $\pm$ 5. Data are expressed as mean $\pm$ SD. Normality was assessed with the Kolmogorov–Smirnov test (by using the Lilliefors modification), and depending on the results, either parametric or nonparametric analysis was performed. Demographic, surgery, and anesthetic data as well as doses of drug administered were analyzed and compared by using the Student *t* test. Pain, sedation, and patient satisfaction verbal rating scale scores were analyzed by using the Fisher exact or Mann–Whitney U-test, with $P < 0.05$ considered statistically significant. Means were analyzed using a type III sum of squares ANOVA, where model = treatment. Frequencies of events were analyzed using a chi-square test. Correlation coefficients for the relationships between the mean total patient-controlled analgesia morphine use and the median ver-

Table 1. Demographic Characteristics, Anesthetic Drugs, and Operative Data for the Three Study Groups

	Control	Bupivacaine 0.25%	Bupivacaine 0.5%
Patients (n)	12	12	12
Age (yr)	61 ± 8	55 ± 11	58 ± 14
Sex (M/F), n	10/2	8/4	7/5
Weight (kg)	83 ± 7	74 ± 12	83 ± 18
ASA physical status (III/IV), n	9/3	8/4	8/4
Anesthesia time (min)	296 ± 38	289 ± 52	311 ± 30
Surgery time (min)	236 ± 51	226 ± 37	222 ± 58
Cross-clamp time (min)	58 ± 25	72 ± 18	63 ± 27
CPB time (min)	90 ± 39	92 ± 28	96 ± 28
Sufentanil dose (μg)	248 ± 112	195 ± 66	189 ± 58
Midazolam dose (mg)	5.4 ± 3.4	3.8 ± 2.4	4.7 ± 2.3

Values are numbers (n) and mean ± SD.

ASA = American Society of Anesthesiologists; CPB = cardiopulmonary bypass.

bal pain scores were calculated for each of the three treatment groups using a multiple regression model.

Results

A total of 45 patients were enrolled in the study. However, nine patients were excluded from the data analysis because of failure to initiate the therapy or protocol violations (*e.g.*, premature termination of the therapy). In six cases, the local anesthetic catheters either were not placed by the surgeon at the end of the operation (four cases) or were inadvertently removed within 24 h (two cases). Two patients developed serious bradyarrhythmias during the postbypass period (and were withdrawn from the study before initiating the therapy), and one patient (in the control group) developed a cerebrovascular accident and died on the second postoperative day. There were no differences between the three study groups with respect to age, weight, height, American Society of Anesthesiologists physical status, midazolam premedication, anesthesia and surgery times, aortic cross-clamp time, cardiopulmonary bypass time, and the amount of intraoperative opioid medication administered (table 1). Of the 12 controls, 10 underwent coronary artery bypass grafting, and two underwent valve replacement procedures. In the bupivacaine-0.25% group, six patients underwent coronary artery bypass grafting, three underwent valve replacements, two underwent atrial septal defect repairs, and one underwent an atrial myxoma excision procedure. In the bupivacaine-0.5% group, eight patients underwent coronary artery bypass grafting, three underwent valve replacements, and one underwent atrial septal defect repair.

No statistically significant differences were found in the average times to tracheal extubation (table 2). Patients in the bupivacaine-0.25% group recovered bowel sounds and were able to ambulate significantly earlier than were controls (table 2). The urinary catheter was removed significantly earlier in the bupivacaine-0.5% group than in the other two study groups (table 2). More importantly, all patients in the bupivacaine-0.5% group were able to sit up in a chair and ambulate with assistance on the first postoperative day. Patients in the bupivacaine-0.5% group were also able to meet discharge criteria from the hospital significantly faster than were patients in the other two study groups (table 2).

Patients in both bupivacaine treatment groups reported significantly less pain 4, 8, 12, and 24 h after surgery than did controls (fig. 1). The patient-controlled analgesia morphine use was significantly reduced in the bupivacaine-0.5% group compared with the control and bupivacaine-0.25% groups (figs. 2 and 3). In the two

Table 2. Recovery Times after Surgery in the Three Treatment Groups

	Control	Bupivacaine 0.25%	Bupivacaine 0.5%
Extubation time (min)	300 ± 118	396 ± 138	304 ± 140
First bowel sound (min)	444 ± 302	231 ± 161*	353 ± 258
Normal dietary intake (d)	2 ± 0.7	1 ± 0.6*	1 ± 0.4†
Urinary catheter removal (d)	2 ± 1	2 ± 1	1 ± 0.5†
Sitting up in chair (d)	1.2 ± 0.7	1 ± 0.6	1
Able to ambulate (d)	2 ± 7	1 ± 0.6*	1†
First bowel movement (d)	4.6 ± 1.4	4.3 ± 1.3	4 ± 1.5
ICU stay (h)	34 ± 12	40 ± 15	30 ± 10
Hospital stay (d)	5.7 ± 2.1	5.0 ± 1.0	4.2 ± 0.8†

Values are mean ± SD.

* Control group *versus* bupivacaine-0.25% group, $P < 0.05$. † Control group *versus* bupivacaine-0.5% group, $P < 0.05$.

ICU = intensive care unit.

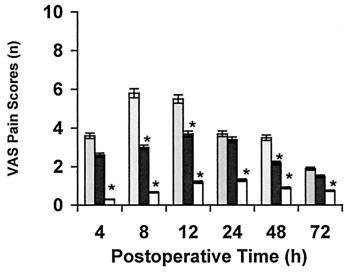

Fig. 1. Pain scores in the control group (*gray bars*), bupivacaine-0.25% group (*black bars*), and bupivacaine-0.5% group (*white bars*) during the first 72 h after surgery as assessed by the patient using a verbal rating scale (VAS), with 0 = no pain to 10 = worst pain imaginable. *$P < 0.05$, values significantly different from those of the control group.

bupivacaine treatment groups, a positive correlation was found between the average patient-controlled analgesia morphine use and the patient's median pain verbal rating scale score, with r values of −0.168, 0.638, and 0.392 in the control, bupivacaine-0.25%, and bupivacaine-0.5% groups, respectively (fig. 3). Some statistically significant differences were also found in patient satisfaction with pain management scores between the two bupivacaine treatment groups and the control group (fig. 4). The overall incidences of postoperative nausea and vomiting during the 72-h observation period were 36%, 25%, and 33% in the control, bupivacaine-0.25% and bupivacaine-0.5% groups, respectively.

The bupivacaine concentrations in the mediastinal drainage fluid were consistently higher than the serum bupivacaine concentrations in both bupivacaine treatment groups (table 3). At 24 h after surgery, there was no significant difference in the serum bupivacaine concentrations between the two bupivacaine treatment groups. However, at 48 h (end of the infusion period), the serum bupivacaine concentrations were significantly higher in the bupivacaine-0.5% group than in the bupivacaine-0.25% and control groups (1.3 ± 0.7 *vs.* 0.5 ± 0.5 and <0.5 μg/ml, respectively). Importantly, the serum bupivacaine concentrations in all bupivacaine-treated patients were less than 4 μg/ml at the end of the 48-h infusion period. Complications related to the local anesthetic delivery system included a catheter tip that was inadvertently broken off during its removal from the incision site, which required reexploration of the wound under local anesthesia.

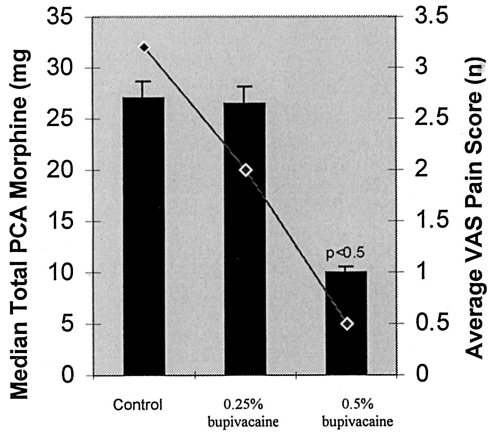

Fig. 3. Relationship between the mean (± SD) total patient-controlled analgesia (PCA) morphine use (mg) during the 72-h study period (*black bars*) and the average (median) verbal pain score (*diamonds*) on an 11-point verbal rating scale (VAS), where 0 = no pain to 10 = worst pain imaginable. The correlation coefficients were −0.168, 0.638, and 0.392 in the control, bupivacaine-0.25% and bupivacaine-0.5% groups, respectively.

Discussion

Mortality and morbidity after surgery seem to be related, in part, to the pathophysiologic response to the surgical trauma and to postoperative complications.[18] Postoperative pain and the use of large doses of opioid under medications can increase adverse effects, which

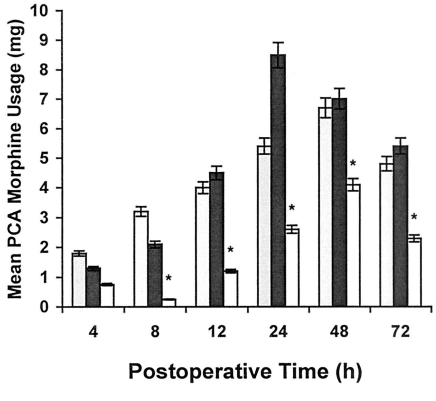

Fig. 2. Postoperative opioid analgesic requirements in the control (*gray bars*), bupivacaine-0.25% group (*black bars*), and bupivacaine-0.5% group (*white bars*) that were assessed using patient-controlled analgesia (PCA) morphine use during the first 72 h after surgery. *$P < 0.05$, values significantly different from those of the control group.

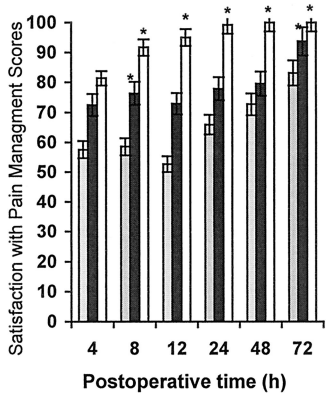

Fig. 4. Patient satisfaction with their postoperative pain management during the first 72 h after surgery in the control group (*gray bars*), bupivacaine-0.25% group (*black bars*), and bupivacaine-0.5% group (*white bars*) on a 100-point verbal rating scale, with 1 = highly dissatisfied to 100 = highly satisfied. *$P < 0.05$, values significantly different from those of the control group.

Table 3. Bupivacaine Concentrations in the Chest Tube Drainage 4 h after Surgery and Serum Concentrations 24 and 48 h after Surgery in the Three Treatment Groups

	Control (Saline)	Bupivacaine 0.25%	Bupivacaine 0.5%
Chest tube drainage concentration at 4 h (μg/ml)	<0.5	1.8 ± 2	3.2 ± 2*
Serum concentration at 24 h (μg/ml)	<0.5	0.5 ± 0.2	0.8 ± 0.6*†
Serum concentration at 48 h (μg/ml)	<0.5	0.5 ± 0.5	1.3 ± 0.7*†

Values are mean ± SD.

* Control group *versus* bupivacaine-0.5% group, $P < 0.05$. † Bupivacaine, 0.25% group *versus* bupivacaine-0.5% group, $P < 0.05$.

contribute to delays in postoperative recovery after major surgery.[19,20] Therefore, the use of opioid-sparing analgesic techniques that can improve postoperative pain control with less opioid medication might facilitate the recovery process and rehabilitation (*e.g.*, resumption of dietary intake and physical activity).[21] Analgesic techniques that improve pain control while minimizing the respiratory depressant effects of opioids in the early postoperative period are essential for fast-tracking patients through the recovery process after cardiac surgery.[8–11]

This "proof of concept" study demonstrated that the use of a continuous infusion of bupivacaine 0.5% (4 ml/h) at the sternotomy site during the early postoperative period is an efficacious method for improving pain control after open-heart surgery. Analogous to the findings described for patients undergoing major orthopedic surgery procedures,[14,22–26] continuous infusion of local anesthetics at the surgical site seems to produce an opioid-sparing effect, which can lead to greater patient satisfaction with their pain management after cardiac surgery. These findings also confirm the anecdotal reports describing local anesthetic (tissue) infusions after bone graft harvest and laparoscopic surgery procedures.[27,28] As suggested Todd and Brown,[29] the modern concept of postoperative analgesia appears to be moving toward peripheral local anesthetic techniques.[21]

Although we failed to demonstrate an improvement in all key outcome variables (*e.g.*, tracheal extubation and length of ICU stay), this study involving a relatively small series of patients was not adequately powered to examine the effect of the local analgesic technique on all of the secondary outcome variables. The differing types of cardiac surgery procedures (*e.g.*, coronary artery bypass grafting, valve replacement, and atrial septal defect repair) may have exerted a significant impact on the recovery and discharge times because of the small group sizes. The failure to demonstrate a benefit of the opioid-sparing action of the local anesthetic infusion on the times to tracheal extubation and ICU discharge was probably related to the fact that there was no attempt by the ICU staff to "fast-track" these cardiac patients at our university teaching hospital. Furthermore, opioid-related adverse effects (*e.g.*, nausea, vomiting, urinary retention, constipation, and ileus) are not strictly dose related. It is also important to note that this study examined a fixed infusion (4 ml/h) of either bupivacaine 0.25% or bupivacaine 0.5%. Further studies are needed to determine the "optimal" infusion rate for and concentration of the local anesthetic. Another valid criticism of this study relates to the location of the local anesthetic infusion catheters. A better outcome might have been achieved with continuous paravertebral intercostal nerve blockade and/or placement of both catheters at deeper tissue planes (*i.e.*, subfascial placement).[30]

Another concern relates to the high incidence of catheter-related problems (*e.g.*, inadvertent removal during dressing changes and breakage on removal) in this "proof of concept" study. Although attempts were made to in-service all ICU nurses and surgery house staff, mistakes were made and interfered with the successful completion of the study in 13% of the cases. Our evaluation of the safety of this local anesthetic technique was limited to monitoring the patients' cardiac rhythm and plasma drug concentrations. Of importance, even in the bupivacaine-0.5% group, plasma concentrations remained below the alleged toxic concentration for this local anesthetic in all patients (table 3). Although no ventricular arrhythmias were observed during the 48-h postoperative period, the use of higher infusion rates for bupivacaine 0.5% (> 4 ml/h) may result in plasma bupivacaine concentrations that could produce cardiotoxicity. Whether the use of ropivacaine or levobupivacaine would provide an additional margin of safety when using continuous local anesthetic infusion systems remains to be established in future comparative studies.

In conclusion, the use of a continuous infusion of bupivacaine 0.5% at the median sternotomy site reduced postoperative pain and the need for opioid analgesics after cardiac surgery. The use of infusion of bupivacaine 0.5% also improved some patient outcome variables (*e.g.*, time to ambulation) and patient satisfaction with their pain management. This nonopioid pain management technique has the potential to facilitate the recovery process (*i.e.*, fast-tracking) after open-heart surgery.

References

1. Mueller XM, Tinguely F, Tevaearai HT, Revelly JP, Chiolero R, von Segesser LK: Pain location, distribution, and intensity after cardiac surgery. Chest 2000; 118:391–6

2. Paiement B, Boulanger M, Jones CW, Roy M: Intubation and other experi-

ences in cardiac surgery: The consumer's view. Can Anaesth Soc J 1979; 26: 173–80

3. Bettex DA, Schmidlin D, Chassot PG, Schmid ER: Intrathecal sufentanil-morphine shortens the duration of intubation and improves analgesia in fast-track cardiac surgery. Can J Anaesth 2002; 49:711–7

4. Boldt J, Thaler E, Lehmann A, Papsdorf M, Isgro F: Pain management in cardiac surgery patients: Comparison between standard therapy and patient-controlled analgesia regimen. J Cardiothorac Vasc Anesth 1998; 12:654–8

5. Ranucci M, Cazzaniga A, Soro G, Isgro G, Rossi R, Pavesi M: Postoperative analgesia for early extubation after cardiac surgery: A prospective, randomized trial. Minerva Anestesiol 1999; 65:859–65

6. Nastasy EL: Identifying environmental stressors for cardiac surgery patients in a surgical intensive care unit. Heart Lung 1985; 14:302–3

7. Tsang J, Brush B: Patient-controlled analgesia in postoperative cardiac surgery. Anaesth Intensive Care 1999; 27:464–70

8. Zarate E, Latham P, White PF, Bossard R, Morse LS, Douning LK, Shi C, Chi L: Fast-track cardiac anesthesia: Use of remifentanil combined with intrathecal morphine as an alternative to sufentanil during a desflurane anesthesia. Anesth Analg 2000; 91:283–7

9. Scott NB, Turfrey DJ, Ray DAA, Nzewi O, Sutcliffe NP, Lal AB, Norrie J, Nagels WJB, Ramayya GP: A prospective randomized study of the potential benefits of thoracic epidural anesthesia and analgesia in patients undergoing coronary artery bypass grafting. Anesth Analg 2001; 93:528–35

10. Priestley MC, Cope L, Halliwell R, Gibson P, Chard RB, Skinner M, Kleinberg PL: Thoracic epidural anesthesia for cardiac surgery: The effects on tracheal intubation time and length of hospital stay. Anesth Analg 2002; 94:275–82

11. Mehta Y, Juneja R, Madhok H, Tehran N: Lumbar *versus* thoracic epidural buprenorphine for postoperative analgesia following coronary artery bypass graft surgery. Acta Anaesthesiol Scand 1999; 43:388–93

12. Lahtinen P, Kokki H, Hendolin H, Hakala T, Hynynen M: Propacetamol as adjunctive treatment for postoperative pain after cardiac surgery. Anesth Analg 2002; 95:813–9

13. Hynninen MS, Cheng DC, Hossain I, Carroll J, Aumbhagavan SS, Yue R, Karski JM: Non-steroidal anti-inflammatory drugs in treatment of postoperative pain after cardiac surgery. Can J Anaesth 2000; 47:1182–7

14. Ilfeld BM, Morey TE, Wang RD, Enneking FK: Continuous popliteal sciatic nerve block for postoperative pain control at home: A randomized, double-blinded, placebo-controlled study. ANESTHESIOLOGY 2002; 97:959–65

15. Fredman B, Shapiro A, Zohar E, Feldman E, Shorer S, Rawal N, Jedeikin R: The analgesic efficacy of patient-controlled ropivacaine instillation after cesarean delivery. Anesth Analg 2000; 91:1436–40

16. Fredman B, Zohar E, Tarabykin A, Shapiro A, Mayo A, Klein E, Jedeikin R: Bupivacaine wound instillation via an electronic patient-controlled analgesia device and a double-catheter system does not decrease postoperative pain or opioid requirements after major abdominal surgery. Anesth Analg 2001; 92: 189–93

17. Haberthur C, Lehmann F, Ritz R: Assessment of depth of midazolam sedation using objective parameters. Intensive Care Med 1996; 22:1385–90

18. Kehlet H: Multi-modal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 1997; 78:606–17

19. Naughton C, Prowroznyk A, Feneck R: Reasons for prolonged hospital stays following heart surgery. Br J Nurs 1999; 8:1085–7

20. Capdevila X, Barthelet Y, Biboulet P, Ryckwaert Y, Rubernovitch J, d'Athis F: Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. ANESTHESIOLOGY 1999; 91:8–15

21. Brown DL: Peripheral nerve blocks: Regional anesthesia for the new millennium (editorial). Reg Anesth Pain Med 1998; 23:237–40

22. Pinzur MS, Garla PGN, Pluth T, Vrbos L: Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. J Bone Joint Surg 1996; 78:1501–5

23. Savoie FH, Field LD, Jenkins RN, Mallon WJ, Phelps RA: The pain control infusion pump for postoperative pain control in shoulder surgery. Arthroscopy 2000; 16:339–42

24. Barber FA, Herbert MA: The effectiveness of an anesthetic continuous-infusion device on postoperative pain control. Arthroscopy 2002; 18:76–81

25. Klein SM, Grant SA, Greengrass RA, Nielsen KC, Speer KP, White W, Warner DS, Steele SM: Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. Anesth Analg 2000; 91:1473–8

26. White PF, Issioui T, Skrivanek GD, Early JS, Wakefield C: The use of a continous popliteal sciatic nerve block after surgery involving the foot and ankle: Does it improve the quality of recovery? Anesth Analg 2003; (in press)

27. Borris TJ, Scuba JR: Continuous postoperative pain control after bone graft harvest using a pump delivery system. J Oral Maxillofac Surg 2001; 59:707–8

28. Stringer NH, Rodino KL, Edwards M, Kumari NV: On-Q system for managing trocar site pain after operative laparoscopy. J Am Assoc Gynecol Laparosc 2000; 7:552–5

29. Todd M, Brown DL: Regional anesthesia and postoperative pain management: Long-term benefits from a short-term investigation. ANESTHESIOLOGY 1999; 91:1–2

30. Yndgaard S, Holst P, Bjerre-Jepsen K, Thomsen CB, Struckmann J, Morgensen T. Subcutaneously *versus* subfascially administered lidocaine in pain treatment after inguinal herniotomy. Anesth Analg 1994; 79:324–7