Thoracic Epidural versus Intravenous Patient-controlled Analgesia after Cardiac Surgery

A Randomized Controlled Trial on Length of Hospital Stay and Patient-perceived Quality of Recovery

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**Background:** Perioperative thoracic epidural analgesia reduces stress response and pain scores and may improve outcomes after cardiac surgery. This prospective, randomized trial was designed to compare the effectiveness of patient-controlled thoracic epidural analgesia with patient-controlled analgesia with intravenous morphine on postoperative hospital length of stay and patients' perception of their quality of recovery after cardiac surgery.

**Methods:** One hundred thirteen patients undergoing elective cardiac surgery were randomly assigned to receive either combined thoracic epidural analgesia and general anesthesia followed by patient-controlled thoracic epidural analgesia or general anesthesia followed by patient-controlled analgesia with intravenous morphine. Postoperative length of stay, time to eligibility for hospital discharge, pain and sedation scores, degree of ambulation, lung volumes, and organ morbidities were evaluated. A validated quality of recovery score was used to measure postoperative health status.

**Results:** Length of stay and time to eligibility for hospital discharge were similar between the groups. Study groups differed neither in postoperative global quality of recovery score nor in five dimensions of quality of recovery score. Time to extubation was shorter ($P < 0.001$) and consumption of anesthesia was lower in the patient-controlled thoracic epidural analgesia group. Pain relief, degree of sedation, ambulation, and lung volumes were similar between the study groups. There was a trend for lower incidences of pneumonia ($P = 0.085$) and confusion ($P = 0.10$) in the patient-controlled thoracic epidural analgesia group, whereas cardiac, renal, and neurologic outcomes were similar between the groups.

**Conclusions:** In elective cardiac surgery, thoracic epidural analgesia combined with general anesthesia followed by patient-controlled thoracic epidural analgesia offers no major advantage with respect to hospital length of stay, quality of recovery, or morbidity when compared with general anesthesia alone followed by to patient-controlled analgesia with intravenous morphine.

PREVIOUS studies on the effects of perioperative thoracic epidural analgesia/analgesia (TEA) as an adjuvant to general anesthesia in cardiac surgery have mainly been focused on postoperative morbidity. Studies have shown that TEA attenuates the surgical stress response, improves hemodynamic stability, and decreases the incidence of new supraventricular arrhythmias, as well as myocardial ischemia, after coronary artery bypass surgery (CABG).1–3 Furthermore TEA decreases pain scores,4,5 permits earlier extubation,1–3,5 and has the potential to decrease the incidence of lower respiratory tract infections, acute renal failure, and acute confusion3 compared with conventional treatment with intravenous opioids. In a recent meta-analysis6 including more than a thousand patients, it was shown that TEA was associated with improvements in faster time to tracheal extubation, decreased pulmonary complications and cardiac dysrhythmias, and reduced pain scores, whereas there were no differences in the rates of mortality or myocardial infarction after CABG with TEA. Despite these potentially beneficial effects with TEA after CABG, the application of TEA in connection with cardiac surgery is still controversial.7,8 Fear of epidural hematoma formation has led to reluctance among anesthesiologists to place epidural catheters in these patients who receive high-level anticoagulation.

Despite the apparent improvement in some measures of morbidity, few studies have been focused on the effects of TEA on hospital length of stay (LOS) as a primary outcome variable. Furthermore, to our knowledge, there are no studies on the effects of TEA on the patients' perception of their outcome in terms of quality of recovery. It has recently been shown that a poor quality of recovery early after cardiac surgery can predict a poor quality of life 3 months after surgery.9

We therefore designed a prospective, randomized controlled trial in an elective group of consecutive patients scheduled to undergo various cardiac surgical procedures to compare the effectiveness on postoperative outcome of two techniques of anesthesia and analgesia: combined thoracic epidural and general anesthesia followed by postoperative patient-controlled thoracic epidural analgesia (PCTEA), using a combination of bupivacaine and fentanyl, or general anesthesia followed by patient-controlled analgesia (PCA) with intravenous morphine. The main endpoint variable was the actual length of hospital stay. Secondary outcome variables were patients' perception of their quality of recovery, time to
eligibility for hospital discharge, adequacy of pain relief, degree of ambulation, and prospectively defined postoperative complications.

Material and Methods

The Human Ethics Committee of the Sahlgrenska Academy, Göteborg University, Göteborg, Sweden, approved the study protocol, and all patients gave written informed consent. The study was conducted for 21 months from April 1, 2002, to December 31, 2003. Inclusion criteria were elective cardiac surgery (CABG), cardiac valve procedures, combined CABG and valve procedures or the Maze procedure, with or without CABG), absence of contraindications to epidural anesthesia, abnormal coagulation tests (i.e., partial thromboplastin time > 45 s or prothrombin time [international normalized ratio] > 1.5 or a platelet count < 80,000), or recent (< 1 week) treatment with thrombolytic or potent antiplatelet drugs (streptokinase, alteplase, clopidogrel, abciximab, tirofiban, integrin). Aspirin treatment was not considered a contraindication to the placement of a thoracic epidural catheter.

Demographic data, preoperative medications, and surgical and medical history were taken from the patient and the medical record. Preoperative histories of hypertension (requiring chronic pharmacologic treatment), insulin-dependent or non–insulin-dependent diabetes, myocardial infarction (transmural, subendocardial, or both), and respiratory disease including restrictive or obstructive respiratory disease (requiring chronic pharmacologic treatment) were recorded.

Patients were randomly assigned (sealed envelopes) the day before surgery to one of two regimens. The PCA group received general anesthesia followed by postoperative PCA with morphine. The interventional group received general anesthesia plus intraoperative thoracic epidural anesthesia followed by postoperative PCTEA. Treatment with PCA or PCTEA continued for 3 postoperative days. All subjects received preoperative written and oral instructions for use of PCA or PCTEA.

The day before surgery, patients in the TEA group had epidural catheter (Braun, Melsungen, Germany) inserted in the thoracic region between T2 and T5 by one of the senior staff anesthesiologists. Epidural puncture was done using the median hanging-drop or the loss-of-resistance technique, and the catheter was inserted 3–5 cm into the epidural space. Four milliliters lidocaine, 1%, was used to confirm placement. Full treatment with heparin or low-molecular-weight heparin was stopped at least 6 and 12 h, respectively, before the epidural catheter insertion. Patients on warfarin or aspirin treatment had their medication suspended 1 week or the day before surgery, respectively. If a bloody tap was encountered, epidural puncture was performed at another interspace. Before we started the study, the neurosurgeons and the neuroradiologists were carefully informed about the nature of the study, and a written “Urgent Management Program” was agreed on in case of a suspected spinal hematoma in our patients.

Premedication in each group consisted of 1–2 mg midazolam 1 h before surgery. β-Adrenergic blockers were continued during the perioperative period, including the morning of surgery, whereas angiotensin-converting enzyme inhibitors, calcium channel blockers, and other cardiovascular medications were suspended the day before surgery.

All patients received infusions of propofol and remifentanil to a target anesthetic depth of 15–25 AAI using an auditory evoked response monitor (Alaris AEP Monitor; Dannmeter A/S, Odense, Denmark). The total intraoperative doses of propofol and remifentanil were recorded. Tracheal intubation was facilitated with 0.5 mg/kg atracurium. After induction of anesthesia and insertion of monitoring devices, patients in the PCTEA group received an epidural 0.1-ml/kg bolus dose followed by a continuous 0.05-ml · kg⁻¹ · h⁻¹ infusion with bupivacaine (5 mg/ml). All patients had a median sternotomy, and all patients undergoing CABG also had leg vein incision(s). Intraoperative hypotension was treated with fluids, norepinephrine infusion, or both, and hypotension was treated with infusion of sodium nitroprusside at the discretion of the attending anesthesiologist. Cardiopulmonary bypass was performed using a COBE Duo membrane oxygenator (COBE, Arvada, CO) after administration of heparin (300 U/kg). The activated clotting time was maintained at greater than 400 s. The circuit was primed with 1,500 ml Ringer’s solution and 200 ml mannitol, 15%, and a nonpulsatile flow of 2.4 l · min⁻¹ · m⁻² was used. In all patients, hypothermia (32°–34°C) and cold hyperkalemic blood cardioplegia were used during cardiopulmonary bypass. After weaning from cardiopulmonary bypass (36.5°–37°C), anticoagulation was reversed with protamine sulfate, given at a ratio of 1 mg/100 U heparin. Target mean arterial pressure during cardiopulmonary bypass was 50–90 mmHg.

In the PCTEA group, postoperative pain treatment was achieved by epidural bolus doses of 2 ml of the mixture 1 mg/ml bupivacaine plus 2 µg/ml fentanyl plus 2 µg/ml adrenaline, a lockout interval of 20 min, and a background epidural infusion of 0.1 ml · kg⁻¹ · h⁻¹. An epidural 0.1-ml/kg loading dose of this mixture was given at the end of surgery. Patients who had CABG received aspirin (160 mg daily), and patients undergoing valve procedures received postoperative 5,000 U subcutaneous heparin three times daily from the first postoperative day. Warfarin treatment was started on the fourth postoperative day, and heparin treatment was continued until the international normalized ratio was 2.1 or greater. The epidural catheter was removed on the morning of the fourth postoperative day at least 2 h
before subcutaneous heparin. In the PCA group, postoperative pain treatment was achieved by intravenous PCA morphine with bolus doses of 0.01 mg/kg and a lockout interval of 6 min with no background infusion. A loading dose of 0.1 mg/kg morphine was given in the operating room when remifentanil infusion was stopped. In both groups, PCA was commenced when the patients responded to verbal commands and were able to report pain (nonverbally, if intubated). All patients received in addition 1 g oral acetaminophen four times daily for 3 postoperative days. Nonsteroidal antiinflammatory agents were administered if the above-mentioned treatment was not adequate.

In the intensive care unit (ICU), the patients were sedated with propofol before extubation. Patients underwent extubation when they fulfilled the following criteria: (1) responsive to verbal commands, (2) body temperature greater than 36.5°C, (3) chest tube drainage less than 100 ml/h, (4) arterial partial pressure of oxygen 70 mmHg or greater at an inspired oxygen fraction less than 0.5, (5) arterial partial pressure of carbon dioxide less than 50 mmHg and respiratory rate 20 or less at a pressure support ventilation of 10 cm H2O, and (6) hemodynamic stability, i.e., not requiring significant inotropic support. Time to extubation was recorded in each patient. If there were no postoperative complications necessitating ICU treatment, the patients were discharged to the surgical ward on the first postoperative morning. Time to ICU discharge was not assessed, because all patients at our institution routinely stay one night in the ICU. If adequate analgesia was not provided with the PCTEA regimen, PCTEA patients were treated with PCA morphine or had a new epidural catheter inserted before ICU discharge.

Patient-perceived quality of recovery was assessed using a translated version of a recently validated quality of recovery score (QoR-40) designed to measure the patient’s health status after surgery and anesthesia.9,10 QoR-40 is a 40-item quality of recovery score measuring the five dimensions: physical comfort (12 items), emotional state (9 items), physical independence (5 items), psychological support (7 items), and pain (7 items). Each item is rated on a five-point Likert scale (for positive items, 1 = none of the time, 5 = all of the time; for negative items, the scoring was reversed. The QoR-40 has a possible score of 40 (extremely poor quality of recovery) to 200 (excellent quality of recovery). Quality of recovery was measured preoperatively, on days 1, 2, and 3 after surgery (where day of surgery is day 0). Patients unable to complete the questionnaires independently were asked for verbal responses to each item by one of the investigators. On the first postoperative day, all patients discharged from the ICU took part in a mobilization program that continued until hospital discharge. The level of mobilization was assessed by a physiotherapist (one of the authors) using a mobilization scale graded from 1 to 8, where 0 = unable to mobilize, 1 = sitting on the bedside, 2 = standing at the bedside, 3 = walking 25 m, 4 = walking 50 m, 5 = walking 75 m, 6 = walking more than 100 m, 7 = walking more than 100 m plus climbing one stair, 8 = walking more than 100 m plus climbing two stairs. In each patient, the postoperative day when level 6 was achieved was also assessed.

Analgesia was assessed by one of the authors for 3 postoperative days, at rest and after coughing, using the 100-mm visual analog scale in which 0 represents no pain and 10 represent the worst pain imaginable. The level of sedation was assessed by one of the investigators for 3 postoperative days using a four-point sedation scale: 0 = fully awake, 1 = mildly sedated (seldom drowsy and easy to awaken), 2 = moderately sedated (often drowsy and easy to awaken), 3 = severely sedated (somnolent, difficult to awaken).

Spirometric estimation of forced vital capacity, forced expiratory volume in 1 s, and peak expiratory flow were performed with the patient in the sitting position in a standardized manner according to the European Respiratory Society11 using a vitalograph (Wicat test 3; Mijnhardt, Odijk, The Netherlands) and a peak flow meter (Wright, London, England) preoperatively and for 3 postoperative days. Chest radiographs were taken preoperatively and at least on day 2 in all patients. Atelectasis was defined as new area(s) of lobar or sublobar atelectatic consolidation with an air bronchogram by a radiologist blinded to treatment.12

The hospital LOS, including the day of admittance (the day before surgery) and the day of discharge was recorded for each patient. The decision to allow hospital discharge was taken by the surgical team not blinded to treatment. Furthermore, the day on which patients were eligible for hospital discharge was assessed. A patient was eligible for discharge when fulfilling all of the following criteria: (1) hemodynamically stable without arrhythmias, (2) moving freely and eating without assistance, (3) afibrile without clinical signs of infection, (4) normal voiding and defecation, (5) full oral feeding, (6) pain controlled with or without oral analgesics, (7) walking greater than 100 m plus climbing two stairs, and (8) normalized mentation.

Evaluation of QoR-40, level of mobilization, pain, degree of sedation, lung function, and eligibility for hospital discharge was performed between 1:00 and 3:00 pm each day by either of two investigators. These were blinded to the assigned treatment. The infusion bag of the PCA pump was covered with red plastic, and the patients in the PCA group had a dummy thoracic epidural catheter attached before leaving the ICU. The injection ports of the epidural catheter (true/dummy) and the left subclavian central venous catheter were covered by surgical gauze, making it impossible to reveal whether a patient received pain treatment through a left
subclavian central venous catheter (PCA) or a TEA catheter (PCTEA). The infusion bag (250 ml) of the PCA pump was changed only once during the postoperative treatment period (72 h) by the nursing team, which was neither blinded to treatment nor involved in the assessment of the patients. The blinded investigators were not involved in the nursing of the patients. Less than 5% of the PCTEA patients revealed by mistake to the blinded observer the presence of the epidural catheter.

Postoperative complications were defined as follows:

Respiratory: postoperative mechanical ventilation for more than 24 h; need for noninvasive positive-pressure ventilation; pneumonia, defined as pulmonary infiltrate with positive microbial cultures from sputum or fever, high leukocyte count, or high levels of C-reactive protein.

Cardiac: myocardial infarction, defined by new Q-waves or creatine kinase-MB isoenzyme concentration of 50 or greater; heart failure requiring two or more inotropic agents with or without intravenous balloon counterpulsation; 12-lead standard electrocardiogram-detected atrial fibrillation requiring treatment with antiarrhythmic medication with or without electrical cardioversion.

Renal: Postoperative increase of serum creatinine by more than 50% from the preoperative level; the need for dialysis.

Neurologic: stroke, defined as a new central neurologic deficit; confusion, defined as inability to cooperate or communicate with the nurses or disorientation in time and place or excessive motor activity requiring treatment with haloperidol with or without propofol sedation.

Infection: Wound infection requiring surgical excision or antibiotic therapy, or positive microbial culture (other than pneumonia).

Statistical Analysis

In a prospective pilot study of 95 consecutive unselective patients undergoing cardiac surgery, it was found that the hospital mean LOS was 9.9 days (SD = 3.9 days). We considered a 2.5-day reduction (25%) in LOS to be clinically important. To detect a potential relative reduction in LOS by 25% in the PCTEA group, an estimated 40 clinically important. To detect a potential relative reduction in LOS by 25% in the PCTEA group, an estimated 40 patients in each group were needed at a statistical power of 80% (β = 0.8) and a significance level of 5% (α = 0.05). Allowing for failures to complete the study, more than 100 patients were recruited. Values are presented as mean ± SD. Baseline and outcome variables were compared using the Student unpaired t test and Pearson chi-square test where appropriate. The effects of treatment on QoR-40, visual analog scale score, mobilization score, peak expiratory flow, forced vital capacity, and forced expiratory volume in 1 s were evaluated by a two-way analysis of variance for repeated measurements.

Time to hospital discharge and eligibility for hospital discharge as well as time to reach level 6 on the mobilization scale were plotted by the Kaplan-Meier technique, and differences between treatment groups were tested by the log rank test. All analyses were performed by assigned treatment (intention to treat). A P value less than 0.05 was considered statistically significant.

Results

One hundred thirty-six patients were evaluated for study participation. One hundred thirteen patients were randomized, 110 patients received allocated treatment, and 97 patients were eventually analyzed (fig. 1). Three patients were excluded because of inability to place the epidural catheter. In 1 of these patients, the catheter was positioned intradurally, and 1 patient did not cooperate. Malfunctioning epidural catheter was considered in 7 patients after extubation. Three of these patients had the epidural catheter replaced in the ICU, and 4 patients were treated with intravenous PCA morphine. These 7 patients were analyzed on an intention-to-treat basis.

Preoperative characteristics were comparable between the two study groups (table 1). The study groups did not differ in intraoperative data except for a higher incidence of off-pump CABG in the PCTEA group and a longer cardiopulmonary bypass time in the PCA group (table 2). Patients in the PCTEA group received less remifentanil and propofol during surgery.

The proportion of patients discharged from the hospital and the proportion of patients being eligible for discharge within 14 days are shown in figure 2 and figure 3, respectively. There were no differences between the study groups in probabilities of hospital discharge (P = 0.54), eligibility for hospital discharge (P = 0.95), or probability of reaching a mobilization score of 6 (P = 0.22; fig. 4) after surgery, as evaluated by the Kaplan-Meier technique. The mean hospital LOS was 7.5 ± 3.3 days for the PCTEA group and 7.9 ± 2.8 days for the PCA group (P = 0.47).

The QoR-40 scores are shown in figure 5. The global QoR-40 declined maximally on day 1 and gradually improved during days 2 and 3 in both groups. The two study groups differed neither in postoperative global QoR-40 nor in the five dimensions of QoR-40. Visual analog scale pain scores at rest and during coughing were comparable between the study groups (table 3). There were no differences between the two groups with respect to mobilization scores (table 3). Three patients (6.5%) in the PCA group versus none in the PCTEA group (P = 0.082) were moderately sedated on the first postoperative day. None of the patients were moderately sedated on the second or third postoperative days. PCTEA did not improve forced vital capacity, forced
expiratory volume in 1 s, or peak expiratory flow after surgery when compared with the PCA group (table 4). There were no differences between the two groups with respect to incidences of postoperative myocardial infarction, heart failure, atrial fibrillation requiring treatment, or the use of intraaortic balloon counter pulsation (table 5). Time to extubation was significantly shorter in the PCTEA group. There was no significant difference in the incidence of pneumonia ($P = 0.085$) or the need for postoperative noninvasive positive-pressure ventilation between the study groups. The incidences of stroke and renal dysfunction were comparable between the study groups. None of the patients required dialysis. There was no significant difference in the incidence of wound infections between the two groups. There were no neurologic complications related to epidural placement in the PCTEA group. Bloody tap was encountered in two patients (3.6%).

A higher proportion of patients underwent off-pump CABG in the PCTEA group compared with the PCA group ($P = 0.04$; table 2). Because of this unbalance with respect to type of CABG surgery, post hoc analyses of covariance were performed on time to hospital discharge, time to eligibility for hospital discharge, and global QoR-40 score as dependent variables and type of CABG surgery as the covariate. These analyses revealed no differences between the study groups with respect to time to hospital discharge ($P = 0.24$), time to eligibility for hospital discharge ($P = 0.29$), or global QoR-40 score ($P = 0.65$).

Discussion

To our knowledge, this is the first randomized controlled trial on the effects of perioperative TEA on postoperative outcome in patients undergoing various types of elective cardiac surgery. The major finding of the

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**Fig. 1.** Trial profile. ICU = intensive care unit; PCA = patient-controlled intravenous morphine analgesia; PCTEA = patient-controlled thoracic epidural analgesia.
null
the overall postoperative morbidity. However, one problem with the use of LOS as an endpoint variable is that this variable is affected by many factors not related to the postoperative pain regimen itself, which, on the other hand, would have been evenly distributed between the two groups. A second problem is that the surgeons responsible for the decision to allow hospital discharge were not blinded to postoperative pain treatment. To circumvent this problem, the time to fulfillment of prospectively defined criteria for hospital discharge was assessed for each patient by observers blinded to treatment.

Traditionally, outcome studies in anesthesia and surgery have focused on measurements of organ complications and mortality rates. A patient’s perception of his or her immediate postoperative well-being is also important, because a poor quality of recovery after surgery is likely to delay discharge from hospital. Myles et al.\(^9,10\) have developed a quality of recovery score (QoR-40) to measure postoperative health status early after surgery. QoR-40 was recently validated in cardiac surgical patients and was found to measure meaningful changes in health status after surgery. Lower QoR scores were associated with longer duration of surgery, postoperative complications, and increased hospital LOS.\(^9\) It was also demonstrated that a poor quality of recovery could pre-
dict a poor quality of life 3 months after surgery. In the current study, PCTEA and PCA had comparable effects on both global QoR-40 score and QoR-40 dimensions, suggesting that the more complicated PCTEA technique offers no major advantage in terms of patients’ perception of quality of recovery after cardiac surgery.

In the current study, there was a trend for a reduced incidence of confusion and pneumonia in the PCTEA group, findings that confirm the results of the largest study (420 patients) on the perioperative use of TEA in connection with cardiac surgery. Those investigators found that PCTEA decreased the incidence of lower respiratory tract infections by 50% and that the incidence of postoperative confusion was three to four times higher in the PCA group. The combination of a lower consumption of anesthetics intraoperatively, as shown in the current study, and the avoidance of parenteral opioids might explain the lower incidence of confusion with PCTEA after cardiac surgery. Quicker extubation times3–5 might to some extent explain the lower incidence of postoperative pulmonary complications seen after cardiac surgery.3,6 Furthermore, PCTEA increases the capability to cough by a greater expiratory muscle strength,14 which might improve the ability to clear the airways. However, TEA does not seem to affect the loss of lung volume after cardiac surgery, as demonstrated previously4,5,14 and also in the current study. One could argue, however, that the beneficial effects of TEA on time to extubation, and the incidences of confusion and pneumonia are seen only when combined with short-acting anesthetics, propofol–remifentanil or propofol–alfentanil,3 and that these beneficial effects of perioperative TEA might be less pronounced when combined with another anesthetic technique.

The results from previous studies on the potential beneficial effects of perioperative TEA on the incidence of postoperative atrial fibrillation are conflicting. Scott et al.5 demonstrated that TEA decreased the incidence of atrial fibrillation by 50% in patients undergoing coronary artery bypass surgery, results that could not be confirmed by data from Priestley et al.,5 Jide´us et al.,15 or the current study. This discrepancy could be explained by the fact that β blockers were not used intraoperatively or postoperatively in any patient of the study by Scott et al.,5 whereas the majority of the patients received β blockers in the immediate postoperative period in the study by Jide´us et al.15 as well as in the current study (75–80%). The perioperative use of β blockers was not described in the study by Priestley et al. Therefore, the question whether perioperative TEA offers any advantage over, or has additive effects to, perioperative treatment with β blockers in the prevention of atrial fibrillation after cardiac surgery remains to be elucidated.

In the current study, PCTEA did not offer any benefit over PCA with intravenous morphine in terms of postoperative pain control, a finding that is in contrast to the results of two previous studies in patients undergoing coronary artery bypass surgery.4,5 In those studies, postoperative analgesia consisted of an epidural infusion (3–5 or 5–14 ml/h) of ropivacaine (1 or 0.2%) and fentanyl (5 or 2 μg/ml) for 48 h in the TEA groups and PCA morphine in the control groups. Analgesia was improved in the TEA group at rest and during coughing only within 24 h after surgery in the study by Priestley et al.5 and for 48 h in the study by Royse et al.4 One could therefore speculate that a continuous epidural infusion of a local anesthetic and an opioid seems to provide more efficient analgesia than PCTEA after cardiac surgery.

### Table 3. Postoperative Analgesia and Mobilization

<table>
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<tr>
<th></th>
<th>VAS (Rest)</th>
<th>VAS (Cough)</th>
<th>Mobilization Score</th>
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<tr>
<td></td>
<td>PCTEA</td>
<td>PCA</td>
<td>PCTEA</td>
</tr>
<tr>
<td>Day 1</td>
<td>0.95 ± 1.62</td>
<td>1.10 ± 1.62</td>
<td>3.79 ± 1.74</td>
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<tr>
<td>Day 2</td>
<td>0.88 ± 1.54</td>
<td>1.14 ± 1.51</td>
<td>5.60 ± 2.02</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.69 ± 1.30</td>
<td>0.70 ± 1.17</td>
<td>6.25 ± 1.89</td>
</tr>
<tr>
<td>ANOVA</td>
<td>P = 0.51</td>
<td></td>
<td>P = 0.35</td>
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ANOVA = analysis of variance; PCA = patient-controlled intravenous morphine analgesia; PCTEA = patient-controlled thoracic epidural analgesia; VAS = visual analog scale.

### Table 4. Postoperative Pulmonary Function

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<tr>
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<th>PVC, l</th>
<th>FEV₁, l</th>
<th>PEF, l/min</th>
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<tbody>
<tr>
<td></td>
<td>PCTEA</td>
<td>PCA</td>
<td>PCTEA</td>
</tr>
<tr>
<td>Day 1</td>
<td>1.66 ± 0.62</td>
<td>1.61 ± 0.69</td>
<td>1.33 ± 0.56</td>
</tr>
<tr>
<td>Day 2</td>
<td>1.58 ± 0.54</td>
<td>1.66 ± 0.65</td>
<td>1.25 ± 0.46</td>
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<tr>
<td>Day 3</td>
<td>1.70 ± 0.61</td>
<td>1.79 ± 0.71</td>
<td>1.33 ± 0.52</td>
</tr>
<tr>
<td>ANOVA</td>
<td>P = 0.83</td>
<td></td>
<td>P = 0.86</td>
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ANOVA = analysis of variance; FEV₁ = forced expiratory volume in 1 s; PVC = forced vital capacity; PCA = patient-controlled intravenous morphine analgesia; PCTEA = patient-controlled thoracic epidural analgesia; PEF = peak expiratory flow.
One important limitation of this study was that, despite proper randomization, the two groups were unbalanced with respect to type of surgery. There was a higher incidence of off-pump CABG in the PCTEA group (23 vs. 9%). A vast number of studies have demonstrated that off-pump CABG is associated with shorter hospital LOS and lower mortality and morbidity (e.g., Bucur et al.,16 Zamvar et al.,17 Lee et al.,18 Stamou et al.19). Despite this confounding factor, which would favor a better outcome in the PCTEA group, there were no significant differences in LOS, quality of recovery, or morbidity between the PCTEA and the PCA groups. This could be explained by the fact that only a minority of patients (16%) in the current study underwent off-pump CABG, and therefore, the influence of type of CABG surgery was of less importance with respect to the group outcomes. Furthermore, our post hoc analyses of covariance with type of surgery as the covariate revealed no differences between the study groups with respect to time to hospital discharge, time to eligibility for hospital discharge, or global QoR-40 score.

In general, few previous studies reported data on epidural failure rates. Epidural insertion failure was 5.2% (3 of 58) in the current study. Two previous randomized studies in cardiac surgical patients reported an insertion failure rate of 5.4–6.7%.4,20 Malfunction of already placed epidural catheters was 12.7% (7 of 55) in the current study. In the study by Priestley et al.,5 catheter malfunction was seen in 6.9%. One explanation for the lower malfunction rate in their study could be that they assessed catheter function only before induction of anesthesia, whereas we tested catheter function both after insertion and, more importantly, after surgery in all patients before discharge from the ICU. Furthermore, in 3 of the 7 patients with a malfunctioning catheter, an epidural catheter was successfully inserted before discharge from the ICU. That is, 51 of 55 patients (93%) allocated to treatment with PCTEA did actually receive PCTEA during the time period when main and secondary endpoint variables were collected.

One major concern with the use of TEA for cardiac surgery is the potential for increased risk of epidural hematoma with high-level anticoagulation. In a mathematical analysis, Ho et al.21 suggested that, at the most, one epidural hematoma secondary to catheter placement would occur for every 1,520 patients undergoing CABG. Although no cases of spinal hematomas were reported in the randomized controlled trials of the recent meta-analysis,6 Rosen et al.22 recently described in a case report the occurrence of a hematoma related to TEA on postoperative day 2 after aortic valve replacement complicated by motor and sensory loss necessitating surgical decompression. Given the severity of this complication and the lack of major benefits in terms of morbidity from TEA in cardiac surgery, as demonstrated by us and others, we seriously doubt that the risks are worth the potential benefits. Furthermore, there are other clinical disadvantages with the technique described in the current study, when fully implemented, e.g., logistic and manpower issues (anesthesiologists, nurse anesthetists) for catheter insertion the day before surgery, increased postoperative monitoring, and consequently increased costs.

In the future, adequately powered randomized controlled studies on the perioperative use of TEA on patients undergoing cardiac surgery should be focused on patients with a high risk of development of postoperative pulmonary complications (e.g., patients with severe obesity or chronic obstructive lung disease) or confusion (e.g., elderly patients). Moreover, patients with severe unstable angina, refractory to pharmacologic treatment, are another interesting group in this respect. These patients have significant perioperative morbidity and mortality,23 and ongoing unstable angina is an independent predictor of myocardial damage after CABG.24 It has previously been shown that TEA exerts an anti-ischemic effect in patients with severe unstable angina25–28 and therefore has the potential to provide perioperative cardioprotection in this particular group of high-risk patients.

In conclusion, in this prospective, randomized trial, the effectiveness of TEA combined with general anesthesia followed by PCTEA and the effectiveness of general anesthesia alone followed by PCA morphine were compared with respect to postoperative hospital LOS, patients’ perception of their quality of recovery, and postoperative complications after cardiac surgery. PCTEA did not offer any major advantage with respect to LOS, quality of recovery, and morbidity compared with PCA.

<table>
<thead>
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<th>Table 5. Postoperative Complications</th>
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</tr>
<tr>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Heart failure, %</td>
</tr>
<tr>
<td>Intraaortic balloon pump, %</td>
</tr>
<tr>
<td>Attributed malfunction, %</td>
</tr>
<tr>
<td>Time to extubation, h</td>
</tr>
<tr>
<td>Need for NIPPV, %</td>
</tr>
<tr>
<td>Pneumonia, %</td>
</tr>
<tr>
<td>Mechanical ventilation &gt; 24 h</td>
</tr>
<tr>
<td>Peak serum creatinine, μm</td>
</tr>
<tr>
<td>Creatinine increase &gt; 50%, %</td>
</tr>
<tr>
<td>Stroke, %</td>
</tr>
<tr>
<td>Confusion, %</td>
</tr>
<tr>
<td>Wound infection, %</td>
</tr>
</tbody>
</table>

NIPPV = noninvasive positive-pressure ventilation; PCA = patient-controlled intravenous morphine analgesia; PCTEA = patient-controlled thoracic epidural analgesia.

References


