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# Epidural Anesthesia Improves Outcome and Resource Use in Cardiac Surgery: A Single-Center Study of a 1293-Patient Cohort

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## ABSTRACT

Thoracic epidural anesthesia (TEA) combined with general anesthesia in cardiac surgery has the potential to initiate earlier spontaneous ventilation and extubation, improved hemodynamics, less arrhythmia or myocardial ischemia, and an attenuated neurohormonal response. The aim of the current study was to characterize the correlation between TEA and postoperative resource use or outcome in a consecutive-patient cohort. The study was performed in a tertiary care, 3-surgeon, university-affiliated hospital that performs 350 to 400 cardiac surgeries per year. All 1293 adult patients who underwent cardiac surgery between July 1, 2002, and February 1, 2006, were included. Patients were assigned to anesthesiologists practicing TEA (TEA group, n = 506) or not (control group, n = 787) for cardiac surgery. The preoperative parameter values and Parsonnet scores for the 2 groups were similar. The 2 groups had the same distribution of surgery types. The TEA group presented with fewer intensive care unit (ICU) complications, such as delirium, pneumonia, and acute renal failure, and presented with better myocardial protection. The TEA group presented with a higher proportion of immediately postoperative extubations and with shorter ventilation times and ICU stays. Total ICU costs decreased from US $18,700 to $9900 per patient. Combining TEA and general anesthesia for cardiac surgery allows a significant change in anesthesia strategy. This change improves immediate postoperative outcomes and reduces the use and costs of ICU resources.

## INTRODUCTION

Adequate postoperative analgesia is a priority during perioperative care: it reduces patient discomfort, decreases the postoperative catecholamine surge, and may reduce postoperative pulmonary complications. Thoracic epidural anesthesia (TEA) is a valuable adjunct to general anesthesia for cardiac surgery and might have several advantages in terms of hemodynamic stability, postoperative respiratory function and early extubation, myocardial blood flow, and neuroendocrine response to surgery. The first application of epidural anesthesia in cardiac surgery dates back more than 50 years [Clowes 1954]. In 1976, Hoar et al demonstrated better hemodynamic control with a combination of general and epidural anesthesia [Hoar 1976]. In 1992, Liem and coworkers randomized 54 patients scheduled for coronary artery bypass grafting (CABG) to receive either TEA combined with general anesthesia or general anesthesia alone. In the epidural group, these investigators demonstrated a 60% reduction in the duration of ventilation, better hemodynamic stability, less tachycardia and myocardial ischemia, and a lower neuroendocrine acute-phase response [Liem 1992a, 1992b, 1992c]. Despite a meta-analysis that showed reduced rates of complications [Liu 2004], the routine application of TEA in cardiac anesthesia has been infrequent, mainly because of the inherent risk of anticoagulation-related hematoma [Chaney 2006].

Ultrafast-track cardiac anesthesia aims at avoiding postoperative ventilation [Walji 1999; Oxelbark 2001; Straka 2002; Brucek 2003; Hemmerling 2004; Cheng 2005]. This technique has routinely been applied in our hospital setting since 2001. The aim of this study was to examine outcomes and the use of intensive care unit (ICU) resources for a cohort of consecutive patients who underwent cardiac surgery with or without TEA.

## MATERIALS AND METHODS

### *Settings*

The hospital setting was a university-affiliated 300-bed hospital. The surgical team consisted of 3 surgeons, all of whom have performed surgeries with TEA combined with general anesthesia. Coronary artery revascularization was systematically performed off-pump (>95%) unless contraindicated. Six out of the 13 anesthesiologists had performed TEA for cardiac surgery. For billing reasons, cases were evenly

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distributed to the 13 anesthesiologists under a strict schedule that allowed the members the same number of cases each year.

### *Anesthesia Technique*

The patients in the TEA group were managed according to an ultrafast-track strategy [Djaiani 2001; Oxelbark 2001; Hemmerling 2004; Cheng 2005]. Epidural catheters were placed on the day of the surgery in the postanesthesia care unit (PACU) or in the operating room. After low-dose midazolam (1-2 mg) and/or fentanyl (25-75 μg) premedications were administered intravenously, epidurals were placed via a median approach with the patient sitting at the T2-T3 or T3-T4 level. A 18G Tuohy needle and a 20G, 3-eye, closed-end nylon catheter (Portex continuous epidural tray; Sims Portex, Keene, NH, USA) were inserted 5 cm into the epidural space and secured to the skin with a skin clamp (Lockit epidural catheter clamp; Sims Portex). A 5-mL test dose of 1.5% lidocaine with 1:200,000 epinephrine was given through the epidural catheter. The block was loaded with 6 to 8 mL of 0.125% or 0.25% bupivacaine, and the presence of a block was tested with cold just prior to induction. After arterial-line placement, anesthesia was induced with propofol (1-2 mg/kg), fentanyl (2-4 μg/kg), or sufentanil (0.2-0.5 μg/kg) and rocuronium (0.6 mg/kg). All patients were equipped with a central venous access, and most of them also had a transesophageal echocardiography probe. In the TEA group, anesthesia was maintained at a minimum alveolar concentration (MAC) of 1 to 1.2 with either sevoflurane or desflurane under bispectral index (BIS) monitoring for a target of 40 to 60. Additional opioids and neuromuscular blocking agents were given as required. Thoracic epidural analgesia was maintained by a continuous infusion of 0.1% bupivacaine at a rate of 6 to 14 mL/hour, and additional 3- to 5-mL boluses were administered as indicated. In the TEA group, cumulative intravenous fentanyl doses were between 3 and 7 μg/kg. If at the end of the procedure the temperature was adequate (>35°C), the patient was hemodynamically stable, and a neuromuscular transmission evaluation showed a train-of-four ratio of greater than 0.9 at the adductor pollicis muscle, the patient was extubated in the operating room. Atrial pacing with normal atrioventricular conduction was not a contraindication to immediate extubation. Patients who met these extubation criteria were extubated in the operating room, transferred to the PACU, and then transferred after 3 hours to the ICU or, in the case of off-pump CABG (OPCAB), to the cardiac surgery ward after the PACU [Hemmerling 2006]. Postoperative pain control was achieved with 0.1% bupivacaine at a rate of 6 to 14 mL/hour for up to 3 days. Additional intravenous or subcutaneous doses of morphine were available for leg pain.

In the control group, anesthesia was maintained with intravenous opioids (up to 10-15 μg/kg of fentanyl), benzodiazepines (5-10 mg midazolam), and sevoflurane (1-1.5 MAC). Whenever extubation criteria were met, patients were extubated in the operating room and transferred to the PACU. Intubated patients were transferred directly to the ICU. In the ICU, patients were entered into a strict sedation and analgesia protocol and a respiratory therapist–driven weaning and extubation protocol. Postoperative analgesia was achieved with patient-controlled analgesia (PCA) of 1 mg morphine at a lockout of 6 minutes for up to 3 days.

### *Surgical Technique and Cardiopulmonary Bypass*

Surgery in all cases was carried out by median sternotomy and with open saphenous vein graft harvesting. Left internal mammary arteries where harvested in almost all CABG cases. Bilateral mammary arteries were seldom used, and no radial artery grafts were used. OPCAB was carried out by pericardial suspension with the Cor-Vasc heart stabilizer (ConoNéo, Montréal, Québec, Canada). Nonpulsatile roller pump cardiopulmonary bypass (CPB) was used under mild hypothermia for valve surgeries and on-pump coronary surgeries. Unfractionated heparin (150 U/kg) was given for OPCAB, and 300 U/kg was administered for CPB cases. Heparin (10,000 U) was primed into the CPB unit, and additional doses were given according to the activated coagulation time. Heparin was reversed with protamine on a 1-to-1 basis, and reversal was monitored by monitoring the activated coagulation time. Pericardial and mediastinal drainage tubes were placed in all patients, and chest tubes were placed in the pleural spaces when the chest was opened. All patients received $2 \times 10^6$ U aprotinin (Trasylol; Bayer HealthCare, Toronto, Ontario, Canada) during induction, and CPB patients received an additional $2 \times 10^6$ U in the pump prime and 500,000 U/hour in the bypass.

### *Data Acquisition*

The Perioperative Cardiac Research Group (PeriCARG) has prospectively acquired data from July 1, 2002, for all of the patients who underwent cardiac surgery. The perfusionist and the PACU nurses summarized all anesthesia-related data. Data were entered into the PeriCARG database.

Since this date, the ICU team has used a custom-made computerized research database deployed over a local network. All of the coded diagnoses (International Classification of Diseases, ICD-10), the procedures used (ICD-9-CM), the ICU resources used, the ICU complications (ICD-10), and the microbiological samples taken and their results were entered into the database. Delirium was diagnosed with the Confusion Assessment Method–ICU (CAM-ICU) scale [Ely 2001], and nosocomial infections were diagnosed according to the US Centers for Disease Control and Prevention definitions [Garner 1996]. Acute renal failure was defined as a creatinine level greater than 180 μmol/L or a requirement for extracorporeal renal replacement therapy. Three research assistants or a medical archivist collected the data daily for each patient. Bedside data collected daily included resource use (mechanical ventilation, renal support, catheters, tubes, and so forth), the fluids and blood products administered, nutritional support, microbiological sampling, and antibiotic treatments. The attending senior ICU staff prospectively validated diagnoses and procedures, and the ICU pharmacist validated all antibiotic treatments. The Parsonnet score was computed at ICU admission on the basis of preoperative data [Lawrence 2000]. Because no Holter monitoring was available, only atrial fibrillation requiring antiarrhythmic treatment was taken into account. Owing to the building of the software interface, blood gas and biochemistry laboratory data have automatically been entered into the ICU outcome database only since January 1, 2005, and complete laboratory data were available for 250 patients (84 in the epidural group and 166 in the nonepidural group). Databases were censored on February 1, 2006. PeriCARG and ICU databases were merged on the basis of the hospital record number and the date of surgery [SAS Institute 2003] and transferred to the statistical software. Costs were derived from recently published data for surgical patients [Dasta 2005]. The hourly costs for ICU use and mechanical ventilation were derived from Dasta et al [2005] for the first, second, and subsequent ICU days and were calculated for each patient. Epidural costs were calculated from previously published supply, pharmacy, and hourly PACU costs [Song 2004]. Surveillance costs, nursing costs, and costs of pump use were not taken into account, considering that these costs are similar for PCA and an epidural. Costs in Canadian dollars were converted to US dollars on a one-to-one basis. The ethics committee of the University Hospitals approved the database and waived informed consent from the patients for data acquisition. The Director of Professional Services approved the ICU and cardiac surgery database as a tool of quality of care.

### *Statistics*

Data were analyzed with SAS software [SAS Institute 2003]. Normally distributed continuous variable were analyzed by analysis of variance under the assumption of unequal variances. Because of their nonparametric nature, the data for length of ICU stay, mechanical ventilation time, and costs for the 2 groups were compared with a Wilcoxon-Kruskal-Wallis test, and the results of analyses were expressed as the median (95% interval). To allow comparisons of resource use and costs that included patients with complications who were high consumers of resources, we also expressed values as the mean (95% confidence interval [CI]). The 2-sided 95% CIs of single proportions [Newcombe 1998b] and comparisons of 2 proportions [Newcombe 1998a] were calculated according to the Wilson method. The CI for the diagnostic odds ratio was calculated as described by Armitage and Berry [1994]. The analysis of the use of resources, such as need for mechanical ventilation, use of blood products, or antibiotic administration, was done by intention to treat: patients who did not receive the therapy were taken into account by assigning them a zero value. Patients who remained in the ICU for more than 24 hours were counted separately, because the length of stay in the ICU could interfere with the operating room schedule on the following day, resulting in operating room cancellation on account of a bed shortage in the ICU. We computed a composite outcome including patient death, ventilation duration longer than 24 hours, and an ICU stay of more than 72 hours. A multivariate analysis including type of procedure, blood product administration, and epidural use was carried out by a nominal logistic analysis for nominal $Y$ (death, composite outcome) or by the least-squares method for continuous $Y$ (length of ventilation, length of ICU stay). In the least-squares analysis, the parameters were expressed as the estimate.

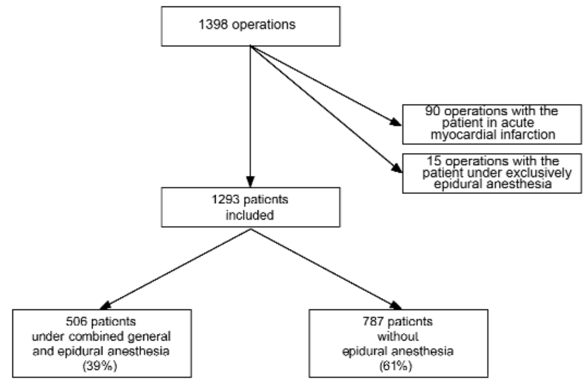


Figure 1. Patients enrolled in the present study. All patients who underwent operations from July 1, 2002, to February 1, 2006, were included in this prospective cohort study.

## RESULTS

A total of 1398 patients had a cardiac surgery procedure during the study period (Figure 1). After we excluded 15 patients who underwent operation exclusively with local-regional anesthesia [Hemmerling 2005] and 90 emergency procedures, 1293 patients remained for the final analysis: 506 patients who received a combination of epidural and general anesthesia (epidural group) and 787 patients who received general anesthesia only (control group) (Table 1). The 2 groups in this cohort were comparable with respect to the measured preoperative variables and Parsonnet scores (Table 2). The 2 groups were the same with respect to the distribution of procedure types, except that there were fewer cases of combined procedures in the epidural group (not statistically significant by chi-square analysis). The combined procedures in the control group consisted of CABG (1 graft, 25 patients; 2 grafts, 14 patients; 3 grafts, 8 patients; >3 grafts, 4 patients) plus valve surgery (aortic, 23 patients; mitral, 24 patients; tricuspid, 3 patients; pulmonary, 1 patient) in 51 patients and double valve surgery in 3 patients. The 3 patients in the epidural group who

Table 1. Types of Procedures*

| | No Epidural, n | Epidural, n | Total, n |
|---|---|---|---|
| CABG | | | |
| Off-pump CABG | 545 (60%) | 357 (40%) | 902 |
| On-pump CABG | 9 (24%)† | 29 (76%)† | 38 |
| Aortic valve surgeries | 134 (59%) | 93 (41%) | 227 |
| Mitral valve surgeries | 45 (65%) | 24 (35%) | 69 |
| Combined surgeries and other | 54 (95%)† | 3 (5%)† | 57 |
| Total | 787 (61%) | 506 (39%) | 1293 |

*Data are present as the number (percent) of patients undergoing each type of procedure done without and with an epidural catheter. CABG indicates coronary artery bypass grafting.

†$P < .05$ for comparison of the 2 groups.

Table 2. Patient Characteristics*

| | No Epidural (n = 787) | Epidural (n = 506) | P |
|---|---|---|---|
| Male-female sex ratio, %/% | 68/32 | 71/29 | NS |
| Age, y | 65.8 (65.0-66.6) | 64.9 (63.9-66.0) | NS |
| Weight, kg | 77.6 (75.3-79.9) | 76.9 (75.5-78.3) | NS |
| LV ejection fraction, % | 58 (56-60) | 58 (57-59) | NS |
| Cardiovascular risk factors, n | | | |
| Active smoker | 118 (15%) | 97 (19%) | <.05 |
| Hypertension | 322 (41%) | 196 (39%) | NS |
| Morbid obesity | 48 (6%) | 33 (7%) | NS |
| Diabetes | 189 (24%) | 142 (28%) | NS |
| Chronic pulmonary disease | 71 (9%) | 72 (14%) | <.001 |
| Parsonnet score | 10 (3-17) | 11 (3-17) | NS |
| Prior myocardial infarction, n | 258 (33%) | 166 (33%) | NS |
| Recent or ongoing intravenous heparin, n | 93 (12%) | 3 (0.6%) | <.001 |
| Emergency surgery | 5% | 5% | NS |
| Length of surgery, min | 126 (122-130) | 124 (121-127) | NS |
| No. of grafts in CABG patients | 3.3 (2.8-3.8) | 2.9 (2.8-3.1) | NS |
| Postoperative temperature, °C | 35.7 (35.6-35.8) | 35.7 (35.6-35.8) | NS |
| Cumulative ischemia time for OP CABG, min | 19 (17-20) | 18 (17-19) | NS |
| CPB time in on-pump cases, min | 58 (52-63) | 59 (56-62) | NS |

*Continuous data are presented as the mean (95% confidence interval), Parsonnet scores are presented as the median (interquartile range), and other data are presented as n (%). NS indicates not statistically significant; LV, left ventricular; CABG, coronary artery bypass grafting; OP, off-pump; CPB, cardiopulmonary bypass.

underwent a combined surgery received a CABG plus mitral plasty, replacement of an aortic valve plus a mitral valve, and mitral valve replacement plus tricuspid annuloplasty. The proportion of CPB cases was the same for the 2 groups (30.7% in the control group versus 29.4% in the epidural group). No epidural hematoma or neurologic epidural-related complications were encountered. No patients had evidence or symptoms of dural puncture. A case of an anterior spinal artery syndrome 24 hours after surgery was probably due to systemic hypotension, use of vasopressors, and generalized arteriosclerosis; the case was resolved without sequelae [Bracco 2007]. Placement of the epidural catheter was successful in all cases. We experienced arterial blood return during catheter placement in 1 patient. In this case, the surgery was postponed 24 hours, and the patient underwent uneventful combined epidural anesthesia on the next morning. The time scheduled for this patient was cancelled, and the next patient planned for the afternoon was done that morning. The afternoon operating time was dedicated to another patient.

The epidural group had significantly lower rates of delirium, pneumonia, and acute renal failure during the ICU stay (Table 3). Because of the low incidence of bloodstream infections and infections involving the central venous catheter, the 2 groups did not differ with respect to the incidence of these complications. Patients in the TEA group had a higher mean arterial bicarbonate level and lower values for parameters of renal dysfunction (Table 4). The proportion of patients with a positive postoperative troponin level in patients with TEA was nearly half that of patients with TEA, with a relative risk of 0.53 (95% CI, 0.28-0.96) and a number needed to treat of 8 (95% CI, 5-76). Mortality was significantly lower in the TEA group, with a number needed to treat of 72.

Although the median lengths of ICU stay for the 2 groups were only slightly different (20.2 hours in the epidural group versus 23.0 hours in the control group; $P < .0001$, Wilcoxon-Kruskal-Wallis test), there was an important difference in the mean length of stay (Table 5). When we analyzed the duration of mechanical ventilation by intention to treat, we found an important decrease in the incidence of mechanical ventilation in the epidural group, because a significant proportion of the patients in this group underwent immediate postoperative extubation. Among the 488 patients who received mechanical ventilation, there was no statistically significant difference between the 2 groups in the duration of mechanical ventilation: a median of 26 hours (interquartile range, 1-63 hours) in the TEA group versus 33 hours (interquartile range, 23-43 hours) in the control group. A multivariate analysis for mortality

Table 3. Postoperative Intensive Care Unit (ICU) Complications*

| Outcome | No Epidural (n = 787), n | Epidural (n = 506), n | P | Relative Risk (95% CI) | No. Needed to Treat (95% CI) |
|---|---|---|---|---|---|
| Acute postoperative delirium | 20 (2.5%) | 4 (0.8%) | <.02 | 0.31 (0.11-0.90) | 57 (31-422) |
| Postoperative atrial fibrillation | 23 (2.9%) | 7 (1.4%) | NS | 0.47 (0.20-1.09) | 65 (32- −502) |
| Catheter infection | 12 (1.5%) | 3 (0.6%) | NS | 0.39 (0.11-1.37) | 107 (47- −265) |
| Positive blood culture | 11 (1.4%) | 1 (0.2%) | NS | 0.14 (0.02-1.09) | 83 (43- −1012) |
| Microbiologically proven pneumonia | 30 (3.8%) | 8 (1.6%) | <.03 | 0.41 (0.19-0.90) | 45 (25-288) |
| Acute renal failure | 15 (2%) | 1 (0.2%) | <.02 | 0.10 (0.01-0.78) | 59 (34-189) |
| ICU mortality | 14 (1.8%) | 2 (0.4%) | <.04 | 0.22 (0.05-0.97) | 72 (38-800) |

*CI indicates confidence interval; NS, not statistically significant.

Table 4. Laboratory Values*

| Outcome | No Epidural (n = 86) | Epidural (n = 171) | *P* |
|---|---|---|---|
| Arterial blood gases | | | |
| Lowest ICU pH | 7.31 (7.30-7.32) | 7.30 (7.28-7.31) | NS |
| Lowest $PaO_2$, mm Hg | 95.1 (89.9-100.3) | 89.5 (84.2-94.8) | NS |
| Highest $PaCO_2$, mm Hg | 47.5 (46.1-48.9) | 45.7 (44.5-46.8) | NS |
| Lowest arterial $HCO_3$, mmol/L | 19.6 (19.0-20.1) | 21.0 (20.4-21.6) | .002 |
| Renal function markers | | | |
| Peak postoperative creatinine, µmol/L | 120 (109-132) | 91 (80-102) | <.001 |
| Peak creatinine increase, % | 26% (18%-34%) | 11% (2%-21%) | <.01 |
| Peak postoperative urea, mmol/L | 9.9 (8.7-11.1) | 7.4 (6.5-8.4) | <.01 |
| Peak urea increase, % | 27% (20%-33%) | 15% (10%-19%) | <.02 |
| Myocardial damage markers | | | |
| Peak postoperative CK, U/L | 549 (447-651) | 469 (372-567) | NS |
| Peak postoperative troponin T, mg/L | 0.81 (0.45-1.16) | 0.20 (0.14-0.28) | <.02 |
| Positive (>0.06 U/L) troponin, n | 42 (25%) | 11 (13%) | <.05 |
| Hemodilution markers | | | |
| Lowest postoperative hemoglobin, g/L | 88 (84-91) | 92 (88-96) | NS |
| Lowest postoperative platelets, $\times 10^9$/L | 146 (135-157) | 170 (156-184) | <.01 |

*Laboratory values were measured in the intensive care unit (ICU). Data are expressed as the mean (95% confidence interval). NS indicates not statistically significant; CK, creatine kinase.

including type of surgery, Parsonnet score, emergency operation, and the use of TEA was not statistically significant (*P* = .084 for type of surgery; *P* = .079 for TEA, because of the low overall mortality incidence [1.2%]). The results for the same model applied to a composite outcome including death, ICU stay >3 days, and ventilation time >24 hours showed a significant effect for type of operation, Parsonnet score, and use of an epidural. In this model, patients in the TEA group had an odds ratio of 0.471 (95% CI, 0.287-0.666; *P* < .001) for the composite outcome, compared with the control group. In a multivariate least-squares model including type of surgery and use of an epidural for predicting length of ICU stay and ventilation time, the epidural group had a statistically significant reduction in the ventilation time by 9.6 ± 2.4 hours (mean ± SD) and a significant reduction in the length of stay in the ICU by 12.7 ± 3.6 hours. These reductions correspond to decreases in ICU and mechanical ventilation costs of US $2700 and US $700, respectively, per patient that are attributable to the use of TEA.

The cost of an epidural includes the costs for the kit (US $18), the dressing (US $1.50), the bupivacaine medication (US $15.24), and 30 minutes of PACU use (US $58.50). The total cost was US $93.24. By comparison, 100 mg of morphine for a PCA pump costs US $11. The physician's fees are the same in Québec (US $71.96) for either an epidural or PCA. Therefore, the additional cost of an epidural (US $82) compared with postoperative PCA is mainly due to PACU use.

We performed a subgroup analysis of the 902 consecutive elective OPCAB patients (Table 6). Patients in the TEA group had a higher median Parsonnet score (10; interquartile range, 3-17) compared with the control group (7; interquartile range, 3-15) (*P* = .01). There were no differences regarding the number of grafts and the duration of ischemia and surgery. Fewer than 10% of the patients with TEA required postoperative mechanical ventilation. Patients in TEA group required less arterial blood gas analysis and received fewer blood products than those in the control group. Mortality could not be evaluated by multivariate analysis in this subgroup because of the low incidence of this event (n = 6). Markers of myocardial protection showed similar maximums in the 2 groups. The median peak creatine kinase concentration was 304 IU/mL (interquartile range, 216-506 IU/mL) in the TEA group, versus 337 IU/mL (interquartile range, 251-481 IU/mL) in the control group (not statistically significant). The peak creatine kinase myocardial muscle isoenzyme (CK-MB) fraction was 6% (interquartile range, 3%-8%) in the TEA group, versus 6% (interquartile range, 4%-10%) in the control group (not statistically significant). The median peak postoperative troponin T concentration was significantly lower in the TEA group (0.05 mg/L; interquartile range, 0-0.15 mg/L) than in the control group (0.10 mg/L; interquartile range, 0.03-0.34 mg/L; *P* = .02). The results of an analysis with a model including Parsonnet score and TEA applied to the composite outcome including death, an ICU stay >3 days, and a ventilation time >24 hours showed a significant effect for type of operation, Parsonnet score, and use of TEA. In this model, patients in the TEA group had an odds ratio of 0.368 (95% CI, 0.135-0.616; *P* < .003) compared with the control group for the composite "bad" outcome. TEA combined with general anesthesia leads to a 40% decrease in ICU costs, a 76% decrease in the cost of mechanical ventilation, and a 25% decrease in ICU costs not related to mechanical ventilation.

Table 5. Use of Intensive Care Unit (ICU) Resources*

| | No Epidural (n = 787) | Epidural (n = 506) | *P* | Odds Ratio or Difference | No. Needed to Treat |
|---|---|---|---|---|---|
| Length of ICU stay, h | 61.4 (52.6-70.3) | 35.5 (24.2-46.6) | <.001 | −25.9 (−42%) | |
| Patients in ICU >24 h, n | 320 (41%) | 132 (26%) | <.001 | 0.51 (0.40-0.66) | 7 (5-11) |
| Ventilation requirement, n | 455 (58%) | 33 (6.5%) | <.001 | 0.11 (0.08-0.16) | 1.95 (1.81-2.13) |
| Ventilation time by ITT, h | 25.3 (19.4-31.2) | 5.9 (0-13.3) | <.001 | −19.4 (−77%) | |
| Requirement for pulmonary artery catheter, n | 173 (22%) | 61 (12%) | <.001 | 0.55 (0.42-0.72) | 10 (7-17) |
| Requirement for catecholamines on ICU admission, n | 74 (9.4%) | 28 (5.5%) | <.05 | 0.59 (0.39-0.90) | 26 (15-113) |
| Arterial blood gas measurement in ICU, n/patient | 7.2 (6.0-8.4) | 4.2 (3.6-4.8) | <.001 | −3.0 (−42%) | |
| Complete blood counts, n/patient | 5.5 (4.5-6.5) | 3.9 (3.3-4.6) | <.05 | −1.6 (−29%) | |
| Transfused red blood cells, n | 177 (22%) | 76 (15%) | .001 | 0.67 (0.52-0.85) | 13 (9-32) |
| Transfusion by ITT, units/patient | 0.82 (0.64-0.99) | 0.30 (0.22-0.38) | <.001 | −0.52 (−63%) | |
| Transfused frozen plasma, n | 96 (12%) | 29 (5.7%) | <.002 | −0.47 (−0.31 to −0.70) | 15 (11-30) |
| Transfused platelets, n | 32 (4.1%) | 8 (1.5%) | <.05 | −0.39 (−0.18 to −0.84) | 40 (23-174) |
| Any allogenic blood product, n | 197 (25%) | 83 (16%) | .002 | −0.66 (−0.52 to −0.83) | 12 (8-24) |
| Allogenic blood products by ITT, mL/patient | 521 (422-621) | 186 (61-310) | <.001 | −335 (−63%) | |
| Therapeutic antibiotics, n | 111 (14.1%) | 44 (8.4%) | <.02 | 0.62 (0.44-0.86) | 18 (11-55) |
| Antibiotics, defined daily doses/patient | 5.0 (3.8-6.1) | 3.3 (2.5-4.1) | <.05 | −1.7 (−34%) | |
| Cost of ICU stay, US $/patient | $18,700 ($16,100-$20,300) | $9900 ($6600-$13,600) | <.001 | −$8900 (−47%) | |
| Cost of mechanical ventilation, US $/patient | $7100 ($5700-$7600) | $1700 ($0-$3900) | <.001 | −$5400 (−76%) | |
| Composite outcome (death, ICU stay >72 h, or ventilation time >24 h), n | 152 (19%) | 41 (8%) | <.001 | 0.37 (0.26-0.53) | 9 (7-13) |

*Data are expressed as n (%) for nominal data and as the mean (95% confidence interval [CI]) for continuous data. The odds ratio and the number needed to treat are expressed as the value (95% CI). ITT indicates intention to treat.

## DISCUSSION

### *TEA in Cardiac Surgery*

High-thoracic epidural analgesia in cardiac anesthesia offers benefits, such as earlier spontaneous ventilation and extubation, better hemodynamic stability [Liem 1992a], a lower incidence of tachycardia [Liem 1992c] or myocardial ischemia [Liem 1992c], and an attenuated postoperative neurohormonal response [Liem 1992a]. Recent data have shown improved myocardial blood flow [Hutcheson 2005] and a shorter length of stay [Petrovski 2006] in patients who underwent operations under anesthesia combined with

Table 6. Resource Use for Patients Undergoing Elective Off-Pump Coronary Artery Bypass Grafting (n = 902)*

| | Control Group (n = 545) | Epidural Group (n = 357) | *P* | Odds Ratio or Difference† | No. Needed to Treat |
|---|---|---|---|---|---|
| Length of ICU stay, h | 47.3 (37.2-57.4) | 30.0 (21.4-38.4) | <.02 | −17.3 (−37%) | |
| ICU stay >24 h | 36% (32%-40%) | 21% (17%-26%) | <.0001 | 0.59 (0.47-0.74) | 7 (5-12) |
| Immediate extubation | 44% (40%-48%) | 94% (91%-96%) | <.0001 | 2.16 (1.95-2.38) | 1.9 (1.7-2.1) |
| Ventilation time, h | 14.9 (10-19.8) | 3.6 (0-9.6) | <.005 | −11.3 (−76%) | |
| Laboratory panels, n/patient | 6.23 (4.88-7.58) | 4.63 (2.90-6.36) | NS | −1.60 (−26%) | |
| ABG in the ICU, n/patient | 2.29 (2.01-2.56) | 1.74 (1.36-2.11) | <.01 | −0.55 (−24%) | |
| Patients transfused | 20% (17%-24%) | 18% (14%-22%) | NS | 0.87 (0.62-1.23) | 48 (−31 to 14) |
| Blood volume transfused, mL/patient | 345 (240-451) | 196 (86-305) | <.05 | −149 (−43%) | |
| Total ICU costs, US $/patient | $14,100 ($11,300-$16,900) | $8400 ($5800-$11,300) | <.0001 | −$5700 (−40%) | |
| Mechanical ventilation costs, US $/patient | $4360 ($2930-$5800) | $1050 ($0-$2810) | <.0001 | −$3310 (−76%) | |
| Composite outcome | 13% (11%-16%) | 7% (5%-10%) | .003 | 0.53 (0.34-0.82) | 16 (10-47) |

*ICU indicates intensive care unit; ABG, arterial blood gases.

†The difference is expressed as the odds ratio (95% confidence interval) for nominal outcome variables or as the absolute and relative difference for continuous outcome variables.

TEA. Liem et al [1992c] randomized patients scheduled for CABG to a conventional strategy and to a combination strategy including TEA and were able to decrease the postoperative ventilation time from 19 hours in the control group to 7.7 hours in the TEA group.

In the present cohort, patients who underwent operation with TEA could be extubated significantly earlier than patients who did not receive TEA, and most of the TEA patients were able to be extubated in the operating room. In addition, the inclusion of TEA significantly reduced postoperative morbidity, with improved pulmonary, infectious, cardiac, and renal outcomes.

### *Risks of TEA*

High-thoracic epidural analgesia is not a risk-free technique [Giebler 1997; Horlocker 2003; Moen 2004]. Despite more than 50 years of experience [Clowes 1954], there is a fear of perimedullary hematoma or neurologic complications following epidural catheter placement in patients who will receive anticoagulation therapy. With an experienced operator performing the placement of the epidural catheter according to strict guidelines [Horlocker 2003; Vandermeulen 2005], the risks can be minimized. The anesthesiologist and the surgeons have to accept the possibility of postponing the surgery if a “bloody tap” occurs. With approximately 12,000 published cases in 2006 using the Wilson method [Newcombe 1998b] the upper limit of the 95% CI is 1:2119. Moen et al [2004] found a similar incidence in the nonobstetric population in a 127-center, 10-year survey of 450,000 epidurals.

There is some controversy on the optimal timing of placing the epidural catheter before cardiac surgery. Some centers insert TEA on the day before surgery. Placement of the epidural catheter on the day before surgery seems to offer more safety in terms of hematoma risk and avoiding the problem of a last-minute surgery cancellation in the event of a bloody tap. There is agreement to allow at least 1 to 2 hours between placing the epidural catheter and systemic heparin administration [Horlocker 2003; Djaiani 2005]. For mechanical valve surgery, it is routine in our hospital setting to remove the epidural catheter on the evening of postoperative day 1 or 2 as the patient gets the first oral dose of anticoagulant. During the study period, only starches of medium molecular weight and a low substitution ratio were used in cardiac surgery patients (260 kd; substitution ratio, 0.4).

### *Costs and Savings of TEA*

TEA is associated with the use of additional resources, mainly material resources and the use of the PACU to place the epidural catheter. The additional costs of US $80 compares favorably with the $8900 reduction in the costs of using ICU resources in the complete group or the $5700 reduction in ICU costs in the OPCAB group. Our cost analysis must be read with the limitations in mind, because the costs were not available at our institution and because they do not include the costs of surveillance nursing, costs of investments such as the pump and teaching, and the costs of any complications.

### *Differences in Outcomes between the 2 Groups*

The differences between the 2 groups of patients were impressive in terms of outcomes and the use of resources. Even with results from several thousand patients in studies of obstetric cohorts, no difference in maternal or perinatal outcomes could be attributed specifically to the use of epidural analgesia during labor [Anim-Somuah 2005]. TEA has a direct mechanistic effect and has indirect effects that allow modifications in the anesthesia and perioperative strategy (Figure 2). The use of TEA facilitates immediate postoperative extubation and a significant reduction in the perioperative use of opioids. Better postoperative pain control might allow better postoperative pulmonary function with less (mechanical ventilation-associated) pneumonia. The lower incidence of delirium could be attributed to the decrease in the use of psychotropic agents such as benzodiazepines and lower doses of opioids. Lower postoperative troponin levels might also be attributed to the use of TEA, which might increase coronary blood flow [Hutcheson 2005] and myocardial oxygen availability [Lagunilla 2006]. Troponin results have to be analyzed with caution, because they may be due to ischemic myocardial damage or to myocardial handling. The difference may represent better protection against an ischemic myocardium or better protection against nonischemic myocardial injury.

A contribution of a bundle effect is likely (Figure 2). With the objective of combining general and epidural anesthesia and rapid extubation, we used a more restrictive fluid-administration strategy that led to less hemodilution, fewer transfusions, and less hyperchloremic acidosis. The lower incidence of postoperative renal dysfunction could be attributed to less mechanical ventilation-related reductions in renal blood flow [Kuiper 2005] or in the distribution of intrarenal blood flow [Hall 1974].

### *Hemodynamic Effects of Epidurals*

Epidural agents have been classically linked with hypotension because of sympathetic blockade; however, the extent and territories involved in sympathetic blockade depend on the placement of the epidural catheter. Lumbar and lower-thoracic epidural placement seems to be related with more venous pooling and hypotension than high-thoracic epidural placement [Taniguchi 1997; Waurick 2005]. These observations may explain the similar degrees of vasopressor usage in the epidural and control groups.

### *Resource Use*

Resources in health care are scarce, and strategies that aim at optimizing their use are welcome. The use of TEA decreases the proportion of patients remaining in the ICU longer than 24 hours. Because all patients share the same ICU resources, we were unable to assess the effect of anesthesia type on the number of operating room cancellations. Local-regional anesthesia and immediately postoperative extubation allow a reduction in the use of resources; however, to use these techniques to their maximum effect requires optimizing the organization of the perioperative management of these patients [Cheng 1995; Cheng 2005].

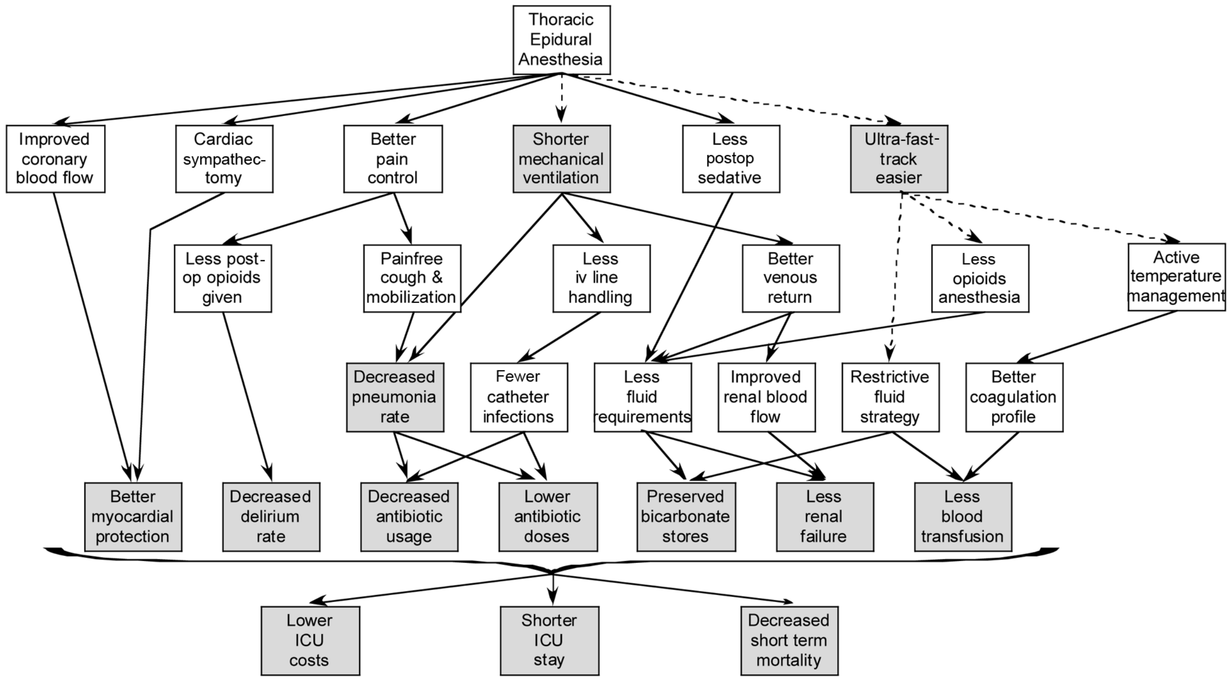


Figure 2. Proposed mechanistic and associated effects of thoracic epidural anesthesia (TEA) in cardiac surgery. TEA has a direct mechanistic effect (solid lines) and an indirect associated effect by allowing changes in the anesthesia strategy (dashed lines). Parameters with a significant difference between the 2 groups are shown as a gray box. Parameters in a white box either were not measured or did not reach statistical significance. Postop indicates postoperative; iv, intravenous; ICU, intensive care unit.

### *Study Limitations*

When we evaluated rare events, such as catheter infection or positive results in blood cultures, we found the number of positive events in each group to be low. Such low incidences yield very low statistical power, very large CIs for relative risk and numbers needed to treat, and an inability to reach a .05 level of statistical significance. This situation was apparent for myocardial protection in the OPCAB group. There was a slightly statistically significant difference in peak postoperative troponin T level that did not translate to a lower incidence of postoperative myocardial infarction. For infrequent events, a larger cohort would be required to achieve statistical significance; however, such larger cohorts may lose the homogeneity characterized by our single-center, 3-year consecutive audit. We also found differences in bicarbonate and platelet levels, which reflected a more restrictive fluid-resuscitation strategy in the TEA group, but these differences probably had no clinical impact. To control for any confounding factors, we explored covariate analysis by surgeon, by surgery itself, and by anesthesiologist. The analysis by anesthesiologist yielded different immediate-extubation rates, which confirmed the different practices of the individual anesthesiologists and were unrelated to patient conditions.

Observational prospective cohort studies are not randomized control trials; they have built-in limitations [Grimes 2002]. There was no randomization between patients using and not using TEA [Rochon 2005]. In the present cohort, this deficiency was corrected in part by the anesthesiologist assigned to the case: 6 of the 13 staff members performed epidural anesthesia for cardiac surgery, and the other 7 staff did not perform this technique. This situation may be described as a form of partial randomization. Despite this lack of randomization, however, there were no differences in preoperative and intraoperative characteristics that favored either of the 2 groups. Patients in the TEA group were more frequently smokers, more often had chronic obstructive pulmonary disease, and had a higher median Parsonnet score than patients in the control group. There seems to have been more combined surgeries in the control group, but we have to point out that these patients received a limited number of CABG grafts plus a single valve. There were no cases of adult congenital defects or more complex procedures, which may add additional risk.

A cleaner study design would have to randomize patients into an epidural group with local anesthesia and an epidural group with saline infusion. Although such a strategy would seem to be a better scientific design, it would be unethical to expose patients to an epidural without an anesthetic in it. This design would also add perioperative and postoperative management problems. What does the anesthesiologist do when the surgeon has the sternal saw in hand and the clinician is not aware whether the epidural is active or a placebo? Further simple, blind randomized trials involving anesthesiologists familiar with ultrafast-track anesthesia are required to better control for confounding factors and the specific effects of epidural anesthesia.

### *Confounding Factors*

Cohort studies usually require multivariate analysis to correct for potential confounding factors [Mamdani 2005]. To be a confounding factor, the risk factor has to be statistically different across the various groups [Normand 2005; Rochon 2005]. In the present cohort, we explored several potential confounding factors but were unable to detect relevant preoperative factors that were different between the groups. Hidden confounding factors are possible, however. There was a greater proportion of patients in the control group who received intravenous heparin before surgery. Hidden confounding factors may have an effect on rare events such as death or catheter infections, but such factors did not change the proportion of cases with postoperative mechanical ventilation from 58% to 6.5%. Therefore, we can assume that the differences in postoperative mechanical ventilation, postoperative morbidity, ICU length of stay, and costs are not related to confounding hidden preoperative factors.

## CONCLUSIONS

Out study indicates that combining TEA with general anesthesia for cardiac surgery might allow a significant change in anesthesia strategy that would include immediate postoperative extubation. This strategy is associated with improved outcomes in the immediate postoperative period and lower use of resources in the ICU, which thereby reduce ICU costs.

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