Thoracic epidural analgesia improves pulmonary function in patients undergoing cardiac surgery

L'analgésie péridurale thoracique améliore la fonction pulmonaire chez les patients subissant une chirurgie cardiaque

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Purpose: Pulmonary dysfunction commonly occurs following coronary artery bypass graft (CABG) surgery, increasing morbidity and mortality. We hypothesized that thoracic epidural anesthesia (TEA) would improve pulmonary function and would decrease complications in patients undergoing CABG surgery.

Methods: This prospective, randomized, controlled trial was conducted with Ethics Board approval. Fifty patients, undergoing CABG surgery, were randomized to the epidural group or to the patient-controlled analgesia morphine group. Patients in the epidural group received a high, thoracic epidural, preoperatively. Intraoperatively, 0.75% ropivacaine was infused, followed postoperatively, by 0.2% ropivacaine for 48 hr. Outcome measurements included: visual analogue pain scores; spirometry; atelectasis scores on chest radiographs; and the incidence of atrial fibrillation.

Results: Twenty-five patients were enrolled in each group. Patients in the epidural group had significantly less pain on the operative day, and for the subsequent two days. Compared to baseline, the forced expiratory volume in one second was significantly higher in the epidural group, on the first and second postoperative days (43.7 ± 12.2% *vs* 36.4 ± 12.0%, $P < 0.002$, and 43.3 ± 12.5% *vs* 38.4 ± 11.0%, $P < 0.05$). There was significantly more atelectasis in the control group, four hours postoperatively ($P < 0.04$); however, on the third, postoperative day, the groups were similar with regards to this outcome. The incidence of atrial fibrillation was similar in both groups, and there were no complications related to the epidural.

Conclusions: High TEA decreases postoperative pain and atelectasis and improves pulmonary function in patients undergoing CABG surgery. Our results support the use of TEA in this group of patients.

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Objectif *: Des troubles pulmonaires surviennent fréquemment à la suite d'une chirurgie de pontage aortocoronarien (PAC), ce qui augmente la morbidité et la mortalité. Nous avons émis l'hypothèse que l'anesthésie péridurale thoracique (APT) améliorerait la fonction pulmonaire et réduirait les complications chez les patients subissant une chirurgie de PAC.*

Méthode *: Après avoir obtenu l'accord du Comité d'éthique, nous avons mené cette étude prospective, randomisée et contrôlée. Cinquante patients subissant une chirurgie PAC ont été randomisés dans deux groupes, péridurale ou analgésie contrôlée par le patient avec de la morphine. Les patients du groupe péridurale ont reçu une péridurale thoracique haute avant l'opération. Pendant l'opération, ils ont reçu une perfusion de ropivacaïne 0,75 %, puis de la ropivacaïne 0,2 % pendant 48 h après l'opération. Les résultats mesurés étaient les scores de douleur sur l'échelle visuelle analogue, la spirométrie, les scores d'atélectasie sur les radiographies pulmonaires et l'incidence de fibrillation auriculaire.*

Résultats *: Chaque groupe comprenait 25 patients. La douleur chez les patients du groupe péridurale était considérablement moins élevée le jour de l'opération et les deux jours suivants. Par rapport aux données de base, le volume expiratoire maximal en une seconde était significativement plus élevé dans le groupe péridurale le premier et le deuxième jour postopératoire (43,7 ± 12,2 % vs 36,4 ± 12,0 %, $P < 0,002$, et 43,3 ± 12,5 % vs 38,4 ± 11,0 %, $P < 0,05$). L'atélectasie a été significativement plus élevée dans le groupe témoin quatre heures après l'opération ($P < 0,04$) ; toutefois, le troisième jour postopératoire, les groupes ont montré*

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des résultats d'atélectasie similaires. L'incidence de fibrillation auriculaire était semblable dans les deux groupes, et il n'y a pas eu de complication associée à la péridurale.

***Conclusion**: L'analgésie péridurale thoracique haute réduit la douleur postopératoire et l'atélectasie et améliore la fonction pulmonaire chez les patients subissant un PAC. Nos résultats appuient l'utilisation de l'APT chez ce groupe de patients.*

REGIONAL anesthesia techniques, in cardiac anesthesia, are increasing in popularity.[1] Many benefits have been attributed to the use of thoracic epidural analgesia (TEA), including: suppression of the stress response; decreased myocardial ischemia; improved analgesia; and decreased myocardial injury.[2] The effects on pulmonary function have also been studied; however, conflicting results have been reported.[3–7] Scott *et al.*[3] reported superior pre-extubation vital capacity in coronary artery bypass graft (CABG) surgery patients with thoracic epidurals. Conversely, Sternest *et al.*[4] infused 0.5% bupivacaine postoperatively, and did not find a difference in postoperative spirometry in CABG surgery patients. Priestley *et al.*[5] administered ropivacaine 1% with fentanyl, postoperatively, and documented no difference in postoperative spirometry. One of the reasons for this lack of benefit may be explained by Tenling's[7] study, published in 2000, which showed that preoperative administration of epidural bupivacaine 0.5% caused a 15% decrease in vital capacity and a reduction in the rib cage contribution to tidal volume. Presumably, this was caused by motor blockade of intercostal muscles. Thoracic epidural analgesia has also been shown to decrease the incidence of atrial fibrillation in patients undergoing thoracic surgical procedures.[8] However, conflicting results have been obtained in CABG patients.[3,9] Therefore, we undertook a randomized controlled trial, to assess the effects of TEA on postoperative lung function and atrial fibrillation, in patients undergoing CABG surgery. We compared the effects of TEA, on patients using epidural ropivacaine 0.2%, to those with patient-controlled analgesia (PCA) with morphine.

Methods

The Ethics Review Board of the University of Manitoba Health Sciences Centre approved this study, and all participants gave written informed consent. Patients scheduled for elective or semi-elective CABG surgery, between July 1, 2003 and June 30, 2004, were invited to participate in this study, at the time of their preoperative anesthesia assessment. Patients less than 80 yr of age, who were deemed appropriate for our facilitated recovery program, were included. Exclusion criteria included: previous cardiac surgery; combined procedures; serum creatinine greater than 150 $mmol \cdot L^{-1}$; pre-existing coagulopathy, or use of antiplatelet agents other than ASA; active liver disease; severe spinal deformity; ejection fraction less than 30%; and a body mass index > 35 $kg \cdot m^{-2}$. Randomization occurred immediately after enrolment. Patients were assigned a sealed envelope that contained the group assignment. There were equal numbers of epidural and PCA envelopes at the start of the trial. We decided that insertion of sham epidural would be unethical; consequently, this was not a blinded study, and group allocation was not concealed from the patients. It was also deemed impossible to conceal group allocation from the attending anesthesiologist, nursing staff, and respiratory therapists, as it is not possible to conceal an epidural catheter.

All patients had baseline laboratory assessments including; a complete blood count, coagulation profile, serum chemistry, arterial blood gas, an electrocardiogram (ECG), a chest radiograph, and spirometry. Patients were instructed in the use of a visual analogue scale (VAS) for pain quantification, and the control patients were informed about PCA.

Patients, randomized to the epidural group, were scheduled to have their surgery in the afternoon, to allow a safety window for epidural catheterization on the morning of surgery. The epidural catheters were placed at least four hours prior to systemic heparinization. The technique was performed using an 18G Tuohy needle and a single orifice, epidural catheter. The epidural catheters were placed between the second and fifth thoracic vertebrae, using the paramedian approach. A 2.5-mL test dose of 2% lidocaine, with 1:200,000 epinephrine, was used to rule out intrathecal and intravenous placement.

Patients were maintained on their usual medications up to the day of surgery, and these were resumed on the first postoperative day. Premedication, with 0.1 $mg \cdot kg^{-1}$ of diazepam *po*, was given 90 min preoperatively, to all patients. Patients in both groups received a standardized general anesthetic consisting of sufentanil 0.5 $\mu g \cdot kg^{-1}$ *iv*, sodium thiopental 3–5 $mg \cdot kg^{-1}$ *iv*, or propofol 1–2 $mg \cdot kg^{-1}$ *iv*, followed by rocuronium 1.0 $mg \cdot kg^{-1}$ *iv*. General anesthesia was maintained in both groups with isoflurane (0.5–1.5% end-tidal), before, during, and after cardiopulmonary bypass. Monitors consisted of: 5 lead ECG; pulse oximetry; invasive arterial lines; central venous pressure monitors; transesophageal echocardiography; and bispectral index monitors.

Mean arterial blood pressure (MAP) was maintained between 55–80 mmHg. Intravenous fluid, ephedrine, phenylephrine, nitroglycerin, and esmolol were administered, as appropriate to maintain the target MAP.

Management of cardiopulmonary bypass was similar in both groups. All patients received 300 $U \cdot kg^{-1}$ of unfractionated heparin, and an activated clotting time (ACT) > 400 sec was required, prior to initiating cardiopulmonary bypass. Flow was maintained at 2.4 $L \cdot min^{-1} \cdot m^{-2}$, and the MAP was maintained between 55 and 80 mmHg. Temperature was maintained between 34 and 36°C during cardiopulmonary bypass. Cold blood cardioplegia was administered for myocardial protection. Protamine was administered, after separation from cardiopulmonary bypass, to normalize the ACT.

Patients in the epidural group received a 3-mL test dose of 2% lidocaine, prior to induction of general anesthesia. Next, they received a 5-mL bolus of 0.75% ropivacaine and 200 μg of hydromorphone in the epidural catheter, followed by an infusion of 0.75% ropivacaine at 5 $mL \cdot hr^{-1}$, for the duration of surgery. Postoperatively, patients in the TEA group received a continuous epidural infusion lasting 48 hr and consisting of 0.2% ropivacaine, with 15 $\mu g \cdot mL^{-1}$ of hydromorphone titrated to maintain a sensory block between T1 and T7. After sternal closure, patients in the control group received morphine 0.1 $mg \cdot kg^{-1}$ *iv* and were maintained with PCA morphine, using 1.0 mg *iv* boluses with a five-minute lockout for 48 hr. Patients in both groups also received indomethacin suppositories (100 mg), postoperatively, and twice daily naproxen (500 mg), according to our usual practice, so long as no contraindications existed.

Postoperatively, the patients' tracheas were extubated, when subjects were hemodynamically stable, awake, able to follow commands, with an oxygen saturation ≥ 97%, with a $F_1O_2 \leq 60\%$, and an end-tidal $CO_2 \leq 50$.

Assessment tools included the following: four hours postoperatively, and then twice daily for the next three days, VAS pain scores were collected, while at rest and with deep breathing and coughing, using a vertical, 10 cm scale. Chest radiographs were performed, four hours postoperatively and then again on the third postoperative day. These were interpreted by a thoracic radiologist, using a previously validated atelectasis scoring system as follows; 0 = no changes, 1 = plate-like atelectasis, 2 = segmental atelectasis, 3 = partial lobar collapse, and 4 = complete lobar collapse.[10] The radiologist was unaware of group assignment. Spirometry was assessed daily, by a registered respiratory therapist, for the first three postoperative days. All patients were attached to Holter monitors for the first three postoperative days, to assess for atrial fibrillation. The presence of clinically significant atrial fibrillation was defined as a need for pharmacologic treatment.

TABLE I Patient characteristics

	Control (n = 25)	*Epidural (n = 25)*
Age (yr)	60.8 ± 9.4	60.1 ± 6.3
BMI $kg \cdot m^{-2}$	27.2 ± 3.6	27.8 ± 3.0
Smoking (pack years)	15.7 ± 17.8	16.8 ± 18.6
Diabetes (*n*)	5 (20.0%)	9 (36.0 %)
Ejection fraction (%)	59.1 ± 8.9	52.9 ± 7.5
Hypertension (*n*)	12 (24%)	17 (34%)
B-adrenergic blockers (*n*)	22 (88%)	21 (84%)
FEV_1 ($L \cdot min^{-1}$)	3.3 ± 0.7	3.2 ± 0.7

BMI = body mass index; FEV_1 = forced expiratory volume in one second.

An improvement in forced expiratory volume in one second (FEV_1) was the primary endpoint. Previous work at our institution predicts a postoperative FEV_1 of 1.3 L, with a standard deviation of 0.3, following CABG surgery.[11] These numbers were used in our sample size estimation that determined 22 patients in each group would be required for a power of 80%, to detect a between-group difference of 20% in postoperative FEV_1. Statistical analysis, using SAS version 8.2 (SAS Institute Inc, Cary, NC, USA), was conducted in consultation with our biostatistical unit, in accordance with the intention to treat principle. Statistical tests included two sample *t* tests for parametric data, and two sample Wilcoxon and Chi-square tests, for nonparametric data. Repeated measures ANOVA, followed by least squares means, were used for multiple comparisons. Data are presented as mean ± standard deviation. A P value < 0.05 was considered significant.

Results

After screening 200 potentially eligible candidates, 100 were deemed eligible. Fifty patients were enrolled in the study with 25 patients in each group. Due to incomplete data collection, two patients were excluded from each group. Importantly, our data has been analyzed according to the intention-to-treat principle. We were unable to insert an epidural in one patient, and the epidural was not use, postoperatively in another patient, because of quadraparesis on emergence (see below for the details of this subject). Preoperatively, both groups were similar (Table I), except for higher mean ejection fractions in the control group (59.1 ± 8.9% *vs* 52.9 ± 7.5%, $P < 0.01$). Intraoperative variables were also similar (Table II), except for phenylephrine requirements, which were lower in the control group (2.1 ± 1.8 mg *vs* 4.3 ± 2.8 mg, $P < 0.001$).

TABLE II Intraoperative variables

	Control (n = 25)	*Epidural (n = 25)*	*P value*
CPB duration (min)	64.8 ± 36.9	72.8 ± 24.5	0.30
CPB (*n*)	22	24	0.52
Grafts (*n*)	3.0 ± 1.1	3.0 ± 1.1	0.64
Lowest temperature (°C)	34.7 ± 0.8	34.6 ± 1.0	0.68
Temperature in PACU (°C)	35.8 ± 0.5	35.7 ± 0.6	0.20
Phenylephrine (mg)	2.1 ± 1.8	4.3 ± 2.8	< 0.001
Ephedrine (mg)	11.6 ± 13.4	16.2 ± 21.3	0.71
Time to tracheal extubation (min)	10.3 ± 12.6	15.3 ± 37.6	0.26

CPB = cardiopulmonary bypass; PACU = postanesthesia care unit.

TABLE III Visual analogue scale pain scores

	Deep breathing		*Rest*	
	Epidural	*PCA*	*Epidural*	*PCA*
4 hr	1.7 ± 1.8*	5.3 ± 2.2	1.1 ± 1.2*	3.6 ± 2.3
POD 1 a.m.	1.6 ± 1.4*	5.6 ± 2.2	0.8 ± 1.2*	2.8 ± 1.6
POD 1 p.m.	2.2 ± 1.7*	4.2 ± 2.2	0.9 ± 1.4*	2.3 ± 1.6
POD 2 a.m.	1.8 ± 2.1*	3.8 ± 2.4	0.5 ± 0.9*	1.7 ± 1.4
POD 2 p.m.	1.4 ± 1.8*	2.6 ± 1.9	0.3 ± 0.6	0.8 ± 0.8
POD 3 a.m.	1.5 ± 1.9	1.6 ± 1.5	0.7 ± 1.5	0.9 ± 1.1
POD 3 p.m.	1.0 ± 1.7	1.9 ± 1.6	0.7 ± 1.4	0.8 ± 1.1

*Statistically significant; PCA = patient controlled analgesia; POD = postoperative day.

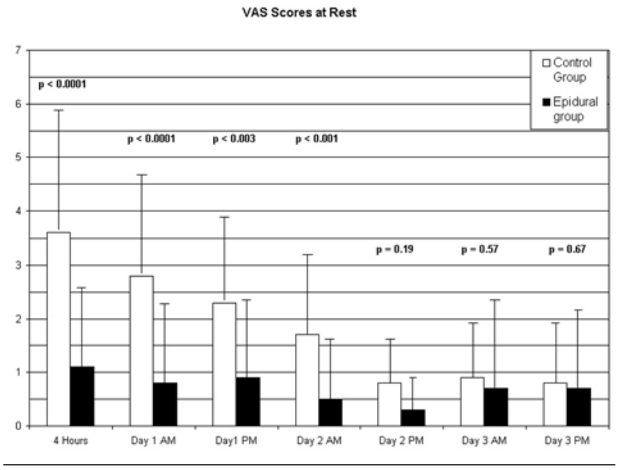

FIGURE 1 Visual analogue scale (VAS) pain scores, at rest. There was significantly better pain control, at rest in the epidural group, until the evening of postoperative day two.

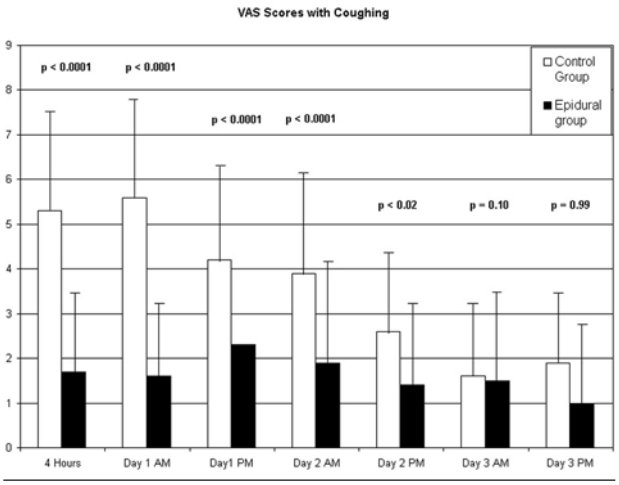

FIGURE 2 Visual analogue scale (VAS) pain scores, with coughing. There was significantly better pain control, with coughing in the epidural group, until the morning of postoperative day three.

Visual analogue pain scores, at rest and with deep breathing and coughing, are shown in Figures 1 and 2. At rest, the VAS scores were lower ($P < 0.05$) in the epidural group compared with the PCA group, until the evening assessment on the second postoperative day and were lower, up to the third day, with deep breathing and coughing. There was no difference between groups with respect to postoperative utilization of non-steroidal anti-inflammatory medications.

Figure 3 shows the effects of epidural analgesia on postoperative FEV_1, presented as the percent of baseline values. Thoracic epidural analgesia effectively moderated the decrease in FEV_1 values on the first and second postoperative days (43.7 ± 12.2% *vs* 36.4 ± 12.0%, $P < 0.002$ and 43.3 ± 12.5% *vs* 38.4 ± 11.0%, $P < 0.05$). By the third postoperative day, mean FEV_1 values were similar in the two groups (46.3 ± 12.4% *vs* 46.7 ± 10.5%, $P = 0.77$).

Atelectasis scores are presented in Figure 4. In comparison to the PCA group (atelectasis score = 4), atelectasis occurred less frequently in the TEA group (atelectasis score = 3), four hours postoperatively ($P < 0.05$). However, atelectasis scores were similar in the two groups by the third postoperative day (atelectasis scores = 3).

Postoperatively, new-onset atrial fibrillation was observed in six patients in the TEA group (24%) *vs* 9 (36%) in the PCA group ($P = 0.29$). One patient in the epidural group developed ventricular fibrillation, 6 hours postoperatively, in association with an "R on T" phenomenon. He was defibrillated successfully, experienced no further evidence of ventricular ectopy, and was discharged from hospital five days postoperatively. One patient in the epidural group awoke from anesthesia quadraparetic. As per study protocol, an emergent neurology consultation and a computed tomography scan were obtained. The quadraparesis

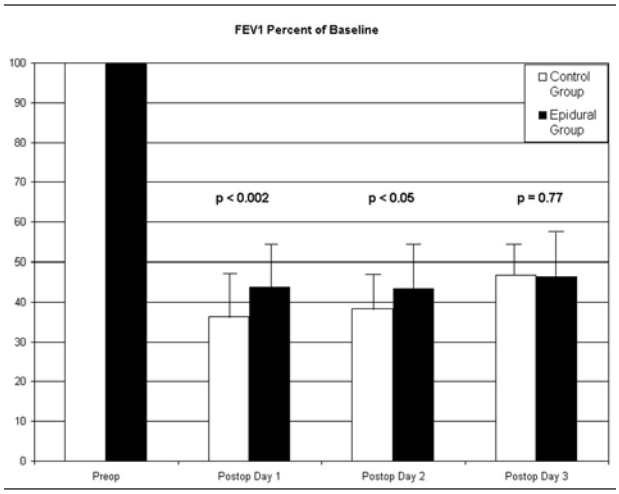

FIGURE 3 Forced, expiratory volume in one second (FEV_1). The data are presented as a percent of the patients' preoperative FEV_1. There was a significant decline in FEV_1, in both groups, postoperatively. The decline in FEV_1 was less in the epidural group, on postoperative days one and two. Both groups were similar by postoperative day three.

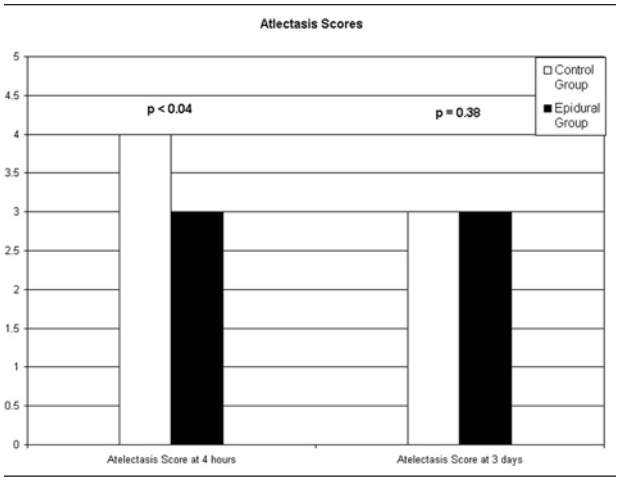

FIGURE 4 Atelectasis scores. There was less atelectasis in the epidural group, at four hours postoperatively. There was no difference between groups by postoperative day three.

resolved within one hour, and there were no neurological sequalae. The cause of the transient quadraparesis was spinal stenosis.

Discussion

This randomized controlled trial demonstrates that TEA provides superior analgesia, improved pulmonary function, and decreased atelectasis in patients undergoing CABG surgery. Previous investigations have also demonstrated superior analgesia with TEA,[2,10] and this was an anticipated result. However, there have been conflicting reports regarding the effects of TEA on postoperative pulmonary function and atelectasis.[3–6] A recent meta-analysis by Liu *et al.*[12] with a combined total of 1,178 patients, found that TEA decreased the incidence of pulmonary complications.

In the present study, TEA was associated with a significant improvement in pulmonary function during the first two postoperative days, using FEV_1 as a surrogate for pulmonary function. Although the increase in FEV_1 was modest, it does represent a statistically significant improvement. The clinical significance of this finding is probably quite minimal in the majority of patients undergoing CABG surgery. However, in patients with borderline lung function at baseline, any improvement in FEV_1 would be important, as this may be the important determinant for the requirement of ongoing postoperative ventilation. This is a common clinical situation, as more and more patients with severe pulmonary dysfunction, are now presenting for surgery.

Pulmonary dysfunction is common following cardiac surgery, and there are many proposed mechanisms, including: diaphragmatic dysfunction; uncoordinated rib cage movements, secondary to the sternotomy and pain, which restricts tidal volume, leading to atelectasis and potentially, lower respiratory tract infections.[13,14] Scott *et al.*[3] have shown that TEA can significantly decrease the incidence of lower respiratory tract infection, and they attribute this effect to the superior analgesia and increased lung volumes associated with TEA. Therefore, measuring lung volume may be appropriate as a predictor of pulmonary complications.

Atelectasis was observed more frequently in patients without epidurals, four hours after surgery. However, the groups were similar with respect to this outcome, by the third postoperative day. These results differ from those of Priestley *et al.*[5] who were unable to show a difference, on chest radiographs, between the groups of patients with and without epidurals. It is plausible that the atelectasis scores were initially lower in the epidural group, because these patients had significantly less pain, and were, therefore, more compliant with deep breathing and coughing exercises. By the third postoperative day, patients in the control group had similar VAS pain scores compared to patients in the epidural group, and this was evident in the similarity of atelectasis scores, at that time.

We did not demonstrate a difference in mean times to tracheal extubation, which contrasts with results from other investigations.[4,5,7,14] However, patients with epidurals in these studies, were extubated three to five hours postoperatively, while tracheal extubation took place within minutes of the conclusion of the operation in our study, the majority of the time

while patients were in the operating room. The details of our ultra-fast track program have been described elsewhere.[15]

The incidence of new-onset atrial fibrillation was similar in the two groups. However, this study was powered to detect a difference in spirometry data, and not to identify the incidence of atrial fibrillation. A secondary power analysis determined that 180 patients would be required to determine a significant between-groups difference with respect to the frequency of postoperative atrial fibrillation. Many believe that TEA will decrease the incidence of atrial fibrillation following cardiac surgery secondary to sympathetic blockade. In fact, Scott *et al.*[3] were able to demonstrate a dramatic reduction in this rate with TEA. However, these investigators included clonidine in the epidural solution, which may have systemic effects. A further difference between that study and the current investigation, is the use of β-adrenergic blocking drugs. We continued this group of medications throughout the perioperative period, whereas Scott *et al.* did not. A recent publication that examined 4,657 patients worldwide, found an overall incidence of postoperative atrial fibrillation in CABG patients to be 32.3%, similar to our control group.[16] The potential influence of TEA on the incidence of atrial fibrillation following CABG, warrants further investigation.

Epidural hematoma, resulting in permanent neurologic damage, is the most feared complication when using epidural analgesia in fully heparinized patients for cardiac surgery. The risk of this catastrophic event is still unknown, but has been estimated to be 1:1500.[17] We chose to insert the epidural catheter, at least four hours preoperatively, as a precautionary measure, despite the fact that many anesthesiologists insert epidurals immediately preoperatively.[3,18] This issue was addressed in recent guidelines from the American Society of Regional Anesthesia and Pain Medicine[19] which recommends at least a one-hour interval between catheter placement and heparinization. However, the same guidelines point out a paucity of data supporting this practice. There has been one report in the literature describing a case of epidural hematoma two days following aortic valve replacement surgery.[20] However, the management of this case was somewhat unusual and does not comply with standard practice, mainly because this patient was anticoagulated while the epidural catheter remained *in situ*, and the catheter was then removed, while the patient was fully anticoagulated. Removal of the epidural catheter is as likely to result in hematoma formation, as is placement of the catheter.[21]

In conclusion, TEA improves postoperative pulmonary function in patients undergoing CABG surgery. Although the benefits in the current study were modest, there may be outcome benefits in patients at high risk for pulmonary complications following cardiac surgery, including the morbidly obese, and those with severe, pre-existing, pulmonary dysfunction. Therefore, further investigations are warranted in this patient population, to further assess this promising technique.

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