

# Epidurals for Cardiac Surgery

## Can We Substantially Reduce Surgical Morbidity or Should We Focus on Quality of Recovery?

**I**N this issue of ANESTHESIOLOGY, there are three articles that show no benefit,<sup>1</sup> some benefit,<sup>2</sup> or considerable benefit<sup>3</sup> to the use of high thoracic epidural analgesia (HTEA) in cardiac surgery. The fundamental difference relates to the outcomes being measured and perhaps an unrealistic expectation of the potential effect size from an anesthetic intervention on surgical outcomes (morbidity or mortality).

As a specialist discipline, we were tantalized by Yeager *et al.* in 1987<sup>4</sup> at the prospect of reducing mortality and morbidity by perioperative epidural analgesia. To detect mortality advantage in a trial of 53 patients was truly astounding. In 1991, Baron *et al.* published a larger randomized trial in a similar patient cohort and found no difference in morbidity outcomes.<sup>5</sup> Twenty years later, we continue to try and show that regional anesthesia and analgesia can substantially alter surgical outcomes without success. Is it realistic for an anesthetic intervention to have a large effect on surgical morbidity or mortality, particularly in major operations where there are so many potential interplays of surgical technique, patient comorbidities, or postoperative care paradigms? Although Svircevic *et al.*<sup>1</sup> have conducted the largest randomized trial of HTEA in cardiac surgery to date (654 patients), it was entirely predictable that they did not find a positive benefit of HTEA. Although their combined morbidity outcome was correctly estimated at approximately 15%, they powered this study to find a 50% reduction in combined incidence of myocardial infarction, pulmonary complications, renal failure, and stroke. A 50% reduction in perioperative complications by using an epidural would not only be “clinically relevant,” it would actually be fantastic and astounding.

The meta-analysis by the same group<sup>2</sup> examined 2,731 patients and found trends toward mortality and myocardial infarction production of approximately 20% (risk ratio 0.80) and significant reductions for respiratory complications or supraventricular arrhythmias. In noncardiac surgery, the MASTER trial<sup>6</sup> randomized almost 1,000 high-risk patients and was unable to detect a difference in mortality and cardiovascular complications. The estimated effect size was a 20% reduction, although the actual effect size was only 6%. In pharmacologic interventions (such as perioperative  $\beta$ -blockers), the effect size is on the order of 15%, and the recent POISE study showed increased mortality with that

particular paradigm of  $\beta$ -blocker use,<sup>7</sup> but randomized more than 8,000 patients to detect this. Similarly, the ISIS-2 study randomized more than 8,000 patients in each group to show a 11.8% mortality reduction with aspirin after myocardial infarction.<sup>8</sup> Wijeysondera *et al.*<sup>9</sup> used propensity-score methods to construct a matched-pairs cohort to compare perioperative epidural use in major noncardiac surgery in 88,188 patients and found a small but significant mortality advantage to perioperative epidural use (risk ratio 0.89, 95% CI 0.81–0.98,  $P = 0.02$ ). A realistic effect size for reduction in postoperative morbidity or mortality therefore lies somewhere between 10% and 20%. For a 15% baseline composite morbidity, and assuming a 15% reduction with an anesthetic intervention, 4,200 patients in each group would be required to demonstrate that no effect exists. The study by Svircevic *et al.*<sup>1</sup> can be added to the series of studies that failed to demonstrate that an anesthetic intervention can make a very large difference in surgical outcomes, but remain substantially underpowered to show that no effect occurs.

Perhaps it is time to move away from trying to prove that anesthetic interventions will reduce morbidity or mortality and to focus on tangible benefits to patients or their families. Epidurals are used primarily to provide excellent analgesia, and any other benefits are a bonus. Postoperative quality of recovery is a new horizon in anesthetic research with outcomes primarily focused on patient well-being, rather than on doctor, hospital, or funding agency outcomes. Aspects of quality of recovery can include physiologic and safety parameters, pain and nausea, emotional well-being, return to activities of daily living, satisfaction, and cognitive recovery. The third article by Caputo *et al.*<sup>3</sup> focuses on aspects of quality of recovery rather than morbidity outcomes. They demonstrated a reduction in hospital length of stay and improvements in multiple domains of recovery (mobility, sedation, pain, upper and lower limb motor function, and nausea). Interestingly, although patients were more likely to require vasoconstrictor infusions with

◆ This Editorial View accompanies the following three articles: Svircevic V, Nierich AP, Moons KG, Diephuis JC, Ennema JJ, Brandon Bravo Bruinsma GJ, Kalkman CJ, van Dijk D: Thoracic epidural anesthesia for cardiac surgery: A randomized trial. ANESTHESIOLOGY 2011; 114:262–70; Svircevic V, van Dijk D, Nierich AP, Passier MP, Kalkman CJ, van der Heijden GJ, Bax L: Meta-analysis of thoracic epidural anesthesia versus general anesthesia for cardiac surgery. ANESTHESIOLOGY 2011; 114:271–82; Caputo M, Alwair H, Rogers C, Pike K, Cohen A, Monk C, Tomkins S, Ryder I, Moscarillo C, Lucchetti V, Angelini, GD: Thoracic epidural anesthesia improves early outcomes in patients undergoing off-pump coronary artery bypass surgery: A prospective randomized controlled trial. ANESTHESIOLOGY 2011; 114:380–90.

Accepted for publication September 27, 2010. The author is not supported by, nor maintains any financial interest in, any commercial activity that may be associated with the topic of this article.

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an epidural, this did not lead to increased length of stay nor affect the quality of recovery indicators, and so should not be viewed as a negative outcome.

What of risk? For more than 20 yr, the use of HTEA has been shrouded in controversy because of the potential for epidural hematoma and the concern that this will increase in frequency associated with systemic anticoagulation. Although epidural hematoma has been reported, the frequency has not increased compared with noncardiac surgery use, with the latest published risk estimate of 1:12,000.<sup>10</sup> Paraplegia is a disaster, but disasters are common in cardiac surgery. In the three studies reported in this issue, the risk of death and stroke (both disasters) was on the order of 1:100. Perhaps we need to consider a “risk-risk” assessment when considering analgesic techniques. If a patient bleeds to death from a gastric ulcer after nonsteroidal antiinflammatory ingestion or suffers hypoxic brain damage after an opiate-induced respiratory arrest, is that any less a disaster than paraplegia? In the context of cardiac surgery, the risk of disaster from HTEA represents a very small component of the risk of disaster to the individual patient. It is sufficiently uncommon that many centers will never have that complication, a few will have one case of paraplegia, and almost none will have two or more disasters. Furthermore, there is no evidence that the use of HTEA in cardiac or noncardiac surgery actually increases the risk to the patient. There are no meta-analyses or randomized trials that have reported paraplegia occurring. In the study by Wijeyesundera *et al.*,<sup>9</sup> the number needed to treat to save one life was 477 patients, and the incidence of laminectomy was approximately 1:5,000 (the same as the nonepidural cohort). Although the small effect size on mortality is insufficient to recommend epidurals to save lives, it does increase our confidence that epidurals do not increase risk. The main take-home message from that study is that for every patient harmed by an epidural, nine lives may be saved.

Are all cardiac operations equal? Most studies have focused on coronary artery graft surgery with or without cardiopulmonary artery bypass, and not on valve surgery, or even the uncommon but interesting “awake cardiac surgery” performed under HTEA alone.<sup>11</sup> Supplemental analgesia may be required for saphenous vein *versus* radial artery harvest, especially when highly lipophilic epidural opiates are used in conjunction with local anesthetic (*e.g.*, fentanyl *vs.* morphine). There is no evidence, however, of increased risk of HTEA-related complications with valve surgery *versus* coronary artery bypass graft surgery. The bias toward investigating coronary artery bypass graft surgery may reflect the greater patient and operative homogeneity compared with valve and other complex cardiac surgeries.

So how do these studies influence our clinical decision on whether to use HTEA for cardiac surgery? If the sole purpose for HTEA use is to substantially reduce postoperative morbidity and mortality, then there is insufficient evidence to recommend that practice. If the primary purpose, however, is to provide optimal pain relief and perhaps improve overall quality of care outcomes, then do not put down your Tuohy needles just yet.

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