Comparing Cardioprotective Effects of Anesthesia Methods in Patients Undergoing Elective Abdominal Aortic Surgery

To the Editor:
The recent article by Lindholm et al. comparing cardioprotective effects of sevoflurane-based anesthesia and propofol-based total intravenous anesthesia in elective abdominal aortic surgery patients was of great interest. Many things of this study were done correctly. The authors used a prospective, randomized, open, parallel-group design and chose a sensitive and well-validated endpoint of myocardial injury: troponin release. They had a large number of subjects (193) and a consistent operation (elective major vascular surgery). Also, they had tried to control most of the known factors that could affect perioperative myocardial injury, such as age, body mass index, American Society of Anesthesiologists physical status classification, preoperative comorbidities and medications, aorta cross-clamp time, hemodynamic changes during surgery, intraoperative blood loss and transfusion, and many others. All these are strengths in the study design. However, to differentiate the effects of one factor on study endpoints, all the other factors have to be standardized in a randomized, controlled trial. In our views, several issues of this study were not well addressed.

First, we would like to know why perioperative hemoglobin levels were not included in data analysis. Actually, preoperative anemia is common among patients undergoing major vascular surgery, and the presence and severity of preoperative anemia have been shown to be independent predictors of perioperative and long-term cardiac adverse events in vascular surgery patients. In addition, in a retrospective study of vascular surgery patients, Valenti et al. even show that preoperative hemoglobin levels, postoperative hemoglobin levels, and intraoperative hemoglobin decreases are all related to an increased risk of 30-day postoperative cardiovascular adverse events, especially for postoperative hemoglobin levels.

Second, the authors did not provide anesthetic dosage (minimum alveolar concentration [MAC]) of sevoflurane used during the surgery. It has been reported that only when concentrations of sevoflurane are 1 MAC or more, pharmacologically preconditioning by sevoflurane can produce a significant protection against myocardial ischemia–reperfusion injury in the rat heart in vivo. Thus, it was possible that sevoflurane-based anesthesia compared with propofol-based anesthesia did not produce more cardioprotective effects because sevoflurane was given at a low dosage. Furthermore, data on the total dosages of fentanyl and remifentanil used in the two groups are lacking as well. In our opinion, it is difficult to homogenize administration of two opioid drugs between groups, because sevoflurane has intrinsic analgesic property whereas propofol does not. This may constitute a bias on the homogeneity between groups. It has been demonstrated that both fentanyl and remifentanil may exert cardioprotective effects by both preconditioning and reducing the cardiovascular stress, especially for remifentanil. So, their administration in general anesthesia could contribute to cardioprotective effects of two anesthesia methods. This further makes interpretation of their results difficult.

Third, dopamine or noradrenaline was given intravenously at the discretion of the attending anesthesiologist to maintain mean artery pressure, and hemodynamic alterations during surgery were not significantly different between groups. However, the authors did not provide and compare the percent of patients with vasopressor use, the time of vasopressor use, and the total vasopressor dosage administered during the surgery. In patients undergoing open infrarenal abdominal aortic aneurysm repair, vasopressor use during the aorta cross-clamp has been identified as an independent risk factor of postoperative complications including myocardial infarction. We are concerned that their results would have been biased by these confounders.

Finally, only one troponin measurement on the first postoperative day was performed for assessment of myocardial injury. In traditional clinical practices, perioperative cardiac adverse events in noncardiac surgery patients have indeed been emphasized more in the more early postoperative stage. However, Barbagallo et al. showed that in patients undergoing major vascular surgery, serum troponin reached the peak level on the third postoperative day, regardless of whether or not patients developed myocardial infarction. In 100 high-risk patients undergoing major noncardiac surgery, Mangano et al. monitored myocardial ischemia during the postoperative first week and found that myocardial ischemia was most severe during the early (days 0–3) versus late (days 4–7) postoperative period, 284 versus 153 episodes. Furthermore, the greatest severity occurred on the third postoperative day, 109 episodes. Similarly, in high-risk patients undergoing noncardiac surgery, Martinez et al. observed that perioperative cardiac injury detected by serum troponin continued to occur frequently after surgery, and serial monitoring of serum troponin on postoperative days 1, 2, and 3 provided the strategy with the highest diagnostic yield for surveillance of myocardial infarction. Accordingly, we would like to accentuate the importance of prolonging the monitoring period after surgery in noncardiac surgery patients. Also, we believe that if the authors had measured serum troponin in the more late postoperative periods, especially in the first 3 days after surgery, a more persuasive result would have been presented.

Competing Interests
The authors declare no competing interests.
References


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In Reply:

We appreciate the comments by (1) Palomero-Rodríguez, Suárez-Gonzalo, and Laporta-Baez, (2) Zaugg and Lucchinetti, and (3) Xue, Cui, Cheng, and Wang regarding our recent publication in *Anesthesiology* “The Anesthesia in Abdominal Aortic Surgery (ABSENT) Study: A Prospective, Randomized, Controlled Trial Comparing Troponin T Release with Fentanyl-Sevoflurane and Propofol-Remifentanil Anesthesia in Major Vascular Surgery.” We are pleased that our study has led to these comments, which raise several important elements.

In their comment, Dr. Palomero-Rodríguez et al. emphasize that thoracic epidural analgesia (TEA) throughout the surgical process concurrently with general anesthesia is beneficial in terms of improved balance of myocardial oxygen supply or demand and greater hemodynamic stability. In the ABSENT study, TEA (thoracic level, 6 to 10) started after opening of the aortic cross-clamp and continued postoperatively. We found no differences in use of TEA between the two groups. However, we cannot exclude that TEA may have had a beneficial effect so that a potential protective effect of an anesthetic agent may be overshadowed by a TEA component, as Palomero-Rodríguez et al. suggested.

There are conflicting data on the impact of TEA on perioperative mortality and morbidity in noncardiac surgery. Some meta-analyses have demonstrated reduced mortality and morbidity with neuraxial blockade. However, several studies on abdominal aortic surgery have not shown lower incidence of early myocardial ischemia, myocardial infarction, mortality, or postoperative complications using TEA, compared with intravenous morphine.

In a recent post hoc analysis of the Perioperative Ischemic Evaluation Study, patients with high risk of cardiovascular morbidity in fact had a three-fold increased risk of the primary outcome (cardiovascular death, nonfatal myocardial infarction, and nonfatal cardiac arrest) receiving general anesthesia combined with TEA, compared with general anesthesia without TEA. In addition, a recent meta-analysis did not prove any positive influence of TEA on perioperative in-hospital mortality in patients undergoing noncardiac surgery.

Palomero-Rodríguez et al. suggested that the results of the ABSENT study would have been different if TEA had not been included. Two Cochrane analyses concluded that TEA reduces postoperative pain compared with systemic opioids after abdominal aortic surgery and intra-abdominal surgery. On the basis of this knowledge, we found it unethical to design a study, in which patients would have more postoperative pain than if they were not included. This was the main reason for including TEA in the ABSENT study. In addition, we designed the study to reflect current clinical practice, and today, TEA is an important component of the perioperative analgesic regimen.

In the comment by Zaugg and Lucchinetti, several aspects and interpretations of our study are questioned. They disagree with our conclusion that "potential cardioprotective effects of volatile anesthetics found in cardiac surgery are less obvious in major vascular surgery." Their interpretation