some of the methodologic issues raised, we point out that randomized trials minimize bias because, as Fisher noted, the simple act of randomization assures the internal validity of the test for significance.² In other words, randomization allocates subjects on the basis of the play of chance and thus enables us to consider just 2 orthogonal alternative explanations for any treatment effect observed; that is, that the difference in treatment effect is due to chance or is due to the experimental therapies. Dr Catalá-López is presumably aware of the design advantages of the randomized trials through his regulatory work.

Mixed treatment analyses are commonly used by technology assessment groups, such as the National Institute for Clinical Excellence in the United Kingdom, to summarize data on several treatments for a common condition.³ Our work builds on the thoughtful conventional meta-analysis from which our data were drawn and confirms that no adverse treatment effect associated with aprotinin is found even when we take this approach.

Small-study bias is less likely to be an issue when it comes to comparative studies; in any case, however, it is likely to be of smaller magnitude than the bias in nonrandomized studies. Thus Catalá-López seems to be missing the point; however we analyze the data from randomized trials, we cannot find a problem associated with aprotinin use, and the regulatory concern and action surrounding this potentially useful agent thus has not been to the benefit of patients.

Finally, we wonder whether employment by a regulatory body that made an incorrect decision to withdraw the use of aprotinin does constitute a declarable conflict of interest.

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IMPORTANCE OF STANDARDIZATION OF SURGICAL TECHNIQUES IN ANALYZING NEUROLOGIC OUTCOMES

To the Editor:

We read with great interest the article by Chaudhuri and colleagues¹ about carbon dioxide insufflation in open-chamber cardiac surgery. Insufflation of carbon dioxide in the pericardial cavity to prevent the development of cardiac or neurologic damage from air embolism has been mentioned in the literature since 1967.² Manual deairing proved to be highly inefficient in the elimination of air emboli even when it was done with very meticulous technique. Improvement was seen when echocardiography was introduced as a standard clinical method for recording air bubbles in the process of deairing heart cavities, with the deairing procedure performed under visual control.³

With the help of transcranial Doppler ultrasonography, it was found that despite the detailed deairing, one of the biggest sources of air embolism occurs during distribution of blood from the heart–lung machine to the empty, beating heart, when the heart begins to eject actively.⁴ In that respect the article provides the necessary safety guidance on the duration of the deairing procedure with and without carbon dioxide insufflation in pericardial cavity without fear for the development of neurocognitive damage. In addition to age, hypercholesterolemia, aortic burden, and coronary artery disease, however, neurologic outcome after cardiac surgery is also influenced by other factors as a consequence of applied surgical technique.

We do not want to split hairs, but remarks that we discuss here are regularly the subject of fierce debate at our clinic. In addition to aortic burden, surgical manipulation on the aorta has significant impact on development of neurologic sequelae or recovery from the same. Patients who underwent surgical myocardial revascularization as additional procedure with open heart cavities make up a quarter of patients in the study of Chaudhuri and colleagues.¹ The increased number of surgical manipulations on the aorta as a result of the revascularization strategy, single or multiple clamping applied during the formation of the proximal anastomosis, could lead to a higher degree of neurocognitive impairments.⁵ This concern is especially pronounced in light of the multicenter character of study, which did not allow the possibility of selecting the surgical techniques that would be used in the study, because some surgeons probably had rigid personal views about issues of technique. Occurrence of gross neurologic outcomes, such as stroke, transient ischemic attack, or delirium, was not described in the postoperative period, although such could be expected in a study of this size on the basis of previous studies.⁶

In summary, we emphasize the significance of proper surgical technique as an extremely important factor in both neurologic and cognitive outcomes after cardiac surgery. We believe that in future study designs it is paramount to use a single standardized surgical technique or, if multiple techniques are used, to stress the differences among them to collect the objective data necessary for forming proper conclusions and avoiding bias. We congratulate Chaudhuri and colleagues¹ on their useful and elegantly conducted research.

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Reply to the Editor:

We thank Borojevic and colleagues for their interest in our article and for

their letter. They quite rightly point out the importance of surgical technique, in particular standardization of that technique, in any trial that looks at neurologic outcomes after cardiac surgery. We are well aware of the evidence that shows that a single-crossclamp technique is superior to multiple cross-clamping and other manipulations of the aorta in terms both of high-intensity transient signals on transcranial Doppler ultrasonography and of neurologic outcome.¹ This was further demonstrated in a meta-analysis of off-pump coronary artery bypass grafting with and without aortic manipulation.²

We can reassure Borojevic and colleagues that all of our surgeons who took part in the trial used a uniform technique with respect to aortic cross-clamping (all used a single-crossclamp technique), manipulation of the aorta, and mechanical deairing of the cardiac chambers. This was also true across both sites of the trial, because only surgeons who were already involved in the trial at the primary site (The Alfred Hospital) were involved at the secondary site (The Epworth).

We did report gross neurologic outcomes in our study (cerebrovascular accident), which were included in the Appendix Table 2, although we did not collect or report data on delirium. No patient in our study cohort sustained a transient ischemic attack. We thank Borojevic and colleagues for their comments.

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SHOULD IATROGENIC TYPE A AORTIC DISSECTION IN PATIENTS WITH PREVIOUS CARDIAC SURGERY BE MANAGED CONSERVATIVELY? To the Editor:

Should iatrogenic type A aortic dissection (AD) in patients with previous cardiac surgery (CS) be managed conservatively? We read with interest the report by Timek and colleagues¹ presenting the clinical course of a 55-year-old patient with a history of coronary artery bypass grafting and coronary catheter-induced acute type A AD. This hemodynamically stable patient was treated conservatively, and the vascular injury healed uneventfully.

The decision as to whether to operate on AD in a patient with previous CS can be difficult. Recent guidelines are inconclusive, and mandatory surgical treatment has recently been questioned.² Patients with type A AD and a history of CS were found to be twice as likely to be managed medically as those with spontaneous AD, perhaps because of a perceived excessive risk of surgery.³ The argument in favor of conservative management in this case was based on the patient's clinical stability, morbid obesity, previous sternotomy, and mechanism of dissection.¹ In fact, however, rupture and instability are rare because of postcardiotomy scarring and protective adhesions.⁴ Contrary to expectation, body mass index, diabetes, sex, type of primary surgery, and acuity of dissection, among others, were not identified as significant determinants of operative outcome in a series of patients with AD after previous CS.⁴

Although the term "iatrogenic AD" is frequently used regardless of the mechanism of aortic injury, we believe that catheter-induced aortic injury must be clearly distinguished from other etiologies. As Timek and colleagues¹