CARDIOPROTECTIVE EFFECT OF PROPOFOL CANNOT BE EXTRAPOLATED FROM THE PLACEBO- CONTROLLED,

RANDOMIZED CONTROLLED TRIAL

To the Editor:

We eagerly read the article by Rogers and colleagues.¹ This is an important clinical study for anesthetic processes during cardiac surgery. However, we would like to emphasize and discuss some conflicting points.

First of all, propofol was suggested as cardioprotective. However there was no statistically significant difference between groups for myocardial troponin T concentration levels during the postoperative period. Without powerful statistical support it is difficult to recommend adding propofol to cardioplegia. We previously published a study² comparing the in vivo effects of isoflurane, sevoflurane, and propofol anesthesia on ischemia and reperfusion-mediated free radical injury and oxidative stress during coronary artery bypass grafting surgery and comparing the effects of these anesthetic agents on levels of the end products of lipid peroxidation and nitric oxide in human right atrial tissue and blood. In our study² we suggested that inhaled anesthetics such as isoflurane and sevoflurane better preserve cardiac function after cardiopulmonary bypass (CPB) from myocardial damage than propofol. Furthermore, propofol induced lower blood levels of lipid peroxidation than isoflurane and sevoflurane. Propofol also increased glutathione peroxidase activity but induced less nitric oxide production compared with sevoflurane. These findings support the cardioprotective properties demonstrated by patients' hemodynamic parameters.

Second, therapeutic hypothermia is a different strategy to decrease myocardial injury secondary to ischemia during cardiac surgery with CPB.² In the study by Rogers and colleagues¹ there is no information about hypothermia and the body temperature of the patient during the surgical procedure. This is also an important issue for cardioprotection.

Third, during the pre-CPB period all patients' anesthesia maintenance was supported with the volatile anesthetic agent isoflurane, which itself has cardioprotective effects. Isoflurane may have added to the cardioprotective effect observed with propofol. To observe the pure cardioprotective effect of propofol there should have been a group solely treated with propofol.

Another multicenter, randomized controlled study³ did not demonstrate any difference between sevoflurane anesthesia and propofol total intravenous anesthesia on the composite end point of prolonged intensive care unit stay, mortality, or both in patients undergoing cardiac surgery.

Finally, using a lipid solution for placebo may not be proper because the cardioprotective effects of lipid solutions have not been shown in humans. Existing studies in the literature about this are limited to animal models.

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PROPHYLACTIC AMIODARONE: USE IT OR NOT?

To the Editor:

Ad and colleagues¹ reported that prophylactic amiodarone can reduce atrial fibrillation (AF) recurrence.

The primary outcome occurred in 52% of the nonamiodarone group (23 of 44) and 19% of the amiodarone group (8 of 43; $P = .001$). Prophylactic use of amiodarone after surgical AF ablation has been debated for a long time, mostly because of its life-threatening adverse effects. As intensivists, we do want to know whether prophylactic amiodarone use is associated with better long-term outcomes for our patients.

The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors should: • Include no more than 500 words of text, three authors, and five references. • Type with double-spacing. • See <http://jtcvs.ctsnetjournals.org/misc/fora.shtml> for detailed submission instructions. • Submit the letter electronically via jtcvs.editorialmanager.com. Letters commenting on an article published in the JTCVS will be considered if they are received within 6 weeks of the time the article was published. Authors of the article being commented on will be given an opportunity of offer a timely response (2 weeks) to the letter. Authors of letters will be notified that the letter has been received. Unpublished letters cannot be returned.

TABLE 1. Early atrial fibrillation recurrence between crossovers and noncrossovers

Groups	Crossovers	Noncrossovers	Total
Amiodarone group	18	27	45
Early AF recurrence	1	7	8
Nonamiodarone group	18	27	45
Early AF recurrence	18	5	23

AF, Atrial fibrillation.

In this study, however, there were 18 (40%) crossovers in each group, with a similar mean time to crossover (13 vs 11 days), which indicates that in the nonamiodarone group, 18 of 23 cases of AF recurrence may occur within 30 days after surgery (Table 1). Studies have raised the caution that early AF recurrence after ablation is a risk factor for long-term AF recurrence.^{2,3} It is common, however, for arrhythmias to recur early after surgical ablation; most of these are transient and can be resolved within 1 month.⁴ Thus it is perhaps more meaningful to separate the AF recurrences within 30 days from the other recurrences. In addition, amiodarone is a routine treatment choice for AF recurrence. So the clinicians may be more interested in comparing the long-term outcomes of prophylactic amiodarone and therapeutic amiodarone uses.

With respect to the long-term outcome, Ad and colleagues¹ have also pooled an analysis that removed any rhythm status not verified by long-term monitoring (6 weeks, 12 weeks) and found out that AF recurred more often in the nonamiodarone group than in the amiodarone group (22 of 40 vs 8 of 37). We believe, however, that this conclusion about the long term should be interpreted with caution. First, 18 patients in the nonamiodarone group crossed over to the amiodarone group at an early time, but the final analysis was made on the basis of the initial randomization, which increased the bias. Second, in this study, long-term monitoring was executed at 6 weeks and 12 weeks, but 6 weeks is really not a long time, so an analysis of the outcomes at 12 weeks may be more meaningful.

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PROPHYLACTIC AMIODARONE REDUCED THE RECURRENCE OF ATRIAL ARRHYTHMIAS

Reply to the Editor:

We appreciate the comments of Yanfei Shen, MD, on our study, in which we sought to clarify the need for prophylactic antiarrhythmic medication in the first few months after surgical ablation of atrial fibrillation. We conducted a prospective, randomized controlled trial to determine whether amiodarone treatment after surgical ablation is effective in reducing the risk of early recurrence of atrial arrhythmia (ie, within <3 months). We found that prophylactic amiodarone did reduce early recurrence of atrial arrhythmia.

We agree with Dr Shen about the importance of knowing whether the prophylactic use of amiodarone is associated with better long-term outcomes. However, we certainly would not classify the outcome in this study as “long term,” as all recurrences were defined as those arising within the first 12 weeks after surgery. In addition, long-term outcome was not the focus of our investigation. Rather, we used long-term *rhythm monitoring* techniques, in which patients wore monitors that recorded for 48 to 72 hours, and this monitoring occurred at 6 and 12 weeks after surgery, which does not qualify as a long-term outcome.

Our analysis, which includes only long-term *rhythm monitoring*, was intended to show that even when this more reliable method of rhythm verification was used, the results did not differ from those of the full analyses of the primary outcome. We are therefore uncertain as to why Dr Shen cautions the reader about this finding, which is simply a subset of our primary outcome analysis but with more-rigorous monitoring.

Crossovers from no-amiodarone to amiodarone treatment represent not bias, but rather incidence of the primary outcome. As stated in our Methods section, “crossover from the no-amiodarone to the amiodarone group due to atrial arrhythmia at any time in the first 3 months after surgery” is part of the definition for the primary outcome. In addition, we state in the Methods section that any “recurrence of atrial arrhythmia at 6- or 12-week follow-up monitoring or at any point during the first 3 months after surgery” was included in the primary outcome definition. Therefore, if patients experienced recurrence of atrial arrhythmia at 12 weeks after surgery, this event would