Intravenous Lidocaine and Postoperative Cognition: Comment

To the Editor:

We read with great interest the article by Klinger *et al.*[1] regarding the effect of intravenous lidocaine on neurologic outcomes after cardiac surgery. We appreciate and congratulate the authors for setting up a clearly structured randomized trial with a large sample size and sharing such useful findings. There are, however, two important points of concern.

First, patients with hypertension are believed to be more susceptible to cerebral hypoperfusion resulting from inappropriate blood pressure and impaired autoregulation of cerebral blood flow while underdoing cardiac surgeries, and cerebral hypoperfusion has been considered an important risk factor contributing to postoperative cognitive dysfunction.[2] In this trial, participants with hypertension made up a sizeable proportion (59% in lidocaine group *vs.* 61.2% in placebo group; $P = 0.268$) of the overall population, the authors used the common practice of maintaining mean arterial pressure from 50 to 80 mmHg through cardiopulmonary bypass, but it was not mentioned whether there were differences in the mean arterial pressures, the durations of intraoperative hypotension, the durations of cerebral desaturation, or any other data that could suggest cerebral perfusion between the two groups.

Second, some variables that might influence the occurrence of postoperative cognitive dysfunction were not mentioned in the study. Such confounding variables include the occurrences of stroke, cardiovascular or cerebrovascular events after cardiac surgery,[3] anesthesia duration, dosage of anesthetic agents, depth of anesthesia,[4] and rewarming rate.[5]

Competing Interests

The authors declare no competing interests.

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Intravenous Lidocaine and Postoperative Cognition: Reply

In Reply:

We thank Drs. Cao and Zhu for their correspondence regarding our study on the effect of intravenous lidocaine on postoperative cognitive dysfunction after cardiac surgery.[1]

Postoperative cognitive dysfunction has a complex pathophysiologic basis without a clear singular etiology in current understanding. As Drs. Cao and Zhu point out, intraoperative hypotension has been associated with an increased risk of postoperative delirium and cognitive dysfunction, although the evidence is conflicting. Chronic hypertension, along with other comorbidities, has long been thought to produce a rightward shift in the cerebral autoregulation curve, suggesting a higher

risk of cerebral hypoperfusion in these patients. However, some studies have failed to find a difference in mean arterial pressure (MAP) at the lower limit of cerebral autoregulation in patients with these comorbidities and have generally found predicting the MAP to target during cardiopulmonary bypass (CPB) difficult based on clinical history and preoperative blood pressure.[2] While it is generally believed that intraoperative MAP goals should be individualized to the patient's physiology, how to monitor and target cerebral perfusion remains difficult without specialized equipment for real-time cerebral autoregulation monitoring. Near-infrared spectroscopy-based methods may provide an acceptable alternative for monitoring cerebral autoregulation during cardiac surgery, yet studies demonstrating the ability of this and similar monitoring techniques to improve neurocognitive outcomes after cardiac surgery remain limited by small cohort size, short duration of follow-up, and mixed results.[2,3] Furthermore, cardiac surgical patients are at risk of hemodynamic instability beyond the intraoperative period; thus, cerebral hypoperfusion may occur outside of the monitored intraoperative environment and remains difficult to detect and preempt postoperatively. Given that blood pressure was not the focus of our current study, we did not employ specialized monitoring of cerebral autoregulation.

Drs. Cao and Zhu further correctly identify other factors that may influence postoperative neurocognitive outcomes, including anesthetic depth and duration, rewarming during CPB, and cerebrovascular events. CPB times, and thus presumably anesthetic duration, were not different between the groups in our study. While we did not specifically record and report anesthetic depth, the literature again lacks convincing evidence that the use of routinely employed anesthetic depth monitors (*i.e.,* processed electroencephalography monitors) can prevent postoperative delirium or cognitive decline.[3] Electroencephalography-based anesthetic titration shows greater promise in reducing postoperative cognitive decline in older adults,[3] but was not used in our study. Based on our previous findings,[4] standard institutional practice is to warm patients at a slower rate, maintaining no more than 2° C difference between nasopharyngeal and CPB perfusate temperature. Rate of rewarming was therefore unlikely to have had a significant effect in our study. Finally, cerebrovascular events, regardless of etiology, are certainly influential with regard to cognitive outcomes after cardiac surgery. We did report on the rate of stroke in our study cohort, which was overall quite low, occurring in two patients in the lidocaine group and six patients in the placebo group (not statistically different). Furthermore, we included these stroke patients in our sensitivity analysis, assigning them to worst cognitive performance, and still failed to find a difference in postoperative cognitive dysfunction between treatment groups. This suggests that the few patients who suffered early postoperative stroke did not skew the findings of our study.

Competing Interests

The authors declare no competing interests.

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Opioid-induced Miosis Is Unaltered by Obstructive Sleep Apnea: Comment

To the Editor:

We read with interest the article by Montana *et al.*[1] "Opioid Sensitivity in Children with and without Obstructive Sleep Apnea." The authors are to be commended on their measurement of *in vivo* remifentanil