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### Title

Response: Does Perioperative Dexmedetomidine Improve Mortality after Coronary Artery Bypass Surgery?

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## LETTER TO THE EDITOR

## Response: Does Perioperative Dexmedetomidine Improve Mortality after Coronary Artery Bypass Surgery?

To the Editor:

We thank Dr. Xue and colleagues for their careful and insightful review and thoughtful comments on our study that demonstrated perioperative dexmedetomidine use was associated with better outcomes of coronary artery bypass surgery.<sup>1</sup> Dr. Xue and colleagues are concerned about preoperative anemia and the outcomes of cardiac surgery. We all agree that preoperative anemia is associated with outcomes of patients undergoing coronary artery bypass surgery. However, anemia was not a factor here in this study since both groups had the same preoperative hemoglobin level. On the other hand, patients in both groups were prepared the same way preoperatively and included the adjustment of blood pressure control and preoperative anemia improvement according to the institutional protocol. This was the same with intraoperative anesthesia management. We believe none of our cardiac surgeons and anesthesiologists deviated too far away from our institutional standard. We also agree with Dr. Xue and colleagues' comments that perioperative transfusion has been suggested to worsen the outcomes in coronary artery bypass surgery.<sup>2</sup> Again, we did not include blood and blood product transfusion because we did not believe dexmedetomidine adversely affected coagulation.

This was an observational cohort study in the patient population with routine cardiac surgery. Multivariate regression in combination with propensity score adjustments were applied to this study population to reduce evident biases; however, the potential confounding biases associated with a non-randomized study remain. Data only could be included for analysis that was documented specifically on medical record. Because the data for our study was extracted from our institutional STS database, which is a voluntary database, under-reporting would be very unlikely.

Although this study demonstrated that the risk of postoperative cardiocerebral events include MI, heart block, cardiac arrest, stroke, and coma, there appeared to be no significant decrease during perioperative use of dexmedetomidine after CABG surgery; the OR value of these events were all in favor of perioperative use of dexmedetomidine. Studies have demonstrated the effectiveness of dexmedetomidine as a stress-

suppressing, anti-inflammatory, and anti-I/R injury agent in the prevention and treatment of cardiovascular events.<sup>3-5</sup> Catecholamines potentially may exacerbate myocardial injury and cause perioperative myocardial ischemia, which has been shown to increase the risk of postoperative mortality. Therefore, reducing the incidence of perioperative myocardial ischemia reduces the mortality by blunting the sympathetic-adrenal-axis response through decreasing central sympathetic activity at the locus ceruleus.<sup>6,7</sup> Laboratory studies have demonstrated that  $\alpha_2$  adrenergic agonists have protective effects against myocardial ischemia by reducing plasma norepinephrine levels and preserving myocardial blood flow to the endocardium by increasing the cAMP level and enhancing adenosine-induced coronary vasodilation effect.<sup>8-10</sup> Dexmedetomidine also reduces inflammation and delirium that contribute to mortalities. A pre-clinical study demonstrated that dexmedetomidine reduced inflammatory reaction and mortality. Therefore, we believe the reduction of mortality represents the overall effects of dexmedetomidine.

We share the commentators' concerns on how to interpret the results. We never mentioned anywhere in our article there is a causal relationship. Instead, we repeatedly have stated that perioperative dexmedetomidine use was associated with a decrease in postoperative mortality up to 1 year and decreased incidence of postoperative complications and delirium in patients undergoing coronary artery bypass surgery. We stated in our conclusion that a prospective, multicenter, randomized study focused on the use of dexmedetomidine in patients undergoing coronary artery bypass surgery is indicated to confirm these findings.<sup>1</sup> However, this study was conducted in the real world; we will never find the ideal experimental condition in our everyday clinical practice.

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