patients undergoing cardiac surgery. Contrast-induced nephropathy is independently associated with increased risks of postoperative adverse renal events.[2]

Second, perioperative hemoglobin levels were not provided. Preoperative anemia is not rare among patients undergoing cardiac surgery and is an important risk factor for postoperative AKI. Anemic patients undergoing cardiac surgery are more susceptible to transfusion-related AKI than nonanemic patients are.[3]

Third, as shown in table 1,[1] mean volumes of blood transfusion and fluids during surgery and the postoperative period were not significantly different between the two groups. But total input volumes at all observed points had highly variable ranges. It was unclear whether serum creatinine levels applied in diagnosis of postoperative AKI had been adjusted based on the perioperative fluid balance of patients. Moore *et al.*[4] showed that using Acute Kidney Injury Network criteria for diagnosis of AKI, without adjusting serum creatinine levels for fluid balance, can underestimate the incidence and severity of AKI after cardiac surgery.

Finally, when assessing the association of albumin with postoperative AKI by multivariable analysis, only preoperative and intraoperative covariates were adjusted in this study. It has been shown that postoperative complications including low cardiac output syndrome, hypoalbuminemia, anemia, and sepsis are independent risk factors of AKI after cardiac surgery.[5] We argue that not taking postoperative covariates into account would have biased the true effect of exogenous albumin administration on the occurrence of postoperative AKI in this study.

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Drs. Zhang and Xue for their interest in our article[1] and appreciate the opportunity to answer their questions. First, we agree that preoperative coronary angiography with contrast media may be related to the development of postoperative acute kidney injury (AKI).[2] However, as shown in table 1 in our article,[1] there was no significant difference in the number of patients who underwent coronary angiography less than or equal to 7 days before surgery between the two groups. Additionally, our previous study showed that the timing of the coronary angiography, the type of contrast agent, or the amount of contrast agent did not affect the development of postoperative AKI in patients who underwent off-pump coronary artery bypass surgery.[3] Thus, this is not likely to have had an impact on our results.

Second, although we agree that perioperative anemia and transfusion are important risk factors for postoperative AKI,[4] we do not agree that "perioperative hemoglobin levels were not provided." We presented the preoperative hematocrit level, the intraoperative lowest hematocrit level, and the number of packed red blood cell units transfused during or after surgery in tables 1 and 2 in our article,[1] all of which were similar between groups. As we stated in our article, we also performed adjustment for preoperative hematocrit using logistic regression.

Third, we agree that adjustment of creatinine for fluid balance has been proposed for a more accurate assessment of AKI.[5] However, in our study, we did not calculate corrected serum creatinine for fluid balance due to inaccurate fluid balance information including incorrect counts of bleeding. Therefore, it is possible that the positive fluid balance may influence the diagnosis of postoperative AKI, and the differences in fluid balance between the two groups influenced our results. However, as shown in table 2 in our article,[1] although there was no significant difference between the two groups, slightly higher postoperative weight gain, which indicates more positive fluid balance, was shown in the control group. Given that the effects of adjustment are larger in patients with more positive fluid balance, the incidence of AKI in the control group may be more masked than that in the albumin group.

Finally, we also agree on the point that several confounding postoperative events could affect our results. Therefore, as the authors suggested, we performed additional analyses to assess the effects of adjustment for postoperative confounding variables (except postoperative hypoalbuminemia and sepsis due to the possibility of mediator and no occurrence, respectively). After additional adjustment for postoperative low cardiac output syndrome and anemia using logistic regression, similar protective effects of albumin treatment were found (odds ratio, 0.409; 95% CI, 0.195 to 0.859; $P = 0.018$ and odds ratio, 0.411; 95% CI, 0.196 to 0.862; $P = 0.019$, respectively).

Competing Interests

The authors declare no competing interests.

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Complications of One-lung Ventilation: Is It the Blood Flow or the Ventilation?

To the Editor:

The results of the study of management of one-lung ventilation by Blank *et al.*[1] suggest that adequate positive end-expiratory pressure (PEEP) is an important factor in reducing pulmonary complications. Blank *et al.*[1] provide an excellent discussion of the mechanical mechanisms and implications. I suggest an alternative or additional possible explanation of the beneficial effects of PEEP. The ventilated lung is subjected to increased blood flow, and this hyperemia may create additional shear stress, resulting in damage to the endothelial glycocalyx, which can then result in clinically significant respiratory complications.[2–4] Studies support the concept that increased pulmonary blood flow may induce lung injury or aggravate a preexisting injury state.[5–9] PEEP to the ventilated lung may reduce this hyperemia and hence reduce complications. Lower tidal volumes and the resultant reduced inspiratory pressure may result in more hyperemia, thus offsetting any potential beneficial effect of the expected reduced volutrauma. If we find a way to protect the glycocalyx or otherwise reduce the hyperemia to the ventilated lung, it is possible that lower tidal volumes may have a net beneficial effect. Larger tidal volumes to the ventilated lung may increase inspiratory pressure, resulting in less hyperemia and less damage to the glycocalyx, but damage from volutrauma could still occur.

Unfortunately, this hypothesis creates a clinical dilemma. Reducing blood flow by the application of PEEP to the ventilated lung may result in a greater shunt with potential desaturation. Applying continuous positive airway pressure (CPAP) to the operative lung to treat desaturation may not be as much of a problem. While the percentage of blood flow to the ventilated lung may increase, thus reducing shunt, it is unclear if there is an absolute increased blood flow to the ventilated lung as a result of the CPAP; the CPAP may just reduce blood flow to the operative lung with no change in blood flow to the ventilated lung.

This hypothesis is consistent with their results. Blank *et al.*[1] found that low tidal volume and low PEEP, conditions that would be expected to increase blood flow to the ventilated lung, are associated with increased pulmonary complications. In the presence of PEEP, which would be expected to decrease blood flow to the operative lung, low tidal volume ventilation is protective.

The concept of pulmonary hyperemia being a cause of pulmonary complications is also consistent with the observations that pulmonary complication rates increase with increased amounts of pulmonary resection. For a given cardiac output, hyperemia may occur because of the reduced pulmonary vascular bed. In the most extreme case of a pneumonectomy, hyperemia would be expected to be maximal and complication rates are the highest; pulmonary edema may result from hyperemia-induced damage to the glycocalyx.

Further studies that incorporate measures of pulmonary blood flow would be helpful. Additional studies should also evaluate carbon dioxide management. Hypercarbia causes pulmonary artery vasoconstriction, which may reduce hyperemia, would require less minute ventilation, thus reducing the risk of volu- or barotrauma while trying to normalize the partial pressure of carbon dioxide, and may by itself be pneumoprotective. Permissive hypercarbia also permits lower respiratory rates, thus reducing the risk of potentially damaging air trapping.

Competing Interests

The author declares no competing interests.

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This letter was sent to the author of the original article referenced above, who declined to respond.— Evan D. Kharasch, M.D., Ph.D., Editor-in-Chief.