Commentary: Should goal-directed fluid therapy be used in every cardiac surgery patient to prevent acute kidney injury?

Alexander Zarbock, MD,^a and Daniel T. Engelman, MD^b

From the ^aDepartment of Anaesthesiology, Intensive Care Medicine and Pain Medicine, University Hospital Münster, Münster, Germany; and ^bHeart and Vascular Program, Baystate Health, Springfield, Mass.

Disclosures: A.Z. receives speaking honoraria from Baxter, Astute Medical, Fresenius, Ratiopharm, Amomed, bioMerieux, and Braun. A.Z. received funding support from German Research Foundation, GIF, BMBF, Fresenius, Astellas, and Astute Medical. D.T.E. consults for bioMerieux and Edwards Lifesciences.

Received for publication April 17, 2019; accepted for publication April 17, 2019; available ahead of print May 31, 2019.

Address for reprints: Daniel T. Engelman, MD, 759 Chestnut St, Springfield, MA 01199 (E-mail: Daniel.Engelman@baystatehealth.org).

J Thorac Cardiovasc Surg 2020;159:1878-9

0022-5223/\$36.00

Copyright © 2019 by The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2019.04.044>

Cardiac surgery–associated (CSA) acute kidney injury (AKI) is a common and serious complication that contributes to a significantly increased morbidity and mortality.¹ Cardiac output, hemoglobin level, vascular tone, blood pressure, and microcirculatory competence are the physiologic determinants of oxygen delivery to the kidney. During and after cardiac surgery, patients frequently experience hemodynamic instability, manifested by perturbations in cardiac output and blood pressure. This may be due to changes in circulating blood volume, anemia, and systemic vascular resistance, and a reduced cardiac output may be caused by myocardial stunning. The reduced circulating blood volume may be caused by blood loss, fluid shifts, and dilution. Changes in systemic vascular resistance may be a consequence of hypotension and a systemic inflammatory response syndrome triggered by the surgery itself.² Short episodes of hypotension in the perioperative period are associated with end-organ injury, including AKI.³ Reduction in blood pressure of previously normotensive or hypertensive patients may be associated with the subsequent development of AKI.⁴ Optimizing hemodynamics and volume status may therefore reduce the occurrence of CSA-AKI.⁵ Recently, the PrevAKI trial demonstrated that the implementation of a bundle of supportive measures in high-risk patients, as identified by urinary biomarkers, significantly reduced the rate of CSA-AKI.⁶

In this issue of the *Journal*, Johnston and colleagues⁷ present the results of an observational retrospective cohort trial investigating whether a goal-directed resuscitation protocol with fluid and vasoactive agents could reduce the occurrence of CSA-AKI. In this before-and-after design study, Johnston and colleagues⁷ used a standardized protocol to achieve quantifiable physiologic goals. In the post-implementation period, a multivariable analysis demonstrated a 37% reduction in the odds of AKI after implementation of a goal-directed resuscitation protocol centered on patient

Goal-directed fluid therapy may reduce perioperative acute kidney injury (AKI).

Central Message

Implementing a goal-directed resuscitation protocol after cardiac surgery may reduce the occurrence of acute kidney injury.

See Article page 1868.

fluid responsiveness. Secondary outcomes, including operative mortality, however, were not different between the groups.

One major limitation is the study design. Before-and-after study designs are inherently susceptible to bias, including selection and assignment, Hawthorne effect, test-retest, and regression to the mean bias, which are subtle but can invalidate conclusions.⁸ Another limitation is that the protocol was applied to every patient, and some patients may have received unnecessary fluids that could, in fact, contribute to AKI. Although several trials and an expert group^{2,9} and guidelines¹⁰ support the use of goal-directed resuscitation after cardiac surgery, the use of such protocols should be individually tailored. Combining the protocol with kidney stress biomarkers would allow patients with negative biomarker results to “fast track” without extra fluid.¹¹ The AKI reduction might have been even more significant had the protocol been used only in patients with positive biomarker results.¹² Before widespread adoption, goal-directed volume resuscitation protocols need to be validated in larger, multicenter trials with heterogeneous patient populations.

References

1. Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005;16:3365-70.
2. Nadim MK, Forni LG, Bihorac A, Hobson C, Koyner JL, Shaw A, et al. Cardiac and vascular surgery–associated acute kidney injury: the 20th international

- consensus conference of the ADQI (acute disease quality initiative) group. *J Am Heart Assoc.* 2018;7(11).
3. Smeltz AM, Cooter M, Rao S, Karhausen JA, Stafford-Smith M, Fontes ML, et al. Elevated pulse pressure, intraoperative hemodynamic perturbations, and acute kidney injury after coronary artery bypass grafting surgery. *J Cardiothorac Vasc Anesth.* 2018;32:1214-24.
 4. Liu YL, Prowle J, Licari E, Uchino S, Bellomo R. Changes in blood pressure before the development of nosocomial acute kidney injury. *Nephrol Dial Transplant.* 2009;24:504-11.
 5. Haase M, Bellomo R, Story D, Letis A, Klemz K, Matalanis G, et al. Effect of mean arterial pressure, haemoglobin and blood transfusion during cardiopulmonary bypass on post-operative acute kidney injury. *Nephrol Dial Transplant.* 2012;27:153-60.
 6. Meersch M, Schmidt C, Hoffmeier A, Van Aken H, Wempe C, Gerss J, et al. Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial. *Intensive Care Med.* 2017;43:1551-61. Erratum in: *Intensive Care Med.* 2017;43:1749.
 7. Johnston LE, Thiele RH, Hawkins RB, Downs EA, Jaeger JM, Brooks C, et al. Goal-directed resuscitation following cardiac surgery reduces acute kidney injury: a quality initiative pre-post analysis. *J Thorac Cardiovasc Surg.* 2020;159:1868-77.e1.
 8. Ho AM, Phelan R, Mizubuti GB, Murdoch JA, Wickett S, Ho AK, et al. Bias in before-after studies: narrative overview for anesthesiologists. *Anesth Analg.* 2018;126:1755-62.
 9. Aya HD, Cecconi M, Hamilton M, Rhodes A. Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis. *Br J Anaesth.* 2013;110:510-7.
 10. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. Guidelines for Perioperative Care in Cardiac Surgery: Enhanced Recovery After Surgery Society Recommendations. *JAMA Surg.* 2019 [Epub ahead of print].
 11. Engelman DT, Germain MJ. Looking to prevent acute kidney injury after cardiac surgery? Just check the urine. *J Thorac Cardiovasc Surg.* 2019;157:1554-5.
 12. Engelman DT, Crisafi C, Germain M, Greco B, Nathanson B, Tiwary A, et al. Implementation of a multidisciplinary acute kidney response team triggered by urinary biomarkers reduces acute kidney injury after cardiac surgery. Presented at: The American Association for Thoracic Surgery 99th Annual Meeting; May 5, 2019; Toronto, Canada.