Commentary: Predicting acute kidney injury in pediatric cardiac surgery

Nathalie Roy, MD, FRCSC

From the Department of Cardiac Surgery, Boston Children's Hospital and Department of Surgery, Harvard Medical School, Boston, Mass.

Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication Jan 11, 2019; accepted for publication Jan 11, 2019; available ahead of print March 4, 2019.

Address for reprints: Nathalie Roy, MD, FRCSC, Department of Cardiac Surgery, Boston Children's Hospital, 300 Longwood Ave, Bader 273, Boston, MA, 02115 (E-mail: nathalie.roy@cardio.chboston.org).

J Thorac Cardiovasc Surg 2019;157:2452-3

0022-5223/\$36.00

Copyright © 2019 by The American Association for Thoracic Surgery

<https://doi.org/10.1016/j.jtcvs.2019.01.038>

Acute kidney injury (AKI) is a frequent complication of congenital heart surgery that is associated with increased morbidity in the acute period. Early diagnosis is critical to manage fluid overload, prevent additional nephrotoxic insults, and maintain frequently used drugs such as milrinone and antibiotics within therapeutic range. A rise in serum creatinine is often delayed by 1-3 days after renal injury. In this edition of *The Journal of Thoracic and Cardiovascular Surgery*, Penk and colleagues¹ have authored a multi-institutional retrospective analysis entitled "Furosemide Response Predicts Acute Kidney Injury in Children Following Cardiac Surgery." Their major findings were that urinary flow rate in response to furosemide was significantly lower through 2 and 6 hours in the patients who had development of AKI according to the creatinine-defined Kidney Disease Improving Global Outcomes criteria. Lower urinary flow rate also led to an increased length of stay, independent of AKI. In their study, despite development of AKI in 33% of patients, no patient required renal replacement therapy, and mortality was low. In addition, Penk and colleagues¹ present a receiving operating characteristic analysis for prediction of severe AKI with ideal cutoff points.

This is a multi-institutional study composed of patients with complex congenital operations, across a wide age range. Because of its retrospective nature, however, the dose of furosemide was not standardized, and the timing of administration varied widely (median, 14.0 hours; interquartile range, 9.5-19.3). Furthermore, Penk and colleagues¹ could not control for patients' hemodynamics and fluid status at the time of furosemide administration or for variations in perfusion strategies. This publication, as well as 2 recent single-center retrospective studies in neonates and infants referenced therein, all demonstrated similar associations between AKI with lower urinary flow rate after furosemide administration. Nevertheless, there are important differences between their methodologies and that of the standardized furosemide stress test, which has been validated prospectively in adult critically ill patients.²

An early predictor for AKI would be clinically relevant in pediatric cardiac surgery for postoperative outcomes.

Nathalie Roy, MD, FRCSC

Central Message

Functional testing with furosemide is promising for predicting acute kidney injury after pediatric cardiac surgery, and it should be evaluated prospectively in conjunction with renal biomarkers.

See Article page 2444.

Interrogating the reserve capacity of the kidney with a functional study could improve risk stratification and possibly allow for early intervention. Furthermore, loop diuretics may offer renal protection by reducing oxygen consumption and apoptosis. In addition, volume overload contributes to morbidity in AKI—such as prolonged ventilation and length of stay—and the early use of loop diuretics can mitigate excess fluid. Therefore, as Penk and colleagues¹ point out clearly, a prospective trial validating the furosemide stress test in the pediatric population is a critical next step. Such a trial should monitor early urinary biomarkers validated in the pediatric cardiac surgical population,^{3,4} such as neutrophil gelatinase-associated lipocalin, markers of cell cycle arrest (tissue inhibitor of metalloproteinase combined with insulin-like growth factor-binding protein 7), and plasma cystatin C.⁵ Ideally, an optimal combination of biomarkers and functional studies would predict AKI early and with high reliability, thus allowing modulation of intraoperative and perioperative renal protection strategies.

References

1. Penk J, Gist KM, Wald EL, Kitzmiller L, Webb TN, Li Y, et al. Furosemide response predicts acute kidney injury in children after cardiac surgery. *J Thorac Cardiovasc Surg*. 2019;157:2444-51.
2. Chawla LS, Davison DL, Brasha-Mitchell E, Koyner JL, Arthur JM, Shaw AD, et al. Development and standardization of a furosemide stress test to predict the severity of acute kidney injury. *Crit Care*. 2013;17:R207.

3. Dong L, Ma Q, Bennett M, Devarajan P. Urinary biomarkers of cell cycle arrest are delayed predictors of acute kidney injury after pediatric cardiopulmonary bypass. *Pediatr Nephrol.* 2017;32:2351-60.
4. Adams PS, Vargas D, Baust T, Saenz L, Koh W, Blasiole B, et al. Associations of perioperative renal oximetry via near-infrared spectroscopy, urinary biomarkers, and postoperative acute kidney injury in infants after congenital heart surgery: should creatinine continue to be the gold standard? *Pediatr Crit Care Med.* 2019;20:27-37.
5. Cantinotti M, Giordano R, Scalese M, Molinaro S, Storti S, Murzi B, et al. Diagnostic accuracy and prognostic value of plasmatic cystatin-C in children undergoing pediatric cardiac surgery. *Clin Chim Acta.* 2017;471: 113-8.