Editorial

# Renal resistive index as a biomarker for acute kidney injury in aortic valve surgery

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*Provenance:* This is an invited Editorial commissioned by Executive Editor-in-Chief Jianxing He (Director of the Thoracic Surgery Department, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China).

*Comment on:* Andrew BY, Cherry AD, Hauck JN, *et al.* The Association of Aortic Valve Pathology With Renal Resistive Index as a Kidney Injury Biomarker. Ann Thorac Surg 2018;106:107-14.

Submitted Aug 31, 2018. Accepted for publication Sep 11, 2018.

doi: 10.21037/jtd.2018.09.45

**View this article at:** http://dx.doi.org/10.21037/jtd.2018.09.45

Acute kidney injury (AKI) is a common complication of cardiac surgery. Depending on the severity level, the incidence of AKI after cardiac surgery ranges from 3–30%, with AKI requiring renal replacement therapy in the 3% range and mild AKI in the 30% range (1,2). Several consensus guidelines and definitions have been developed to diagnose and grade AKI, including the Kidney Disease: Improving Global Outcomes (KDIGO) AKI guidelines, the Acute Kidney Injury Network (AKIN) guidelines, and the Risk-Injury-Failure-Loss-End-Stage Kidney Disease (RIFLE) criteria by the Acute Dialysis Quality Initiative Group (2-4). Several of these guidelines and definitions have been adopted and validated for the assessment, diagnosis, and reporting of AKI in several settings, including cardiac surgery. Based on these definitions, AKI of all severity levels, including mild AKI, are associated with increased short-term and long-term morbidity and mortality for patients undergoing cardiac surgery (1-4). Thus, it is imperative that the perioperative and surgical team ensure that the risk of AKI is minimalized during the perioperative period.

The pathophysiology of AKI in patients undergoing cardiac surgery is not completely understood. Several factors can contribute to the development of AKI in patients undergoing cardiac surgery including susceptibility to pre-renal azotemia, exposure to nephrotoxins such as intravenous contrast dye, decreased intraoperative renal perfusion, impairment of renal autoregulation, systemic inflammation related to cardiopulmonary bypass, hemodilution, microembolic events, and adrenergic/neurohormonal activation (2). The multifactorial nature and limited understanding of the pathophysiology of AKI make it challenging to predict which patients are particularly susceptible. Serial measurements of serum creatinine and monitoring urine output are currently the most widely used methods of measuring and diagnosing AKI. The utility and validity of other biomarkers are unclear.

Various groups are currently investigating different approaches to predicting and detecting AKI in patients undergoing cardiac surgery. One approach is to measure a multitude of serum or urine biomarkers and correlate them with the development of AKI (5,6). For example, Enger and colleagues found that increased baseline plasma levels of neopterin and N-terminal pro-brain natriuretic peptide along with decreased levels of plasma lactoferrin were associated increased risk of developing AKI after cardiac surgery (5). However, a meta-analysis done by Ho *et al.* found that most serum and urine biomarkers were poor predictors of AKI in the perioperative period for cardiac surgery (6). The meta-analysis also revealed another important point—most current biomarkers are not measured intraoperatively, a period in which the surgical and perioperative team can intervene. Other approaches utilize patient demographic factors and comorbidities to predict the risk of developing severe AKI (7-9). For example, the widely used Cleveland Clinic

Acute Renal Failure (ARF) score developed by Thakar *et al.* uses preoperative demographic and comorbidity data in addition to preoperative serum creatinine to predict the risk of developing AKI after cardiac surgery (9). Based on validation studies, these risk prediction models utilizing clinical data tend to be more predictive than biomarkers alone (6). An important limitation of these models, however, is that they are currently only predictive of severe AKI requiring renal replacement therapy. Though it is clear that a suitable predictor of AKI after cardiac surgery is needed, an ideal candidate has yet to be identified.

One potential biomarker that is currently being investigated for the prediction of AKI is the renal resistive index (RRI) via transabdominal or transesophageal ultrasonography. The RRI is a Doppler-derived value [RRI = (peak systolic velocity – end diastolic velocity)/peak systolic velocity] measured at the arcuate or interlobar arteries of the kidneys and provides an index of renal function. A threshold RRI of >0.70 is suggestive of decreased renal function (10,11). Many studies have investigated the utility of RRI in the critically ill and perioperative population (10,12). These studies are especially relevant in cardiac surgery patients given the higher rate of AKI in this patient population (11,13,14). Benefits of RRI as a biomarker for the prediction of AKI include reproducibility, cost-effectiveness, availability, and immediate feedback.

Andrew *et al.*'s retrospective study, published earlier this year in *The Annals of Thoracic Surgery* explores the nuances of aortic valve disease on the utility of the RRI in predicting the development of AKI post-cardiac surgery (15). Andrew *et al.* should be commended on their study, as they are the first group to report on the relationship between aortic valve pathology and RRI. In their study, patients were divided into four distinct groups depending on their predominant aortic valve pathology: normal aortic valve, predominantly aortic insufficiency (AI), predominantly aortic stenosis (AS), and combined insufficiency/stenosis (AI/AS). Determination of AKI was done using the KDIGO criteria. They find several relevant findings in their study population. Patients with predominantly AI or combined insufficiency/stenosis were found to have significantly elevated RRI pre-operatively. Yet, rates of AKI were not significantly different for the AI and AI/AS groups compared to the other groups.

Increased RRI found in patients with AI may be related to the hemodynamic disruption and decreased diastolic renal blood flow caused by aortic regurgitation. Similar to Andrew *et al.*'s findings, Sinning *et al.* also found elevated RRI in their population of patients with moderate to severe paravalvular leak after transcatheter aortic valve intervention (TAVI) (16). However, the hemodynamic disruption and subsequent elevated RRI may not correlate clinically with increased rates of AKI as shown in Andrew *et al.*'s study. A clear explanation for this is not readily available at this time but the data does provide some further insight on the utility of RRI as a biomarker for AKI, especially in the setting of aortic valve pathology. As more studies investigate the utility of RRI as a biomarker for prediction of AKI, investigators must take into account the effects of regurgitant aortic lesions and adjust their RRI measurements as necessary. For example, Andrew *et al.* make the suggestion of decreasing the measured RRI depending on whether the patient has AI or AI/AS to more accurately predict the development of AKI, however validation of this remains to be completed. Perhaps, the use of RRI in the setting of lesions such as AI should be avoided altogether given the poor correlation of RRI and AKI in this population.

Several studies have already assessed the utility of RRI in the setting of cardiac surgery. A prospective cohort study done by Bossard *et al.* demonstrated that patients with increased RRI in the immediate post-operative period had an increased risk for the development of AKI (14). Increased RRI was also associated with worsening severity of AKI in their cohort. Interestingly, pre-operative RRI in this cohort was not associated with the development of AKI. Hertzberg *et al.* found that a pre-operative RRI of >0.70 was associated with a three-fold increase in risk of developing AKI after cardiac surgery (11). Regolisti *et al.* found a correlation between immediate post-operative RRI and the development of AKI after cardiac surgery. However, their receiver operating characteristic (ROC) analysis found that immediate post-operative RRI had poor predictive value for determining which patients would develop AKI (13). These studies in addition to Andrew *et al.*'s findings suggest that the RRI has great potential for prediction and earlier detection of AKI in patients undergoing cardiac surgery to allow for more expedient intervention. However, there are still issues to resolve prior to implementing RRI in routine clinical practice. Nonetheless, Andrew *et al.* provide further understanding on the consequences of AI on the measurement of RRI and help guide future studies on the utility of RRI as a predictor of AKI. Continued work to determine reliable predictors of AKI is essential for the guidance of therapies to prevent this common and potentially devastating complication of cardiac surgery (17-19).

 

## Acknowledgements

None.


## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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**Cite this article as:** Vo TX, Boodhwani M. Renal resistive index as a biomarker for acute kidney injury in aortic valve surgery. J Thorac Dis 2018;10(Suppl 33):S4010-S4012. doi: 10.21037/jtd.2018.09.45

 