

EDITORIAL

# Modifying the Risk of Contrast-Associated Acute Kidney Injury in Percutaneous Coronary Interventions and Transcatheter Aortic Valve Implantations

Briggs S. Carhart , MPH; Meagan E. Stabler , PhD; Jeremiah R. Brown , PhD, MS

**C**ontrast-associated acute kidney injury (CA-AKI) remains a clinical quandary that increases the rate of morbidity and mortality in patients undergoing various coronary procedures.<sup>1,2</sup> Researchers within the last decade have synthesized and elucidated the various pathophysiological mechanisms of developing this form of nephropathy from iodinated contrast media.<sup>2,3</sup> A recent study estimated the incidence of CA-AKI in percutaneous coronary intervention (PCI) was about 7.7%.<sup>4</sup> Using the Acute Kidney Injury Network criteria, CA-AKI is considered when there is an absolute increase in serum creatinine of  $\geq 0.3$  mg/dL, a relative serum creatinine increase of  $\geq 50\%$  from baseline, or a significant reduction in urine output (ie,  $< 0.5$  mL/kg per hour for more than 6 consecutive hours), within 48 hours.<sup>5</sup> Catheter administration of contrast, as seen in PCI or transcatheter aortic valve implantation (TAVI), are of particular interest because of the higher volume of contrast media being used during the procedure.<sup>2</sup> Contrast load in addition to release of arthroemboli from the catheter increases the risk for CA-AKI to occur. As there is greater understanding about which patients are at higher risk for CA-AKI, the next step is to determine how to approach a patient's risk profile and understand how to prevent CA-AKI.

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See Articles by Shoji et al. and Venturi et al.

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In this issue of the *Journal of the American Heart Association (JAHA)*, Shoji and colleagues examined the risk profiles of a retrospective cohort ( $n=14\ 702$ ) and compared these profiles to the amount of contrast used in their PCI procedures. An increase in contrast quantity is associated in a dose-response manner with AKI risk.<sup>6</sup> The study calculated NCDR (National Cardiovascular Data Registry) Cath-PCI Registry AKI-risk scores for each patient.<sup>7</sup> These scores were mapped to contrast quantity and found a uniform quantity across all quartiles. This raises the concern that overall CA-AKI risk was not considered when determining the amount of contrast that was to be used during the case. Although overall risk did not map to contrast volume, estimated glomerular filtration rate (eGFR) was correlated with a higher quartile of risk receiving less contrast (figure 3 of Ref. [7]). This is a promising result because eGFR, a tool for renal function estimation, is a risk factor in a vast number of preconceived risk scores.<sup>4,8-15</sup> Approximating a patient's renal function is one of the better predictors of CA-AKI because eGFR is heavily weighted in the risk

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Correspondence to: Jeremiah R. Brown, PhD, MS, DHMC 1 Medical Center Drive, Lebanon, NH 03756. E-mail: jbrown@dartmouth.edu

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calculation for most risk models. For the NCDR risk model, a severe GFR increases risk of CA-AKI by almost 5% without other risk factors present.<sup>4</sup> When a patient presents with accompanying risk factors, such as diabetes mellitus, myocardial infarction, intra-aortic balloon pump, etc, the interaction of multiple risk factors exponentially increases CA-AKI risk. For clinicians to gravitate toward eGFR as a tool for determining contrast volume is a good sign that some risk modification is occurring in the field already. A caveat to Shoji et al is the NCDR risk model was derived and validated in 2014 whereas some participants received their intervention as early as 2008. This makes it challenging to attribute the lack of adjustment of the contrast volume to the overall risk quartiles to an evidence-to-practice gap. However, the NCDR risk model was validated for the incidence of CA-AKI with 66.5% (750/1127) of the patients who developed CA-AKI being from the highest risk quartile.<sup>7</sup> Although the majority of the covariates in the risk model are not modifiable, it reinforces its viability to determine the priority of reducing risk in the patient before the coronary angiogram or PCI.

Moreover, also in this issue of *JAHA*, Venturi et al investigated the staging of TAVIs in conjunction with PCIs as an area of potential risk modifications, comparing staged strategy versus concomitant strategy. Studies in this area previously compared the safety of staged procedure. Staged strategy (SS) is defined as having the coronary angiogram/PCI before the TAVI was performed. Concomitant strategy (CS) is defined as having the coronary angiogram/PCI performed at the same time as the TAVI. Studies comparing SS and CS have largely focused on overall morbidity and mortality, not CA-AKI specifically.<sup>16</sup> To compare the absolute difference in risk of CA-AKI, 339 patient records were retroactively analyzed. When considering individuals developing AKI after the TAVR, the SS and CS group were comparable with 10.6% and 10.1% developing CA-AKI, respectively (figure 4 of Ref. [17]); however, the SS group had an additional 19.9% of their group develop nephropathy after the initial staging procedure within the 30-day window before the TAVI.<sup>17</sup> Venturi et al characterize the hemodynamics of the patient in the SS to be less stable when going for a SS versus the CS catheterization. Hemodynamic stability is one of the factors that drive CA-AKI risk.<sup>3,9</sup> Interestingly, the patients with eGFR <60 mL/min per 1.73 m<sup>2</sup> received hydration therapy/volume expansion as a measure to reduce risk.<sup>18</sup> This study was successful at outlining the potential risk reduction methods to protect patients from CA-AKI during TAVI procedures by changing the staging process.

The challenge with CA-AKI is that the risk reduction methods will not be consistent with each patient. CA-AKI is an iatrogenic condition from essential diagnostic and intervention tools that aid in the reduction of

cardiovascular events in a variety of contexts. Similar intervention methods are used in outpatient care as well as in the acute care setting. Because of time constraints, emergent coronary interventions limit opportunities to consider and reduce the risk of patients developing CA-AKI. These acute cases need extra consideration. If a high-risk patient is not considered during PCI/TAVI, correcting one condition might have downstream consequences that question the utility of hospital resources. In the instance that excess caution causes a patient with preexisting chronic kidney disease to be refused necessary treatment (or “renalism”). To avoid these extremes, we offer suggestions.

First, when a patient presents with multiple risk factors of CA-AKI, map the risk factors to a risk score calculation to determine the overall risk. In the acute setting, focusing on eGFR would be the minimum, if that information was able to be ascertained. Formulating a self-made risk calculator is common for most conditions, not just contrast-associated nephropathy; however, using a validated tool will aid in considering all preprocedural risk factors because eGFR, although heavily weighted, is one of many risk factors used in modern calculations.<sup>4,8–15</sup> Shoji et al outlined important covariates that should have indicated a decrease in contrast volume, such as intra-aortic balloon pump and heart failure for the previous 2 weeks. Instead, those were associated with an increase in contrast volume.<sup>7</sup> This result could be from residual confounding and stratification could elucidate if these patients also had other risk factors that would increase their individual probability of contrast-associated nephropathy. If a patient’s risk score surpasses a high threshold, patient engagement and shared decision making will be paramount to minimize risk of CA-AKI and treat the underlying acute cardiovascular disease. If the patient is decompensating in an acute setting, then PCI is warranted regardless of AKI risk. For elective procedures, delay and follow-up with the patient are recommended to see if the eGFR would recover or if hemodynamics can stabilize. If this delay is not expected to improve risk, then PCI/TAVI can proceed.

Second, all patients will benefit from having shorter nothing by mouth times (2 hours prior to procedure for clear fluids), pre-, peri-, and postprocedure hydration and limited contrast volume. Isotonic saline (0.9%) being administered at a rate between 1 and 3 mL/kg per hour before the procedure can aid in preventing CA-AKI.<sup>17–19</sup> The POSEIDON (Study of Durvalumab + Tremelimumab With Chemotherapy or Durvalumab With Chemotherapy or Chemotherapy Alone for Patients With Lung Cancer) trial studied pressure guided volume expansion based on the patient’s left ventricular end-diastolic pressure.<sup>19</sup> This recommendation would be contraindicated for a patient in cardiogenic shock, fluid overloaded, or

in congestive heart failure. Furosemide-induced diuresis can benefit the patient when prescribed at the optimal dose.<sup>20</sup> The RenalGuard system from the REMEDIAL II (Renal Insufficiency After Contrast Media Administration II) trial was able to achieve a low dose of furosemide that was also effective at maintaining the balance of fluid overload and volume depletion.<sup>20</sup> Volume expansion remains a modifiable risk factor that can be implemented if time permits among patients with normal cardiac output. In Venturi et al, emergency cases were not considered in that portion of the study when 1 mL/kg per hour was not able administered.

Lastly, Venturi et al discusses the benefits of transcatheter aortic valve implantations being concomitant with PCI and other interventions. The authors acknowledge the limitation of the number of single-center, retrospective studies. More investigation into this area is encouraged, but that does not exclude current practices from using the CS to prevent CA-AKI in high-risk patients. Other studies suggest the CS, although more protective for CA-AKI, could be associated with a marginal increase in mortality within the first 30 days.<sup>16</sup> There is limited evidence on the optimal time for staging procedures; therefore, we recommend the clinical care teams make the decision on the appropriate timing based on the untreated lesions, initial contrast load from the first case, and safety of the patient to comply with aggressive medical management until the staged procedure. On average, contrast clears and serum creatinine normalizes levels in 14 days<sup>21</sup>; though, Venturi et al included patients with a median staging interval of 22 days.<sup>17</sup> More investigations should be conducted before this recommendation can be open to low-risk patients.

In summary, CA-AKI continues to be an area of active research with the goal of decreasing its incidence and associated rates of morbidity and mortality. Cardiac catheterization and PCI have been the focus of CA-AKI discussions, however, TAVI procedures are becoming more commonplace and CA-AKI must take its seat at the table when factoring in risk and major adverse events. These studies represent the current issues of encouraging clinical practices to better manage CA-AKI and investigate realms of kidney injury in TAVI beyond the initial staging. Modern practices need to consider all avenues of risk reduction to protect patients from further iatrogenic effects. There must remain active awareness of the clinical decisions that may bias treatment decisions for patients with preexisting chronic kidney disease and focus on preventive practices to minimize procedural risk of CA-AKI. New team-based interventions to implement evidence-based practices are being evaluated to aid in center-wide prevention of CA-AKI.<sup>22,23</sup>

## ARTICLE INFORMATION

### Affiliations

Geisel School of Medicine at Dartmouth, Hanover, NH (B.S.C.); Department of Epidemiology (M.E.S., J.R.B.) and Department of Biomedical Data Science, Geisel School of Medicine at Dartmouth, Hanover, NH.

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