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Editorial

Acute Kidney Injury Following Percutaneous Coronary Intervention: Trying to Get Whole Eggs From an Omelette

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See article by Shacham et al., pages 1240-1244 of this issue.

Diseases of the heart and kidneys are inherently linked because they share many common and overlapping risk factors. In fact, recent classification schemes have added the term "cardiorenal" to focus and draw attention to the dysfunction the 2 organs commonly share.[1] Over the past few decades, tremendous progress has been made in the interventional and medical treatment of acute coronary syndromes. In stark contrast, during the same time frame there have been minimal therapeutic advances in the prevention of acute kidney injury (AKI), which often complicates acute percutaneous coronary intervention (PCI). Thus, the development of AKI and its association with the need for dialysis and risk of death can be viewed as a rate-limiting step to improving outcomes in patients with acute coronary syndromes.

The recognition that AKI is broadly associated with worse outcomes has led to a paradigm shift. Current classification schemes dissociate from the etiologic origin of AKI and focus solely on the degree of kidney injury. This development is both evidence based, because even mild levels of kidney dysfunction are associated with increased mortality, and pragmatic, because patients with AKI rarely undergo a kidney biopsy procedure. An inherent limitation of this approach is the difficulty of disentangling direct causes of AKI from its associated risk factors.

This problem is well illustrated in patients in whom AKI develops after PCI. Tsai et al.[2] developed a risk model in > 900, 000 patients that identified age, chronic kidney disease (CKD), chronic heart failure, diabetes, ST-segment–elevation myocardial infarction (STEMI), and cardiogenic shock (among others) as predictors of AKI development after contrast exposure.[2] However, many of these risk factors (congestive heart failure [CHF] and cardiogenic shock) may inherently be causative of AKI, independent of contrast exposure. Nevertheless, a large proportion of research to date has focused on prevention and treatment of contrast-induced AKI.

Attempting to distinguish eggs (the source) from the omelette (the outcome) is important because it may lead to differences in preventive therapy. For example, in patients with active decompensated CHF (a contributor to AKI), the goal may be relief of congestion with removal of extracellular salt and water to reduce the risk of AKI. This is a direct contradiction, as many clinicians are all too aware, to the use of intravenous volume expansion to prevent renal injury from contrast exposure.

In this issue of the *Canadian Journal of Cardiology*, Shacham et al.[3] present data attempting to disentangle the cause of postcontrast AKI in a group of high-risk patients with STEMI. Using a retrospective single-centre cohort study design of 1656 patients who underwent PCI, they found that AKI developed in roughly 10%. Baseline kidney function was determined at hospital admission, and AKI was defined by the validated Acute Kidney Injury Network criteria based on a rise in the serum creatinine (SCr) level or a decline in the urine output, or both. In patients without overt CHF, intravenous fluids were administered after PCI. In adjusted models, AKI was associated with factors termed "hemodynamic impairment," such as critical state, reduced left ventricular ejection fraction, CHF, and delays in therapy. The authors conclude that these additional factors should be considered in addition to intra-arterial contrast exposure with PCI.

Examination of baseline characteristics reveals some interesting and important information. Patients in whom AKI developed after PCI were older, had a history of hypertension or diabetes (or both), had a longer time to reperfusion, and most importantly had a lower estimated glomerular filtration rate (eGFR) at admission and a higher proportion of patients with an eGFR < 60 mL/min. In other words, some of these patients had likely experienced AKI before hospital admission, with "hemodynamic impairment" resulting from STEMI being the likely cause as opposed to a risk factor. This observation could explain many of the further study findings, such as the lack of an association between AKI and a reduced eGFR (< 60 mL/min) at baseline or between AKI and contrast volume.

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The determination of a true baseline SCr level would have provided insight into the heterogeneous study group that likely consisted of patients with AKI and patients with CKD. This is an important consideration because CKD is in itself a well-established and important risk factor for AKI. Its accurate determination requires a historical measure of kidney function at a time of steady state, ie, free of concurrent acute illness or volume fluctuations. SCr determination at the time of hospital admission (as the authors report in this study), although convenient in regard to availability, are notoriously inaccurate for determination of baseline kidney function. Multiple strategies to estimate a baseline SCr level in patients admitted to hospital have been examined, including use of the first hospital admission SCr determination, imputation, assumption of a baseline of 75 mL/min/1.73 m^2, and use of an outpatient SCr value within the preceding year.[4] Of these strategies, the use of an outpatient SCr value leads to the least misclassification and should be the preferred method for the determination of baseline kidney function. We encourage investigators to attempt to delineate the true baseline SCr level, before STEMI onset, in future work.

Are there other potential risk factors for AKI? Another often under-recognized factor is the presence and severity of proteinuria. James et al.[5] reported the risk of AKI stratified by degree of proteinuria in a large population-based cohort from Alberta. Heavy proteinuria (defined as 2+ on urinary dipstick measurement) was associated with an unadjusted rate of AKI of 8.8 per 1000 patient-years compared with 1.0 per 1000 patient-years among patients with normal proteinuria and an eGFR $>$ 60 mL/min/1.73m^2. The risk of AKI according to degree of proteinuria persisted even among individuals with a reduced baseline eGFR. In individuals with an eGFR $<$ 15 mL/min/1.73 m^2, the crude rate of AKI was 117 per 1000 patient-years with heavy proteinuria compared with 70 per 1000 patient-years with normal proteinuria. Quantification of proteinuria by urinary dipstick before PCI is a rapid, inexpensive, and readily available method to further risk stratify patients.

A few other limitations of the present study require mention. Patients who died early ($<$ 24 hours after admission) were excluded, with the presumption that it was too early for the development of AKI. This is likely not the case, because early AKI is reported in up to 10% of cases.[6] Furthermore, information on urine output was lacking. The importance of the urine output criterion was recently illustrated in a study by Kellum et al.[7] Examining $>$ 30,000 intensive care unit admissions (74.5% with AKI) they found that AKI defined by the urine output criterion alone was more common than AKI using the SCr level criterion alone. Further, AKI with both criteria (rise in SCr level and drop in urine output) was associated with an increased risk of mortality compared with AKI determined by either criterion alone.

In conclusion, we applaud the effort by Shacham et al.[3] to identify noncontrast risk factors that are involved in AKI after PCI. Whether these were truly risk factors or were causative remains unknown. The challenge for future investigators will be the design of studies or analyses to appropriately differentiate, if possible, the eggs from the omelette.

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