Published in final edited form as:

Coron Artery Dis. 2019 March ; 30(2): 93–94. doi:10.1097/MCA.0000000000000713.

Does Acute Kidney Disease Following Primary Percutaneous Coronary Intervention lead to Chronic Kidney Disease Development and Progression?

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The development of acute kidney injury (AKI) during hospitalization has been shown to be associated with short and long-term mortality, new onset CKD, higher resource utilization and an increased risk of rehospitalization. Non-recovery from AKI is emerging as a potential factor influencing these adverse events and is related to the severity, duration and recurrent episodes of AKI. Underlying comorbidities including diabetes, CKD, proteinuria and advanced age have been identified as risk factors for AKI non-recovery^{1,2}. Processes of care including fluid balance, dialysis requirement and follow up also influence the degree of recovery^{3,4}. The ADQI group has recently reported a consensus statement proposing a standardized classification for recovery⁵. Rapid reversal is considered when serum creatinine is back to reference value within 48 hours; early recovery within 7 days and late recovery within 7 – 90 days. Patients with late recovery are classified as acute kidney disease (AKD) and the degree of dysfunction determined as the AKI staging. These kidney function trajectories can occur in patients with *de novo* AKI or AKI on CKD. However, the heterogeneity of AKI etiology, its recognition and management has been a limiting factor in identifying these events in epidemiologic studies and for individualized patient management. A key issue is the difficulty in distinguishing a new episode of AKI from preexisting CKD and persistent AKI with incomplete recovery^{6–8}.

In this issue of the journal, Kofman et al.⁹ report on the outcomes of patients identified as having AKI following primary percutaneous coronary interventions (PCI) for ST-elevation myocardial infarctions (STEMI) in a single center. Over a course of 8 years, 2122 patients underwent PCI for STEMI, of whom 225 developed AKI within 7 days based on the KDIGO serum creatinine criteria. Patients were considered to have AKD if their serum creatinine level was higher than 0.1mg/dl from admission levels at 7 days, while progression to CKD was based on a comparison of the hospital discharge creatinine to the creatinine values at 90–180 days. These parameters are subject to variation since hospitalization is associated with an overall decrease in serum creatinine due to a loss of muscle mass, volume overload and nutritional status. Consequently, eGFR calculations overestimate renal function in comparison to measured creatinine clearances^{10,11}. Long-term outcomes were ascertained over a range of 3.5+2.5 years. Half of the AKI patients had underlying CKD at the time of PCI, and late recovery/progression to acute kidney disease occurred in 81 (36%)

of all the patients. Non-recovery and development of CKD, assessed between 90 and 180 days, was frequent in AKD patients; 59% in AKD vs. 7% in non-AKD. Patients with AKD had higher 90 day (35% vs. 11%, $p<0.001$) and long-term mortality (35% vs. 17%, $p<0.001$). These findings add further evidence of the influence of early AKI recovery on patient outcomes^{4,12,13}.

Underlying CKD is a known risk factor for contrast-induced nephropathy (CIN), and prior studies have shown these patients are more likely to progress¹⁴. In the Kofman et al. study⁹, AKD was more frequent in patients with underlying CKD. However, there is no information on the distribution of AKD and outcomes among patients with CKD in comparison to *de novo* AKI. Since 60% of AKD patients progressed to CKD at 90 days, it would be essential to distinguish progression in CKD from the development of new-onset CKD, as the interventions may be different^{4,15–17}. The authors used different definitions for ascertaining new-onset CKD based on a decrease in eGFR to a level <60 ml/min/1.73m², at 90–180 days compared to admission eGFR vs. progression based on the change in CKD stage. Since the timing of contrast exposure was known and, patient hemodynamic parameters were monitored, it is reasonable to determine the contribution of these events on the course of AKI in these patients. However, the peak serum creatinine within the first 7 days was the only factor found to be significant in predicting the development of AKD. Although AKD patients were hospitalized for a longer period, it is unclear if they underwent additional interventions that could contribute to recurrent episodes of AKI^{18,19}.

Although the Kofman et al.⁹ study has limitations in being retrospective from a single center and may have misclassified patients as CKD based on estimated GFR rather than objective measures of proteinuria and a documented evidence of CKD, it illustrates several important issues. Measurement of serum creatinine prior to cardiac catheterization is variable pre-procedure and in most instances not done post procedure. Patients with STEMI represent higher acuity, and require hospitalization, however, current guidelines for PCI focus on preventing CIN, and do not indicate the need for renal functional monitoring following the procedure.^{20,21} Prior studies of PCI associated AKI^{22,23} have shown an incidence of AKI of around 10% during the hospitalization, similar to that seen in the Kofman study⁹, however, have not described long-term renal outcomes. In the Action *Get with the Guidelines-CAD* Registry, over 182 thousand patients underwent PCI for STEMI in the US in 2014²⁴. Based on the reported AKI incidence of 10% in prior studies and the Kofman et al.⁹ data, approximately 18000 patients a year would have developed AKI and 6480 would have had AKD with a high risk of developing new-onset CKD, CKD progression and mortality. These numbers would be further magnified if one considers the broader category of PCI for non-STEMI applications²⁴. These findings highlight the need for identifying patients at risk for AKI and AKD, and develop standardized approaches for surveillance and monitoring of renal functional changes post PCI. Patients identified as AKD should be monitored closely and potentially referred for nephrology assessment. With the availability of point of care testing for serum creatinine and urine dipstick for proteinuria, it is now feasible to follow renal function in ambulatory patients at home²⁵. Optimizing management prior to and during the PCI procedure to prevent CIN is well defined in existing guidelines, nevertheless, follow up care focusing on factors associated with renal functional recovery is needed to improve patient outcomes²⁶. Further

epidemiologic studies evaluating AKD and its course would be an important adjunct to current registries for PCI.

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