AKI and Medical Care after Coronary Angiography: Renalism Revisited

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AKI after coronary angiography is commonly related to iodinated contrast administration and has been shown in multiple studies to be associated with serious adverse cardiovascular events, accelerated long-term decline in kidney function, and increased short- and long-term mortality (1–5). Although this condition is potentially preventable in at-risk patients and is very uncommon in those with normal baseline kidney function, efforts to prevent the development of longer-term adverse cardiovascular and renal outcomes in those patients who do experience AKI after angiography are of paramount importance. Key among such efforts is implementing evidence-based therapies to optimize cardiovascular risk reduction and mitigate risk for CKD progression.

In this issue of CJASN, Leung and colleagues report the results of a retrospective cohort study that investigated the association of AKI with use of cardioprotective medications after coronary angiography (6). Utilizing a database from Alberta, Canada, the investigators developed a cohort of older patients who were hospitalized with acute coronary syndrome (ACS) and underwent coronary angiography, had at least one serum creatinine measured within 7 days after the procedure, and survived at least 120 days after hospital discharge. Data on the use of statins, β-blockers, and angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) in the 120 days after hospital discharge were abstracted from a provincial, universal medication coverage plan. The investigators used logistic regression models to analyze the association of AKI after angiography, defined based on Kidney Disease-Improving Global Outcomes criteria, with postdischarge use of statins, β-blockers, and ACEIs/ARBs, as well as Cox proportional hazards models to characterize the association of use of these medications with longer-term survival, stratified by AKI status.

The overall incidence of postangiography AKI was approximately 15%, with the majority of patients manifesting stage 1 AKI. In multivariable analyses, patients with stage 1 AKI had lower odds of receiving ACEIs/ARBs than patients without AKI, whereas patients with stages 2/3 AKI had lower odds of receiving statins, β-blockers, and ACEIs/ARBs than patients without AKI. These associations remained statistically significant in subgroup analyses based on baseline kidney function; history of diabetes, heart failure, and albuminuria; and prior use of these medications. Of particular interest, among patients with albuminuria, individuals with stage 1 and stages 2/3 AKI had statistically significant lower odds of receiving ACEIs/ARBs compared with patients without AKI. The use of statins, β-blockers, and ACEIs/ARBs was each associated with lower longer-term mortality in patients with and without AKI. The investigators concluded that (1) the development of severe postangiography AKI was associated with lower subsequent use of statins, β-blockers, and ACEIs/ARBs, (2) the use of these medications was associated with reduced long-term mortality; and (3) efforts to identify strategies to improve the utilization of these medications in patients who experience AKI after coronary angiography are warranted.

This important study has several key strengths. First, the study cohort was relatively large with a substantial proportion of patients who experienced AKI. Second, by virtue of the universal medication coverage plan for elderly patients, identification of prescriptions for statins, β-blockers, and ACEIs/ARBs was likely comprehensive. Finally, thorough ascertainment of and adjustment for comorbid conditions and other potential confounders reduced the likelihood of unmeasured confounding. There are also important limitations to this study. First, the investigators did not assess post-AKI events (e.g., hypotension) and/or serologic parameters (e.g., elevated serum potassium) that may have contraindicated the use of certain medications. Second, by virtue of the observational study design, a causal association of AKI with medication underutilization could not be determined. Third, the baseline serum creatinine used for AKI determination was measured up to 6 months before angiography and may not have reflected patients’ true level of kidney function just before angiography, hence increasing the possibility of AKI misclassification. Finally, it is important to note that there is no definitive evidence supporting the universal use of β-blockers and ACEIs/ARBs, particularly after successful revascularization, in patients with unstable angina/non-ST elevation myocardial infarction (MI) without left ventricular dysfunction, hypertension, or another indication (7). Thus, some patients in the study by Leung et al. may not have had an unequivocal indication for these particular medications. However, this would not have explained the disproportionate underutilization of these agents in patients with AKI.
Table 1. Studies demonstrating lower use of coronary angiography in patients with CKD

<table>
<thead>
<tr>
<th>Authors</th>
<th>Clinical Presentation</th>
<th>Patients (N)</th>
<th>CKD (%)</th>
<th>Angiography (± PCI) in Patients with CKD versus No CKD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chertow et al.⁸</td>
<td>MI</td>
<td>57,284</td>
<td>26.3</td>
<td>25.2 versus 46.8</td>
</tr>
<tr>
<td>Han et al.⁹</td>
<td>NSTE ACS</td>
<td>45,343</td>
<td>14.5</td>
<td>47.6 versus 73.8</td>
</tr>
<tr>
<td>Goldenberg et al.¹¹</td>
<td>NSTE ACS</td>
<td>13,141</td>
<td>31.8</td>
<td>49.9 versus 67.8</td>
</tr>
<tr>
<td>Szummer et al.¹⁰</td>
<td>MI</td>
<td>57,477</td>
<td>33.3</td>
<td>33.2 versus 58.4⁹</td>
</tr>
<tr>
<td>Nauta et al.¹²</td>
<td>MI</td>
<td>12,087</td>
<td>25³</td>
<td>NS</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; NSTE, non-ST segment elevation; ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; NS, not specified; NSTEMI, non-ST segment elevation myocardial infarction.

¹Denotes the percentage of patients with NSTEMI who underwent revascularization based on CKD status, defined as eGFR<60 ml/min per 1.73 m².

²CKD defined based on eGFR<60 ml/min per 1.73 m².

Notwithstanding these limitations, the study by Leung et al. is of particular clinical importance because it highlights a highly unfortunate phenomenon faced by, and likely unknown to, patients with kidney disease: renalism (i.e., underutilization of diagnostic and therapeutic interventions in patients with kidney disease out of concern that they are more likely to do harm in this patient group). Renalism was initially described by Chertow and colleagues a decade ago in an observational study of >57,000 elderly patients with acute MI, of whom approximately one quarter had CKD (8). This study demonstrated that patients with CKD had >50% lower odds of undergoing coronary angiography compared to patients without CKD after adjusting for clinical predictors of this procedure. When angiography was performed, patients with CKD were less likely to undergo revascularization (54.7% versus 62.0%, P<0.001) than those without CKD. Although the odds of 1-year mortality among patients with CKD were nearly double that of patients without CKD, the odds of death at 1 year were nearly 50% lower among patients with CKD who underwent coronary angiography compared with patients with CKD who did not undergo angiography. The authors hypothesized that concern for the risk of contrast-induced AKI may have explained their findings.

There have since been at least four additional observational studies documenting lower utilization of coronary angiography in patients with CKD and ACS (Table 1) (9–12). Han et al. examined treatment and outcomes of approximately 45,000 patients with non-ST elevation ACS, 6560 (14.5%) of whom had moderate to severe CKD (9). In adjusted analyses, patients with CKD had >50% higher odds of in-hospital death than patients without CKD, yet 48% and 36% lower odds of undergoing coronary angiography and coronary artery bypass, respectively. Using a database of 13,141 patients with non-ST elevation ACS including 4181 (31.8%) with CKD, Goldenberg and colleagues demonstrated that patients with CKD were less likely to undergo coronary angiography (49.9% versus 67.8%, P<0.001) (11). Among patients with CKD, the performance of angiography was associated with 40% lower risk of 30-day mortality. Using a large Swedish registry, Szummer et al. documented lower revascularization rates among patients with eGFR<90 ml/min per 1.73 m² and non-ST elevation MI and progressively lower rates of revascularization with increasing severity of kidney disease (10). Remarkably, among patients with ST elevation MI, reperfusion was also less commonly utilized in patients with stage 4 CKD than in patients with intact kidney function, whereas patients with CKD were more likely to receive thrombolysis and less likely to undergo primary percutaneous intervention than patients without CKD. Collectively, these studies support the potential mortality benefit with coronary revascularization in patients with CKD compared to patients without CKD, including those with ST elevation MI.

Certain past studies also documented lower use of cardioprotective medications in patients with CKD after ACS. In the study by Han et al., patients with CKD were less likely to receive ACEIs, but had similar rates of β-blocker and lipid-lowering therapy at the time of hospital discharge compared with patients without CKD (9). Unlike the current findings of Leung et al., that study did not stratify patients by AKI status. More recently, Nauta and colleagues found that patients with stages 4/5 CKD presenting with MI were less likely to receive aspirin, β-blockers, and statins than patients with intact kidney function, although this study did not evaluate the association of AKI with use of these medications (12). Nonetheless, these prior studies support the presence of renalism related to use of cardioprotective medications.

Although these aforementioned studies and the current study by Leung et al. cannot, by virtue of their study design, prove the existence of renalism or fully explain the reasons for this form of medical bias appears to exist, they are consistent in demonstrating underutilization of effective diagnostic and therapeutic interventions in patients with kidney disease, acute and/or chronic. Although the risks for adverse effects related to angiography, coronary intervention, and certain cardioprotective medications may be increased in the setting of kidney disease, these risks can be effectively attenuated in most instances and should not routinely preclude the use of these interventions. As such, the identification of renalism, yet again, by Leung et al. should alert renal providers of the importance of informing our non-nephrology colleagues of the potential benefits of (and true level of risk associated with) these interventions in order to facilitate the unbiased implementation of indicated therapy in patients with acute and/or chronic kidney and cardiovascular disease.
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References

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