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EDITORIAL COMMENT

Should the AKI-MATRIX Trial Change Our Practice?*

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Acute kidney injury (AKI) after coronary intervention occurs in 10% to 15% of cases and is associated with a 3- to 5-fold increase in mortality (1). The question that remains is whether kidney injury is causal for this mortality or simply a marker of comorbidity and risk. Despite this, the area of contrast-induced AKI has been littered with promising interventions (e.g., N-acetylcysteine) that have been shown to be ineffective in large randomized trials.

Radial access for coronary intervention has been rapidly growing due to randomized trials showing improved outcomes (2,3). The MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox) trial (n = 8,404) was a randomized controlled trial that compared radial with femoral access for coronary angiography and percutaneous coronary intervention (PCI) in patients presenting with acute coronary syndrome (2). The overall trial showed a 17% reduction in net adverse clinical events and a 33% reduction in major bleeding (2). Furthermore, the risk of all-cause mortality was lower in the radial access group (relative risk [RR]: 0.72; 95% confidence interval [CI]: 0.53 to 0.99; p = 0.045) (2). The question that has been asked is whether the radial access site can influence the rate of AKI after coronary angiography and/or intervention.

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As shown in this issue of the *Journal,* AKI-MATRIX was a pre-specified analysis from the MATRIX trial that examined the effect of radial access versus femoral access on AKI after the procedure (4). AKI was defined as an absolute (>0.5 mg/dl) or a relative (>25%) increase in serum creatinine, which is a common definition among intervention trials to prevent AKI. By this definition, AKI was reduced 13% with radial access (15.4% in the radial access group vs. 17.4% in the femoral access group; odds ratio [OR]: 0.87; 95% CI: 0.77 to 0.98; p = 0.018). Dialysis during initial hospitalization was rare and was not significantly different between the groups. In multivariable analysis, radial access remained protective, whereas bleeding was an independent predictor of AKI.

There were significant subgroup interactions with benefit of radial access to prevent AKI that was predominantly observed in patients at the highest risk of AKI; this included those with a Mehran score >10 points and those with a reduced creatinine clearance. This would suggest that radial access is most beneficial for reducing AKI in those at highest risk.

The MATRIX trial had a factorial design, with a second randomization to either heparin or bivalirudin if patients underwent PCI. Surprisingly, there was a significant interaction in the evaluation of heparin versus bivalirudin, with no benefit in the bivalirudin group. A potential biological rationale was that if the mechanism for prevention of AKI was prevention of serious bleeding, then patients on bivalirudin might be at lower risk of bleeding and consequently would derive less benefit. It should be noted that there was no significant interaction for the clinical outcomes, such as major bleeding overall in the bivalirudin subgroup in MATRIX. The more likely explanation was that this was a chance finding with multiple subgroup comparisons.

WHAT IS THE MECHANISM OF BENEFIT OF RADIAL ACCESS FOR AKI?

One potential explanation is that radial access compared with femoral access reduces hemodynamically significant bleeding events, which prevents

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resultant renal hypoperfusion and renal injury. In the MATRIX trial, there was a reduction in Bleeding Academic Research Consortium (BARC) score 3 or 5 bleeding (1.6% in the radial group vs. 2.3% in the femoral group; rate ratio: 0.67; 95% CI: 0.49 to 0.92; p = 0.013) (2). However, because of the high frequency of AKI (17.4% in the femoral group), major bleeding was likely only causal in a minority of AKI cases. As a result, the bleeding reduction might only be a partial explanation for the benefit observed in AKI between radial and femoral access.

Another possibility was the reduction of aortic atheroemboli and cholesterol emboli by avoiding catheter manipulation near renal arteries with radial access instead of femoral access. Although direct measures, including imaging of the kidneys, or indirect measures, like eosinophilia, can be helpful to assess for embolization, such data were not reported as part of the AKI-MATRIX trial publication. Further analyses or studies looking at this issue would help us better understand the association between femoral arterial access catheterization procedures and AKI.

SHOULD THIS STUDY CHANGE OUR PRACTICE?

The overall results of the MATRIX trial and other studies have suggested a radial first approach by operators with the requisite expertise. However, some operators have been concerned about using the radial approach in patients with advanced renal insufficiency due to possible increased contrast use and potential requirement for a future fistula involving the radial artery for dialysis. However, contrast volume was not increased with radial use in MATRIX, and AKI was reduced with radial access, particularly in those with pre-existing renal insufficiency. The caveat is that operators in MATRIX had a high degree of expertise with radial access.

Radial access should be added to the proven methods for AKI prevention after coronary intervention such as pre-hydration. Despite the benefits observed, the high rates of AKI even in the radial group (15%) suggested that further therapies are needed to prevent AKI. Finally, it is unclear if measures that reduce AKI (>0.5 mg/dl or 25% increase in creatinine) can prevent dialysis.

In conclusion, this analysis of the MATRIX trial suggests that radial access is beneficial in preventing AKI after coronary angiography or intervention. This provides another piece of evidence supporting a radial first approach in patients with acute coronary syndrome who are undergoing coronary angiography or intervention.

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