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**DISCOVERY OF
BIOMARKERS THAT
DIAGNOSE KIDNEY
DISEASE
PROGRESSION AND
NOVEL PATIENT
MANAGEMENT
STRATEGIES NEEDED**

**NOW TO PREVENT PROGRESSIVE
KIDNEY DISEASE**

Reply to the Editor:

We read with great enthusiasm the comments of Kalisnik and colleagues on our article published in the *Journal*¹ as they reflected on future directions of our research. In our study,¹ we found that progression to acute kidney disease (AKD) by 2 to 4 weeks after cardiac surgery can be predicted by early postoperative serum creatinine changes when using the KDIGO (Kidney Disease: Improving Global Outcomes) acute kidney injury stages. AKI represents a subchronic disease state with significant implications for patient mortality, need for renal replacement therapy (as our study demonstrated), and quality of life.¹

We found that 67.9% of patients with previously normal kidney function and 81.4% of those with preexisting chronic kidney disease (CKD) had progression to AKD after cardiac surgery if postoperative acute kidney injury (AKI) was diagnosed according to the KDIGO definition. Moreover, we also found that among those patients in whom the diagnostic criteria for postoperative AKI were not met, 32.1% with normal preoperative kidney function and 18.6% with preexisting CKD developed progressive kidney disease (AKD). This is where the comments of Kalisnik and colleagues extend the scope of our study for our community. We are in agreement with their comments that we need to make every effort both to validate biomarkers that can add to the value of creatinine-based AKI definitions and to validate biomarkers that can discriminate patients with latent AKI who will have subsequent progression to

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AKD without showing signs of early creatinine elevation that meet the current diagnosis of AKI. Years of efforts to find a universal biomarker for all AKI (the “troponin equivalent” for kidney injury) have been met with limited success. It is perhaps time to focus on more disease (injury)-specific biomarkers that can help patients after cardiac surgery. It is becoming clearer, however, that a combination of biomarkers may yield better diagnostic precision.²

As research is progressing in the biomarker discovery field, this will offer us an opportunity to extend our studies to include novel biomarkers into our studies of patients for whom serum creatinine-based definitions alone were insufficient predictors.³ Identifying the populations at risk for AKD and CKD after cardiac surgery is paramount if we are to reduce kidney injury-related morbidity and mortality.

One note of caution is that although many of the biomarkers are showing good diagnostic ability of predicting AKI earlier than serum creatinine, they have been less successful in predicting disease progression.⁴ Other approaches may therefore be needed to enable reliable prediction of disease progression to AKD and CKD in the perioperative setting.⁴

We also agree that better monitoring of patients at risk for AKD and disease progression (those that we and others have identified) is essential. These patients will likely benefit from the early application of renal protective care bundles.⁵ This alone could significantly improve outcomes and also enable the use of future strategies of biomarker-based risk stratification (once developed).

We also need to be mindful of how some of the newer initiatives as enhanced recovery after surgery pathways, developed to promote early recovery (initially) for colorectal surgical patients, may affect kidney function. A recent article noted that when restricting fluids to achieve zero balance, the fluid-restricted patients had a higher rate of AKI.⁶ These pathways are now being implemented in cardiac surgery with the intention of optimizing intraoperative fluid balance. Their effects on kidney function will add additional complexity to our ongoing work. It is possible that enhanced recovery after surgery pathways in cardiac surgery may actually decrease the AKI rate by allowing optimal fluid administration rather than the enforcing traditionally extreme fluid restriction in cardiac surgery.

We agree with Kalisnik and colleagues that the expansion of our current research into the areas both of biomarkers and of the changing conditions of management affecting cardiac surgical patients is essential.

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