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**PROGRESSION OF
CARDIAC SURGERY–
ASSOCIATED ACUTE
KIDNEY INJURY INTO
ACUTE KIDNEY
DISEASE: A CASE FOR
ENHANCED EARLY
KIDNEY DIAGNOSTIC**

FINE-TUNING IMPLEMENTATION?

To the Editor:

We read with great interest the study of Mizuguchi and colleagues,¹ which identified patients with cardiac surgery–associated (CSA) acute kidney injury (AKI) at risk for progression to acute kidney disease (AKD) in a graded manner in which higher CSA-AKI stage predicted higher relative risk of AKD, resulting in higher in-hospital and 30-day mortalities in patients both with and without preexisting kidney disease. Of note, 67.9% of patients with AKD progressed from AKI of any stage, but a remarkable one-third of patients had AKD occur as like a bolt from the blue. These observations are in line with the findings of Bouma and associates,² who showed that even a 10% to 25% subclinical increase of creatinine after cardiac surgery translates into substantially higher long-term mortality. These studies urge us to adapt the CSA-AKI definition, not by revising the creatinine-based definitions only but also by detecting clinically silent kidney injury with latent potential for clinically relevant functional deterioration. As previously discussed,³ not replacing but rather adding a kidney injury biomarker might significantly improve the identification of those patients potentially amenable to targeted preventive care strategies, downgrading the frequency and severity of CSA-AKI. Indeed, Albert and colleagues⁴ have demonstrated that positive kidney injury biomarkers carry prognostic information regardless of acute renal function decline. In fact, the need for acute renal replacement therapy and in-hospital mortality were more than 5 times higher in patients with positive biomarkers signifying kidney injury that, because of current creatinine-based definitions, remained in subclinical range. Of note, even the

patients with clinically expressed kidney injury had significantly worse short- and long-term clinical outcomes when they had concomitant injury biomarker positivity.⁴ These findings were conceptually robust regardless of the biomarker used (eg, neutrophil gelatinase-associated lipocalin, midkine, or interleukin-6). Reassuringly, both subclinical AKI (under the creatinine detection threshold) and preclinical AKI (with injury biomarkers preceding diagnostic creatinine rise) were detected within several hours after cardiac surgery.⁴

As solely applying care bundles (avoiding nephrotoxic agents, discontinuation of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers for the first 48 hours after surgery, optimization of volume status) reverses progression of CSA-AKI relative to standard postoperative care,⁵ the study of Mizuguchi and colleagues,¹ opens a new perspective. To start with, how many cases of AKD would really appear as a bolt from the blue if we knew the extent of kidney injury preoperatively or very early after surgery? Finally, Mizuguchi and colleagues¹ are filling a gap by showing that progression of kidney deterioration after cardiac surgery within 2 to 4 weeks in itself dramatically impacts the short-term and late outcomes of surgery. We agree with their conclusion that those patients would benefit from more frequent watchful monitoring. We strongly believe that to improve our results of surgery, hand-in-hand with excellent surgery and in line with the global initiative of International Society of Nephrology, to eliminate preventable deaths due to AKI by 2025, we are challenged to implement postoperative kidney monitoring also qualitatively by quantification of kidney injury, consequently identifying high-risk groups that would benefit most from early application of care bundles.

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The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors should: • Include no more than 500 words of text, three authors, and five references. • Type with double-spacing. • See <http://jtcsc.etsnetjournals.org/misc/fora.shtml> for detailed submission instructions. • Submit the letter electronically via jtcvs.editorialmanager.com. Letters commenting on an article published in the JTCVS will be considered if they are received within 6 weeks of the time the article was published. Authors of the article being commented on will be given an opportunity of offer a timely response (2 weeks) to the letter. Authors of letters will be notified that the letter has been received. Unpublished letters cannot be returned.

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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.