ADULT

almost half of patients on the basis of a test with limited sensitivity and specificity. It is important at the health care level because, citing similarly flawed research, the recent ERAS (Enhanced Recovery After Surgery) guidelines, of which Dr Engleman is lead author, made this use of biomarkers a class IIa recommendation.[4] And the magic does not stop there—these ERAS guidelines were cited in the 2018 annual report of the $2.4 billion revenue biotech company that acquired Astute Medical (who developed this biomarker assay and for whom 3 of the authors consult) for $90 million.[5]

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Commentary: Is it time for a rapid kidney response team?

Richa Dhawan, MD, MPH, and Mark A. Chaney, MD

Acute kidney injury (AKI) after cardiac surgery remains a persistent problem, reliably increasing morbidity, hospital length of stay, cost, and mortality. For decades, researchers have tried to tackle the problem of diagnosis and treatment for AKI, with limited success. In this issue of the *Journal*, Engelman and colleagues,[1] a group of investigators from Massachusetts, reveal that identification of kidney stress through urinary biomarkers during the immediate postoperative period, followed by initiation of therapeutic interventions, may help.

This retrospective quality improvement project focused on 435 patients before and 412 patients after initiation of an AKI reduction protocol. Patients in the protocol had urinary biomarkers measured the morning after cardiac surgery. If markers were elevated above a predetermined level (indicating kidney stress), a multidisciplinary Acute Kidney Response Team was activated, and they initiated therapeutic interventions according to a predetermined

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CENTRAL MESSAGE

Identification of postoperative kidney stress through urinary biomarkers, followed by initiation of therapeutic interventions, may decrease incidence of stage 2 to 3 acute kidney injury.

algorithm that was based on Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The Acute Kidney Response Team was activated for 54% of the 412 patients. Stage 2 to 3 AKI (according to KDIGO criteria) occurred in 10 of 435 control patients (no AKI reduction protocol) yet in only 1 of 412 patients in the intervention group (89% relative reduction, statistically significant). These results indicate that early intervention and preemptive renal salvage techniques in patients at risk for kidney injury decrease progression to severe AKI.

In clinical practice, AKI is diagnosed on the basis of a decrease in urinary output or increase in serum creatinine, both of which lack sensitivity and specificity.[2,3] Serum creatinine is a late marker that takes 48 to 72 hours to

increase after renal injury, at which point substantial injury to the glomeruli has already occurred. Urinary output can be an unreliable marker (affected by nonrenal factors, such as hydration, cardiac output, medications, etc), especially in cardiac surgical patients after cardiopulmonary bypass. Other novel serum and urine biomarkers (neutrophil gelatinase–associated lipocalin, kidney injury molecule 1, interleukin 18, liver-type fatty acid–binding protein, angiotensinogen) have been identified in early AKI; however, their use is limited by cost, availability, and lack of clinical trials demonstrating an improvement in clinical outcome. Insulinlike growth factor–binding protein 7 (IGFBP7) and tissue inhibitor of metalloproteinases-2 (TIMP2; Nephro-Check; Astute Medical, Inc, San Diego, Calif) is the first test approved by the US Food and Drug Administration to identify patients at risk for development of AKI.[4] This presents a pivotal shift in the approach to management of AKI, because the clinician can anticipate and preemptively begin treatment, instead of waiting until organ damage has ensued.

This new concept of subclinical AKI (biomarker leak before development of AKI) requires further evaluation in clinical practice. Should all patients have biomarkers tested after cardiac surgery, or can we identify high-risk patients? Can patients with preexisting renal insufficiency benefit from implementation of KDIGO guidelines? Which phase of care is appropriate for an AKI reduction protocol, perhaps preoperative or intraoperative? This is an exciting time in AKI research, with tremendous implications for patient care. This important clinical trial by Engelman and colleagues[1] not only demonstrates that early goal-directed intervention can significantly decrease postoperative AKI, but also paves the way for larger clinical trials.

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