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(AKI) may have acute tubular damage that is associated with poor outcomes.² Kalisnik and colleagues and de Geus and colleagues³ have advocated that the routine use of biomarkers such as neutrophil gelatinase-associated lipocalin³ and cystatin C should be added to conventional creatinine as necessary perioperative tests, particularly in patients with existing renal dysfunction. Although a recent meta-analysis⁴ supports the potential benefits of biomarkers in the early detection (ie, subclinical) of CSA-AKI, there is still no evidence that using them to make this diagnosis alters outcomes. Therefore, although Kalisnik and colleagues have called for the routine use of subclinical AKI biomarkers to improve the accuracy of early detection of CSA-AKI, this would appear to be putting the cart before the horse. Use of these tests without systematic study would result in additional costs and clinical confusion because teams will be faced with new data in the absence of information on what to do with these results. It is hoped that detection of subclinical AKI will provide the bedside clinician “the best time to apply interventions or new therapeutics aimed at reducing CSA-AKI is a very early stage.” However, to date no proven intervention of this nature has been demonstrated and the notion remains theoretical. Therefore, we reiterate a previous statement⁵ that the routine clinical use of these biomarkers may not yet be ready for prime time and urge such important efforts as led by de Geus and colleagues³ and Kalisnik and colleagues to continue to systematically generate robust evidence that first supports the diagnostic value of these biomarkers and second evaluates therapeutic strategies for taking advantage of them. Until then, the “must do” in the field of CSA-AKI is working to obtain these crucial data.

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References

1. Thakar CV, Arrigain S, Worley S, Yared J-P, Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. *J Am Soc Nephrol*. 2005;16:162-8.
2. Haase M, Kellum JA, Ronco C. Subclinical AKI—an emerging syndrome with important consequences. *Nat Rev Nephrol*. 2012;8:735-9.
3. de Geus HRH, Ronco C, Haase M, Jacob L, Lewington A, Vincent J-L. The cardiac surgery-associated neutrophil gelatinase-associated lipocalin (CSA-NGAL) score: a potential tool to monitor acute tubular damage. *J Thorac Cardiovasc Surg*. 2016;151:1476-81.
4. Zhou F, Luo Q, Wang L, Han L. Diagnostic value of neutrophil gelatinase-associated lipocalin for early diagnosis of cardiac surgery-associated acute kidney injury: a meta-analysis. *Eur J Cardiothorac Surg*. 2016;49:746-55.
5. Arora RC, Rigatto C, Singal RK. Neutrophil gelatinase-associated lipocalin to predict cardiac surgery-associated acute kidney injury: a holy grail or just another fancy cup? *J Thorac Cardiovasc Surg*. 2016;151:1482-3.

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THE CARDIAC SURGERY--ASSOCIATED NEUTROPHIL GELATINASE--ASSOCIATED LIPOCALIN SCORE FOR POSTOPERATIVE

ACUTE KIDNEY INJURY: DOES SUBCLINICAL ACUTE KIDNEY INJURY MATTER?

Reply to the Editor:

We thank Dr Kalisnik and coauthors for their comments on our article.¹ They raise the question of whether the application of a damage marker-based scoring system will have any clinical implications in patients undergoing cardiac surgery. We share their view on our published, concept-introducing personal point of view. Future research will need to further investigate the effects of combining serum creatinine (SCr) and neutrophil gelatinase-associated lipocalin (NGAL) in clinical risk assessment and NGAL-guided clinical intervention studies. A recent multicenter pooled analysis showed that NGAL positivity in absence of SCr-based acute kidney injury (AKI) has an impact on short- and long-term patient- and kidney-related outcome measures.² Therefore, it is anticipated that efforts to reduce perioperative tubular damage will indeed be of clinical relevance.

Kalisnik and coauthors cite the study of McIlroy and colleagues³ as the basis for their concerns. That study showed that NGAL alone might not be an earlier marker compared with clinical AKI based on discrete Δ SCr values. In our view, this statement represents the main pitfall of current AKI-related biomarker research: the definition of the “outcome measure.” In terms of sensitivity, SCr-based

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AKI provides a serious advantage for SCr as a (functional) biomarker compared with a damage biomarker like NGAL. This is statistically defined as “incorporation” bias. The accuracy of damage markers will inevitably be lower compared with SCr that is incorporated into the definition of the endpoint. That is precisely the reason to propose a separate scoring system, such as the cardiac surgery–associated NGAL score (CSA-NGAL score), to increase the sensitivity of AKI diagnosis overall and also to cover the detection of what used to be subclinical AKI. The additional value of adding another functional biomarker along with SCr, such as plasma cystatin-C, to a diagnostic model for AKI based on the study by Spahillari et al,⁴ remains questionable.

Finally, another important aspect of the clinical implication of AKI biomarkers that must be addressed is whether they can help identify patients at the bedside without the risk of subsequent development of AKI.

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References

1. De Geus HR, Ronco C, Haase M, Jacob L, Lewington A, Vincent J-L. The cardiac surgery-associated neutrophil gelatinase-associated lipocalin (CSA-NGAL) score: a potential tool to monitor acute tubular damage. *J Thorac Cardiovasc Surg.* 2016;151:1476-81.
2. Haase M, Devarajan P, Haase-Fielitz A, Bellomo R, Cruz DN, Wagener G. The outcome of neutrophil gelatinase-associated lipocalin (NGAL)-positive subclinical acute kidney injury: a multicenter pooled analysis of prospective studies. *J Am Coll Cardiol.* 2011;57:1752-61.
3. McIlroy DR, Farkas D, Matto M, Lee HT. Neutrophil gelatinase-associated lipocalin combined with delta serum creatinine provides early risk stratification

for adverse outcomes after cardiac surgery: a prospective observational study. *Crit Care Med.* 2015;43:1043-52.

4. Spahillari A, Parikh CR, Sint K, Koyner JL, Patel UD, Edelstein CL. Serum cystatin C versus creatinine-based definitions of acute kidney injury following cardiac surgery: a prospective cohort study. *Am J Kidney Dis.* 2012;60:922-9.

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DOES A GOOD BEGINNING MAKE A GOOD END? THE IMPORTANCE OF BIOCOMPATIBILITY To the Editor:

We carefully read the interesting article by Allen and colleagues¹ suggesting that the most important goal of sternal closure is rigid fixation for both physiologic and economic reasons. They demonstrated significant improvement of sternal healing and fewer sternal complications in patients with sternal closure with rigid plate fixation than with conventional wire cerclage fixation. In their study, a simple computed tomographic scoring scale was applied to the various computed tomographic appearances and indicated that the sternal union rates with rigid fixation were 40.8% at 3 months and 80.2% at 6 months (15.7% and 67.0% with wire cerclage, respectively). Gradual healing was demonstrated by 6 months postoperatively; however, approximately 20% demonstrated incomplete healing with rigid fixation. Our first question is thus is there any other way to achieve union in addition to rigid fixation, or is it satisfactory?

We consider that from the viewpoint of long-term outcomes, biocompatibility as well as the mechanical properties plays a key role in the success of implants applied in the thoracic cage. On the basis of this concept, we have enriched insights about osteoinductive biomaterials. In plastic or orthopedic surgery, improvement of osteosynthesis has been reported with the additional use of bone graft and artificial osteoinductive materials on rigid fixation. These options have already been investigated in sternotomies by several authors. One author in our group² previously reported that bioabsorbable and rigid material that gradually changes to bony tissue showed mechanical strength comparable to that of titanium. Another³ demonstrated that an additional sternum-stabilizing procedure may reduce the incidence of postoperative sternal infection with the use of bioabsorbable material on conventional sternal wiring. The importance of biocompatibility was also implied by the exclusion criteria in the report of Allen and colleagues¹ that the patients with intraoperative use of