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**CARDIAC SURGERY--
ASSOCIATED NEUTROPHIL
GELATINASE-ASSOCIATED
LIPOCALIN SCORE FOR
POSTOPERATIVE ACUTE
KIDNEY INJURY: WHAT
IS THE CLINICAL**

IMPLICATION?

To the Editor:

Cardiac surgery-associated (CSA) acute kidney injury (AKI) affects roughly 40% of patients, yet as many as 6.5% require postoperative renal replacement therapy, with mortalities ranging from 30% to 80%.¹ The best time to apply interventions or new therapeutic modalities aimed at reducing CSA-AKI is at a very early stage; however, serum creatinine-based AKI is unfortunately not recognized at the time of the noxious event. We read with great interest the recent proposition to detect early acute tubular damage by applying the CSA neutrophil gelatinase-associated lipocalin (NGAL) score.² In that article, de Geus and colleagues² suggested a classification of acute tubular damage and postoperative therapy adjustments according to the extent of released NGAL.² We believe that the proposed endeavors represent a major step forward in reasoning as well as in detecting early subclinical AKI; however, McIlroy and associates³ recently found that the determination of AKI by NGAL alone might not provide earlier detection than determination of subsequent clinical AKI on the basis of discrete *delta* creatinine values.³ On the other hand, NGAL combined with creatinine exhibited superior clinical performance to any marker alone.³ Further, cystatin C provides additional information, with the potential to distinguish a higher-risk subgroup of patients, and it could even identify patients at risk of AKI in the presence of normal levels of creatinine.⁴ In our view, combining NGAL with conventional

creatinine, cystatin C, or even both is a “must do,” especially for patients with preexisting impaired kidney function, in whom the values of creatinine and NGAL are less representative.⁵ Such paired biomarker composites might enhance an earlier identification of acute tubular damage, providing the opportunity to institute highly targeted renal-protective strategies.

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**IS ROUTINE USE OF
RENAL INJURY
BIOMARKERS IN
CARDIAC SURGERY
PATIENTS PUTTING THE
CART BEFORE THE
HORSE?**

Reply to the Editor:

The search for a means to identify a reversible phase in new renal dysfunction after cardiac surgery is an important one because significant perioperative renal injury is associated with high rates of morbidity and mortality.¹ Recent information on cardiac surgery-associated acute kidney injury (CSA-AKI) has suggested that a further 15% to 20% of patients who do not fulfill current serum creatinine urine-based criteria for acute kidney injury

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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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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