Reply to “The Neutrophil-to-Lymphocyte Ratio: An Ideal Marker for Early Diagnosis and Short-Term Prognosis of Acute Kidney Injury?”

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We thank Drs. Lang and Schiffel for their interest in our recent study titled “Red Blood Cell Distribution Width and Neutrophil-to-Lymphocyte Ratio in Predicting Adverse Outcomes of Acute Kidney Injury in Hospitalized Patients” [1]. In this study, we provided evidence that neutrophil-to-lymphocyte ratio (NLR) and red blood cell distribution width (RDW) may have prognostic value for acute kidney injury (AKI) patients. Before going to details, we would make the statement that we essentially agree with Drs. Lang and Schiffel that NLR and RDW are not ideal or perfect biomarkers, rather they may be useful additions to the assessment and molecular parameters currently used in clinical settings.

In this retrospective, observational and cross-sectional study, it was difficult to control other potential confounding factors such as inflammation, despite conducting multivariate analysis. In addition, very few biomarkers of AKI were tested simultaneously with RDW or NLR in the patient cohort, making it impossible to compare with other biomarkers in this study. As such, our results do not negate the need and importance of clinical assessment in decision-making for the initiation of RRT. Currently, no single biomarker or test has an efficient predictive ability for patients at risk for AKI, progression of AKI, or mor-

talidity from AKI. Our analyses suggest that increased NLR and/or RDW is an independent risk factor for AKI progression, providing additional information for risk stratification. In this aspect, NLR and RDW are readily available for most patients in their blood cell count reports. Therefore, NLR and RDW may be used along with clinical assessment and other biomarkers, as suggested by our study and those of others [1–4].

The value of NLR was calculated by dividing the counts of neutrophils by lymphocytes. Different labs use different methods for measuring neutrophils and lymphocytes, resulting in a variation in the thresholds for high NLR among different studies. In our study, the cutoff of NLR was determined by receiver-operating curves instead of referring to previous studies. We acknowledge that NLR cutoff values may vary in different studies or hospitals, so interpreting thresholds for high NLR should be based on the cohort measurement instead of a defined value from previous studies.

The cause of AKI is heterogeneous and includes sepsis, renal ischemia, and exposure to nephrotoxic drugs, to name a few. In this study, we tried to include as many as possible of demographic factors and clinical characteristics and made multivariate analysis to test the prognostic

ability of NLR. The prognostic ability of NLR in AKI patients was valid, although demographic and clinical factors were needed to provide more accurate and specific information.

Selection bias may not be a significant factor in our study because we analyzed all hospitalized patients from January 1, 2016, to June 30, 2016, in the Second Xiangya Hospital and all AKI patients were identified according to the KDIGO guidelines in 2012 [5] except urine output criteria. The cutoff value of NLR was proposed in our study. The reference range of NLR in healthy population was not determined in this study because healthy subjects were not included.

Very few studies compared NLR with established biomarkers of inflammation or infection. In the future, a prospective study may investigate the relationship. Our study suggested the predictive ability of NLR in AKI patients. NLR has been reported as a predictor and prognostic marker in other diseases [6, 7], although the underlying mechanism remains unclear.

Finally, we would reiterate that we essentially agree with the comments by Drs. Lang and Schiff. Our work indicates NLR is a risk factor for predicting RRT requirement, but this does not mean NLR can be used as a single, predictive biomarker. It is important to use it in combination with clinical assessment and related laboratory tests.

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Statement of Ethics

This research was approved by the Ethics Committee of the Second Xiangya Hospital at Central South University (Protocol Reference No. 2013-050-01). Written informed consent was not required because of the nonintervention and retrospective chart review design.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

J.Z. drafted the manuscript, and Z.D. revised the manuscript.

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