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Biomarkers of Delirium Duration and Delirium Severity: A Reply

Sikandar H Khan, DO, MS[1,2], **Anthony J. Perkins, MS**[3], **Sujuan Gao, PhD**[3], **Babar A. Khan, MD, MS**[1,4,5,6]

[1]Division of Pulmonary, Critical Care, Sleep and Occupational Medicine, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN

[2]IU Center of Aging Research, Regenstrief Institute, Indianapolis, IN

[3]Department of Biostatistics, Indiana University School of Medicine, Indianapolis, IN

[4]Indiana University Center of Health Innovation and Implementation Science, Indianapolis, IN

[5]Division of Geriatrics and General Internal Medicine, Department of Internal Medicine, Indiana University School of Medicine, Indianapolis, IN

[6]Sandra Eskenazi Center for Brain Care Innovation, Eskenazi Hospital, Indianapolis, IN

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Letter to the Editor

We would like to thank the authors for their insightful comment on our work measuring the association among biomarkers of inflammation, neuroprotection and astrocyte activation and delirium duration and severity in critically ill patients (1-2). As noted by the authors, 52% of patients in our cohort were admitted to the intensive care unit (ICU) with acute respiratory failure and/or sepsis. The authors highlight the limitations of patient-level prognostication using blood biomarkers cleared via continuous renal replacement (CCRT), a therapy frequently utilized in patients with sepsis (3). They also caution about the interpretation of S100B as a delirium biomarker in patients with acute neurologic injury. We agree with Honore et al. that future studies should measure the temporal effects of CRRT on reliability of these biomarkers and their relationship with delirium outcomes. While our study did not conduct sensitivity analyses excluding patients on CRRT, our methodological design may have limited the effects of dialysis on our biomarker analyses for the following reasons. First, we analyzed the association of biomarkers collected at a single timepoint, rather than multiple timepoints. These blood samples were collected around admission to the ICU (within 24 hours of enrollment) when patients are less likely to have received a long duration of CRRT. Second, our biomarker analyses showed significant association with delirium

Corresponding Author Information: Sikandar H. Khan, DO, MS, Regenstrief Institute - IU CAR, 1101 West Tenth Street, Indianapolis, IN 46202, (317) 274-9427, sikhan@iu.edu.

Name of the Institution Where the Work was Performed:
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duration and severity even after adjustment for sepsis diagnoses, and Acute Physiology and Chronic Health Evaluation-II scores (which includes a variable for acute renal failure). Third, as shown in the supplementary materials accompanying the original study, excluding patients with neurologic injury (including those with traumatic brain injury) from the analyses did not change the results. Specifically, S100B levels measured at ICU admission remained associated with fewer delirium/coma free days by 1 week and 30 days post-enrollment. Levels of S100B from ICU admission also remained associated with increased mean delirium severity at one week and hospital discharge, and higher hospital mortality (3). Finally, our findings are similar to studies evaluating biomarkers in non-critically ill patients with delirium (4-5). In these studies, C-Reactive Protein levels measured before and after surgery were associated with increased delirium incidence, duration and severity,(4) and higher levels of S100B were associated with increased incidence of delirium (5). Nevertheless, we agree with the authors that further studies of the reliability of circulating biomarkers and their relationship with delirium duration and severity in patients undergoing renal replacement therapies are needed.

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