Critical Care

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Reply to: angiotensinogen: a new era beyond lactate as a biomarker?

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Dear Editor,

We appreciate the comments from Drs. Shen and Ding [1] regarding our brief research report, "*Stronger association of intact angiotensinogen with mortality than lactate or renin in critical illness: post-hoc analysis from the VICTAS trial* [2]. Their letter addresses several excellent points about the extent and severity of septic shock in the VICTAS cohort in relation to serum lactate. We agree that the serum levels of lactate were not excessively elevated in our patient population which likely reflects the fact that most of the VICTAS patients were not in severe septic shock. Nonetheless, there was significant mortality in this cohort of sepsis patients that was strongly associated with circulating levels of intact angiotensinogen, suggesting under these conditions that intact angiotensinogen as a biomarker outperformed both renin and lactate according to model performance metrics including area under the curve and the Youden index. Thus, we believe intact angiotensinogen may constitute an additional clinical tool in the care of patients in early sepsis or septic shock. We previously showed that active renin also associated with mortality in this cohort consistent with the recent literature that renin may be a predictor of disease severity that outperforms lactate, as well as a potential indicator for exogenous Ang II treatment to maintain blood pressure and tissue perfusion [3–5]. As renin converts angiotensinogen to Ang I and then Ang II through ACE, our results suggest that reduced levels of intact angiotensinogen through excessive renin activity and/or impaired synthesis may also be an indicator of disease severity and may further reveal the need for exogenous Ang II therapy in sepsis patients. The accurate and rapid assessment of plasma Ang II levels is not currently feasible, whereas assay of intact angiotensinogen and active renin or their combination may be a more suitable point-of-care test for critical care patients [2]. We also agree that additional time points in the course of disease are necessary in the assessment of angiotensinogen and other components of the renin–angiotensin–aldosterone system (RAAS) in the critically ill, as well as more detailed assessment of optimal clinical thresholds for each. Indeed, a clinical trial in septic shock patients that directly arose from our present study is currently under way at Wake Forest University School of Medicine that is designed to address several of the issues raised by Drs. Shen and Ding regarding the response of the circulating RAAS and serum lactate.

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Consent for publication
Not applicable.

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