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# Reply to “Potential confounders in linking elevated S100A8/A9 to left ventricular dysfunction in septic shock patients”

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We would like to address the comments by Honoré et al. [1] referring to our recently published paper “Therapeutic S100A8/A9 blockade inhibits myocardial and systemic inflammation and mitigates sepsis-induced myocardial dysfunction” [2].

In their commentary, Honoré et al. highlighted the importance of renal replacement therapy (RRT) as a potential factor that might have impacted the measurement of plasma S100A8/A9 in our study. Since the molecular weight of the S100A8/A9 heterodimer (24 kDa) is lower than the cutoff value of the extracorporeal purification membrane (35–40 kDa), the use of RRT might partly remove S100A8/A9 from the circulation, leading to falsely low values of the protein in plasma. The authors of the comment argue that this might have led to erroneous conclusions regarding the positive relationship between elevated plasma S100A8/A9 and the development of sepsis-induced myocardial dysfunction (SIMD)

demonstrated by our study [2]. The concern regarding the influence of RRT on biomarker values in the context of sepsis is not specific for S100A8/A9 and has previously been expressed by Honoré et al. in reference to other studies [3].

We agree that biomarker washout by RRT is an important factor that might impact both clinical studies and clinical practice, regardless of the initial pathology leading to renal failure. However, we would like to stress that in our study, S100A8/A9 was measured in plasma collected within 12 h from admission to the intensive care unit (ICU), as mentioned in the Methods section [2]. At this early time point, none of the sepsis patients included in the cohort had received RRT. Subsequently, the results of our study showing that plasma S100A8/A9 is elevated in severe sepsis patients with SIMD have not been impacted by the use of RRT and remain valid.

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## Abbreviations

RRT	Renal replacement therapy
SIMD	Sepsis-induced myocardial dysfunction
ICU	Intensive care unit

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## Author contributions

GJ and AS drafted the response. HA and MC verified the data and reviewed the manuscript. All authors approved the final version.

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## Availability of data and materials

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## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

Michelle Chew is a member of the editorial board of *Critical Care*.

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## References

1. Honore PM, Perriens E, Blackman S. Potential confounders in linking elevated S100A8/A9 to left ventricular dysfunction in septic shock patients. *Crit Care*. 2023;27(1):480.
2. Jakobsson G, Papareddy P, Andersson H, Mulholland M, Bhongir R, Ljungcrantz I, Engelbertsen D, Bjorkbacka H, Nilsson J, Manea A, et al. Therapeutic S100A8/A9 blockade inhibits myocardial and systemic inflammation and mitigates sepsis-induced myocardial dysfunction. *Crit Care*. 2023;27(1):374.
3. Honore PM, Redant S, De Bels D. Reliability of biomarkers of sepsis during extracorporeal therapies: the clinician needs to know what is eliminated and what is not. *Crit Care*. 2020;24(1):553.

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