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Potential confounders in linking elevated S100A8/A9 to left ventricular dysfunction in septic shock patients

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Jakobsson et al. investigated the role of S100A8/A9, a pro-inflammatory alarmin, in sepsis-induced myocardial dysfunction (SIMD). They concluded that elevated S100A8/A9 is associated with the development of left ventricular (LV) dysfunction in severe sepsis patients [1].

Patients 18 years of age and older admitted to the intensive care unit (ICU) with septic shock (per Sepsis III) were included in this study [1]. Thirty-five out of sixty-two (56%) patients had LV dysfunction. Plasma S100A8/A9 was significantly higher in LV dysfunction patients (20.1 µg/mL vs. 7.4 µg/mL, $P=0.009$). Nearly half of critically ill patients, especially with septic shock, develop acute kidney injury (AKI), and 20–25% require renal replacement therapy (RRT) within the first ICU week [2]. Considering S100A8 (10.8 kDa) and S100A9 (13.2 kDa) molecular weights, as well as the molecular weight of the S100A8/A9 heterodimer (24 kDa) [3], continuous RRT (CRRT)—which has a cut-off value of 35–40 kDa—might eliminate these molecules, impacting bio marker levels, and potentially leading to artificially decreased S100A8/A9 levels [4, 5]. The absence of CRRT/RRT in the criteria and its impact on each group is a potential major comfounding factor that could heavily influence results [4, 5]. In a clinical setting, this could lead to inaccurate prognosis and unadapted support. It is necessary that a sensitivity analysis should be done after the exclusion of CRRT/RRT patients to clarify the performance of these biomarkers when they are not artificially removed by an extracorporeal purification technique [5].

Abbreviations

LV	Left ventricular
ICU	Intensive care unit
AKI	Acute kidney injury
RRT	Renal replacement therapy
CRRT	Continuous renal replacement therapy

Acknowledgements
Not applicable.

Author contributions
PMH designed the paper. PMH, EP, and SB participated in drafting and reviewing. PMH, EP, and SB read and approved the final version of the manuscript.

Funding
Not applicable.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare to have no competing interests.

This comment refers to the article available online at https://doi.org/10.1186/s13054-023-04652-x.

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Received: 27 November 2023 Accepted: 29 November 2023
Published online: 06 December 2023

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