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

Patrick M. Honore<sup>1\*</sup>, Emily Perriens<sup>2</sup> and Sydney Blackman<sup>2</sup>

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 confounding 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

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\*Correspondence:

Patrick M. Honore  
patrick.honore@chuclnaminur.uclouvain.be

<sup>1</sup> CHU UCL Godinne Namur, UCL Louvain Medical School, Campus Godinne, Avenue G Thérassé 1, 5530 Yvoir, Belgium

<sup>2</sup> ULB University, Brussels, Belgium



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