Critical Care Medicine
July 2026 • Volume 54 • Number 7 • Pages 1837–1838

LETTER TO THE EDITOR

Plasma Levels of Soluble ST2 Reflect Extrapulmonary Organ Dysfunction and Predict Outcomes in Acute Respiratory Failure: Beware of Potential Confounders

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KEYWORDS: acute kidney injury; acute respiratory distress syndrome; acute respiratory failure; confounders; kidney replacement therapy/continuous kidney replacement therapy; ST2

To the Editor:

The recent article by Labar et al (1), published in the issue of *Critical Care Medicine*, is robust and of significant merit, nevertheless a few aspects of the discussion warrant further consideration.

The authors report that "plasma sST2 levels were higher in non-COVID acute respiratory failure (ARF) (863) patients compared with COVID-19 (569) patients ($p < 0.05$)." This interpretation warrants careful reconsideration.

Among patients with ARF, including acute respiratory distress syndrome, acute kidney injury develops in approximately 35% of cases, and nearly 17% require kidney replacement therapy (KRT) within the first week of ICU admission (2, 3).

Soluble ST2 (sST2) has a molecular weight of approximately 30 kDa (4). Contemporary continuous kidney replacement therapy (CKRT) membranes are capable of removing solutes up to 40 kDa (4). Accordingly, sST2 may be at least partially cleared by convective mechanisms during CKRT and potentially also by adsorption when highly adsorptive membranes are used (4). Differences in the use, timing, or modality of KRT/CKRT between the non-COVID and COVID groups could therefore substantially influence measured plasma sST2 concentrations.

Consequently, circulating sST2 levels may not exclusively reflect the underlying pulmonary injury (COVID-19 vs. non-COVID etiologies), but may also be affected by extracorporeal clearance. The lower sST2 concentrations observed in patients with COVID-19 could thus be partially attributable to differences in KRT/CKRT exposure between groups. However, the study does not report the proportion of patients receiving KRT or CKRT in either cohort.

To more accurately assess the discriminatory performance of sST2, a sensitivity analysis excluding patients treated with KRT/CKRT would be advisable. Such an approach would help clarify the biomarker's behavior in the absence of extracorporeal removal and strengthen the validity of the conclusions (5).

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DOI: 10.1097/CCM.0000000000007142

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Drs. Lefèvre and Honore designed the article. All authors participated in drafting and reviewing. All authors read and approved the final version of the article.

The authors have disclosed that they do not have any potential conflicts of interest.

REFERENCES

1. Labar AS, Ulrich BC, Lovelace TC, et al: Plasma levels of soluble ST2 reflect extrapulmonary organ dysfunction and predict outcomes in acute respiratory failure. *Crit Care Med* 2025; 53:e1567–e1580
2. Park BD, Faubel S: Acute kidney injury and acute respiratory distress syndrome. *Crit Care Clin* 2021; 37:835–849
3. Peters E, Antonelli M, Wittebole X, et al: A worldwide multicentre evaluation of the influence of deterioration or improvement of acute kidney injury on clinical outcome in critically ill patients with and without sepsis at ICU admission: Results from the intensive care over nations audit. *Crit Care* 2018; 22:188
4. Honoré PM, Jacobs R, De Waele E, et al: Evaluating sepsis during continuous dialysis: Are biomarkers still valid? *Blood Purif* 2014; 38:104–105
5. 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; 24:553