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LETTER

Methodological and Clinical Gaps in Biomarker-Guided Weaning for Sepsis-Induced ARDS [Letter]

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Dear editor

We read with interest the narrative review by Muhoza et al[1] on circulating and respiratory biomarkers in sepsis-induced ARDS While the paper covers considerable ground, several issues that bear on its clinical applicability were not addressed.

First, the review draws heavily on COVID-19 ARDS cohorts to support thresholds for sRAGE, suPAR, and IL-6, without acknowledging that SARS-CoV-2–induced lung injury is immunobiologically distinct from classical bacterial sepsis-induced ARDS. The two conditions differ in endothelial injury patterns, type I interferon signalling, and complement activation,[2] and cutoffs derived from one context may not translate reliably to the other. A clearer separation of evidence by etiology would substantially strengthen the review's conclusions.

Second, the manuscript proposes specific diagnostic thresholds — such as suPAR ≥14.01 ng/mL — without discussing how renal function affects biomarker clearance. AKI complicates up to 40–50% of sepsis-induced ARDS cases,[3] and suPAR, sRAGE, and presepsin are all partially renally cleared. Elevated plasma concentrations in oliguric patients may therefore reflect impaired clearance rather than inflammatory burden,[4] a distinction with direct implications for bedside decision-making.

Third, the review endorses IL-6 as a key prognostic marker while simultaneously recommending IL-6 receptor antagonists and corticosteroids as standard therapy — an inconsistency that is not reconciled. Active treatment with tocilizumab or dexamethasone suppresses the very markers proposed for monitoring, and declining levels may reflect pharmacological suppression rather than genuine clinical improvement.[5] Rather than relying on absolute concentration thresholds, future studies should examine the rate of biomarker change over 24–48 hours, which has been shown to carry independent prognostic information even in treated patients.[6]

Fourth, the evidence presented is almost entirely cross-sectional. Serial measurements of IL-6, Ang-2, and syndecan-1 have been shown to outperform single time-point values in predicting weaning outcomes and mortality,[7,8] yet no guidance is offered on when during a spontaneous breathing trial biomarkers should be measured or how they might be integrated with clinical indices such as rapid shallow breathing index into a composite prediction model.[9,10] Beyond study design, practical barriers receive little attention: without rapid point-of-care assays,[11] many of these markers will remain research tools rather than clinical instruments.

Finally, the review attributes geographic variation in ARDS prevalence to healthcare-system factors but overlooks two sources of biological heterogeneity that are equally important. Host genetic variation — including SNPs in the AGER gene encoding sRAGE and in the IL6 promoter — can drive baseline biomarker differences unrelated to disease severity,[12] potentially leading to misclassification in precision-medicine frameworks. Separately, the exclusive focus on humoral markers neglects the mechanical dimension of weaning failure: sepsis-induced diaphragmatic dysfunction contributes substantially to extubation failure and cannot be captured by circulating proteins alone. Incorporating diaphragm ultrasound-derived indices or neural respiratory drive measurements alongside biomarker panels[13] would provide a more complete picture of a patient's readiness for liberation from mechanical ventilation.

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We thank the authors for a thorough review of a clinically important topic and hope these remarks are of use.

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Data sharing is not applicable to this article as no data were created or analyzed in this communication.

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References

1. LS MBG, Niyonkuru E, Sun T. Circulating and respiratory biomarkers in sepsis-induced ARDS: diagnostic and prognostic insights – a narrative review. *J Inflamm Res*. 2026;19:1–35. doi:10.2147/JIR.S571504
2. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in covid-19. *N Engl J Med*. 2020;383(2):120–128. doi:10.1056/NEJMoa2015432
3. Peerapornratana S, Manrique-Caballero CL, Gómez H, Kellum JA. Acute kidney injury from sepsis: current concepts, epidemiology, pathophysiology, prevention and treatment. *Kidney Int*. 2019;96(5):1083–1099. doi:10.1016/j.kint.2019.05.026
4. Jabaudon M, Blondonnet R, Pereira B, et al. Plasma sRAGE is independently associated with increased mortality in ARDS: a meta-analysis of individual patient data. *Intensive Care Med*. 2018;44(9):1388–1399. doi:10.1007/s00134-018-5327-1
5. Meduri GU, Tolley EA, Chrousos GP, Stentz F. Prolonged methylprednisolone treatment suppresses systemic inflammation in patients with unresolving acute respiratory distress syndrome: evidence for inadequate endogenous glucocorticoid secretion and inflammation-induced immune cell resistance to glucocorticoids. *Am J Respir Crit Care Med*. 2002;165(7):983–991. doi:10.1164/ajrccm.165.7.2106014
6. Schuetz P, Birkhahn R, Sherwin R, et al. Serial procalcitonin predicts mortality in severe sepsis patients: results from the multicenter procalcitonin monitoring sepsis (MOSES) Study. *Crit Care Med*. 2017;45(5):781–789. doi:10.1097/ccm.0000000000002321
7. Yang P, Iffrig E, Harris F, Holder AL, Martin GS, Esper AM. Serial measurements of protein biomarkers in sepsis-induced acute respiratory distress syndrome. *Crit Care Explor*. 2022;4(10):e0780. doi:10.1097/cce.0000000000000780
8. Liu Z, Li J, Chen D, et al. Dynamic Interleukin-6 level changes as a prognostic indicator in patients with COVID-19. *Front Pharmacol*. 2020;11:1093. doi:10.3389/fphar.2020.01093
9. Trivedi V, Chaudhuri D, Jinah R, et al. The usefulness of the rapid shallow breathing index in predicting successful extubation: a systematic review and meta-analysis. *Chest*. 2022;161(1):97–111. doi:10.1016/j.chest.2021.06.030
10. Stivi T, Padawer D, Dirini N, Nachshon A, Batzofin BM, Ledot S. Using artificial intelligence to predict mechanical ventilation weaning success in patients with respiratory failure, including those with acute respiratory distress syndrome. *J Clin Med*. 2024;13(5):1505. doi:10.3390/jcm13051505
11. Plebani M. Point-of-care testing in the era of value-based laboratory medicine. *Clin Chem Lab Med*. 2026. doi:10.1515/cclm-2026-0309
12. Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. *Lancet*. 2021;398(10300):622–637. doi:10.1016/s0140-6736(21)00439-6
13. Dres M, Dubé BP, Mayaux J, et al. Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. *Am J Respir Crit Care Med*. 2017;195(1):57–66. doi:10.1164/rccm.201602-0367OC

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