Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Response to: MR-proADM has a good ability to predict mortality in critically ill patients with SARS-CoV-2 pneumonia: Beware of some potential confounders!

To the editor:

We appreciate the comments of professor Honore and colleagues concerning the potential confounding effect of continuous renal replacement therapy (CRRT) on the validity of mid-regional proadrenomedullin (MR-proADM) measurements in severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) pneumonia patients. As MR-proADM can be removed by CRRT and non-survivors were treated with CRRT three times more compared with survivors, the letter authors propose that CRRT could have artificially lowered MR-proADM levels and introduced confounding.

We note that professor Honore and colleagues have reversed the key results in their letter: Our study showed MR-proADM to be lower rather than higher in survivors (1.01 vs. 1.88 in survivors vs. non-survivors at baseline). The true MR-proADM difference between survivors and non-survivors would therefore be larger rather than smaller.

Nevertheless, the authors make an interesting point and we ourselves have mentioned that MR-proADM levels could decrease faster during CRRT [1]. Nine out of 105 patients (8.6%) received CRRT during ICU stay and it was used three times more (16.7% vs 5.3%) in the non-survivor group. However, biomarkers were collected during the first seven days and only two patients were on CRRT when biomarkers were collected [1]. When we excluded these two patients the difference in baseline MR-proADM between survivors and non survivors did not change (median value 1.01 nmol/L (IQR 0.80–1.28) vs. median value 1.88 nmol/L (IQR 1.29–2.61), $p < 0.001$).

In all, we are confident that this specific biasing mechanism did not artificially inflate the difference between survivors and non-survivors. Even so, we need to account for other potential biases. By performing a single-centre prospective observational study with a limited number of patients we may have introduced selection, collider, and observational bias, which may have led to underestimation of the prognostic performance of MR-proADM. We therefore plan to perform a larger multi-centre study in the near future.

Authors's contributions

JO, HJG, DL, AG designed the paper. All authors participated in drafting and reviewing. All authors read and approved the final version of the manuscript.

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Reference

[1] van Oers JAH, Kluiters Y, Bons JAP, de Jongh M, Pouwels S, Ramnarain D, et al. Endothelium-associated biomarkers mid-regional proadrenomedullin and C-terminal proendothelin-1 have good ability to predict 28-day mortality in critically ill patients with SARS-C0V-2 pneumonia: A prospective cohort study. J Crit Care. 2021. https://doi.org/10.1016/j.jcrc.2021.07.017 Jul 20:S0883–9441(21)00157-x.

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