Response to 'Procalcitonin is a biomarker for disease severity rather than bacterial coinfection in COVID-19' by Heer *et al*.

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We thank Heer *et al*. for their comment (p. 315) on our paper on the role of procalcitonin in the management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. Indeed, as concluded in their paper [1], procalcitonin measures during ICU stay are associated with ICU mortality [2], whereas their accuracy in identifying bacterial coinfections is low within the current pandemic context [2]. Other markers have been proposed such as the ferritin to procalcitonin ratio [3].

While reaching similar conclusions, we observed some different methodological approaches in the above-mentioned paper [1] that should be taken into account when assessing the results.

The first difference is that while our paper studies the accuracy of procalcitonin measures at hospital admission, Heer *et al*. [1] studied procalcitonin peak concentrations measured as far as 5 ± 4 days from admission. Moreover, they did not specify whether the studied values of procalcitonin were systematically sampled before the identified positive cultures or if positive cultures could have been drawn before the studied procalcitonin values. In our view, these two differences weaken any conclusion that could be made on the diagnostic value of procalcitonin in supporting the use of antibiotics in suspected bacterial coinfections.

Second, it can be observed that a logarithmic transformation of procalcitonin values was used by Heer *et al*. [1], whereas most of the literature relies on nontransformed procalcitonin values. This might represent a potential limitation for two reasons. First, logarithmic transformation might not be practical when implementing procalcitonin in clinical practice. Second, logarithmic transformation, as any data transformation, should be applied very cautiously as the results of standard statistical tests performed on log-transformed data are often not relevant for the original, nontransformed data [4].

Finally, the association of procalcitonin to mortality was inferred based on a multivariable regression model that was constructed on a backward selection that excluded relevant measured covariates such as age, Charlson comorbidity index or mechanical ventilation. Backward selection is discouraged as it is associated with methodological weaknesses, whereas historical selection of confounders might have been more appropriate when selecting covariates for multivariable regressions [5]. Excluding age, Charlson comorbidity index or mechanical ventilation when studying mortality might represent a possible limitation of the analysis.

Altogether, as suggested by Heer *et al*. [1], clinicians should not rely on procalcitonin values alone to decide on whether initiating antibiotics in patients with suspected infections during the current SARS-CoV-2 pandemic.

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Conflicts of interest

There are no conflicts of interest.

References

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What is the cause of increased mortality in normothermic patients with suspected infection?

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We would like to congratulate Schuttevaer *et al*. [1] on their excellent paper regarding treatment delays in patients with suspected infections in the emergency department. The authors clearly demonstrate significant associations between body temperature, the initiation of antibiotic therapy, and 30-day mortality in their cohort. We appreciate the hypothesis that body