Critical Care

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Response to: Understanding the null hypothesis (H0) in non-inferiority trials

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See related Letter by Mallat, https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1685-2

We thank Dr. Mallat for their interest in our study of stepwise lactate kinetics-oriented hemodynamic therapy and for putting forward a statistical problem [1]. Central venous oxygen saturation (ScvO2)-targeted therapy was recommended by the Surviving Sepsis Campaign (SCC) guidelines in 2012 [2] and we initially envisaged that the stepwise lactate kinetics strategy was, at least, not inferior to the ScvO2 target strategy. Therefore, the design of non-inferiority analysis was adopted at the beginning of the trial.

We rechecked and recalculated the data by non-inferiority and superiority test. The lactate kinetics group mortality rate (P1) was 18.3% and the Scvo2 group mortality rate (P2) was 27.9%. The standard error for the mortality difference between the two groups was 0.0441, and thus the mortality difference was −0.0944 (95% confidence interval −0.1809 to −0.0080). The upper limit of the interval is less than 0, and thus the superiority conclusion is established. At this point, regardless of the non-inferior value (0.15 or 0.10), non-inferior conclusions must be established.

Additionally, the non-inferiority threshold of 10% is indeed more reasonable according to a previous study [3].Therefore, regardless of whether the non-inferiority threshold is set at 10% or 15%, no effect on the final conclusion was seen in this study.

Last, but not the least, the latest sepsis guidelines released by the SCC in 2016 have weakened early goal-directed therapy (EGDT) and highlighted the importance of normalization of lactate [4], which also supports the conclusion we draw that stepwise lactate kinetics-oriented hemodynamic therapy can reduce mortality in patients with sepsis-associated hyperlactatemia compared with ScvO2-oriented therapy.

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Abbreviations
EGDT: Early goal-directed therapy; SCC: Surviving Sepsis Campaign;
ScvO2: Central venous oxygen saturation

Availability of data and materials
Not applicable.

Authors' contributions
XZ, LS, and DL drafted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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