

LETTER

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Response to “Association between metformin use prior to admission and lower mortality in septic adult patients with diabetes mellitus: beware of potential confounders”

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To the Editor:

We thank Dr. Honore and his colleagues for their attention on our study in *Critical Care* [1]. First, we agree with their point that RRT has a protective effect on the mortality of patients with metformin (MET)-associated lactic acidosis [2]. However, there are some reasons to demonstrate that the lower mortality in septic patients with diabetes is due to MET treatment, rather than the metformin eliminated by RRT. First, the study of Doeniyas-Barak et al. [3], one of the included studies in our meta-analysis [1], showed that the use of RRT between the MET-treated population and non-MET users was 38.6% and 21.2%, but there was no difference between the two groups ($p = 0.13$). More importantly, after removing this included study [3], we reworked the pooled effect of the remaining four studies and the result was consistent with our meta-analysis [1]. Furthermore, the study of Jochmans et al. [4] showed the use of RRT is higher in non-MET users than MET users (18.2% vs. 17.1%), but it also indicated that the protective effect of MET use in septic patients with diabetes. In addition, the metformin treatment can improve the liver injury and inflammatory response and even ameliorate the mortality of septic mice in our ongoing experimental study. Finally, we believe that studies in the future to assess the association between metformin and mortality in septic patients with diabetes will be performed.

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None.

Authors' contributions

LHY and DXF designed the study. STW edited the English text of this manuscript. All authors participated in drafting and reviewing the manuscript. The authors read and approved the final version of the manuscript.

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Availability of data and materials

Not applicable.

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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References

1. Liang H, Ding X, Li L, Wang T, Kan Q, Wang L, Sun T. Association of preadmission metformin use and mortality in patients with sepsis and diabetes mellitus: a systematic review and meta-analysis of cohort studies. *Crit Care (London)*. 2019;23(1):50.
2. Peters N, Jay N, Barraud D, Cravoisy A, Nace L, Bollaert PE, Gibot S. Metformin-associated lactic acidosis in an intensive care unit. *Crit Care (London)*. 2008;12(6):R149.

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3. Doenyas-Barak K, Beberashvili I, Marcus R, Efrati S. Lactic acidosis and severe septic shock in metformin users: a cohort study. *Crit Care* (London). 2016;20:10.
4. Jochmans S, Alphonsine JE, Chelly J, Vong LVP, Sy O, Rolin N, Ellrodt O, Monchi M, Vinsonneau C. Does metformin exposure before ICU stay have any impact on patients' outcome? A retrospective cohort study of diabetic patients. *Ann Intensive Care*. 2017;7(1):116.

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