Critical Care

CORRESPONDENCE

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Authors' reply to the comment from Uchida et al.

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We thank Uchida and Hayashi for their comments on our study [1]. As pointed out by Uchida et al. [2], we acknowledge the potential survivor treatment selection bias resulting from the use of data from a retrospective observational study (the JSEPTIC-DIC study) to identify the best criteria for polymyxin B hemadsorption (PMX-HA). However, because the derived criteria were validated in the analysis using data from the EUPHRATES trial, in which treatment allocation is randomized, we believe that the impact of selection bias was well minimized.

To address the potential immortal time bias [3], we analyzed only those cases that were alive for at least 54 h after randomization (i.e., the maximum time from randomization to the end of the standard regimen of two PMX-HA regimens) [4, 5]. As shown in Additional file 1: Fig. S1, the hazard ratios up to 28 days using the Cox proportional hazard model, adjusted for baseline APACHE II and SOFA scores, are 0.79 (95% CI 0.53–1.19, $p=0.26$) and 0.64 (95% CI 0.41–0.99, $p=0.04$) in all and targeted population, respectively. Therefore, we believe that these results from the analysis considering immortal time remained consistent with the original findings. However, it should be noted that the results of this additional analysis may underestimate the effect of PMX-HA by assuming that early deaths in the control group that were excluded from the analysis considering immortal time, could have been saved if they had been assigned to the PMX-HA group.

Although the two potential biases indicated by Uchida et al. could pose limitations to our study, they do not significantly undermine the target subpopulation of PMX-HA when considering the results of our additional analysis. However, the validity of our findings needs to be verified in future prospective studies.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-023-04606-3.

Additional file 1: Fig. S1. Kaplan-Meier curves of patients in all and targeted population of the validation cohort considering immortal time.

Author contributions

IO had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. IO and KD wrote and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

The data from the JSEPTIC-DIC study are publicly available (*Sci Data.* 2018;5:180243). The data from the EUPHRATES trial will not be shared beyond the requests from investigators of its trial.

Declarations

Ethics approval and consent to participate

The study protocol entitled "Targeted therapy using Polymyxin B hemadsorption in patients with sepsis" was approved by the Institutional Review Board of the University of Tokyo Hospital (No. 2022332NI) on February 27, 2023. This study was a secondary data analysis of de-identified data, and therefore, the requirement for informed consent was waived.

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Consent for publication
Not applicable.

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

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