Shen et al. Critical Care (2020) 24:543
https://doi.org/10.1186/s13054-020-03263-0

Critical Care

LETTER Open Access

Hyperthermia is a predictor of high mortality in patients with sepsis

Yanfei Shen[1], Yangfang Lou[2] and Shiping Zhu[2*]

To the Editor,

In a recent study, Shimazui et al. [1] reported that body temperature (BT) on ICU admission exhibited different predictive values in elderly and non-elderly patients with sepsis, and only hypothermia (BT < 36.0 °C) was associated with increased mortality in non-elderly patients while hyperthermia (BT > 38.3 °C) was not. A few issues should be noted.

First, the grouping method may underestimate the impact of hyperthermia. In the current study, the whole cohort was divided into the hyperthermia and non-hyperthermia groups, using a cutoff value of BT at 38.3 °C. One limitation is that under this grouping method, both hypothermia and normothermia were classified as non-hyperthermia. Thus, the comparison between the hyperthermia and non-hyperthermia groups could be susceptible to the proportion of patients with hypothermia. For instance, in two hypothetical cohorts (cohort 1: hypothermia $n = 80$, normothermia $n = 20$, hyperthermia $n = 100$ vs. cohort 2: hypothermia $n = 20$, normothermia $n = 80$, hyperthermia $n = 100$), the comparison of mortality between the hyperthermia and non-hyperthermia groups could be quite different in these two cohorts, as the non-hyperthermia group in cohort 1 (high proportion of hypothermia patients) may have high mortality. In addition, several studies [2] also reported that in sepsis, hyperthermia (T_{max}) was also a significant risk for high mortality. Furthermore, one randomized controlled trial (RCT) found that fever control using external cooling to maintain BT between 36.5 and 37.0 °C significantly reduced mortality in septic shock [3]. For validation, we explored the association between BT and mortality in another cohort from MIMIC-III database (Fig. 1). A total of 4201 adult patients with sepsis were included. Consistent with the current study, different associations between BT and mortality were also found in old (≥ 75) and young (< 75) patients. However, in patients with age < 75, both hypothermia and hyperthermia exhibited increased trends of in-hospital mortality (Fig. 1 black bars).

Second, the author mentioned that the impact of hypothermia duration on mortality remained unclear. Noteworthy, in a median analysis of previous RCT [3], Schortgen et al. [4] found that 73% of the impact of

* Correspondence: zsping0908@163.com
[2]Department of Respiratory Medicine, Hangzhou Hospital of Traditional Chinese Medicine, No. 453, Tiyuchang Road, Hangzhou 310000, Zhejiang, China
Full list of author information is available at the end of the article

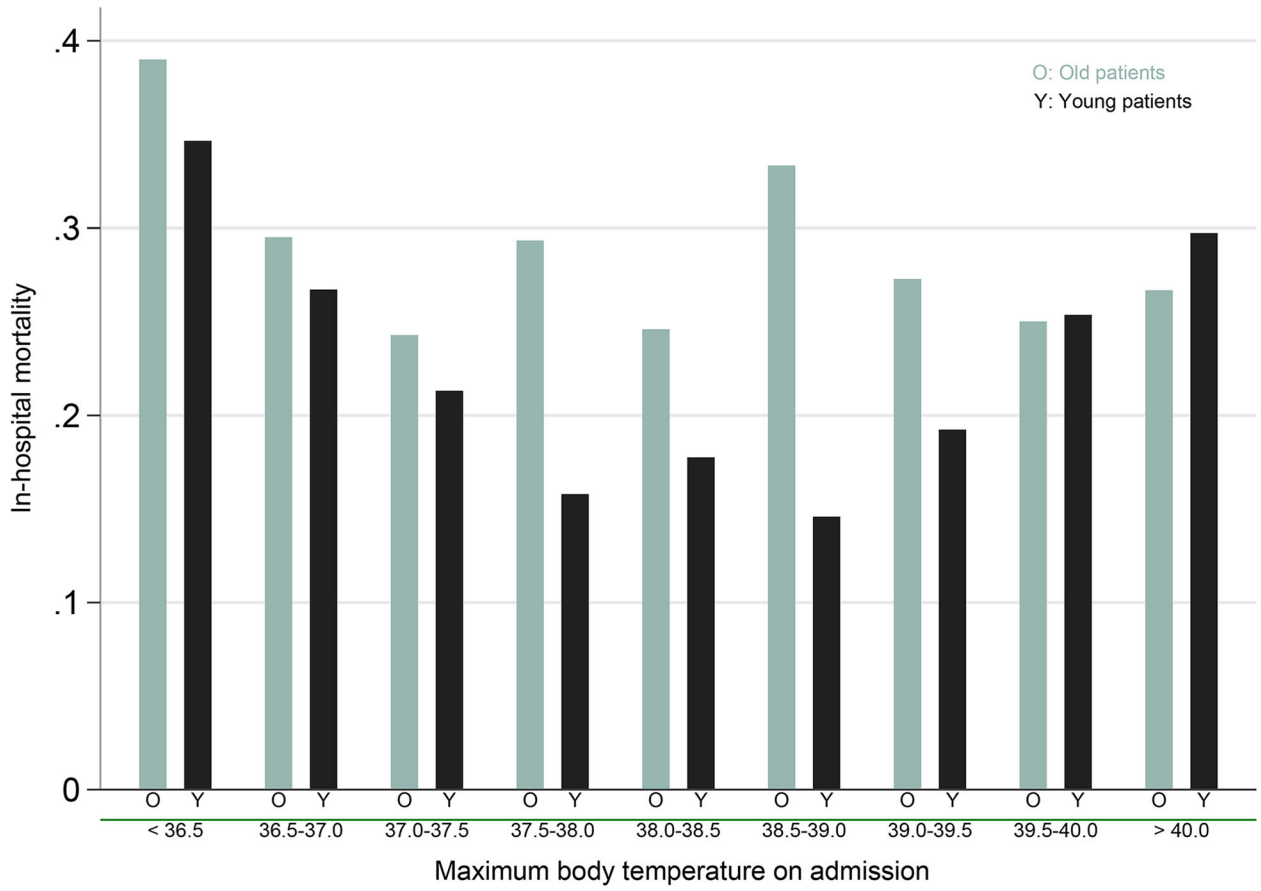

Fig. 1 Association between body temperature and in-hospital mortality in old (≥ 75 years old) and young (< 75 years old) patients with sepsis

external cooling on mortality was mediated by the duration of BT < 38.4 °C. Thus, focusing on a single BT record may increase the bias risk. Temperature load (TL) [5] may be a method to this limitation, defined as the sum of BT above/below the targeted temperature level multiplied by the duration (hours). For instance, the TL of hyperthermia (> 38.3 °C) within 72 h should be calculated as follows—step 1: $\overline{t_i} = \frac{t_i + t_{i+1}}{2}$ - 38.3; step 2: $\mathrm{TL} = \sum_{i=1}^{72} \overline{t_i} \times 1$ hour.

Acknowledgements
Not applicable.

Authors' contributions
S.Z. and W.C. came up with the question, and S.Z. was responsible for the writing. The authors read and approved the final manuscript.

Funding
YS received funding from the Zhejiang medical and health science and technology project (no. 2018261355).

Availability of data and materials
Not applicable.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
None.

Author details
[1]Department of Intensive Care, Zhejiang Hospital, 1220#, Gudun-Road, Hangzhou, Zhejiang, China. [2]Department of Respiratory Medicine, Hangzhou Hospital of Traditional Chinese Medicine, No. 453, Tiyuchang Road, Hangzhou 310000, Zhejiang, China.

Received: 18 August 2020 Accepted: 24 August 2020
Published online: 03 September 2020

References

1. Shimazui T, Nakada TA, Walley KR, Oshima T, Abe T, Ogura H, Shiraishi A, Kushimoto S, Saitoh D, Fujishima S, et al. Significance of body temperature in elderly patients with sepsis. Crit Care. 2020;24(1):387.
2. Wu DY, Lu SQ. The effects of abnormal body temperature on the prognosis of patients with septic shock. Ther Hypothermia Temp Manag. 2019. Epub ahead of print. PMID: 31895653. https://doi.org/10.1089/ther.2019.0012.
3. Schortgen F, Clabault K, Katsahian S, Devaquet J, Mercat A, Deye N, Dellamonica J, Bouadma L, Cook F, Beji O, et al. Fever control using external

cooling in septic shock: a randomized controlled trial. Am J Respir Crit Care Med. 2012;185(10):1088–95.
4. Schortgen F, Charles-Nelson A, Bouadma L, Bizouard G, Brochard L, Katsahian S. Respective impact of lowering body temperature and heart rate on mortality in septic shock: mediation analysis of a randomized trial. Intensive Care Med. 2015;41(10):1800–8.
5. Rahmig J, Kuhn M, Neugebauer H, Juttler E, Reichmann H, Schneider H. Normothermia after decompressive surgery for space-occupying middle cerebral artery infarction: a protocol-based approach. BMC Neurol. 2017; 17(1):205.

Publisher's Note