

CORRESPONDENCE

Open Access



Confounding factors in article stating that Ubiquitin C terminal hydrolase predicts poor neurological outcome after cardiac arrest

Patrick M. Honoré^{1*}, Emily Perriens², Ibrahim Bousbiat², Nahida Harim³, Elena Germain³, Patrick El Nawar³ and Sydney Blackman²

Keywords Ubiquitin C, Correlation with poor neurological outcome, Potential confounders

Song et al. conclude that novel serum biomarkers predict poor neurological outcome after cardiac arrest (CA) with high accuracy [1]. Cutoffs from two large existing studies (TTM and COMACARE substudy) were externally validated in their study [1]. According to Song et al., the predictive power of novel biomarkers was the highest 72 h after CA [2].

In their analysis, the predictive performance of Ubiquitin C terminal hydrolase (UCHL) was seen in patients with poor outcome [1]; higher values of UCHL were observed in these patients [1]. Nearly half of critically ill patients—especially those with shock—had or developed acute kidney injury (AKI) and 20–25% needed renal replacement therapy (RRT) within the first week of hospitalization [2]. In Song's study, the out-of-hospital cardiac arrest (OHCA) group was very sick on admission with lactate between 6 and 9 mmol/L [1]. Therefore, we could make the assumption that 20–25% of these patients would require RRT or continuous RRT (CRRT). As the study did not provide numbers regarding RRT, this assumption

may also overestimate any negative impact on the estimated effect. UCHL's molecular weight of 25 kDa makes it theoretically very easily removable by RRT and CRRT [3]. Although theoretically possible, there is little to no published data on this issue. CRRT is performed using membranes with a cut off of 35–40 kDa; it is, therefore, logical to assume that a potential portion of UCHL is eliminated by the CRRT [4]. New highly adsorptive membranes (HAMs) are able to adsorb molecules with molecular weights greater than 35 kDa, further increasing the removal of UCHL [5]. Not taking into account the effect of RRT and CRRT on UCHL can mislead evaluations and conclusions by artificially reducing the level of UCHL and underestimating its effects in each group (good versus poor neurological outcome) [1]. Nevertheless, only a study looking into UCHL clearance could precisely quantify the loss of it by RRT and the potential impact on the results of the study. If the findings of this new study show that UCHL is significantly removed by RRT, it is necessary to exclude patients with AKI that may need RRT or CRRT to avoid potentially underestimating the levels of UCHL in each group (good versus poor neurological outcome) undergoing RRT or CRRT.

This comment refers to the article available online at <https://doi.org/10.1186/s13054-023-04400-1>.

*Correspondence:

Patrick M. Honoré

patrick.honore@chuclouvain.uclouvain.be

¹ ICU Department, CHU UCL Godinne Namur, UCLouvain Medical School, Avenue G Thérasse 1, 5530 Yvoir, Belgium

² ICU Brugmann University Hospital, ULB University, Brussels, Belgium

³ ULB University, Brussels, Belgium

Abbreviations

CA	Cardiac arrest
UCHL	Ubiquitin C terminal hydrolase
AKI	Acute kidney injury
RRT	Renal replacement therapy
CRRT	Continuous RRT



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Acknowledgements

None.

Author contributions

PMH designed the paper. PMH, EP, IB, NH, PEN, EG and SB participated in drafting and reviewing. PMH, EP, IB, NH, PEN, EG and SB read and approved the final version of the manuscript. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

Not applicable.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare to have no competing interests.

Received: 23 April 2023 Accepted: 25 April 2023

Published online: 15 May 2023

References

1. Song H, Bang HJ, You Y, et al. Novel serum biomarkers for predicting neurological outcomes in postcardiac arrest patients treated with targeted temperature management. *Crit Care*. 2023;27:113. <https://doi.org/10.1186/s13054-023-04400-1>.
2. Peters E, Antonelli M, Wittebole X, et al. A worldwide multicentre evaluation of the influence of deterioration or improvement of acute kidney injury on clinical outcome in critically ill patients with and without sepsis at ICU admission: results from the intensive care over nations audit. *Crit Care*. 2018;22(1):188. <https://doi.org/10.1186/s13054-018-2112-z>.
3. Li J, Yu C, Sun Y, Li Y. Serum ubiquitin C-terminal hydrolase L1 as a biomarker for traumatic brain injury: a systematic review and meta-analysis. *Am J Emerg Med*. 2015;33(9):1191–6. <https://doi.org/10.1016/j.ajem.2015.05.023>.
4. Honoré PM, Jacobs R, De Waele E, et al. Evaluating sepsis during continuous dialysis: are biomarkers still valid? *Blood Purif*. 2014;38(2):104–5. <https://doi.org/10.1159/000363497>.
5. Honoré PM, De Bels D, Spapen HD. An update on membranes and cartridges for extracorporeal blood purification in sepsis and septic shock. *Curr Opin Crit Care*. 2018;24(6):463–8. <https://doi.org/10.1097/MCC.0000000000000542>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.