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Dear Editors-in-Chief,

we are submitting our invited article: „Can adequate hemodynamic management of brain-dead donors improve donor organ procurement?“ after our minor revision for publishing in the *World Journal of Transplantation* under the category of *Letter to the Editor*. We confirm that all authors have read and approved the submission and have contributed significantly to the content of the article. In our opinion, this letter to the editor merits reporting as it presents an interesting commentary on a recent article from the Journal – “Hemodynamic management in brain dead donors“. We hope You will find this manuscript with interest as it may represent an important contribution to the understanding and management of brain-dead donors.

We confirm that our article is original and it has not previously been published in print or electronic form, and it is not under consideration by another publication. If accepted, authors will sign an exclusive license to publish. We confirm there are no ethical problems or any potential conflicts concerning the exclusive nature of the paper and that we have not received any financial or editorial assistance to support the article. We have a full control of all primary data and agree to allow the journal to review our data if requested.

We would like to thank the Company Editor-in-Chief, Science Editor, and Reviewers for their thoughtful review and consideration for publication of our paper. We have followed all the suggestions and improved the paper as applied to the requested corrections.

We would like to thank **Reviewer #1** for the thoughtful review, comment, as well as for the compliments. As per the comment regarding DBD abbreviation, we have carefully checked the abbreviations and amended the manuscript using the abbreviation DBD for “Donation after Brainstem Death”.

We would like to thank **Reviewer #2** for the thoughtful review, comments and suggestions.

1) *Lazzeri et al. have not described requirement of PAC in their review.*

Response: Thank you. We have already mentioned this in our discussion.

2) *Along with acceptance of more marginal donors with comorbidities and worldwide variability in donor management strategies due to various constraints.*

Response: Thank you. Based on this comment, we have amended the manuscript with the following included in the text: “Lack of evidence from randomized controlled trials still remains one of the main issues regarding the management strategies in donation after brainstem death (DBD) along with acceptance of more marginal donors with comorbidities and worldwide variability in donor management strategies due to various constraints.”

3) *Both the article and the commentary have not mentioned i) the role of initial intravascular volume replacement ii) choice of crystalloid or colloid iii) need for assessment of volume status. Since they are addressing hemodynamic management, it was a valid recommendation of the 2015 guidelines (ref12).*

Response: Thank you. Based on this comment, we have amended the manuscript with the following included in the text: “However, appropriate hemodynamic monitoring is a prerequisite in assessment of volume status and response to therapy; therefore, the authors should have

addressed the role of initial intravascular volume replacement and the need for assessment of volume status. Pathophysiological changes in DBD donors make the clinical assessment of volume status even more challenging, hence appropriate monitoring is of paramount importance in guiding fluid replacement. Recent guidelines suggest that euvolemia, even while is the primary therapeutic goal, and isotonic crystalloid solutions are the preferred choice for volume replacement (12).”

However, the choice of crystalloid or colloid is still very controversial and varies among different units; it is also beyond the scope of this short commentary to discuss in more detail such important topic. Hope this meets with the Reviewer’s understanding.

4) These guidelines recommend dopamine as first line; with addition of NE, when the requirement of DA exceeds 10mcg/kg/min. However, the data on this is variable with a retrospective analysis (Kutschmann M et al, Transpl Int. 2014) stating otherwise.

Response: Thank you. Based on this comment, we have amended the manuscript with the following included in the text: “These guidelines recommend the use of dopamine as a first line therapy, with addition of NE when the requirement of dopamine exceeds 10 mcg/kg/min. However, the data on this is variable with a retrospective analysis stating otherwise (13).”

We have also added the reference: **Kutschmann M**, Fischer-Fröhlich CL, Schmidtman I, Bungard S, Zeissig SR, Polster F, et al. The joint impact of donor and recipient parameters on the outcome of heart transplantation in Germany after graft allocation. *Transpl Int.* 2014;27(2):152-61. doi: 10.1111/tri.12221.

5) In order to increase the credibility of quoted literature, articles in PUBMED database are considered in a review.

Response: Thank you. We agree with the reviewer and based on this comment, we have amended the statement with the following included in the text: “However, as the authors did not perform systematic review, this could lead to extrapolation bias.”

We would like to thank **Science Editor** for the thoughtful review, suggestion, as well as for the compliments.

1) *The manuscript describes the importance of dead brain donors (DBD) in preserving blood stability as transplanted organs. The manuscript is well written and can be helpful for the readers to ameliorate the therapeutic approach for this scenario.*

Response: Thank you for the compliments.

2) *I suggest that the author summarize a table and collect relevant literature, which will be conducive to knowledge dissemination.*

Response: Thank you for your suggestion. *Lazzeri et al.* have provided a valid and interesting review on this topic, and they have already collected relevant literature. We have made our comments on their review manuscript in the format of a Letter to the Editor and we have discussed strengths and weaknesses of their review manuscript while also referring to a few important references. However, providing and collecting more literature on this topic would be out of the scope of the Letter to the Editor and we would like to avoid any further interference with the respect to the authors of this review manuscript.

We have also amended our Letter to the Editor as per reviewers’ comments and requested minor revision. Hope this meets with the Editor’s understanding.

We would like to thank **Company Editor-in-Chief** for the thoughtful review and compliments.

1) I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Transplantation, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response: Thank you. We have also amended the title of our Letter to the Editor to reflect better the topic and in order to improve visibility of the manuscript.

We hope that these changes to the manuscript will facilitate the decision to publish this Letter to the Editor in your *World Journal of Transplantation*.

With much appreciation,

Dr. Davorin Sef

London, 19th March 2022