

PEER-REVIEW REPORT

Name of journal: *World Journal of Transplantation*

Manuscript NO: 82500

Title: Haemodynamic management in brain death donors: influence of aetiologies of brain death

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05346206

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2022-12-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-24 04:32

Reviewer performed review: 2022-12-29 13:55

Review time: 5 Days and 9 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

There are two questions need to be explicated: 1. Whether the abbreviation of brain death donors (DBD) should be BDDs? 2. Please supplement the statistical P value of utilization rate.

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Peer-review model: Single blind

Reviewer's code: 00054549

Position: Peer Reviewer

Academic degree: BSc

Professional title: Doctor

Reviewer's Country/Territory: Australia

Author's Country/Territory: Italy

Manuscript submission date: 2022-12-20

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-01-30 02:20

Reviewer performed review: 2023-02-01 05:34

Review time: 2 Days and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript attempts to show that the hemodynamic profiles of potential organ donors around the time of determination of brain death vary according to the underlying cause of brain death, hence the management also varies. One of the major flaws with the data as presented is that it is not clear as to when brain death was determined from the data that are provided. Was this at time point 1 or 2 or was at after these two predetermined time periods? Plus do these time periods encompass the duration of all of the potential organ donors in this study in the ICU or does it only represent the earlier stages of their duration in ICU? Out of interest how many of these potential organ donors in each subgroup proceed to organ recovery? This would also be useful information to include -the so called utilization rate does not seem adequate because it is unclear what this represents. How the data are presented is confusing. Would it not be easier to include all of the relevant data for each of the data elements of interest for each of the time points for each subgroup of donors into one large Table? Or instead have a Table for each subgroup of donors with the measurements/data for each time point then included? Of note the terminology for how potential organ donors post



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

determination of brain death are mentioned in the literature is evolving <https://jamanetwork.com/journals/jama/article-abstract/2769149> You might wish to consider updating all of the relevant references made to brain death in the manuscript to a more current term. The manuscript Title could do with work as well. Do you not mean that management of the potential donor appears to be a reflection of the hemodynamic alterations etc associated with the underlying cause of the significant brain injury leading to death? This also needs to be rectified in the conclusions of the abstract as well. The Introduction section of the manuscript suffers from a number of sweeping statements being made which are problematic. You need to make it clear in the early part of the Introduction section that you are referring to potential organ donors. Plus the statement in the first para of the Introduction of how many potential organ donors are not able to be supported in the ICU to the next stage of organ recovery needs to have a lower percentage limit included from the published literature (this figure varies depending on other factors-ie completeness of reporting, experience, etc). The statement in the Introduction " Strong recommendations on therapies for hemodynamic management in DBDs are still lacking" is only partly correct. There have been attempts at formulating Consensus guidelines on the hemodynamic management of potential organ donors (some of which are published), Are you referring to your own country/region? If so you need to provide some background information. Plus you have provided a set of old references for donor management goals. far more has been published on this topic. You need to include references to the relevant literature both in the Introduction and Discussion sections of the manuscript. For eg see the attached word document. You mention machine preservation in the Introduction section but do not include any data on the outcomes of organ recovery/transplantation in your results. You also need to expand on what you mean by reducing the incidence of DGF independent of machine preservation. In the Methods section you need to reference the relevant



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Italian guidelines/statement for the declaration of brain death. Also in the Methods section in the first sentence in the subsection on donor management you need to clarify what the (XX) is following the statement "All potential donors were managed as previously described". So was none of this management for this particular study cohort new or was some of it new? The Discussion section is extremely limited. There is utility in analyzing the results of larger data sets (which occurs in Spain routinely now). You need to mention the utility of the relevant data on potential organ donors being reported to a central agency/registry and how this can be used for audit, to drive practice improvement, develop consensus statements etc. Plus, you need to mention whether there is a move in your region/country for more uniform reporting/management of this subgroup of potential organ donors (and how this compares to other countries in Europe/other regions of the world).

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Peer-review model: Single blind

Reviewer's code: 03755399

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Consultant Cardiac Surgeon

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Italy

Manuscript submission date: 2022-12-20

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-01-30 14:49

Reviewer performed review: 2023-02-07 13:57

Review time: 7 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Authors have presented an observational single centre study (138 DBDs) on hemodynamic donor management and aimed to analyse whether it can be affected by the aetiology of brain death. However, there are several drawbacks which limit the scientific value of this manuscript: 1. What does “n.71 DBD donors” stands for? Pls correct 2. Please state in the abstract and main text to which donor organ donation your study refers to. 3. Conclusions consist of overstatements and need to be re-written as the only conclusion the authors have is that post-anoxic encephalopathy had higher requirements for inotropic and vasopressor support. Also, pls remove “aggressive treatment” as higher need for ino- support is sufficient. I suggest to remove the conclusion on utilization rate as your subgroups are too small to comment on such conclusion. Particularly, as you did not provide the results of utilization rate of every organ. 4. Why the authors did not correlate aetiology of brain death with success of HTx and survival outcomes? 5. Pls remove statement: “factors affecting hemodynamic management in DBDs are to date poorly investigated “. Improved hemodynamic management including serial echocardiography can guide hemodynamic management

in potential donors to increase number and quality of donor hearts. As there are many references missing, pls add more that are relevant to your Introduction: a) Thet MS et al. Can adequate hemodynamic management of brain-dead donors improve donor organ procurement? World J Transplant. 2022 Apr 18;12(4):79-82.; b) McKeown DW et al. Management of the heartbeating braindead organ donor. Br J Anaesth. 2012;108 Suppl 1:i96-107. 6. In the Methods pls correct "XX" 7. Most importantly, how did you provide data on BP, lactates etc? Was it min, max or average value? 8. When discussing the results in the Results section pls refer to exact numbers and avoid saying just "were the youngest", "lowest values"... 9. Pls avoid commenting "no differences" if there were "no significant differences between the subgroups" 10. Pls use DBD instead of BD donors and be consistent throughout the text 11. What is "donor manager protocol"? 12. Pls re-phrase the comment on Sandroni et al. study as it is unclear 13. Pls avoid statements such as "for the first time" 14. Pls explain why do the authors believe that management in donors with post anoxic encephalopathy is more challenging? 15. Limitations are written poorly. Pls mention bias of retrospective study, lack of data on utilization rate of each specific organ, survival and outcomes post-transplant, lack of other relevant donor data 16. Table 1 is missing some p values

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 00054549

Position: Peer Reviewer

Academic degree: BSc

Professional title: Doctor

Reviewer's Country/Territory: Australia

Author's Country/Territory: Italy

Manuscript submission date: 2022-12-20

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2023-03-13 02:34

Reviewer performed review: 2023-03-13 03:37

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Can you please upload the revised version of your manuscript complete with the two Tables. The latest version of the manuscript-82500-is missing the two Tables.

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Professional title: Consultant Cardiac Surgeon

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Italy

Manuscript submission date: 2022-12-20

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2023-03-13 07:42

Reviewer performed review: 2023-03-13 14:04

Review time: 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have only partially improved their manuscript according to my previous comments. If they do not engage in improving their manuscript according to the comments, the article cannot be considered to be published in the current form. My comments: 1. Please use DBD instead of BDD, as DBD and DCD are standard terms. 2. Pls correct: "DBD donors who sustained post-anoxic encephalopathy " instead of "BDDs from post anoxic encephalopathy" 3. Can the authors provide post-transplant survival? It does not need to be prospectively and this is important for the understanding of your study. 4. Pls use "single-centre" 5. The authors did not explain which data on BP, lactates have they used in their results. Was it minimal, maximal or average value? 6. "No differences were detectable among the three subgroups" – the authors did not correct previous comment not to use only "no differences". There can be statistically significant or non-significant difference. Pls correct! 7 Pls read the previous comment carefully - Pls use DBD, and not BDD throughout the text. 8 Again – pls correct "donor manager protocol" and write "donor management..." 9 The authors did not re-phrase the comment on Sandroni et al. study. I suggest referring to "donor kidney", and not only kidneys, livers etc... Also, word "livers" does not exist in standard English language. The authors need to use English language editing service. pls correct weird wording such as - "from post-anoxic encephalopathy" . The manuscript has obviously not been revised by a mother-tongue expert. 10 The authors did not amend their Limitations of the study. I suggest to add 3-4 more.