

ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 21537-review.doc). We appreciated the time, constructive criticism, and suggestions of all the reviewers. We have addressed each of their concerns as outlined below.

Title: Potential approaches to improve the outcomes of donation after cardiac death liver grafts

Author: Mahboub P, Bozorgzadeh A, Martins PN

Name of Journal: *World Journal of Transplantation*

ESPS Manuscript NO: 21537

The manuscript has been improved according to the suggestions of the reviewers:

Reviewer #1:

This mini-review describes the current status of organ transplantation and statistical numbers, emphasizing lack of donors. The manuscript focuses on several methods to preserve liver grafts from donors after cardiac death (DCD). There is no doubt that the manuscript will help provide a quick overview of currently available methods to store DCD liver grafts. The title is also very accurately reflects the focus and the content of the manuscript. Major comment 1. none. Minor comments 1. Do you think "DCD" is OK to use in the title instead of spelling it out? If the manuscript were published in liver transplantation journal, it would be fine, but not sure if "DCD" is a popular word across all transplantation fields. 2. Very minor formatting issue: It is probably better to add one spacing line between sections. I know it does not matter at the end, but it will help reviewers and publishers.

Response: The title has been changed. We have spelled out DCD instead of the abbreviation. The one spacing line request has been addressed.

Reviewer #2:

The manuscript entitled, "Potential approaches to improve the outcomes of DCD liver grafts", reviewed the ways of the mechanical perfusion to improve the outcome of liver transplantation with DCD grafts. I have some comments. Comments to author 1. The references seem relatively old. Authors should stick to more recent literatures. Please re-survey the literatures. 2. Authors should discuss the abdominal regional perfusion when reviewing the way to improve outcome of DCD program.

Response: The new references have been added in the text. Such as references number 22, 37, 42, 43. The abdominal perfusion region part has been added to the manuscript.

Reviewer #3:

Dear Authors, Liver graft improvement after ex vivo preservation interventions is an issue under expansion that has gained great interest recently. In this way, the topic chosen by the authors is

attractive not only for those ones interested in improving the quality of the DCD donors, but also to the transplant centers seeking to rescue grafts with expanded criteria. However, there are a couple of topics that should be included and explored in order to expand the interest of the manuscript. Ex vivo perfusion techniques have demonstrated positive results also with kidney grafts. Thus, the authors might include a paragraph exploring the differences between liver and kidney ex vivo perfusion interventions. Although, there is enough evidence showing the protective effects of ex vivo perfusion methods, a few centers have used these strategies as a routine. Explain why there is no widespread use around the world of the Liver graft improvement after ex vivo preservation interventions is an issue under expansion that has gained great interest recently.

Response: The paragraph "Using HMP in other organs such as kidney is more common. There have been several clinical trials done on kidney HMP and it has become routine to use this method to preserve human kidneys in Europe and in US. cold static storage is still the most common method of preservation in liver since cannulation and perfusion is more complicated in liver, and currently there is no FDA approved liver perfusion machine for clinical use." was added in the HMP section.

Reviewer #4:

Authors reviewed the innovational methods for preserving livers from Donation after Cardiac Death (DCD). I suggest to add a table summarizing (dis)advantages of different methods.

Response: The table of the disadvantages has been added in the manuscript.

Reviewer #5:

The manuscript offers an overview of the attempts to improve the quality of donation after cardiac death liver grafts and liver transplant outcomes, by means of innovative preservation techniques. Both the goal and the content of the paper deserve attention and are worth publication. However, the manuscript requires minor editing because there are few mistakes or imprecisions. For example: - the word "increase" is often mis-spelled ("increas"); - in the Introduction section, line 4, "has been increased" should be "has increased"; - in the "Characteristics of DCD Donors" section, line 2, "in 1990s" should read "in the 1990s"; - in the "Oxygenated cold storage (Persufflation)" section, line 8, "by Fischer group" should be "by the Fischer group"; - in the "Oxygenated cold storage (Persufflation)" section, line 9, "large animal" should be plural "animals"; - in the "Oxygenated cold storage (Persufflation)" section, line 12, "The livers underwent of..." do not require "of"; - in the "Hypothermic machine perfusion", line 10, "during four the weeks" obviously needs to be corrected into "during the four weeks". Once the imprecisions listed above are corrected, and after a complete abbreviations list is provided, the paper could be published, as it holds an important message.

Response: All requested spelling correction has been addressed.

Thank you again for publishing our manuscript in the *World Journal of Transplantation*.

Sincerely yours,

A handwritten signature in black ink, consisting of a stylized first letter followed by a series of loops and a long horizontal stroke at the bottom.

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A handwritten signature in black ink, consisting of a series of loops and curves, positioned to the right of the contact information for Paulo Martins.

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