

COVER LETTER

Dear Lian-Sheng Ma,

We would like our revised version of our manuscript entitled *“Machine perfusion and the prevention of ischemic type biliary lesions following liver transplant. What is the evidence?”* to be considered for publication in *“World Journal of Gastroenterology”*.

After a positive initial review, we have extensively reviewed our manuscript and have addressed point-by-point all the suggestions and comments from the reviewers. Changes have been marked in red. We are very grateful to the reviewers and editors for their positive feedback. The manuscript has improved its quality.

We are aware that *“World Journal of Gastroenterology”* is a leading international journal, and thus we would be very grateful if you would consider our revised version for publication in your journal, as it will review an important topic what is ITBL in liver transplantation and the current evidence on its prevention by different machine perfusion techniques. The full manuscript including Tables and Figures has been formatted and accepted by all authors to meet the publication guidelines of the journal.

Yours sincerely,

Manuel Durán-Martínez, MD.

REVIEWER REPORTS

Reviewer 1

The article reflects an important topic in non-anastomotic biliary structures. It explains the effect of machine perfusion techniques after DCD donor recruitment and graft outcome. This has a great impact on graft survival, patient survival, quality of life and cost of living after DDLT. Also, the treatment of the non-anastomotic structures could be challenging, so establishing a protocol to avoid them is beneficial especial with expanding donor pool. A limitation of the study is that there is no head-to-head RCT to show the impact of different techniques on graft outcome

Concerns:

(1) A limitation of the study is that there is no head-to-head RCT to show the impact of different techniques on graft outcome.

R. Thank you for your comment. The authors agree with the reviewer that the current evidence is supported by cohort studies. The only RCTs that have been performed have been to compare different machine perfusion techniques versus SCS. We hope that in future years, RCTs will be developed and this situation may be addressed.

Reviewer 2

In the manuscript, authors have comprehensively reviewed recent literature and summarized current progress in clinical applications of MP for potentially preventing ITBL. This topic is interesting and important, since biliary complications after liver transplant remain unconquered and the development of mechanical perfusion techniques might be promising for ITBL prevention. Overall, the manuscript was well-organized and written. However, there remains some comments taken for consideration during revision. 1. 1.0 INTRODUCTION, the author should briefly introduce the potential

mechanism (elevated ROS, infiltration of immune cells, etc.) and prevention strategies of ITBL. 2. The last paragraph in 2.2, the study about the comparison between A-NRP and HOPE has been aforementioned in 2.1 (Ref [36]). And an adequate citation should be executed in the last paragraph in 2.2. 3. Fig. 1, were there any ethic announcement to using MRCP images? 4. In Acknowledgments, authors mentioned that “Figures created with biorender.com, accessed on January 2023.” Except MRCP images, no other figures have been found. 5. Please check the abbreviations and definitions. E.g. NRP-A or A-NRP?

Concerns:

(1) 1.0 INTRODUCTION, the author should briefly introduce the potential mechanism (elevated ROS, infiltration of immune cells, etc.) and prevention strategies of ITBL.
R. Thank you for this interesting comment. Although the aim of this review is not to go into the pathogenesis of LTBI in depth, we have added a paragraph in the introduction that briefly introduces it. (Page 10, paragraph 2)

(2) The last paragraph in 2.2, the study about the comparison between A-NRP and HOPE has been aforementioned in 2.1 (Ref [36]). And an adequate citation should be executed in the last paragraph in 2.2. 3.
R. Thank you for this comment, we agree that it is important to avoid duplication. However, we consider it is important to mention this study in both sections, due to it facilitates the understanding of the reader and also, different aspects of the study are mentioned. Finally, the citation has been correctly referenced. (Page 16, paragraph 2, line 3)

(3) Fig. 1, were there any ethic announcement to using MRCP images?
R. Thank you for your comment. An ethical statement regarding this has been added. (Page 11, paragraph 1, line 19)

(4) In Acknowledgments, authors mentioned that “Figures created with biorender.com, accessed on January 2023.” Except MRCP images, no other figures have been found.

**R. Thank you for your comment. This grammatical error has been corrected.
(Page 3, paragraph Acknowledgements, line 3)**

(5) Please check the abbreviations and definitions. E.g., NRP-A or A-NRP?

R. Thank you for your comment. All abbreviations in the manuscript have been checked. The abbreviations have been arranged alphabetically. (Page 6, paragraph Abbreviations, line 1)