2-May-2019

Prof. Lian-Sheng Ma

Editor-in-Chief

World Journal of Gastroenterology

Dear Chief Editor Lian-Sheng Ma,

We, sincerely, thank all the members of your Editorial Board and the reviewers for their hard work for our manuscript, and we are grateful for the valuable comments from reviewers and editors. We are pleased to submit our revised manuscript entitled "Bioartificial liver support systems for acute liver failure：Systematic review and meta-analysis of the clinical and preclinical literatures" (Manuscript ID 47378) to be reconsidered for publication in your journal *World Journal of Gastroenterology*.

In the revised manuscript, according to the comments of reviewers and editors, we have made some improvements regarding the contents and layout of the article as follows. (1) we have reorganized the author's contribution, funding, and adding the biostatistics statement and article highlights; (2) registered the study protocol in PROSPERO on April 24, 2019, but it needs about 20 working days until the final approval; (3) the bias risk of non-RCT studies has been assessed according to the Newcastle-Ottawa Quality Assessment Scale for cohort studies and reported in the results and Appendix table 3; (4) luckily, we have got the full-text of two included articles that was not available before (only abstract), thus we had supplemented the information in the tables and updated the relative data in the results; (5) Figure 1 (Flow chart of study selection) and Figure 2 (Forest plot of meta-analysis) have been presented in the editable PPT file; (6) The entire manuscript has been edited again by the professional English language editing company to eliminate non-native language errors; (7) Other specific responses to the issues raised by the reviewers are given point by point as below.

Yours sincerely,

Ji Bao, PhD.

Laboratory of Pathology;

Key Laboratory of Transplant Engineering and Immunology, Ministry of Health

West China Hospital, Sichuan University

Address: No.37 Guoxue Xiang, Chengdu, Sichuan, China, 610041

Phone number: 86-028-85164030

Fax number: 86-028-85164034

Email: baoji@scu.edu.cn

Reviewers' Comments to Author

Reviewer 1: Number ID 00227359

Comments to the Author: Please clearly point out the searching key words. Was the study registered to any recording database?

Response to reviewer: Thank you very much for your comments. Accordingly, we have attached the keywords for our literature searching in the appendix. Moreover, we have registered our research protocol in the PROSPERO website on April 24, 2019, but it needs about 20 working days until the final approval.

Reviewer 2: Number ID 03727922

Comments to the Author: Very interesting manuscript. However, I suggest some important improvements in this systematic review. Firstly, you should use and describe better the heterogeneity and sensitivity analysis in these studies. Furthermore, to a better evaluation of the studies and the level of evidence you need to use some scores or scale, as New Castle score (Ottawa Quality Assessment Cohort Studies) for nonrandomized clinical trials and Jaded Scale for randomized clinical trials. Moreover, you must need to stablish de Mesh-terms and inform the correct search done. I suggest you to register this systematic review in the International Database of Prospectively Registered Systematic Reviews. Finally, I recommend you

to stablish the scientific hypothesis and clearly describe how the search was done. The search you need to stablish the patient, intervention, comparison, or control, outcome structure.

Response to reviewer: Thank you very much for your important comments. We accepted all your suggestions and made the corresponding improvement in our manuscript. We (1) described more detail in the results about the heterogeneity between studies used for meta-analysis, and supplemented the sensitivity analysis by changing the effect measures (odds ratio vs. relative ratio), pooling methods (Peto vs. M-H), and statistical models (fixed- vs. random-effects) in the method and results; (2) assessed the bias risk of non-RCT studies according to the Newcastle-Ottawa Quality Assessment Scale for cohort studies, and the scores were presented in Appendix Table 3; (3) registered the research protocol in the PROSPERO website on April 24, 2019, but it needs about 20 working days until the final approval; (4) described more detail about the searching strategy in the method, e.g. PICOS, and listed the keywords used for literature searching in the Appendix. Thank you again and best wishes!

Reviewer 3: Number ID 02544416

Comments to the Author: The topic is adequately evaluated and the results are correctly presented.

Response to reviewer: Thanks very much for your comments to our research.