Author’s response to reviews

Title: Multiparametric functional magnetic resonance imaging for evaluation of hepatic warm ischemia-reperfusion injury in a rabbit model

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Version: 1 Date: 18 Oct 2017

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To

Carlo Pulitano

BMC Gastroenterology

Dear Carlo Pulitano:

Thank you for giving us the opportunity to revise and resubmit the manuscript BMGE-D-16-00592R1 which titled "Multiparametric functional MR imaging for evaluation of hepatic warm ischemia-reperfusion injury in a rabbit model". We have updated the manuscript in response to the comments from editor and reviewers, and would like to resubmit the revision. We hope that the revised version could meet the criteria for publication in BMC Gastroenterology.

According to the questions mentioned in the editor’s decision letter, a point-by-point response we’ve addressed in the revision was listed as below:
Editor comments:

1. This is an interesting and original study. However the authors should review grammar and style of discussion.

Response: Thanks for your affirmation. I have reviewed the grammar and style of discussion, and invited someone who is fluent in English to review my manuscript.

2. As stressed by the reviewer, the authors should better define the difference between the two groups in terms of biochemical parameters, SOD, etc. Please also comment regarding histological comparison between the two groups.

Response: Thank you for your suggestion. We’ve added detailed biochemical parameters results and quantitative histopathological analysis/grading in Abstract section, Materials and Methods section, Results section, and Discussion section.

Reviewer 1 comments:

The study has a original think. It investigates the relationship between MR investigation and warm ischemia-reperfusion injury. The study is a preliminary study and the numbers of the animals are few. On the other way Ischemia-reperfusion injury is a dynamic process but the measurment of MR is nondynamic. The study must be supported further with many new studies. As a new sudy, It can be accepted for this journal.

Response: Thanks for your affirmation. Just as the limitations we discussed, this paper was an exploratory pilot study and we reported our preliminary findings. And now, we are doing a longitudinal, dynamic, time-dependent study about MR evaluation of hepatic WIRI, the results will be presented in other articles.

Reviewer 2 comments:

1. This is an interesting article, and this work will give clinical insight on how to use MRI techniques for diagnosis hepatic pathologies over liver biopsy techniques

Response: Thanks for your affirmation.
2. Topic: Multiparametric functional MR imaging for evaluation of hepatic warm ischemia-reperfusion injury in a rabbit model, The authors should consider changing to "Multiparametric functional magnetic resonance imaging for evaluation of hepatic warm ischemia-reperfusion injury in a rabbit model"

Response: Thank you for your suggestion. We have changed the title as “Multiparametric functional magnetic resonance imaging for evaluation of hepatic warm ischemia-reperfusion injury in a rabbit model”.

3. Abstract: page 2: The abstract is ok. But, there is minor grammatical mistake
Page 2 line 24-26: The authors compared MR parameters between two groups. Where are the two groups in the abstract? The two groups should be mentioned in the material and methods of the abstract for clarity.

Line 30-31: The authors should consider writing PF, MD and MD in full

Line 42-45: The authors give only histopathological summary of WIRI group. What about the second group?

I therefore, recommend the histopathological summary of the second group. The histopathological of both groups should be compared for clarity.

Response: Thank you for your suggestion. I have reviewed the grammatical mistake in Abstract. We’ve added and corrected some sentences in Abstract section.

4. Introduction: Page 3 line 30-37: I do believe that hepatic WIRI resulted to oxidative stress due to reactive oxygen species(ROS) production which eventually lead to antioxidants imbalance and inflammatory cells response. I suggest, the authors should explain in brief, "the role of WIRI in ROS production", since they assayed for oxidative stress markers in this study.

Response: Thank you for your suggestion. We’ve added one sentence in Introduction section.
5. Materials and Methods: Page 6 line 25-27: Described from were written together. I believe that is not the correct spelling.

Page 7 line 1: I suggest, the authors should explain: How the animals were sacrificed, How the venous blood was collected from each animal and How the serum blood was collected and/or separated from RBCs before using it for liver function parameter.

Line 14-15: Why did the authors assayed for only superoxide dismutase (SOD)? There are other enzymatic (catalase CAT, glutathione peroxidase GPX, glutathione S transferase etc) and non-enzymatic antioxidants (reduced glutathione GSH) that they can assay for. These are just to make the study more detailed.

Line 20-30: I recommend addition of the liver histological scores of the two groups

Response: Thank you for your suggestion. We’ve corrected the spelling error and added the detailed explanation in this section. Meanwhile, We’ve added quantitative histopathological analysis/grading, that is, the stages of hepatic inflammation/necrosis (I score) and liver fibrosis (F score) using the METAVIR classification system (Materials and Methods section, Results section, and Discussion section). Because this paper was just an exploratory pilot study and we reported our preliminary findings, so we only measured SOD. In the future study, we will assay for other antioxidant enzymes and non-enzymatic antioxidants which the reviewer mentioned.

6. Results: Page 8 line 35-39: The authors should state clearly the statistical or significant difference in ALT, AST, LDH, MDA, MPO and SOD among the two groups. Are they higher or lower in WIRI group compared to control? Not really clear. This session required more statistical difference details of all these parameters.

Generally, the authors should give more statistical details of the two groups.

Response: Thank you for your suggestion. We’ve added one sentence in Results section.
7. Discussions: This is ok. Page 9 line 45-48: I suggest, the authors should do hepatic histological scores for the two groups to confirm the hepatocyte death, swelling and inflammatory cell infiltration.

Response: Thank you for your suggestion. We’ve added one sentence in Discussion section.

8. In general, this is an interesting article, the results and conclusions well conveyed, but this is just a pilot study. More research work with larger population of subjects should be carried out. The article needs slight grammatical corrections.

Response: Thanks for your affirmation. I have reviewed grammatical mistakes, and invited someone who is fluent in English to review my manuscript. Now we are doing advanced studies with larger population of rabbits, and dynamic evaluation about MR evaluation of hepatic WIRI, the results will be presented in other articles.

We’ve also updated the manuscript according to the comments. Thank you for the re-considering of the updated version.

With best regards.

Sincerely yours,

Guang Ming Lu

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