

June 3, 2019

**RE: Revised Manuscript NO-48037 entitled "The effect of Low-dose aspirin administration on long-term survival of cirrhotic patients after splenectomy: a retrospective single-center study" by Zhaoqing Du, Junzhou Zhao, Jian Dong, Jianbin Bi, Yifan Ren, Jia Zhang, Bilawal Khalid, Zheng Wu, Yi Lv, Xufeng Zhang, Rongqian Wu.**

Dear Editors and Reviewers:

Thank you very much for your email dated May 31, 2019 in which you informed us that our manuscript has been reviewed and invited us to revise and resubmit the manuscript for further consideration. We appreciate the consideration of publishing our manuscript. We also thank you for including the critiques from the referee that were very useful for improving our manuscript. The comments, our point-by-point responses to them, and changes made in the text are listed in separate pages.

We sincerely hope that the extensive changes made in the revised manuscript meet with your approval as well as the approval of the referees and, therefore, our manuscript is now acceptable for publication in *World Journal of Gastroenterology*. If there are any further questions, please do not hesitate to contact us.

Sincerely yours,

Rongqian Wu, MD, PhD

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## Responses to Reviewers' Comments

### Reviewer: 1

*“It is a very interesting study which demonstrated the increased survival of patients on aspirin following splenectomy for complications of portal hypertension as a result of hepatitis induced liver cirrhosis. Cirrhosis of the liver is a premalignant condition for HCC and takes at least 10 yrs for the dysplastic transformation.*

We thank the reviewer for the excellent summary of our work and the positive comments.

*Your conclusion that aspirin decreased the incidence of HCC is not exactly true. It may have slowed the progression of the disease which was already there in that cohort of patients especially at that advanced stage of the disease.*

Our research investigate the effect of long-term low-dose postoperative aspirin on the development of hepatocellular carcinoma and long-term survival of cirrhotic patients after splenectomy after analysing the clinical data of 264 adult patients with viral hepatitis-related cirrhosis who underwent splenectomy at the First Affiliated Hospital of Xi'an Jiaotong University from January 2000 to December 2014. We found that long-term post-splenectomy administration of low-dose aspirin reduced the incidence of hepatocellular carcinoma and improved the long-term overall survival in patients with viral hepatitis-related cirrhosis. Thus, long-term low-dose aspirin therapy should be recommended to cirrhotic patients with hypersplenism after splenectomy. However, the data in this study originated from a single center, the sample size was relatively small and the incidence of postoperative mortality and morbidity was low. For instance, a relatively small proportion of patients died during follow-up which may have limited the robustness of the multivariable analysis for adjustment for confounding factors. Hence, as the retrospective nature of this study, the results are subject to some uncontrollable biases, so the further prospective and multi-center researches should be obtained and verify our conclusions.

### Reviewer: 2

*The authors have presented their experience of low-dose aspirin administration post-splenectomy for hypersplenism in cirrhotic patients and recorded the incidence of hepatocellular carcinoma (HCC) and survivals. They have shown reduced incidence of HCC and improved survival in aspirin-treated group. The paper does have novelty and I recommend its publication in the WJG.*

Thank you for the positive comments and excellent summary of our work, which encourages us a lot for the better research in the further.

*I would recommend to pay attention to some of the English language issues and also cite more recent references which are available in the PubMed.*

Based on your comments, I have done some changes of the English language issues and also cite more recent references from *PubMed* database.”

Thanks.