

*Lian-Sheng Ma*

*Founder and CEO,*

*World Journal of Hepatology*

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*Dear Lian-Sheng Ma,*

*We were very glad to receive your e-mail dated August 12, 2019, detailing the reviewers' comments on our manuscript entitled "Prospective validation to prevent symptomatic portal vein thrombosis after liver resection" (Manuscript NO.: 66372, Prospective Study).*

*We have revised our manuscript and addressed the comments from the reviewers as thoroughly as possible. All changes made to the text have been underlined and marked in bold. A revised version of the manuscript including highlighted text is presented in the file named "Main Body R1 highlighted", and the revised manuscript file without underlining and bold markings is entitled "Main Body R1".*

*We believe that the presentation of our manuscript has been improved significantly thanks to the input from the reviewers. We hope that you will find these revisions appropriate and that the manuscript will now prove acceptable for publication in the World Journal of Hepatology.*

*We appreciate your kindness and thank you once again for the time and effort taken in re-reviewing our manuscript.*

*Respectfully yours,*

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**We have replied to all comments from Reviewers #1 in point-by-point manner, as indicated below.**

*Reviewer #1:*

*Specific Comments to Authors: This paper presents an early detection and treatment of PVT after hepatectomy by enhanced CT. As PVT following hepatectomy is potentially life-threatening, it is an interesting topic and worthy of being studied. But the paper needs some improvement before acceptance for publication. My detailed comments are as follows:*

*1. Just as described in this paper, the occurrence of PVT was reported in the first 5–7 days after hepatectomy. However, this time point was shifted to the first day after surgery, which resulted in the problem of less cases in this study. Moreover, the difficulty of finding microthrombi is the main reason, E-CT might be not sufficient. Besides, blood flow, hypercoagulable state, and endothelial injury are described in this paper as Virchow's triad, can one of these be used as an early PVT predictor?*

**We agree with the reviewer's comment that the event of PVT was small at the first day. As we encountered a patient who had severe PVT and it lead to hepatic failure at the first 7 days, therefore, we want to manage severe PVT as early as possible. We hypothesized the severe PVT may occurred from the first day and small PVT is easy to treat with anticoagulant therapy. As the result, we found 6 small PVT at the first day and there was no patient who had adverse event resulting by PVT.**

As indicated by the reviewer, E-CT is not sufficient to find microthrombi. We routinely performed ultrasound study at the end of operation and at the first day in case of major resection. However, US was not performed in all cases due to insufficient observation especially in the umbilical portion where was the most frequent occurrence area of PVT.

We disappointingly to answer that coagulation markers were measured only pre-operation. So, we added a sentence about this limitation to the DISCUSSION.

**Page12, line 17-19**

**Forth, E-CT alone is not sufficient to detect a small PVT on day 1. It is necessary to combine coagulation makers as well as images.**

2、In “METHODS”: *the follow-up time and follow-up plan are not stated. Dose all patients received hepatectomy had continuous follow-up and no other PVT case have been found?*

Thank you for your kind input about Methods, to avoid miss-reading for readers, we explained more detail the follow-up time and plan of this study in METHODS.

**Page 7, line 17-19**

**E-CT was performed in all treated cases for one week after starting anticoagulant therapy to confirm the degree or new appearance of PVT.**

**Page 7, line 20 and Page 8, line 1-3**

**The patient who had no PVT on E-CT at the first day after surgery did not perform E-CT until discharge. While, all patients received E-CT on 2 or 3 months after discharge as a routine follow-up after liver resection.**

3, In "METHODS": The plan and basis of anticoagulation treatment are not explained. Anticoagulant efficacy, evaluation criteria are not provided. And pictures of before and after anticoagulation should be provided.

As indicated by the reviewer, we explained the plan and basis of anticoagulation treatment in METHODS. We also add a pictures of before and after anticoagulant therapy in figure 3.

**Page 7, line 13-17**

**In small PVT, a short half-life heparin was used just after detecting PVT by CT, while in cases of large PVT, intravenous heparin combined with oral anticoagulation (warfarin or direct oral anticoagulant) were used as an initial treatment. Then, the heparin was changed to an oral anticoagulant from 10 days after operation.**

**Figure 3 Before and after anticoagulation therapy**

**(A)In case 7, PVT found in umbilical portion (UP). (B)PVT disappeared on 140 days after the starting of anticoagulant therapy.**

4, "Anatomical resection is the only independent predictor for the occurrence of PVT. Anatomical resection tends to be associated with longer operation time, hepatic clamping time, and wider transection surface." But there is no statistics difference in operation time and hepatic clamping time. The relevant results do not draw conclusions cited above.

As indicated by the reviewer, operation time and hepatic clamping time did not reach statistical difference. We correct about the following sentence.

**Page 11, line 17**

**We changed "anatomical resection" to "sectionectomy".**

**Page 12, line 18-19: Removed**

**Anatomical resection tends to be associated with longer operation time, hepatic clamping time, and wider transection surface.**

*Reviewer #2:*

*Specific Comments to Authors: The incidence of portal vein thrombosis after hepatectomy for hepatocellular carcinoma is extremely low, about 2-4% reported in the literature, and it is likely to occur after right hepatic lobectomy. The number of cases provided in this article is small, and the diagnostic rate of postoperative contrast-enhanced computed tomography (E-CT) examination is also questionable. It is recommended to increase the case data and publish it after further research.*

As you pointed out, the number of cases is small to point out portal vein thrombosis. We are ongoing this protocol to analyze larger population again. We added to this concern in the discussion.

**Newly added: Page12; line 12-14.**

**The statistical power to analyze the risk factors for PVT was not optimal therefore, this protocol is ongoing to analyze larger population in the future.**