January 5, 2017

Prof. Damian Garcia-Olmo, Stephen Strom, Andrzej Tarnawski

World Journal of Gastroenterology

Dear Profs. Garcia-Olmo, Strom, and Tarnawski,

Scientific editor: Ze-Mao Gong

Subject: The submission of our revised manuscript entitled, "*The possible role of soluble fibrin monomer complex (SFMC) after gastroenterological surgery*"

Thank you for your letter regarding our manuscript (Manuscript NO: 31413), which was dated 24 December 2016. The manuscript was revised in accordance with the reviewer's suggestions. We herein submit the revised manuscript for your consideration.

Our responses to the reviewer's suggestions and the revisions that were made are summarized in the text below. We hope that the revised manuscript is now suitable for publication in *World Journal of Gastroenterology*.

Sincerely,

Manabu Shimomura

Response to the reviewer's comment

Thank you for your valuable comments. The manuscript was extensively revised in response to your suggestions. Our responses to your comments are noted below.

Reviewer code: 00502831

Comments:

The authors examined the role of SFMC in the prediction of hypercoagulable state after gastroenterological surgery, and they concluded that the SFMC on POD 1 strongly predicted the hypercoagulable state after gastroenterological surgery than the clinical risk factors and the other fibrin related markers. VTE is serious problem after surgery. This article is thought to be significant for prediction of hypercoagulable state on early phase after gastroenterological surgery. But I have some comments as bellow.

#1. The authors should described the recommendation about the strategy of anticoagulant therapy on high SFMC on POD 1 cases.

Response:

The authors appreciate this comment. As described in the manuscript, the selective administration of anticoagulant therapy to patients in the SFMC-high group would be effective for preventing the development of VTE. We added following statement to the Discussion (page 12, Lines 28-30): ", and the selective administration of anticoagulant therapy to the patients of the SFMC-high group would be effective for preventing the development of VTE."

#2. There were sixteen cases which had high D-dimer (POD7) and low SFMC (POD1). The authors should explained about these cases.

Response:

As the reviewer indicated, there were cases in which the patients had high D-dimer (POD 7) and low SFMC (POD 1). This was related to the fact that the sensitivity of SFMC in the present study was 63%. Since it might be difficult to select all patients with a hypercoagulable state after surgery based on SFMC (POD 1) alone, we plan to add measurements on the second and third days in further clinical studies.

#3. How about relationship between preoperative state of SFMC, D-dimer and VTE after surgery?

Response:

As the reviewer indicated, the relationship between the preoperative SFMC and D-dimer levels and the development of VTE after surgery is important. However, the preoperative SFMC and D-dimer levels have been shown to predict VTE in past studies (reference No. 10 and 13). These studies indicate that the preoperative level of SFMC was not increased in patients who developed postoperative VTE. The following publications support this position. Considering these issues, we added the following sentences to the Discussion (page 12, Lines 9-13): "The relationship between the preoperative SFMC and D-dimer levels and the development of VTE after surgery is

important; however, the preoperative SFMC and D-dimer levels could not predict postoperative VTE in previous studies[10,13]. These studies indicate that the preoperative SFMC level was not increased in patients who developed postoperative VTE.”

#4. The authors should explained about SFMC more in detail using schema.

Response:

We appreciate this comment. We added Figure 1 to explain SFMC in greater detail.

#5. Why did the D-dimer level on POD 7 reflect the occurrence of VTE?

Response:

As the reviewer suggested, the D-dimer level on POD 7 did not always reflect the presence of true VTE. As described in the manuscript, D-dimer elevation is a strong predictor of VTE, and previous studies (Reference No. 10) have shown that D-dimer elevation on POD 7 is associated with the presence of VTE. Thus, we used it as an indicator of a hypercoagulable state.