

## Format for ANSWERING REVIEWERS

May 07, 2014



Dear Editor

Please find enclosed the edited manuscript in word format (file name Shin 9489.doc).

**Title:** Proton pump inhibitor administration may delay rebleeding after endoscopic gastric variceal obturation

**Authors:** Won Seok Jang, Hyun Phil Shin, Joung Il Lee, Kwang Ro Joo, Jae Myung Cha, Jung Won Jeon, Jun Uk Lim

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 9489

### **Answer for review and comments (2445043)**

Thank you for your kind review and comments and I really appreciate your effort.

**1. MELD should be used (instead of the outdated CTP scoring system) for the patient characteristics.**

Thank you for your kind and proper comments. According to your suggestion, we used MELD score and corrected table 1 and results.

**2. I realize there is a low number of patients in the study. However, the same patients should not be used more than once as this creates some inherent bias.**

I agree with your exact opinion. We also worried about the bias but analyzed all cases because of low number of cases. However, according to your comment, we corrected that only one case per patient was included in this study.

After correction, because of limited number of patients, we still can show that bleeding interval was correlated when patients take PPI or not, but can't show the relation between duration of PPI use and rebleeding interval.

**3. In the methods, "hepatic failure" was used as an exclusion criteria but how was this defined. There is likely some degree since all patients had cirrhosis. I would like to see this more clearly defined.**

I agree with your opinion. During the hospital stay of this study, there was no case with hepatic failure. More clearly, we deleted hepatic failure in exclusion criteria and described that there was no patients dying during hospital stay.

**4. In the introduction, you wrote "...treat post-sclerotherapy esophageal ulcers" --> shouldn't this be gastric ulcers?**

Thank you for kind comments. These studies [16-20] are reported about post-sclerotherapy esophageal ulcers, but not reported much about post-sclerotherapy gastric ulcer. Therefore, we studied about PPI use for gastric varices treated by injection therapy and this is the aim of our study.

According to your comment, we changed post-sclerotherapy esophageal ulcers as post-sclerotherapy ulcers.

**5. In the discussion, you wrote "Among the complication of gastric varices, variceal bleeding is fatal." It can be fatal but is not necessarily fatal always as your sentence suggests.**

Thank you for your exact comment. We changed like that variceal bleeding is serious problem.

**6. In the discussion, you wrote "This ulcer is high probability of vessel.exposure." It should be written as "This ulcer has a high probability of vessel exposure."**

Thank you for your kind comment. According to your comments, we corrected.

**7. I think with a study with such a small number of patients, then it should have been easier to standardize and give all patients just one single type of**

### **PPI to be more uniform.**

You're comment is absolutely right. Please understand that this is a retrospective study. In the discussion, we admitted and described "Therefore, additional studies with a larger population with single type of PPI should be used to further elucidate the benefits and effectiveness of PPI in GV patients"

### **8. It also needs some language polishing and utilization of paragraphs to read easier**

The English in this document has been checked by professional English editor, we will check again to be read easier.

### **Answer for review and comments (No. 44945)**

Thank you for your kind review and comments and I really appreciate your effort.

### **Despite the interesting hypothesis, some important data are missing.**

#### **1. how many pts did rebleed?**

Thank you for your very important and proper comment. I admit my mistakes and I have inserted data. Following another reviewer's comment, we analyzed again, not using same patients more than once.

The group that used PPIs had experienced rebleeding in 8 out of 12 patients and the non PPI use group in 3 out of 4 patients.

#### **2. How many episodes?**

Because, we analyzed again, this revised manuscript did not use same patients more than once. Only first bleeding episode were included.

#### **3. How often the bleeding episode could be attributed to ulceration**

Six patients had ulcers at previous injection site. Although, there is a limitation of retrospective study, we think that all these ulcers may be the cause of bleeding because there were no suspected bleeding stigmas except ulcers in these six patients.

## **Answer for review and comments (No. 1560862)**

Thank you for your kind review and comments and I really appreciate your effort.

**This manuscript entitled: Proton pump inhibitor administration can extend the rebleeding interval after endoscopic gastric variceal obturation with N-butyl-2-cyanoacrylate** While an interesting paper, there are some serious concerns with this manuscript. Major comments

**1. This paper is a retrospective study and the sample size is too small.**

I completely agree with your exact opinion. But, reports that address the effectiveness of PPI are rare for gastric varices treated by injection therapy. Therefore, this study can give meaningful message for readers.

**2. It is unclear the rebleeding of the difference gastric variceal bleeding or not variceal bleeding.**

Thank you for proper comment. Because this is retrospective study, we can't confirm that all cases were related with gastric variceal bleeding. Some cases might have been related with esophageal variceal bleeding, but no definite esophageal bleeding were not observed in this study,

**3. This study has a selection bias for PPI use.**

Your comment is right and important. In the discussion, we admitted and described that "Third, the study sample had a selection bias for PPI use based on the clinician's subjective findings. Fourth, kind of PPI is various"

**4. Prospective randomized study is necessary for effectiveness of PPI.**

We admit that this study has limitations. In the discussion, we described "Therefore, additional prospective studies with a larger population with single type of PPI should be used to further elucidate the benefits and effectiveness of PPI in GV patients"

Thank you again for kind review and publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'H. Phil Shin', with a stylized, cursive script.

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