ANSWERING REVIEWERS

February 10, 2014

Dear editor,

We deeply appreciate the opportunity to revise this manuscript for *World Journal of Gastroenterology*. The reviewers' valuable comments on this study made us better understand the issue and inspired us to conduct further research on the topic of this study. We are pleased to inform you that we are ready to resubmit our revised manuscript, taking into account the reviewer's comments.

Thank you again for your kind review. We look forward to your response.

Sincerely yours,

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Title: **Negative impact of sedation on esophagogastric junction evaluation during esophagogastroduodenoscopy**

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Reviewer 1.

The current article presents interesting data concerning a very current discussion about the optimal sedation effect in endoscopies. An excellent view of the EGJ in endoscopy of the upper GI in times of increasing Barrett's esophagus, and esophageal adenocarcinoma is very important. If the effect of no sedation is really the key for a better visualization of this area seems to be questionable. The limitation of this study definitely is that there was no randomization no blinded approach, what to my mind should be no problem in a prospective study of such a frequent examination. It scares me that more than 50% (n=52) had have no excellent grade of visualization which seems to be a problem of the quality of the endoscopy or do all the endoscopists performing gastroscopies every day under sedation or propofol do a bad job. Did the endoscopists in this study themselves apply the sedation or a nurse? The effect of randomization and blinding seems indispensable regarding the distribution of 28.6% vs. 27.3% vs. 91.4% of visualization in the 3 different groups. The conclusion that sedation during EGD has a negative impact on EGJ evaluation cannot be drawn on the bottom of this study. Also the introduction and discussion part could profit from a presentation of what is currently used for sedation (e.g. World J Gastroenterol 2013 January 28; 19(4): 463-481).

Answer: Thank you for your critical comments. We absolutely agree with your point regarding non-randomization and non-blindness design as the limitation of this study. Despite a prospective study, we could not perform randomization for the assignment of each group

from the beginning because many subjects want sedation during EGD and they have the strong preference to the specific kind of sedative agents (propofol or midazolam). In Korea which has a high prevalence of gastric cancer, subjects over 40 years old can have free screening EGD every other year with government support as the national strategy for cancer control since 1999, which means almost participants have the previous experience of EGD. Therefore, it is almost impossible for us to allocate patients to sedation or non-sedation group against their will. We described this point in the Discussion (page 8).

As far as we know, there is no study on the quality of EGJ evaluation during EGD. As there are no criteria on the grading system for EGJ evaluation, we created our own grading system; excellent (100% of the EGJ), good (100% > EGJ ≥ 50%), fair (50% > EGJ), and poor (non-visualized EGJ). We believe that it is quite difficult to obtain 100% of the EGJ territory without patient's cooperation (i.e., inspiration). Therefore, we believe that it is hard to tell this result (50% had no excellent grade of visualization) a problem of the quality of the endoscopy. The number of patients increased up to 77 (74%) when we chose excellent or good grade (>50% EGJ) of EGJ visualization in this study.

Reviewer 2.

Authors deal with EGJ evaluation quality during EGD with sedation. In Western countries sedation during EGD is quite common, but its use makes it impossible for patients to breathe in deeply. So the use of sedative agents during EGD might cause inadequate inspection of EGJ, but there have been few papers regarding the issue. In the sense, this paper is quite important. However, some points should be improved before acceptance.

Major comments: 1. In this manuscript, the primary outcome is not the accuracy of detecting lesions in at the EGJ but EGJ evaluation itself. So, the precise definition of EGJ in this study

is essential. However, in this manuscript, EGJ definition is quite vague. Was deep inspiration necessary or not? Which was laid weight on, the distal end of the longitudinal esophageal vessels or the proximal end of the longitudinal gastric mucosal folds? Please define them in detail.

Answer: Indeed, it is quite difficult to define EGJ endoscopically because of the lack of authoritative guidance in the literature on how to locate the EGJ. In addition, the EGJ definition differs between Asian and Western endoscopists; the distal end of the lower-esophageal palisade vessels is used to define the EGJ in Japan while the land mark is the upper end of the gastric longitudinal folds in Western countries. As upper end of gastric folds has been supported as the definition of EGJ by several studies, we decided to use this definition (Gastroenterology 2006;131:1392-1399, Gastrointest Endosc 2006;64:206-211). We did not ask patients anything regarding respiration during EGD. This aspect was described in Method (page 4) and Discussion (page 8).

2. Moreover, EGJ evaluation grades should be explained more concretely. Authors showed an example in Figure 1, but the difference between “Good” and “Fair” was obscure. This point is also very important, so please add more detailed explanation.

Answer: As there are no criteria on the grading system for EGJ evaluation, we created our own grading system; excellent (100% of the EGJ), good (100% > EGJ ≥ 50%), fair (50% > EGJ), and poor (non-visualized EGJ). We changed the figures and added indicators in Figure 1 for better understanding. Thank you for your crucial comment.

3. Please explain why authors assumed that the proportion of excellent observation in the

sedation group would be 60% in contrast to 90% in the non-sedation group.

Answer: Before initiating this study, we collected preliminary data with 20 subjects (10 from non-sedation, 10 from propofol group). In the preliminary data, 90% (9/10) in non-sedation group and 60% (6/10) in sedation group showed excellent EGJ observation. Based on this data, we assumed the proportion of each group. We added this comment in the Method (page 5).

4. If possible, please tell me why this study was not conducted in a randomized design although authors had calculated the necessary sample size.

Answer: Despite a prospective study, we could not perform randomization for the assignment of each group from the beginning because many subjects want sedation during EGD and they have the strong preference to the kind of sedative agents (propofol or midazolam). In Korea which has a high prevalence of gastric cancer, subjects over 40 years old can have free screening EGD every other year with government support as the national strategy for cancer control since 1999, which means almost all participants have the previous experience of EGD. Therefore, it is nearly impossible for us to allocate patients to sedation or non-sedation group against their will. We described this point in the Discussion (page 8).

Reviewer 3.

The study consists of a smart idea regarding visualization of EGJ during UGI endoscopy with and without sedation. One drawback is what you already mention in the discussion that endoscopies were carried-out in a non-blinded manner, so endoscopist was aware in advance if the subject was sedated or not. In order to overcome this and further validate your study it

could be nice to perform, in some subjects, UGI with and without sedation and so confirm the results of your study if you get similar results in this matched way (each subject to serve as control of him/herself sedated or not.

Answer: Thank you for your comment. Despite a prospective study, we could not perform randomization for the assignment of each group from the beginning because many subjects want sedation during EGD and they have the strong preference to the kind of sedative agents. In Korea which has a high prevalence of gastric cancer, subjects over 40 years old can have free screening EGD every other year with government support as the national strategy for cancer control since 1999, which means almost participants have the previous experience of EGD. Therefore, it is almost impossible for us to allocate patients to sedation or non-sedation group against their will. We described this point in the Discussion (page 8). In the future, we will conduct randomized, blinded study taking into account your comments.

Reviewer 4.

Good work for a nice idea

Answer: We appreciate your positive comment.