

March 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9211-review.doc).

Title: Comparison of a novel bedside portable endoscopy device with nasogastric aspiration for identifying upper gastrointestinal bleeding

Author: Jong Hwan Choi, Jae Hyuk Choi, Yoo Jin Lee, Hyung Ki Lee, Wang Yong Choi, Eun Soo Kim, Kyung Sik Park, Kwang Bum Cho, Byoung Kuk Jang, Woo Jin Chung, Jae Seok Hwang

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9211

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated

2. Revision has been made according to the suggestions of the reviewer

1) Reviewer 1

The most important advantage of this method that was applied in the manuscript is the statistically significant sensitivity, specificity and accuracy of EG scan in the esophageal lesions.

Answer: Thank you for your positive comments.

2) Reviewer 2

① The abbreviations of some medical terminology in the abstract, such as NG, EG, should be given the full name at where they are firstly mentioned.

Answer: We put full name of NG in the first appearance and changed EG to the portable endoscopy in abstract as you requested.

②What's the accurate explanation of the last item of exclusion criteria 'no final esophagogastroduodenoscopy (EGD) evaluation'. Did 'the final EGD' mean that patients who were eligible for this study refused the final EGD?

Answer: Yes, it meant that patients resenting with bleeding symptoms or signs did not undergo EGD for any reason. There were some patients who refused EGD for cost problem or who insisted to go home before taking EGD. We inserted this aspect in page 6 Method.

③ The primary outcome should be described with numerical index other than effectiveness and safety outcome.

Answer: Thank you for your comment. We corrected primary outcome in 7 Method as you requested. "Primary outcome measures were (i) comparison of **the accuracy, sensitivity and specificity of the EG scan in identifying UGI bleeding with NG tube insertion, and (ii) the rate of adverse event of the EG scan procedure.**"

④ Did the study receive the approval of the medical ethics committee?

Answer: Yes, it did. Also, it was registered on the WHO International Clinical Trials Registry Platform. This was described in page 6 Method section.

⑤ The data of the two groups should be listed respectively both in Tables 1 and 2.

Answer: As we described in Method section, both NG and EG scan were conducted in each patient. Please refer to the manuscript page 6. "First, patients suspicious for active GI bleeding who visited the emergency room received NG tube insertion and aspiration with or without lavage to confirm active UGI bleeding according to the International Consensus Recommendations for patients with UGI bleeding.³ Then, the EG scan device was inserted within 12 h from NG tube insertion to identify the focus of the UGI bleeding." Therefore, because patients are the same group, they cannot be separated in Table 1 and 2.

⑥ The number of patients with UGI bleeding was 81 in Table 2, but the sample size of patients with UGI Bleeding in accuracy calculating in Table 4 was 93 (the definition of accuracy in the manuscript, "Accuracy was the proportion of all cases correctly identified by the test"), so how did you get the number?

Answer: Thank you for your critical question. Accuracy means the proportion of all cases correctly identified by the test (true positive + true negative). The 2 X 2 table would be helpful for the understanding.

	Bleeding yes	Bleeding no	
EG scan bleeding yes	A 52	B 7	59
EG scan bleeding no	C 29	D 41	70
	81	48	

Sensitivity: $A/(A+C)$

Specificity: $D/(B+D)$

Accuracy: $(A+D)/(A+B+C+D)$

Therefore, 93 was calculated by sum of true positive (A 52) and true negative (D 41).

⑦ The number of patients with esophagus diseases was 20 in Table 2, but in Table 4

the number was 68, which include what kinds of patients?

Answer: The number of esophagus outcomes in Table 4 (68) was calculated by subtraction definite stomach and duodenal lesions from all cases (129 - 53 - 8). In other words, for specificity outcome (true negative), non UGI bleeding (36) and no definite focus of bleeding (12) was included to true esophageal lesions (20).

⑧ The average time from NG tube aspiration to EG scan was 129.5 ± 190.5 min. It's too long to ensure the reliability of the conclusion, for considering that the UGI bleeding might stop automatically.

Answer: This is a critical weak point of this study. As described in the manuscript, we compared the accuracy of the EG scan and NG tube aspiration in a matched pairwise manner in the same group of patients (NG aspiration then EG scan) rather than a head-to-head comparison in two independent groups of subjects. This was because there might be an ethical issue if we performed the EG scan in a patient without knowing its efficacy or safety. The reason for delay between NG and EG scan might be due to the time taking notification to doctors of gastroenterology division. We added comment on this issue in 12 page of Discussion section.

⑨ Every patient took EGD for final diagnosis, but the author didn't give the time interval, for which would affect the reliability of the conclusion as the UGI bleeding might stop automatically during the interval.

Answer: We absolutely agree with this point which was also crucial in the study. The time delay between EG scan and EGD was approximately 7.3 ± 7.6 hours. However, we could identify the potential bleeding point lesions by EGD even though there was no blood in the stomach, such as gastric or duodenal ulcers with stigmata Mallory-Weiss mucosal tear, and varices with surface erosion. We added time delay between EG scan and EGD in page 8 Result section.

⑩ In this study, patients received NG first, and then received EG. Did the diagnosis of UGI bleeding was made by different doctors. If the doctor check the NG result, and then check EG result subsequently, it may affect his/her diagnosis and result in false positive rate of EG.

Answer: Thank you for your question. They were different doctors between NG and EG scan. Doctors who performed EG scan did not know the result of NG aspiration. We added this point in page 6 Method section.

⑪ Kindly recommend you could read the references : Nirmal SA, Ingale JM, Pattan SR, Bhawar SB. *Amaranthus roxburghianus* root extract in combination with piperine as a potential treatment of ulcerative colitis in mice. *J Integr Med.* 2013; 11(3): 206-212.

Answer: We read this important article with great interest and joy. Thank you for your recommendation.

Reviewer 3

A very interesting paper addressing the important clinical problem of triaging upper GI bleeding. I feel that the most useful role of this new tool would be in identifying food in the stomach which may increase aspiration risk with sedation. This is stated by the authors along with other potential benefits, but I feel this point is the most salient, and other potential advantages stated are overemphasised. The role of EG scan in detecting esophageal bleeding in cirrhotics I feel is not relevant as these patients would all go on to have formal EGD and EG scan may delay this. The poor sensitivity for gastric and duodenal blood and lesions also limit the usefulness of this tool. It is reassuring that this EG scan is not operator dependent, however patients did not appear to tolerate the test very well.

Answer: We absolutely agree with your opinion. EG scan can never replace the EGD for any patients with bleeding symptoms or signs and EGD should not be delayed due to EG scan or NG aspiration. However, we think that it might be helpful to use correct therapeutic agents (PPI or somatostatin) before conducting EGD by differentiating between variceal bleeding and peptic ulcer bleeding in liver cirrhosis patients. Thank you for your critical comments. We added your comment in abstract result section.

3 References and typesetting were corrected.

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

Sincerely yours,

Eun Soo Kim, MD, PhD

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keimyung University School of Medicine, 194 Dongsan-dong, Jung-gu, Daegu 700-712, South Korea. dandy813@hanmail.net