Author’s response to reviews

Title: Evaluation of scoring systems without endoscopic findings for predicting outcomes in patients with upper gastrointestinal bleeding

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Author’s response to reviews:

Editor Comments:

Two referees have reviewed your manuscript and their comments are included at the bottom of this letter. The referees had a number of important concerns regarding your manuscript, especially the cause of bleeding, ulcer bleeding or variceal bleeding should be separated for analysis.

Authors answer:

We sincerely appreciate for your kind advice and comments to our manuscript. We revised the manuscript as per reviewer’s comments. We represents the specific modifications in response to the comments by blue-letters in our manuscript.

Review reports (Wei-Lun Chang, Ph.D.)
This retrospective study compared the applicability of Glasgow-Blatchford score (GBS), modified GBS (mGBS), and pre-endoscopy Rockall score (Pre-E RS) in predicting the need for endoscopic intervention and 30-day mortality. The results are quite similar to previous studies showing that GBS is better at deciding endoscopic intervention. And RS is better for predicting 30-day mortality.

Reviewer question-1

“Based on AUC analyses of sensitivities and specificities, the optimal cutoff mGBS and GBS for the need for interventions was (70.71 % sensitivity, 89.35% specificity) and 9 (73.57 % sensitivity, 82.90% specificity) respectively, and optimal cutoff Pre-E RS for 30-day mortality was 4 (88.0 % sensitivity, 97.52% specificity).” There seemed to be a word missing in this sentence. What is the optimal cutoff for mGBS?

Author answer

Thank you very much for your comments about our mistakes. According to reviewer’s comment, we added missing posts in abstract part.

► Following sentences were added to the abstract parts.

Based on AUC analyses of sensitivities and specificities, the optimal cutoff mGBS and GBS for the need for interventions was 9 (70.71 % sensitivity, 89.35% specificity)…. (2 page, 18 lines)

Reviewer question-2

In page 7 line 3: Octreotide and glypressin are two different drugs, please correct.

Author answer

According to reviewer’s comment, we modified sentence in methods part.

► Following sentences were modified to the methods parts.

The terlipressin (Glypressin® Ferring Pharmaceuticals, Saint-Prex, Switzerland) (7 page, 3 lines)

Reviewer question-3

Table 3 is suggested to include information of hemostatic intervention, so that the paragraph of “Endoscopic findings” can be shortened.

Author answer
We agree with reviewer comment. However, the paragraph of “Endoscopic findings” explained how hemostatic interventions were conducted according to each endoscopic finding. So please acknowledge that the sentences became long.

Reviewer question-4

A table or figure showing the patient numbers in each score and the patient numbers that need interventions of the 3 scoring systems will help readers understand the disease severity and the ratio of intervention in each score.

Author answer

We agree your opinion. We will add a table showing the patient numbers in each score and the patient numbers that need intervention of the 3 scoring systems.

► Following sentence were added to the results parts.

Table 4 lists the patient numbers in each score and the patient numbers that underwent hemostatic interventions (transfusion and hemostatic procedures). (10 page, 16-17 lines)

► Following table were added to the results parts.

"The authors' response letter has been included as a Table 4 in manuscript" (26 page, 4 lines to 27 page, 2 lines)

Reviewer question-5

Besides the above scoring system, “AIMS65” had been shown to be superior in predicting 30-day mortality and rebleeding (Gastrointest Endosc 2016;83:1151-60; J Dig Dis 2016;17:820-828). How about AIM65 in predicting 30-day mortality compare to pre-RS or full RS in their study population?

Author answer

We agree your opinion. But when we planned research, we did not sort out factors involved in AIMS65 because AIMS65 was not considered. If the study is terminated at our hospital, we can’t access the data of patients included in the study. Please understand that we can’t compare with the AIMS65 because it is difficult to identify the factors associated with AIMS65. Please understand the difficulties of this study.

Reviewer question-6

Previous study showed these scoring system were less accurate in predicting outcome of patients with variceal bleeding (J Gastroenterol Hepatol 2016;31:761-7). However, the author included patients with variceal bleeding. Will the result be different if the analyses were stratified by non-variceal vs. variceal bleeding?
Author answer

When we planned this study, we considered a research involving only patients with non-variceal bleeding. However patients with UGIB symptoms and Sign visiting emergency department can’t be distinguished clearly between variceal bleeding and non-variceal bleeding first. So, we analyzed patients with symptoms and signs of UGIB from either variceal or nonvariceal source. According to your advice, we analyzed data involving only patients with non-variceal bleeding.

► Following sentence were added to the discussion parts.

When we planned this study, we considered a research involving only patients with non-variceal bleeding. However patients with symptoms and signs of UGIB who visited emergency department could not be distinguished clearly between variceal bleeding and non-variceal bleeding first. So, we analyzed patients with symptoms and signs of UGIB from either variceal or non-variceal source. However, when we analyzed data involving only patients with non-variceal bleeding, the result was similar with that of this study. (13 page, 9-14 lines)

Reviewer question-7

The selection of optimal cut-off is usually based on youden index, did the author select their optimal value based on it?

Author answer

Yes, we selected optimal value based on youden index.

Reviewer question-8

The statement “However, RS is not suitable for an early decision on need of urgent interventions or predicting 30-day mortality in the management of patients with UGIB, since it requires endoscopic finding” is not true since their data showed Pre-E RS is good at predicting 30-day mortality. Moreover, they do not show the data of RS to predict 30-day mortality. The statement should be modified.

Author answer

We agree your opinion. We will modify the statement according to your advice.

Reviewer question-9

The author stated “Our results suggest that patients with GBS > 9 or mGBS > 9 need hemostatic interventions and have to undergo early gastroscopy”. The author should provide data to show that in patients with GBS or mGBS > 9, a shorter presentation-to-endoscopy time is related to a lower mortality.
Author answer

Thank you for your point-out. According to reviewer’s comment, we provide new data to show that in patients with GBS or mGBS > 9, a shorter presentation-to-endoscopy time is related to a lower mortality. We will comment that in paragraph “The comparison of scoring systems for predicting the need of interventions and 30-day mortality without endoscopic findings” of result.

Following sentence were added to the results parts.

Of 397 patients with GBS > 9, 21 patients died in 30 day from presentation. Of them, 12 patients underwent endoscopy after 24 hours from presentation, and 9 patients underwent endoscopy within 24 hours (X2 = 21.675, p < 0.001). The odds ratio for 30 days mortality was 6.753 (95% CI, 2.729 to 16.712) meaning that the probability of death in the endoscopy performance over 24 hours was 6.753 times higher than in the endoscopy performance within 24 hours.

Of 372 patients with mGBS > 9, 21 patients died in 30 day from presentation. Among them, 12 patients underwent endoscopy after 24 hours from presentation, and 9 patients underwent endoscopy within 24 hours (X2 = 19.380, p < 0.001). The odds ratio for 30 days mortality was 6.215 (95% CI, 2.510 to 15.390) meaning that the probability of death in the endoscopy performance over 24 hours was 6.215 times higher than in the endoscopy performance within 24 hours.

Reviewer question-10


Author answer

Thank you for finding out our fault. I will correct that.

Review reports (Kuei-Chuan Lee)

In this study, IG Ko et al retrospectively reviewed 590 patients with upper gastrointestinal bleeding (UGIB). They aimed to compare the three scoring systems which were used to evaluate the severity and outcomes of patients with UGIB before endoscopy performed. They also investigated the potential cutoff scores to predict the need of interventions and 30-day mortality in applicable scoring systems. This study gives us some good concepts in evaluation of UGIB patient generally. I think the study has some values in practical care of UGIB patients.

Major comments 1.
There were many diseases to cause UGIB, such as variceal bleeding, peptic ulcer disease, malignancy etc…., and different medication or interventions may be performed to treat different causes to UGIB. This study includes all UGIB conditions, as a result, there may be lots of confounding factors. I suggest analyze outcomes of subgroups (variceal bleeding vs. non-variceal bleeding, vs. malignancy) by the scoring systems.

Author answer

When we planned this study, we considered a research which separated patients with variceal, non-variceal, and malignant bleeding. However patients with symptoms and Sign of UGIB who visited emergency department could not be distinguished clearly between variceal bleeding and non-variceal bleeding first. So, we analyzed patients with symptoms and signs of UGIB from either variceal or non-variceal source. According to your advice, we analyzed data involving only patients with non-variceal bleeding. The result was similar with that of this study. We will comment this in discussion.

►Following sentence were added to the discussion parts.

When we planned this study, we considered a research involving only patients with non-variceal bleeding. However patients with symptoms and signs of UGIB who visited emergency department could not be distinguished clearly between variceal bleeding and non-variceal bleeding first. So, we analyzed patients with symptoms and signs of UGIB from either variceal or non-variceal source. However, when we analyzed data involving only patients with non-variceal bleeding, the result was similar with that of this study. (13 page, 9-14 lines)

Major comments 2.

As mention to UGIB prognosis, we do care about rebleeding rate besides mortality. Do you have the rebleeding rate of the study patients after medication or intervention therapy? Were there any relationships between the scores and rebleeding rate?

Author answer

Thank you for your point-out. We evaluated the prognosis through 30-day mortality rather than rebleeding rate. So we were not able to analyze the rebleeding rate during the initial study design. However, we found that, in the case of 30-day mortality, in most cases, the patient's condition deteriorated due to rebleeding, leading to death.

Minor comment-1

Page 2, line 18, "…for the need for interventions was (70.71 % sensitivity, …" Should be "…for the need for interventions was 9 (70.71% sensitivity,…"

Author answer
Thank you very much for your comments about our mistakes. According to reviewer’s comment, we added missing posts in abstract part.

► Following sentences were added to the abstract parts.

Based on AUC analyses of sensitivities and specificities, the optimal cutoff mGBS and GBS for the need for interventions was 9 (70.71% sensitivity, 89.35% specificity)…(2 page, 18 lines)

Minor comment-2

Page 6, "Study population" Since the study were carried out at a teaching center, did you exclude the patients who were referred from other primary hospitals? Because these referred patients may have already received interventions before.

Author answer

Your point out is correct. We excluded the patients who already underwent gastroscopy and hemostatic interventions.

Minor comment-3

Page 7, line 2, "The proton pump inhibitor..." Nowadays we all know that high dose PPI may downgrade the severity of Forrest classification when endoscopy is performed. Do you record the patients' proportion of receiving high dose PPI?

Author answer

Yes. We administered high dose PPI to patients with UGIB. We will that in my manuscript.

► Following sentences were added to the method parts.

The high dose proton pump inhibitor (Pantoloc® Takeda GmbH, Singen, Germany) was administered to all subjects with UGIB intravenously. (7 page, 2 lines)

Minor comment-4

Page 25, "Table 2" Since the patients were reviewed between 2007-2016, were there patients who received clopidogrel or NOAC (novel oral anticoagulant)? Because you only record Aspirin and Warfarin in your table.

Author answer

Your comment is right. Of patienst who took aspirin, there were patients who took clopidogrel or NOAC (novel oral anticoagulant). I will correct my table.