

## Answering reviewers

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: -35383- Revised manuscript.doc)

Title: Scoring systems for peptic ulcer bleeding: Which one to use?

Author: Ivan Budimir, Sanja Stojšavljević, Neven Baršić, Alen Biščanin, Gorana Mirošević, Sven Bohnec, Lora Stanka Kirigin, Tajana Pavić, Neven Ljubičić.

Name of Journal: World Journal of Gastroenterology

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

1 Format has been updated

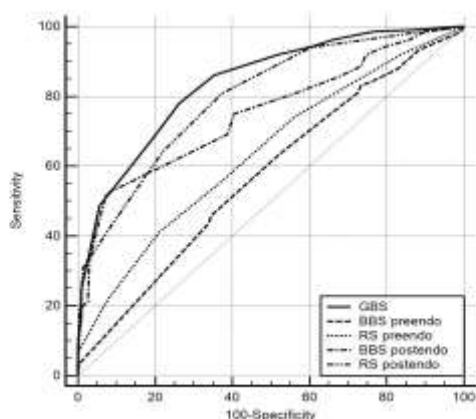
2 Revision has been made according to the suggestions of the reviewers and Editor

To reviewer 02927665:

The manuscript 35383, "Scoring systems for peptic ulcer bleeding: which one to use?" analyzed 1012 consecutive patients admitted with PUB. After comparing the RS, BBS and GBS scores systems, the author found that the RS is the best predictor of mortality and the GBS is the best predictor of rebleeding, need for blood transfusion and surgical intervention in patients with PUB. There is no one 'perfect score' and we suggest that these two tests be used concomitantly. It is an interest research for the PUB and can be published in WJG. However, there were some comments: 1.The authors should present the three scores system in a table and show the difference among these scores. This may be easier for the reader to understand this manuscript. 2.The figures and results should be re-collected as two parts: one is pre-endoscopic scores, the other is the post-endoscopic. In all, this study is an interest study and can be published in WJG after revised.

Thank you for your comments. We have revised the manuscript and the figures and legends were re-collected as two parts – one pre-endoscopic and other post-endoscopic. This has been changed in accordance with your suggestion and we believe that this has brought better understanding of the manuscript. We tried to present all three score systems in one figure but we believe that this is a too

busy figure, as you will see in the following example of Figure - Comparison of the GBS, pre-endoscopic--RS ,pre-endoscopic BBS, post-endoscopic RS and post-endoscopic BBS with AUROC figures for the prediction of need for hospital-based intervention or 30-day mortality [0.83 (CI 95% 0.81 to 0.86)] vs [0.63 (CI 95% 0.59 to 0.68)] vs [0.57 (CI 95% 0.53 to 0.61)] vs [0.79 (CI 95% 0.76 to 0.83)] vs [0.75 (CI 95% 0.71 to 0.78)]



To reviewer 01115220:

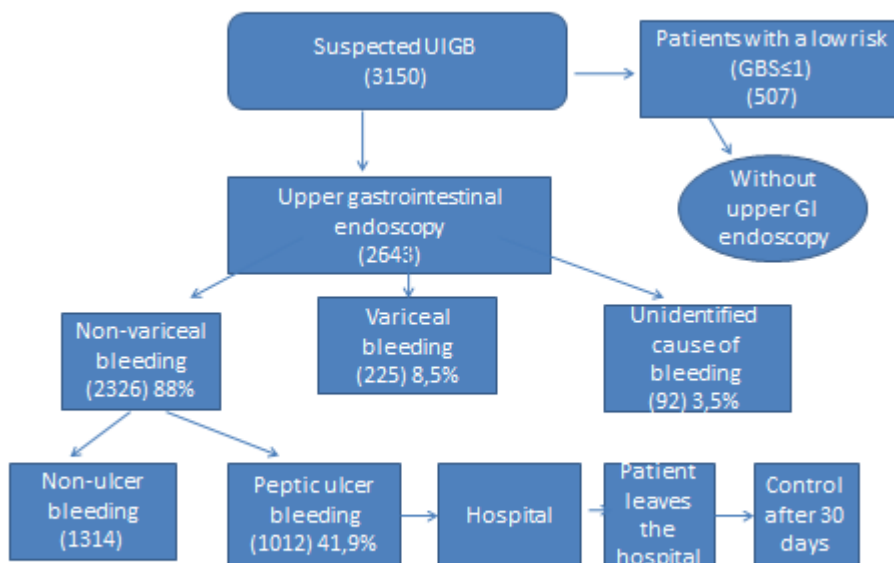
The authors have provided another data set comparing different scoring systems for prognosis in peptic ulcer bleeding. Whilst the authors should be congratulated for collecting together this dataset, there are several others papers comparing the same and arguably performing this slightly better, using the latest scoring systems and the most meaningful outcomes. Obviously it has taken some time to collect this cohort together and as such the paper cannot provide the most modern information as provided in papers such as BMJ. 2017 Jan 4;356:i6432. doi: 10.1136/bmj.i6432, which included over 3000 patients and used the latest scoring systems including AIMS65 and PNED. Hence it would be appropriate to remove the comments in the current paper about the apparent primary of these current analyses as there clearly are other prospective studies. The conclusions of the current paper are in general in concordance with others in that the GBS is usually the best predictor of the need for intervention and the full Rockall is better at predicting death. Whilst these are always useful, the authors should acknowledged that the AUROC scores in most of their analyzed are < 0.80 which is usually taken as the level required to be clinically meaningful measure. The sensitivity and specificity of nearly all their outcomes, although showing a difference between the scores, are really too poor to be used as clinical decision tools. It is unfortunate that the authors have not examined the most important clinical outcomes - the need for admission and intervention. Previous studies have clearly shown the GBS to be the superior score here. Whilst relative prognosis re mortality is somewhat clinical useful, it is much harder to say that a score here clearly alters management. Specific points: 1. the authors have very much

focused on rebleeding as an endpoint and they have not made a very good case for the importance of this. Rebleeding is probably mostly determined by the adequacy of endoscopic hemostasis plus some effects of comorbidity and predicting rebleeding on a pre-endoscopy score seems to be a rather pointless activity. It is important that the authors actually provide the comparison of the GBS and other pre-endoscopy scores, with the full post-endoscopy scores. It is also worth commenting on why the current study showed scores predicting rebleeding but this was not seen in the larger multicenter study (BMJ. 2017 Jan 4;356:i6432. doi: 10.1136/bmj.i6432). 2. Some elements of the methods require further explanation. What was the protocol and indications for transfusion? How was H pylori managed? What endoscopic therapies were applied? How many were taking NSAIDs or aspirin? 3. The cohort studied seems to only include patients admitted with upper GI bleeding. The main utility of the GBS score, of course, is to predict those that do not require admission or further therapy. How may low risk patients were excluded from the analysis? 4. How exactly were the data collected, how were decisions made on co-morbidity scoring, who was responsible for this? How were patients specifically followed up? Were they all seen at 30 days. There should be a chart of subject flow through the study. Some of these data are given, but subject flow should be clearer. 5. Why was high dose PPI used in all subjects? 6. The table listing the subjects included required more details. The individual Forrest classification data should be provided: the most recent data from both the Doppler and PPI-trials are that Forrest 1b lesions are not high-risk for rebleeding and it is not inappropriate to group these in with the Forrest 1a lesions. Much better to provide separate data for each Forrest group. 7. Throughout the paper, including the introduction, page 6, the authors state that scores have been designed to predict rebleeding: this is incorrect/. I am not aware that any score has ever been designed to predict rebleeding. The GBS was designed to predict lower risk bleeds, the Rockall to predict mortality. They may have secondarily applied to rebleeding but they were not designed as such. It is suggest this is corrected. 8. Also in the Introduction, it is rather incorrect to call a GBS score of >1 a high risk patient. This is clearly a higher risk than 0 but the important cut off in the GBS is 1 or less which are very low risk. Most clinicians would regard a GBS of > 12 or so as "high-risk." 9. In the Results section, it would be better to place the text providing the optimal cut-offs at the beginning of the section, rather than after the graphs. 10. In the discussion, there are too many over-interpretation of the relative scoring systems. It is not possible to say that score X is better than score Y, because of the different number of points given to A or B. All it is possible to conclude from these data are that one score is better in some circumstances than another.

Thank you for your extensive comments and constructive insight to our manuscript. We have tried to answer all your questions and implement them throughout the manuscript. The aim of this study was to compare pre-endoscopic and post-endoscopic scores in patients with peptic ulcer bleeding , and in the first version of the manuscript we did not show all the requested information of epidemiological and endoscopic characteristics that we have gathered through our research, but now we have corrected this as you proposed. 1. The Figure 1 represents the need to hospital- based intervention or 30-day mortality and the comparison of the GBS and other pre-endoscopy scores. Rebleeding was as the outcome researched in articles: Bryant RV, Kuo P, Williamson K, Yam C, Schoeman MN, et al. Performance of the Glasgow-Blatchford score in predicting clinical outcomes and intervention in hospitalized patients with upper GI bleeding. *Gastrointest Endosc* 2013;78(4):576-83[PMID: 23790755 DOI: 10.1016/j.gie.2013.05.003], Hyett BH, Abougergi MS, Charpentier JP, Kumar NL, Brozovic S, Claggett BL,

et al. The AIMS65 score compared with the Glasgow-Blatchford score in predicting outcomes in upper GI bleeding. *Gastrointest Endosc* 2013;77:551-7 [PMID: 23357496 DOI: 10.1016/j.gie.2012.11.022] and Laursen SB. Treatment and prognosis in peptic ulcer bleeding. *Dan Med J* 2014;61:B4797 [PMID: 24547604]. We changed the introduction as you suggested. 2. Now table 4. was updated with previously lacking information. 3. Of all patients 507 (16,15) had not had an endoscopy since they were at low risk (GBS<1). 4. Since we have more elaborately explained the mechanism of collected information we are of the opinion that the diagram will not be needed, but we have created one nonetheless if you will insist of incorporating one.

Diagram



5. This was elaborated in the manuscript. 6. Requested information was added in table 4. Comments under 7., 8., 9., and 10. were corrected in the manuscript as requested.

To reviewer 03474116:

General: In this study, the authors investigated to compare the scoring system of the Glasgow Blatchford score, Rockall score and Baylor bleeding score in predicting clinical outcomes and the need for interventions in patients with bleeding peptic ulcers. Finally, authors concluded that although there is no 'perfect score', the Rockall score is the best predictor of mortality and the Glasgow Blatchford score is the best predictor of rebleeding, need for blood transfusion and surgical intervention in patients with peptic ulcer bleeding. Although this study was well written, there were serious problem in this study, as below. Major comments: 1. In general, peptic ulcer disease is caused by *H. pylori* infection and NSAIDs

intake. Authors should add this information. 2. In addition, intake of anticoagulant influence incidence of bleeding. Authors should add this information, and evaluate association with intake of anticoagulant and rebleeding. 3. Endoscopic treatment was required in 58% of patients with ulcer bleeding. Please show how to treat.

Thank you for your comments. 1. We added the requested information that we did not state in the first version of the manuscript regarding H. pylori infection and NSAIDs intake. 2. We have also added the information on intake of antiplatelet and anticoagulant therapy. 3. We now showed how the treat.

To reviewer 00051373:

This is an observation study with evidence base concept to explore the monitor system for upper GI non-varices bleeding control. The manuscript is written so far so good. There are two comments to be revised. The blood transfusion needs to be more detail describe such as the component like PRBC, platelet, plasma or whole blood; and the transfusion amount like 2 units or 10 units. There is very important to predict the outcome and estimate the bleeding severity.

Thank you for your comments, we added in detail what was the threshold and the amount of specific blood units used.

Best regards,

Ivan Budimir

Sanja Stojšavljević