BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

Name of Journal: *World Journal of Gastrointestinal Pathophysiology*
ESPS Manuscript NO: 20912
Manuscript Type: Review

REVIEWER COMMENTS:

Reviewing: 1

This is an interesting and well written article. A following point can be easily incorporated in a revised version. The authors should discuss molecular pathological epidemiology (MPE). In the MPE framework, risk factors are associated differentially with various subtypes of disease including gastrointestinal bleeding. Hence, risk scores are likely different for different subtypes of bleeding. Thus, for future research, the authors should discuss MPE. The authors can quote Gut 2011; Am J Gastroenterol 2014 for the concept of MPE.

We have now discussed the molecular pathological epidemiology (MPE) and have included the following into the "When section" of the manuscript:

"Personalized medicine can help in stratification of patients according to biomarkers and guide optimal treatment and prevention. The molecular pathological epidemiology (MPE) is a recently established interdisciplinary and transdisciplinary field, which emerged from the complex relationship between etiological factors, molecular alterations, and disease evolution[79, 80]. MPE may stratify UGIB into different subtypes according to the pathogenic mechanisms, enabling a more efficient and individualized approach.

To date, most of MPE research is applied to cancer[81, 82], but this approach may also be important to UGIB and further investigation is needed to evaluate its contribution."

Reviewing: 2

This is a review on the characteristics, clinical use and limitations of upper gastrointestinal bleeding risk scores. This is a relevant topic because, although scientific societies guidelines recommend the use of these scores (albeit with a low strength recommendation), its use has not become generally adopted. The review seems thorough and updated. I would like to make some comments:

-Trying to fit the review in the sections who, when and why, as it is described in the title, makes the text somewhat confusing for the reader. The "Who section" seems a brief description of the main available risk scores. The "When section" makes a more deep review of the scores and their main outcomes, but it does not deals with "when" each score should be used. The reader could guess that the "why section" would deal with the reasons for a score to be used over a clinical evaluation, but it starts with a comparison of scores performance for different outcomes, a very interesting question that should fit more appropriately on the previous section.

We agree with the reviewer and to improve the readability we have carefully revised the text and removed the comparisons between various studies on "why section" and placed into the "when section".

In "When section" several sentences were introduced in order to establish deals with "when" each score should be used.

- The "why" section should be the more appealing, since the authors want to persuade the reader to use risk scores when approaching a patient with UGIB

In "WHY or WHY NOT should we use a risk score? section "we aim to demonstrate the importance and the reasons why to use a score on evaluation of patient with UGIB and we introduce some sentences to appeal their use. Also, we aim to present some limitations of these scores and thus justifying the reluctance of its use by most physicians.

- I suggest adding a more practical approach to the use of scores in the conclusion. Which score should be used depending on our objective (e.g. discharging a low-risk patient, early intervention on a high-risk patient, etc.). For instance, guidelines recommend using the Blatchford score to identify very low-risk patients (score 0) amenable to early discharge without endoscopy (Laine L, Am J Gastroenterol 2012). Other authors recommend the use of nonendoscopic scores when first evaluation patients with UGIB, early EGD in patients admitted with UGIB and early discharge if endoscopic low-risk lesions (Das A, Gastrointest Endosc 2004).

As suggested, we introduce the following data in the conclusion in order to clarify the current position of the scores in clinical practice:

"As a means to predict low risk patients amenable to an early discharge and outpatient management, the Rockall and GBS are the two most commonly used and recommended risk stratification systems[13].

T-score, recently described, can potentially be useful to predict high-risk endoscopic stigmata and the need of early intervention[65].

We recommend the use of non-endoscopic scores as the pre-endoscopic Rockall score or the GBS, as a decision tools for patients with acute UGIB. This scores may be useful when endoscopy are not available in the emergency department. A patient with Rockall score or the GBS equal to 0 can be safely discharged.

Moreover, we also advocate early endoscopy (within 12 to 24 hours of admission) and early discharge of patients with low risk lesions or low post-endoscopic risk scores (e.g. post-endoscopic Rockall score ≤ 2)."

- As the authors state, anticoagulants may change the mortality and rebleeding rates and most of the scores do not address this issue. Perhaps the fact that the AIMS65 score includes INR as a risk factor may be emphasized. Summing up, the authors should make the effort to transform this deep review of the available evidence in a more practical tool for practicing physicians.

This information has been added to the "WHY or WHY NOT should we use a risk score? section":

"*However, the AIMS65 includes the INR as a risk factor and an INR > 1.5 has been shown to be independently associated with in-hospital mortality in acute NVUGIB in a recent multicenter UK national audit[78].*"

Following the reviewer's advice, we have reorganized paragraphs and rewritten sentences to provide a more practical approach.

Thank you again for considering our work for publishing our manuscript in the *World Journal of Gastrointestinal Pathophysiology*