Reviewer’s report

Title: Percentage of small platelets on peripheral blood smear and Child-Turcotte-Pugh class can predict the presence of oesophageal varices in newly diagnosed patients with cirrhosis: development of a prediction model for resource limited settings

Version: 0 Date: 10 Jun 2019

Reviewer: Theresa Bucsics

Reviewer’s report:

The manuscript titled "Percentage of small platelets on peripheral blood smear and Child-Turcotte-Pugh class can predict the presence of oesophageal varices in newly diagnosed patients with cirrhosis: development of a prediction model for resource limited settings" by K. Perera et al. describes a newly developed, non-invasive score to predict the presence of varices in patients with cirrhosis. This model incorporates the fraction of small platelets as a novel, but potentially widely available biomarker for portal hypertension.

The manuscript is concise and straightforward, but there are several points that need to be addressed prior to publication:

- This study has not been validated in an independent internal or external cohort of patients. Without validation of any kind, a predictive model cannot be recommended for clinical use. Similarly, 76% specificity and 76% NPV is not "high" as stated in the abstract. Please downgrade your recommendation in the abstract and discussion sections and avoid stating that the model is suitable for "avoiding the need for initial UGIE", since with a reported negative predictive value of 76%, approx. 1 in 4 patients with varices would be missed.
- In the introduction the authors stated that the aim of upper gastrointestinal endoscopy was to "identify those patients who are at increased risk of bleeding from oesophageal varices". However, the authors did not differentiate between presence of (any) varices, and the presence of varices in need of treatment (VNT), defined as either medium-large varices with a diameter >5mm and/or the presence of red spots, which are at highest risk of rupture and require endoscopic treatment with band ligation or sclerotherapy, or treatment with non-cardioselective beta-blockers. Please state the prevalence of VNT in your patient population. Is the score predictive of VNT as well in your patient population? (it should be, considering that the presence of VNT correlates with Child-Turcotte-Pugh class)
- The authors need to add units to ALL tables and graphs! E.g. What does the right-hand y axis on supplementary figure 1 (ROC analysis) refer to?
- The authors need to write out all abbreviations at the point where they are first mentioned. This includes both the abstract and the manuscript.
- Have the authors performed an analysis for statistical power prior to study initiation? Please report.
- The authors must report all data, e.g. variables that were collected for the study as mentioned in the methods section. This includes demographic, clinical, and ultrasonographic parameters as well as...
gastroscopy findings (VNT!). Table 1, listing patient characteristics, is very brief, reporting only age, sex and CTP class. The majority of collected parameters appear to be missing. What were the etiologies of cirrhosis? How many patients had ascites? How many patients had splenomegaly?

- In the discussion section, the authors mentioned to have "collected data on confounding factors of thrombocytopenia and complications of cirrhosis". However, none of these confounding factors were reported. Please add these findings to the results. Did spleen diameter correlate with the fraction of small platelets?

- In addition to reporting units for continuous variables, the authors should add number and fraction of patients to each table column, and categorical variable.

- Please report all variables entered into multivariable analyses. For prediction of presence of variables, the authors should use a binomial regression analysis (with outcomes yes/no) instead of a linear regression model. The authors should repeat this analysis with VNT, as they are in critical need of treatment.

- The authors need to proofread their manuscript for contextual errors. Please delete or rephrase the last paragraph of the results section ("Based on this proposed model a calculated rounded value > 0.0 predicts presence of varices while a calculated rounded value < 0.0 predicts the presence of varices"), which has also been copypasted into the discussion session.

- How do the authors explain the vastly higher rate of normal-sized platelets in patients with oesophageal varices (mean 82.6% vs 57.8% in patients without varices, p=0.008)?

- The main finding of this study was that the fraction of small platelets (%SP) appears to be protective of oesophageal varices, however, there was no difference in %SP between patients who had small and large varices. How do the authors explain this finding pathophysiologically? Please discuss.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Unable to assess

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics
Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

There are no financial or non-financial conflicts of interest with regards to this study. I declare that in the past 5 years I have received travel support from AbbVie, BMS, Medis, and Gilead, as well as fees for lectures from BMS, and a financial award from Medis. I have additionally received financial funding from Gore Medical.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal