

## Comments to reviewers

### REVIEWER 1

- *There seems to be a tendency to abolish the minimum platelet count safety limit for performing various procedures, with the need to individually evaluate each case, but studies of better methodological quality need to be carried out to support such decision making*

We thank the reviewer for his comment. We rewrite the conclusion section to include this issue (paragraph “conclusion”, lines 7-8 and 21-22).

- *I suggest that the authors explore further the results of thrombopoietin receptor agonists in patients with chronic liver disease, as these drugs represent a promising strategy in the treatment of thrombocytopenia (PMID: 34748184, PMID: 30762895, and PMID: 35836089).*

The proposed references were include into the text in the “introduction” paragraph (ref. 26-27-28, lines from 46 to 64).

- *A recent study (PMID: 32810307), involving cancer patients, revealed that a platelet count below  $50 \times 10^9 /L$  was not associated with a higher incidence of post-puncture complications. The aforementioned study may enrich the discussion regarding the topic "lumbar puncture", although it does not specifically involve patients with chronic liver disease.*

We also added in the discussion section the study about post-puncture complications in cancer patients (ref. 111) in lines from 12 to 19 of the paragraph “lumbar puncture”.

- *It would be interesting to address platelet count and bleeding risk in laparotomy and laparoscopy procedures.*

About laparotomy and laparoscopy procedures, evidence in literature is scant at the moment. We add to the discussion section a new paragraph on “significant limitations and future perspectives” (lines from 1 to 27, ref. from 115 to 131) in which we include retrospective studies about urological surgery, cholecystectomy, herniotomy, liver surgery and two different case reports and an original study about coronary artery bypass grafting and cardiac surgery to report the management of thrombocytopenia in cirrhotic patients undergoing major invasive surgery.

### REVIEWER 3

- *It would be worthwhile quoting the recent studies which have reported data on the effect of thrombocytopenia and risks for procedure complications, as these have not been reviewed while making the presently available guidelines. These recent studies will get incorporated in the new guidelines. Moreover, this will add strength to the present review.*

We add in the discussion more studies reporting data on this topic in the different sections according to the type of procedure they refer to (ref. 59-60-65-86-114).

- *The authors should add a paragraph about the significant limitations and future directions in this field.*

We add a new paragraph on significant limitations and future directions about this topic.

- *Moderate thrombocytopenia is defined as 50-100,000. Do the authors mean 50 or 50,000?*

Typo error was corrected. (section "introduction", line 4).

- *The authors should discuss the effect of platelet transfusion in patients with cirrhosis and acute variceal bleeding and associated outcomes in light of recent literature. Recent data suggest that platelet transfusions may be associated with adverse events in patients with variceal bleeding.*

We rewrite the paragraph "endoscopy" including new studies about adverse events and effects of platelet transfusion in patients with cirrhosis and acute variceal bleeding, investigating the associated outcomes from recent studies recently published in literature (ref. 72-73-74-75, lines from 39 to 56).

- *The authors mention: "Platelet transfusion should be considered for low bleeding risk procedures that require arterial access when platelet count is <20,000/ $\mu$ L and for high bleeding risk if platelet count is <50,000/ $\mu$ L, obtaining an appropriate pre-procedural coagulation testing. (28)" As the understanding of coagulation in cirrhosis is being understood better, discuss how thromboelastography has helped in transfusion of blood products before procedures in these patients.*

We expanded the discussion regarding the use of thromboelastography to guide platelet transfusion before procedures in cirrhotic patients in the section "bleeding risk of different procedures and main guidelines" (ref. 32-33-34-35-36, lines from 21 to 41).

- *The grammar needs correction. Many sentences are unclear. E.g. On the other hand, all there were studies that did not show any correlation between bleeding risk and coagulation tests (48). 8. Check spelling throughout the text. Eg.cateter*

The text received professional proof-editing.