

World Journal of Hepatology

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Dear Editor-in-Chief,

Thank you very much for the careful review of our manuscript, which we have amended following the reviewers' suggestions. A copy of the revised manuscript with the changes colored in red has been uploaded to the submission system. Also, please find below an itemized point-by-point response to the reviewers' comments.

We look forward to hearing from you regarding the status of our manuscript, which we hope is now acceptable for publication in the World Journal of Hepatology. Please feel free to contact us if you need any additional information.

Sincerely,

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Reviewer 1

Excellent article, analysis in future should be extended to other transplanted organs.

Response: Thank you for reviewing our manuscript, we appreciate your feedback.

Reviewer 2

The first paragraph in your discussion should be used as a conclusion in the abstract to make it clear that your findings are not original rather retrospective review of your data to confirm previous reports.

Response: Thank you for the relevant comment. As suggested, we have used the first paragraph in the discussion as the conclusion in the abstract.

Reviewer 3

Comments on Low platelet count: predictor of death and graft loss after liver transplantation? Introduction Manuscript's aim is clear: To confirm if platelet count (PC) at 5th postoperative day less than 70K/mm³ has prognostic significance for death or graft failure at some postoperative time points. The scientific rationale for authors' analysis is supported by some clinical observations, but not by a pathophysiologic basis because even those fast recovering patients depict low platelet counts in their pre- and early post transplantation periods. Moreover, the prognostic significance of low PC in the post-operative period could be related not to the platelets themselves, but to a more complicated transplanted patient or an overly harder intra- or early postoperative course. Material and Methods The methods are clearly described and designed for a broad subsequent statistical analysis. Nevertheless, they omit some physiologic postoperative variables taken in account in the pre-transplantation period such as MELD score components, hemodynamics, surgery duration (as a surrogate for intraoperative complications occurrence), etc. In the statistical section, authors tell us that they choose the best performance post-operative PC using the C-statistic. What in the confidence interval of the day 5 PC C-statistic? Was is statistical significant to be included

in the multivariate models? As the author's intention was to validate a post-operative prognostic variable of PC, did other post-operative variable perform as well as PC? Results It is stated that the lowest PC was on postoperative day 3 and the highest on day 7. Maybe, a better prognostic variable is PC recovery from day 3 to day 5 or 7. If this indeed is significant, it might imply that PC is just a surrogate marker of a not yet apparent clinical condition. It is stated that "In the group with $<70 \times 10^9/L$ PC, the recipients were transplanted at later stages of their disease according to the CTP score ($P = 0.014$) and, although without statistical significance". I did not find the CPT score of neither group. How do authors define: "primary graft dysfunction and delayed graft function"? Were these patients the same that those requiring re-transplantation and those who had higher mortality? As this seems to be the case, once again, it suggests that low post-operative PC is a surrogate marker of one or more not yet apparent complications. Discussion It is clear and well written. It correctly emphasize that the retrospective nature of the clinical experience precludes to know if low post-operative PC correction could modify graft and patient prognosis. It is necessary to add a comment about that low PC could be, in fact, be a surrogate marker of an another condition that jeopardize clinical recovery after liver transplantation and that low PC could not be the problem itself. References: OK Figures: OK Table 1 does not contain CTP scores. Table 2: OK Title, Abstract and Core Tips: OK

Response: *Thank you for the relevant comments. Our responses are as follows:*

i) To our knowledge, the articles on negative outcomes observed in patients with thrombocytopenia after LT failed to demonstrate a possible pathophysiologic basis for the relationship between low platelet count in the postoperative period and negative outcomes after LT. Unfortunately, the retrospective nature of our study does not allow us to determine the real role of low platelet count in negative outcomes after LT. Perhaps low platelet count is indeed only a marker of poor prognosis. To address this issue, we added this as a limitation of the study (at the end of the Discussion section).

ii) The cutoff point for platelet count on the fifth postoperative day ($<70 \times 10^9/L$) was defined using the C-statistic, and we acknowledge that not reporting the confidence intervals and P-values was a mistake; therefore, such data were added to the Results in the revised manuscript. Thus, platelet counts $<70 \times 10^9/L$ on the fifth postoperative day were included in the multivariate models, together with other relevant variables that were selected based on similar studies, especially the study conducted by Lesurtel et al. (reference #17 in the manuscript).

iii) The observations regarding the CTP score and primary graft dysfunction are important. In table 1, the CTP score had been presented using an abbreviation different from that used in the text, causing some confusion, for which we apologize; we have corrected this in the revised manuscript. The definitions for primary graft dysfunction and delayed graft function were included in the Materials and Methods (Outcomes subsection). We also rewrote some sentences in an attempt to make it clearer that patients with primary graft dysfunction or delayed graft function were also counted in the total number of deaths and retransplantations.

iv) We would like to explain the absence of the MELD score in the postoperative period of LT. Unfortunately, it is not a routine practice in our service to order tests for bilirubin, creatinine and INR on a daily basis in the postoperative period of LT. Therefore, because we performed a retrospective study, most patients did not have enough data for an accurate calculation of the MELD score in the postoperative period.

v) Finally, as markers for the occurrence of intraoperative complications, we used the need for transfusion of fresh frozen plasma, transfusion of platelets and bleeding volume >2500 mL. As seen in table 1, these variables showed no significant differences between groups. In addition, cold ischemia time was used as an indirect marker for duration of surgery. In fact, duration of surgery and hemodynamic variations during the procedure appear to be very interesting markers and may be used in future studies on this topic.