Author’s response to reviews

Title: Liver transplantation in Jehovah’s witnesses: 13 consecutive cases at a single Institution

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Liver transplantation in Jehovah’s witnesses: 13 consecutive cases at a single Institution
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Dear Editor,

first of all, we should like to thank the Reviewers for the new comments and for the opportunity to improve the quality of the present manuscript.

To differentiate this revision from the previous, the new added text is light-blue highlighted

The following is our point-by-point rebuttal

Technical Comments:
1. Please include sub-sections in the Abstract. Done
2. Please move the Abbreviations section to after the Conclusion. Done
3. Please revise the manuscript headings according to our submission guidelines - Rename the Introduction into Background and provide Conclusion heading. Done
4. Please move the Declarations section to before the References. Done
5. Reformattting of the Declarations section. Done
6. Provide figure 1. Data are provided in Table 1 and not in a figure
Reviewer’s comments

1. Were erythropoiesis stimulating agents used intraoperatively as mentioned in the text? If they were used preoperatively then it needs to be mentioned earlier in the chronology of events, not in the intraoperative management.

We acknowledge that in the present form some confusion could be ingenerated in the reader. Therefore we split the original “Intra-operative and peri operative management” section in 2: “Intra-operative management” (page 4) and “Post-operative management”(page 5). We also better specified in the text that “Postoperatively, erythropoiesis was stimulated when needed following the same criteria and protocol used for pre-OLT preparation”

2. Other factors identified to be associated with increased intraoperative bleeding are “previous abdomen surgery”, “previous evidence of SBP” “Post TIPSS. Were these also considered when selecting cases. Collaterals on CT, evidence of DIC preoperatively are some predictors of bleeding. Single value of INR>2.5 alone may not be a reason enough to require blood products in our experience. Since this is a retrospective review many considerations may not have been clearly stated in the documents which were accessed to write up the paper. Would the authors like to add such parameters, perhaps these were considered by the team managing these patients. Were certain aetiologies also excluded as they can be associated with increasing intraoperatively bleeding like alcohol imduced CLD. Patients on inotropes preoperatively are more likely to required volume and product transfusion. Were sick patients on multiple inotropes excluded?

We agree that many anamnestic, clinical and laboratory characteristics have been associated to an increase risk of bleeding in LT patients. This led to very stringent criteria indicating LT in our population of JW. We agree also that an INR >2.5 alone cannot prevent patients from be considered for LT but, according to literature, we used this parameter not as an indicator of the risk of bleeding but of severe portal hypertension, which is acknowledged as the main risk factor for intraoperative bleeding during LT together with platelets <50x103 µL, grade 3 esophageal varices and stage 2 kidney injury according to the AKIN classification (Methods, page 3). In the revised version of the manuscript we also outlined that “patients with previous upper abdominal surgery and UNOS status 1 and 2 were excluded from listing”

3. Authors could consider adding data on intraoperative use of vasoactive agents. This would give more credibility and a better understanding to those wanting to learn from the article. There is mention of 2 patients who needed inotropes at reperfusion and there is mention of 1 patient who required inotropes post operatively. The conduct of LT without transfusion is indeed commendable. With some more detail it will be more helpful for others to learn how they can do the same

This information was already given in the original text but in the revised version we added the following sentence: Two patients received nor-epinephrine at reperfusion (figure 1), in one of them it was continued for the first 2 postoperative days (peak dose 2.5 mcg/kg/min)

4. Mentions that total duration of study was about 400 minutes. Would the authors like to mention in the
text the importance of focused and expert surgical involvement towards conducting a blood less surgery. Was there any difference in the surgical involvement and conduct in Jehovah’s witnesses vs other transplants

We added the following sentence in the Discussion: During the last decade, blood product requirements in LT patients have significantly decreased in most centres. This improvement was related to different factors including better surgical techniques, LT indication and liver graft preservation techniques9-12. Also, experience of the surgical and anesthesiological team is important. In particular, surgical experience and skill during hepatic dissection and meticulous hemostasis has long been recognized as meaningful in determining the amount of intraoperative blood loss.23 However, experience is difficult to quantify and many unforeseen intraoperative events with the potential occurrence of technical difficulties impart complex changes predisposing to extensive bleeding. Furthermore, there is evidence that transfusional requirements can be reduced if the anesthesia team followed protocols including goal-directed transfusion practices.24 However, comparison of intraoperative transfusion requirements from different transplant centers may be inherently biased by an inability to account for differences in transfusion triggers and clinical practices. Consequently, the predictive models developed in one institution may hardly, if ever, be applicable in others.

We also added 2 new references: # 23 and 24

We hope that our revised article should be taken into consideration for publication.
Kindest regards
Gianni Biancofiore, MD on the behalf of all of the authors