

Dear Editor,

Many thanks for your review of our manuscript. Please find enclosed our responses to the reviewers' comments. We have highlighted any changes to the manuscript in red and comment boxes have been used to elaborate on specific points.

#### Reviewers' comments

##### **Reviewer no. 03648086**

1) Query regarding the suitability of comparison with referenced article [28]. In our study we used the AKIN criteria to identify the incidence of renal dysfunction post OLT. This meant we included, along with multiple rises in creatinine from baseline, the use of renal replacement therapy (RRT) during the post-operative stay on ICU (not just at Day 1) as an assessment of early AKI. Looking at our data, all patients undergoing RRT in the first 7 days post OLT were included in the analysis (classed as stage 3 AKI). All but one had RRT started within 48hours of OLT and the remaining patient at 53hours.

The referenced [28] study defined patients undergoing early RRT as those doing so within 7 days of OLT. As a result we believe the studies are comparable, both in terms of time frame and severity of AKI. As such, our assessment of predictors of early AKI was based not only on the multiple rise in creatinine, but also on the need for RRT.

2) "On page 5, the 'AST1000-2000iu/L' should be 'AST 1000-5000iu/L'"  
This amendment to the text has been made

3) Consolidation of figures  
The number of figures has been reduced from 12 to 6 and the text has been adjusted appropriately to reflect this.

##### **Reviewer no. 03537672**

1) "Case number is small and the study period is short"  
This study was conducted over 1.5 years and covered 140 OLTs before exclusions. The 116 patients analysed may seem a modest number in comparison to some of the trials using data from the large national databases. However we feel that the strength of our single centre study lies in the analysis of data and variables that are not collected in these national databases so benefits from a more detailed assessment of the causes and consequences of early AKI post OLT.

2) "Present data for all patients and for each group separately"  
All data for the patients included in the study have been presented in this article and have been separated according to groups "AKI" and "No AKI" (Tables 1,2 and 3).

3) "Please present intraoperative blood loss"  
We have presented data for the volume of cell salvage blood transfused. Our patients all routinely have cell salvage from the start to the end of the transplant, so the volume of red cells generated is a reflection of the blood lost and collected,

which can then be compared between patients. Clarification of this has been made in the text (methods section)

4) The association between DCD/DBD and HIRI

The reason we have included this association is that although we have shown that HIRI and AKI are associated we feel it is also important to demonstrate the association between DCD transplantation and HIRI, to highlight this clinical issue in context of the increasing use of DCD organs to meet demands.

5) "Too many figures"

The number of figures has been reduced from 12 to 6 and a table has been created to summarise the impact of increasing severity of HIRI, as suggested by this reviewer (Table 5).

**Reviewer no. 03656240**

9) 24h AST, HIRI, AKI: How does this finding contribute to the current risk assessment and management of OLT associated HIRI in patients undergoing liver transplant?

This study has demonstrated that there is a high incidence of AKI post OLT, with a significant impact on recipient outcomes. IR injury and hence graft quality was the only variable that predicated this complication on multivariate analysis. Pre-existing renal dysfunction was not a predictor. Therefore, allocating a marginal graft, as is commonly done, to a recipient with a lower MELD score and no renal impairment still carries with it significant risk, perhaps higher than previously thought. Hence focus should be directed at investigating ways to prevent and treat this graft-related injury.

We hope that these responses have answered the questions and comments put forward. Please let us know if there are any further points that require clarification or if there are any changes that you believe will further enhance the work.

Kind regards

Suehana Rahman  
Brian R Davidson  
Susan V Mallett