



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 58278

**Title:** Early tacrolimus exposure does not impact long-term outcomes after liver transplantation

**Reviewer's code:** 00054549

**Position:** Peer Reviewer

**Academic degree:** BSc

**Professional title:** Doctor

**Reviewer's Country/Territory:** Australia

**Author's Country/Territory:** Spain

**Manuscript submission date:** 2020-08-14

**Reviewer chosen by:** Pan Huang (Quit in 2020)

**Reviewer accepted review:** 2020-10-18 05:34

**Reviewer performed review:** 2020-10-23 02:06

**Review time:** 4 Days and 20 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

## **SPECIFIC COMMENTS TO AUTHORS**

This manuscript is potentially publishable if the authors address a number of the limitations noting the numbers of recipients in each cohort and hence the limited numbers who experienced the adverse outcomes of interest (ie impairment of renal function as well as HCC recurrence). First the abstract is too wordy. The methods section in the abstract can be compressed down. Plus one of the significant findings from the data analysis is not mentioned either in the abstract nor addressed in the discussion section of the manuscript. That is that the mean donor age was significantly higher for the recipients in the Tacro level > 10ng/ml versus for the recipients in the other group. It is known that the age of the donor liver can be a factor that needs to be considered with respect to the dosing of Tacrolimus in the post transplant phase but this has not been mentioned. The decision to place the recipients into either of the two Tacrolimus level subgroups seems extremely arbitrary in that it is based on the median level of a minimum of 5 recorded Tacrolimus levels recorded in the first 30 days. This is problematic as it could have led to confounding of the results (and hence constrained the potential results that could instead have been obtained from a more focussed type of data analysis). Would it not have been better to have obtained a median of all of the Tacrolimus levels that were obtained for each of these recipients for the first 30 days and then place the recipients into the low or high Tacro level subgroups? This would more accurately reflect the Tacrolimus exposure. What would perhaps even more accurately reflect the impact of prolonged Tacrolimus exposure of > 10 ng/ml would be the actual number of days that the Tacro level was greater than this for the recipients in the > 10 ng/ml subgroup. This would facilitate further sub group analysis for the end points that were selected. Did the presence of T-tubes impact the Tacrolimus levels at all noting that these were utilised during the time period this study encompasses? There is some



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-399-1568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**https://**[www.wjgnet.com](http://www.wjgnet.com)

limited published data that biliary diversion can impact on Tacrolimus levels. For example was the bile fed back to the recipients or were the T-tubes all able to be clamped at the same stage post transplant? It may also be useful to mention how this was managed (and refer to the relevant literature).



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Manuscript submission date:** 2020-08-14

**Reviewer chosen by:** Jia-Ru Fan

**Reviewer accepted review:** 2020-12-28 07:39

**Reviewer performed review:** 2020-12-30 04:03

**Review time:** 1 Day and 20 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
<b>Language quality</b>	[ ] Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

I believe that the reviewers questions have been adequately addressed. The authors need to make one final check of the spelling particularly of terminology etc through the manuscript including for Mycophenolate-mofetil and choledochocholedochostomy