

Long Term Liver Allograft Fibrosis: A Review with Emphasis on Idiopathic Post-Transplant Hepatitis and Chronic Antibody Mediated Rejection

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Dear Reviewers and Editors,

Many thanks for your valuable comments regarding our article entitled. We appreciate your interest and precious time spent in going through our article. We have now revised our manuscript taking in to account the comments, critiques and questions highlighted in your reviews. We believe that the revised manuscript now reads well and fulfils the requirements for publication in World Journal of Gastroenterology. If you have any further queries or comments, please do not hesitate to contact us.

Kind Regards

Thank you

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Reviewer #1:

Specific Comments to Authors: Reviewer #1:

Specific Comments to Authors: In the manuscript entitled “Long Term Liver Allograft Fibrosis: A Review with Emphasis on Idiopathic Post-Transplant Hepatitis and Chronic Antibody Mediated Rejection”, authors have summarized the factors contributed to LAF and emphasized on IPLTH and CAMR. There are also some comments taken for consideration: 1. Authors seem to introduced LAF, IPLTH and CAMR individually, but haven’t showed the importance of IPLTH and CAMR in LAF, especially compared with other LAF reasons (like cellular immunity).

Reply: Thank you very much for reviewing our manuscript and for the insightful suggestion. While we described each of the entities individually, we failed to explicitly write about the causality and link between them. We have now edited the manuscript and have added a section which highlights the reviewer’s points.

2. Incidence of allograft fibrosis should be supplemented, especially for the pediatric LT recipients. And What are differences between adult and pediatric LT recipients in LAF? Incidence? Mechanism?

Reply: Thank you for the astute suggestion. We agree with the reviewer; this was a detail which we felt in retrospect was missed by us in the original manuscript. We have rewritten the whole section to incorporate the details.

3. Parts entitled “Metrics for Liver Allograft Fibrosis”, “Complement component 4d (C4d) Immunostaining” and “Operational Tolerance & Liver Allograft Fibrosis: The Equipose” don’t connect tightly with the emphasis of the manuscript. It is suggested to re-organize the text.

Reply: We thank the reviewer's suggestion. The text has been re-organized to provide for a better flow.

4. The manuscript needs to be polished. Some of the descriptions are colloquial and not professional. Please pay attention to the grammar and the word spelling.

Reply: The paper has been proof-read for grammatical errors and syntax. These have now been corrected. We have extensively revised the language of the manuscript to reflect internationally accepted descriptions.

Reviewer #2:

Specific Comments to Authors: 1. Advances in organ preservation techniques, perioperative care and immunosuppression have resulted in greatly improved long-term survival in patients undergoing liver transplantation (LT). Consequently, a continued assessment of the liver allograft in these patients to ensure optimal graft function is becoming increasingly important. Pathological findings are frequently present in liver biopsies obtained after a year post LT. The significance of these findings is uncertain as many of these are seen in protocol liver biopsies from patients with clinically good allograft function and normal liver chemistry parameters. This review has novelty and clinical value. It opens up the research thinking of Liver Allograft Fibrosis and has guiding significance for carrying out relevant research, exploring the new reliable predictive immune biomarkers mode of Liver Allograft Fibrosis and improving the prognosis of liver transplantation. 2. The title, abstract and key words are accurate and basically reflect the study. The language is fluent and there is few grammatical errors. 3. Outlook: look for reliable predictive immune biomarkers to reduce protocol biopsies.

Reply: We sincerely thank the reviewer for the comments. The paper has been proof-read for grammatical errors and syntax, which have now been corrected.