

May 15, 2021

Dear Editors of the World Journal of Transplantation,

We very much appreciate your preliminary decision to accept our manuscript for publication after our revision. We have reviewed and responded to the reviewers' concerns and have edited our manuscript accordingly. Please see below a detailed point-by-point response to the reviewers.

Point-by-point response to article reviewers

Reviewer #1

- Language quality: Grade B (Minor Language Polishing)
 - We have had the manuscript proofread by two separate native English speakers and have incorporated their comments about how the language can be improved into the manuscript.
- The inclusion and exclusion criteria of the subjects are not mentioned in the methods part.
 - We have specified that the inclusion criteria of subjects includes patients who underwent LT at our center between January 2010 and March 2020, and age of 45 years and above.
 - We have specified that the exclusion criteria included patients who underwent multi-organ transplants or repeat transplants.
- Are the primary liver diseases associated with futility of liver transplantation?
 - Table 1 outlines the results of our original futility analysis, which included the indication for transplantation. This included cirrhosis and its various etiologies, as well as hepatocellular carcinoma and acute liver failure. None of these variables were found to be associated with futile outcome.
 - We recognize that this approach did not fully address if the primary cause of liver disease was associated with futile outcome, as the primary cause of liver disease for patients with hepatocellular carcinoma was not indicated. Therefore, we have repeated the analysis with the primary cause of liver disease.

- This additional analysis found that none of the primary causes of liver disease were associated with futile outcome.
- Results of the futility analysis for primary cause of liver disease are now included in Table 1. Etiologies other than the three most common (cirrhosis related to alcohol, NASH or viral hepatitis) were grouped into an “other” category due to very small sample size.
- We have modified the legend to Table 1 to reflect this change.
- Subtitles of each section are needed for readability.
 - Please see subtitles which we have added under the Methods and Results sections.

Science Editor Review

- Reviewer 00052899 pointed out that the inclusion and exclusion criteria of the subjects are not mentioned in the method part.
 - Please see response to reviewer 1 regarding addition of inclusion/exclusion criteria.
- Language quality: Classification: Grade B.
 - Please see response to Reviewer 1’s language quality classification.

We hope that these changes are acceptable. We appreciate your consideration and are looking forward to your response.

Sincerely,

Jamak Modaresi Esfeh

Assistant Professor, Department of Gastroenterology and Hepatology

Cleveland Clinic Foundation