

Editorial Board
World Journal of Transplantation

March 22, 2023

RE: "Pre-Lung Transplant Reflux Testing Demonstrates High Prevalence of Gastroesophageal Reflux in Cystic Fibrosis and Reduces Chronic Rejection Risk"

Dear Editors,

We appreciate the opportunity to revise our manuscript submission to World Journal of Transplantation, and the valuable feedback and comments from the editorial board. We have incorporated the suggestions into a revised manuscript for your evaluation. A point-to-point summary of the changes is included below.

Point-to-point Response:

Reviewer 1:

1. Although the statistical data of the cohort showed that completing pre-transplant reflux testing was an independent predictor for lower risk of developing CLAD, in fact there is no causal relationship between the two. With a limited sample size, a more comprehensive analysis of the influencing factors that would affect reflux in the pre-transplant reflux-tested and non-reflux-tested groups is needed, such as the presence of other gastrointestinal diseases, the use of PPIs, and the presence of reflux-related care.

Author Response: Thank you for this comment. As stated in our limitations, we agree that we cannot assign causality between pre-transplant testing and CLAD based on our results alone. With regards to other influencing factors that would affect reflux pre-transplant, there were no other known major gastrointestinal diseases related to reflux reported in our cohort, such as major esophageal motility disorders or gastroparesis. This was not surprising because patients with major esophageal motility disorders such as achalasia or absent contractility were generally excluded from our institution's transplant list during the study period. However, it is certainly possible that some patients in the no pre-transplant testing group could have undiagnosed esophageal dysmotility, as they did not undergo routine manometry testing. In addition, gastric emptying assessment was not routinely obtained pre-transplant at our institution. For pre-transplant PPI use, we have now included this data in Table 1 (also see response to Comment 3 below regarding pre-transplant PPI). For other reflux-related care, our study has excluded patients with prior anti-reflux surgery before transplantation, as stated in our Methods section. Finally, our sample size and retrospective design also limited our ability to perform more detailed analyses of other potential factors associated with reflux testing. We have also updated our limitations to address this feedback.



Page 9, paragraph 3:

“Conditions that may affect reflux, including major esophageal motility disorders (achalasia, absent contractility) and gastroparesis, were not noted in our study cohort during the pre-transplant period, likely because many patients with known history of these conditions were not transplanted.”

Page 14, paragraph 2:

“Additionally, the sample size and retrospective design also limit the ability to perform more comprehensive analyses of other potential factors that may be associated with performance of reflux testing.”

2. The manuscript mentioned “Patients with CF were less likely to undergo reflux testing during pre-lung transplant assessment compared to those with other pulmonary diagnoses ” but the title implies: Pre-Transplant Reflux Testing Demonstrates High Prevalence of Objective Gastroesophageal Reflux in Cystic Fibrosis. As the main conclusion and the title should be objective.

Author Response: Thank you for this feedback. Our intention with the title is to highlight our findings that patients with CF who did undergo pre-transplant reflux testing had high prevalence of reflux. Because patients with CF were found to be less likely than other pulmonary diagnoses to undergo pre-transplant reflux testing, our conclusion is that more patients with CF should undergo testing. These statements are not contradictory or mutually exclusive.

3. The majority of patients tested before their transplants had significant reflux symptoms, and data on whether the two cohorts used PPIs prior to transplantation should be supplemented.

Author Response: Thank you for this comment. We have revised Table 1 to include this data. There was no statistically significant difference between the two groups in pre-transplant PPI use. We have also added our Results section to reference these additional results.

Page 10, paragraph 1:

“Post-transplant PPI use was very common in both groups, including 83.9% in the pre-transplant testing group compared with 89.5% in the no testing group ($p=0.70$), and higher than pre-transplant PPI use in both groups.”

Editorial Office’s Comments:

The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Author Response: The title has been edited to: “Pre-Lung Transplant Reflux Testing Demonstrates High Prevalence of Gastroesophageal Reflux in Cystic Fibrosis and Reduces Chronic Rejection Risk” per journal specifications.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Author Response: The tables have been edited to comply with these guidelines.

Thank you for your consideration and we look forward to hearing from you.

Sincerely,

A handwritten signature in black ink, appearing to read "Walter Chan", written in a cursive style.

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