

Yale SCHOOL OF MEDICINE
Department of Pathology

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Pathology and Medicine

Dear Dr. Ghosh and Editorial Board Members,

Please find enclosed the edited manuscript in Word format titled "**Primary sclerosing cholangitis associated colitis: Characterization of clinical, histologic features, and their associations with liver transplantation**" by Aranake-Chrisinger et al.

We appreciate the thoughtful and constructive comments of the reviewer. Our responses to comments are in bold. All the changes which were made to the main text and tables are highlighted in yellow. We think the manuscript has been improved by the suggestions of reviewers. Reviewer comments are in bold text.

Reviewer #1:

- 1. Table 4 is somewhat confusing because only p values are shown. Obviously authors compared cases with liver transplantation vs. those without liver transplantation in PSC-UC and in PSC-IBD patients respectively. Thus, it would be much better to show include all data in the Table 4 (number of patients, percentage, and p-value for each variable).**

Thank you very much for your review and comments. We completely agree that Table 4 needed more clarification and data. The authors made a new Table 4 and re-arranged the data. In order to prevent from repeating data that was previously discussed (table 3 summarizes all patients with OLT), and to be able to discuss the statistically significant data, we only included the select histologic data of PSC-IBD patients with and without

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OLT (We tried including all available which made a very dense and confusing table). The text was also updated to reflect these changes. While we think this revision really helped us emphasize the important aspects, we hope it also reflects the revisions requested by the reviewer.

- 2. In addition, some of the data do not match the main text: activity scores in the left colon of PSC-UC patients with OLT vs. those without OLT, $p=0.0568$ in the main text but 0.0599 in the Table 4. Please inspect the data carefully and fix them.**

Thank you very much for bringing this to our attention. We simplified all of our numeric values on all the tables, made changes, and correlated them with the text.

- 3. How did authors define PSC-CD? Although authors followed “established guidelines”, many of the PSC-CD cases apparently had overlapping features with UC. As authors discussed in the “Discussion” section, it would have been difficult to diagnose PSC-CD unless there was no ileal stricture or granuloma. Please provide more detailed clinicopathologic features that led to the diagnosis of PSC-CD: characteristic colonoscopic, radiologic, or histologic appearances. Some supplementary figures of those characteristic features might be helpful for readers.**

We think our reviewer brings up important and valid questions regarding the PSC-CD group. As stated in the methods the diagnosis of PSC-CD vs PSC-UC was made by the treating gastroenterologist. All of the PSC-CD patients had ileal involvement compared to PSC-UC and two had ileal strictures. On colonoscopy, however, only 50% of them showed ileal inflammation or stricture. It's certainly possible that some of the other subtle clinical findings that helped make this clinical distinction, were not reflected in the patient's clinical chart. These points were further explained in the discussion part. Unfortunately, we were not able to include any additional figures or data to this manuscript, to further prove this diagnosis. We hope these changes would be sufficient enough for the reviewer.

Thank you in advance for considering our revised manuscript for publication in "World Journal of Gastroenterology" We hope our responses and modifications will be well-received by the members of the editorial board and the reviewer. We look forward to your decision regarding its suitability.

Sincerely,

A handwritten signature in black ink, consisting of the letters 'jke' in a cursive style. A long, thin horizontal line extends from the bottom of the 'j' to the right, ending in a small arrowhead.