

Dear Editors and Reviewers:

Thank you for your letter and for reviewing our manuscript entitled “Contrast-enhanced ultrasound imaging for intestinal lymphoma” (Manuscript NO.: 67186). Those comments are very valuable and helpful for revising and improving our paper. We have studied all the comments carefully and made correction accordingly.

We have tried our best to improve the manuscript and we hope this version could meet with your approval.

We look forward to your decision.

Yours Sincerely,
Yong Wang & Yan-Tao Tian

Responds to the reviewer’s comments:

Reviewer #1: I read the manuscript written by Ningyi and others with great interest. In my honest opinion, the topic is interesting and the retrospectively studies novel enough to attract the readers’ attention. This might provide additional information for clinical diagnosis and treatment of intestinal lymphoma.

Response: Thank you for your positive comments.

- 1. Title: Appropriate. It reflects the main content of the study.**

Response: Thank you for your positive comments.

- 2. Authorship: Is correct. Institutions: are correct. ORCID number: is correct. Supported foundation: is correct.**

Response: Thank you for your positive comments.

- 3. Abstract: Is a structured abstract according to the required format. In 289 words authors showed a summary of the content of the manuscript.**

Response: Thank you for your positive comments.

- 4. Key words: 3 that reflect the content of the study. However, I suggest adding another 3-5 keywords that reflect the theme.**

Response: Thank you for your professional comments and valuable suggestions. We have added three additional keywords to the new manuscript, they are “Histopathological features”, “Lactate dehydrogenase” and “Quantitative diagnosis”.

- 5. Core Tip: In 61 words authors reflect properly aspects that should call attention to the readers.**

Response: Thank for your positive comments.

- 6. Background: Intestinal lymphoma is a rare tumor. CEUS findings of intestinal lymphoma have not been reported previously, and the relationship between CEUS and clinicopathological features and prognostic factors is still unknown.**

Response: Thank you for your positive comments.

7. Method: Authors made the detailed description of the investigations.

Response: Thank you for your positive comments.

8. Results: The author clearly presents the data to be observed in the method.

Response: Thank you for your positive comments.

9. Discussion: Authors made a detailed an informative discussion of the results.

Response: Thank you for your positive comments.

10. Illustrations: They show 3 figures and 4 tables with their corresponding legend. All figures and tables are showing clearly making and adequate support of the results.

Response: Thank you for your positive comments.

11. Biostatistics: This work met the requirements of biostatistics.

Response: Thank you for your positive comments.

12. References: The references are quite appropriate to the subject of research, but I think authors can also add some recent research.

Response: Thank you for your professional comments and valuable suggestions. We have added three researches published in the last five years to the revised version as references. They are reference 11, 13, 31.

13. Comments to the author: In this manuscript authors investigate the correlation of CEUS and histopathological features. Their findings on intestinal lymphoma contribute to knowledge of CEUS imaging. Although US is not the primary imaging modality in diagnosis of intestinal lymphoma, it can play an important role in guidance of biopsy and provide more information.

Response: Thank you for your positive comments.

Reviewer #2: In the manuscript “Contrast-enhanced ultrasound imaging for intestinal lymphoma”, the authors tried to describe the B-mode and CEUS features of intestinal lymphoma and investigate the correlation of CEUS and histopathological features. Until now, there are few studies on the diagnosis of intestinal lymphoma, most of which are case reports. However, some studies have already shown that US is an effective method for detecting gastrointestinal lesions, especially in experienced hands. Ningyi Cui et al. performed a single-center retrospective study of eighteen patients with histologically confirmed intestinal lymphoma underwent B-mode US and CEUS examinations. They summarized the features of B-mode US and CUES imaging of intestinal lymphoma and compared the frequency of tumor necrosis in intestinal lymphomas with reference to different pathological subtypes and clinical stage. Finally, they revealed an unexpected CEUS enhancement pattern with a high rate of tumor necrosis, which was found more frequently in aggressive than in indolent subtypes. The topic of this work is interesting. Their conclusion might provide additional information for clinical diagnosis and treatment of intestinal lymphoma. The manuscript is well written and well organized, and authors presented also the limitations of the study. I recommend that the manuscript can

be published. Sincerely

Response: Thank you for your positive comments.

Reviewer #3:

- 1. When something is not enhancing does not mean it is necrotic. The use of ultrasound may represent an alternative to the more reproducible cross sectional imaging techniques, however the limitations should be well stated.**

Response: Thank you for your professional comments and valuable suggestions. We are aware that necrosis assessed by CEUS (represented by unenhanced areas in the tumor) is not equal to necrosis assessed by histological examinations. Because of the retrospective nature of this study, histopathological analysis of necrotic tumor sites at CEUS was not available. Although the pathogenesis of unenhanced areas at CEUS in intestinal lymphomas remains unclear, it can be speculated that it correlated with aggressive subtypes. And in the revised manuscript, we added the limitations of ultrasound at the end of the discussion section.

- 2. The authors should discuss which cases would benefit of the use of CE ultrasound compared to CT or MR or PET.**

Response: Thank you for your professional comments and valuable suggestions. We added relevant content at the end of the discussion section. We admit that the comparison between CEUS and other imaging methods (CT, MRI, and PET) is very important in disease diagnosis. However, we did not compare this in this study because 1) this is a retrospective study, the pathological results were known before enrollment, thus lack of the diagnostic accuracy; 2) some patients only underwent ultrasound examination thus no other imaging data. We think this is a good research direction, we will continue to explore the advantages of CEUS in the diagnosis of intestinal lymphoma in future prospective studies.