

April 5, 2013

Lian-Sheng Ma,
Editor-in-Chief

Dear Editor-in-Chief,
Please find enclosed the edited manuscript in Word format (file name: 2596-edited 2.doc).

Title: Diagnostic accuracy of endoscopic ultrasound in pancreatic neuroendocrine tumors: A systematic review and Meta analysis

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 2596

We want to thank the reviewers for the comments. We believe their insightful comments have made this manuscript stronger. Please find enclosed our revised manuscript entitled "Diagnostic accuracy of endoscopic ultrasound in pancreatic neuroendocrine tumors: A systematic review and Meta-analysis" for your consideration for publication in world journal of gastroenterology. All authors have contributed meaningfully to the study, have access to all data, have no conflict of interest to report, and have seen and approved submission of the final manuscript.

We have made all the changes that the reviewers have suggested. Also, please find below the point to point answers to all the reviewers comments.

Because the results of this meta-analysis provide novel contribution to the field, we believe that world journal of gastroenterology is an ideal forum.

Thank you for your consideration of our work.

Sincerely, 

Srinivas R Puli, M.D
Division of Gastroenterology and Hepatology
University of Illinois at Peoria,
Telephone: +1- 309-624-9400 **Fax:** +1-309-624-2291

Email: srinivaspuli@yahoo.com

MAJOR

1. Pls describe any diagnostic criteria that were adopted by the studies to diagnose PNT
Answer: The studies that were selected into the analysis used surgery as a gold standard for diagnosing PNETs. This is described in the methods section of the manuscript.
2. From experience, it would be difficult for EUS to "diagnosis" PNT without FNA. I agree that EUS may be the best modality in localizing/detecting the lesion but not diagnosing. Pls clarify in the manuscript
Answer: we agree with the reviewers view point that EUS is good modality for localizing. The manuscript prior wording which used diagnosing has been changed to localizing or detecting in the edited version.
3. Did any of the studies performed EUS + FNA? Pls calrify
Answer: There were only 2 studies that used EUS FNA data to see if further improved accuracy. A subset analysis could not be performed as there was limited data. This is described in the discussion section of manuscript.
4. Did any of the studies used special techniques, e/g contrasted enhanced EUS?
Answer: This is an excellent question. None of the studies that were included into the analysis used contrast EUS as a modality. Additional subset analysis could not be performed due to lack of data in the included studies.
5. Did any of the studies compared EUS to another imaging modality?
Answer: The reviewer makes a valid comment. The goal of our study was to assess only the diagnostic accuracy of EUS alone as a modality for evaluation of PNETs but not to compare with other non-invasive studies.
6. Pls add a paragraph on how EUS compares to other modalities in detecting PNT as this is probably more clinically relevant.
Answer: Our current analysis did not assess for comparative accuracies between studies. A paragraph (9) in the discussion was added on comparative accuracy of EUS with CT scan alone
7. Was the EUS accuracy influenced by tumor size or tumor localization in the pancreas? What is the position of EUS in the diagnostic algorithm in PNETs? What is the relationship between application of EUS and other common imaging modalities used for PNETs (CT scan, MRI, radiolabeled somatostatin receptor scanning)?
Answer: We appreciate the comments as it makes a practical sense in how we could approach this issue as accuracy could vary by size. The size reported in the studies included in the analysis was varied and or were not reported at diagnosis. We took a position and added a paragraph in the discussion section of the manuscript. Additionally our study was undertaken to purely look at accuracy of EUS with surgery specimens as gold standard. We did not intend to look at comparison with other imaging techniques but since the data is sparse on it we recommend EUS be an adjunct to imaging modalities.
8. Nevertheless they never indicate the identified criteria chosen in EUS to raise the diagnosis. In addition, authors should be very prudent in their conclusion because the aspect of a neuroendocrine tumor even if nearly certain in some case should only be undergone with biopsy. Of note, Authors should modify their conclusions in line with the usefulness of a biopsy.

Answer: Thank you for the comments. Firstly, the manuscript has been reedited to change the terminology from diagnosis to localize or detect to avoid confusion as EUS alone at this time does not have any specific endosonographic findings to confirm PNETs without biopsy. A section in the discussion is in place to address the role of EUS with FNA.

9. Considering that sentences should be added in the discussion section, to clearly indicate the impact of neuroendocrine tumors (median overall survival) of the pancreas that an adenocarcinoma.

Answer: the literature is sparse on the impact of EUS on the impact of overall survival.

10. Detecting a neuroendocrine neoplasm in the pancreas helps not only with treatment but also helps improve prognosis. This is not correct

Answer: The sentence has been revised to address the statement as we clarified in the prior statement that the literature is sparse regarding the impact on survival.

MINOR

1. 22., 23., 24., 27 and 29. are not in in a different format than the others.

Answer: References have been reformatted.\

2. Abstract are missing

Answer: Abstract is added to the edited manuscript.

3. Discussion, Paragraph 1, Sentence 1: Rewrite as follows: Localizing or detecting a neuroendocrine neoplasm in the pancreas helps not only with the planning of treatment but also when detected early might improve overall prognosis

Answer: This change was made in the manuscript

4. Discussion, Paragraph 3 revised: Relocated to paragraph 7 to include in the limitation of the analysis.

Answer: This change was made in the manuscript.

5. Discussion, Paragraph 7: Rewrite

Answer: This change was made in the manuscript

6. Discussion, Paragraph 8: Added new paragraph

Answer: This change was made in the manuscript

7. Discussion, Paragraph 9: Rewrite.

Answer: This change was made in the manuscript

8. References: Be consistent with the format. Would refer to author guidelines.

Answer: This change was made in the manuscript