Response letter

Manuscript Number: 82925

Journal: World Journal of Gastrointestinal Oncology

Title: Diagnostic accuracy of apparent diffusion coefficient to differentiate intrapancreatic accessory spleen from pancreatic neuroendocrine tumors

Dear editors and reviewers,

We sincerely thank the editors and all reviewers for the critical review and the chance for revision. Your comments are highly insightful and constructive. We have revised the manuscript accordingly and marked the changes using red color fonts. We hope the revised manuscript has been improved to the quality that is suitable for publication now. We will be happy to edit the text further, based on helpful and valuable comments from both editors and reviewers. We are looking forward to your favorable final decision.

Best regards.

Reviewers' comments:

Reviewer #1:

Conclusion: Minor revision

A very interesting and well thought-out retrospective analysis is presented here. The aim of this work was to prevent unnecessary surgery in IPAS patients. Unfortunately, no information can be obtained from the manuscript as to whether this goal was achieved. There is a lack of essential data on the patients examined. Especially how many IPAS patients were operated on. The radiologist is certainly pleased with the good results. However, the clinician wonders whether this is a relevant problem at all.

Authors response: We thank the reviewer for the constructive and valuable comments. An intrapancreatic accessory spleen (IPAS) is usually less than 3 cm in size and is generally an innocuous condition. The main clinical importance of this lesion is to not mistake it for a small (< 3cm) hypervascular pancreatic neuroendocrine tumor (PNET) which shares similar imaging findings with IPAS to avoid unnecessary surgery and the associated increase in morbidity (1–4). Therefore, it is of clinical

significance to noninvasively characterize the IPAS and differentiate this lesion from small (< 3 cm) hypervascular PNET.

In addition, we provided relevant information about examined patients in the revised paper. A total of 132 patients were identified from the database search (51 IPAS and 81 PNETs). According to inclusion criteria, 38 IPAS patients were excluded from the study, i.e. 34 patients without available CE-MRI or DWI/ADC, one patient with surgically-proven cystic changes within the lesion, and three patients was diagnosed based on imaging findings although the follow-up period was less than 18 months. Finally, 13 patients with IPAS whose diagnosis was made by surgery (n = 4), biopsy (n = 3), and typical imaging findings (n = 6, follow-up period ≥ 18 months) were included into this study.

For PNETs, 65 patients with PNETs were excluded from the study, i.e. 49 patients without available CE-MRI or DWI/ADC, five patients with hypovascular enhancement pattern or surgically-proven cystic changes within the lesion, eight patients with a mass size > 3 cm and three patients with metastasis. Finally, 16 patients with PNETs whose diagnosis was made by surgery (n = 11) and biopsy (n = 5) were included into this study.

Reviewer #2:

Conclusion: Minor revision

Dear Authors, The use of the expression (< 3cm) in the title of the article was not appropriate. It will be sufficient to specify what is meant by small in the material method section.

Authors response: An intrapancreatic accessory spleen (IPAS) is usually less than 3 cm in size and is generally an innocuous condition. The main clinical importance of this lesion is to not mistake it for a small (< 3 cm) hypervascular pancreatic neuroendocrine tumor (PNET) which shares similar imaging findings with IPAS to avoid unnecessary surgery and the associated increase in morbidity (1–4). As suggested, the revised title is "Diagnostic accuracy of apparent diffusion coefficient to differentiate intrapancreatic accessory spleen from pancreatic neuroendocrine tumors". We accordingly clarified the meaning of "small" in the revised paper.

Gadopentetate dimeglumine is the content of Magnevist. I am not sure if a drug with this content is produced by GE Healthcare. Please verify the composition of the

contrast agent used.

Authors response: Thanks for your careful reading and valuable comments. Gadopentetate dimeglumine (Bayer HealthCare Pharmaceuticals, Berlin, Germany) was intravenously injected at a dose of 0.2 mmol/kg body weight followed by a 20-mL saline flush. We corrected that in the revised paper.

In how many of the patients was the diagnosis of IPAS made histopathologically? There is no precise information about this in the article. Please specify the material in the method section.

Authors response: We really appreciate your constructive comments. Finally, 13 patients with IPAS whose diagnosis was made by surgery (n = 4), biopsy (n = 3), and typical imaging findings (n = 6, follow-up period ≥ 18 months) were included into this study; And 16 patients with PNETs whose diagnosis was made by surgery (n = 11) and biopsy (n = 5) were included into this study. More details were given in the revised paper.

The work you use as the first reference almost exactly coincides with your work. Therefore, please compare the results of the study of Pandey A. et al. in detail in the discussion section.

Authors response: The general comments are thoughtful and impressive. Our study showed an equal performance of both absolute ADC and normalized ADC values in the discrimination of IPAS from PNETs and revealed a high degree of inter-reader reliability, which corroborated the findings a previous study have demonstrated [4]. However, this study has an unbalanced data with 51 PNETs and 11 IPASs and no algorithm was used to balance the data for further analysis. Additionally, all patients underwent MRI scans using a 1.5-T MRI system; And a single scanner from one vendor was used to scan the patients and it is unclear whether the results can be generalized to all vendors. A recent study showed that ADC measurements of the pancreas may be affected by MRI scanner's field strength [5]. Our studies further validated that both absolute ADC and normalized ADC values are useful in the discrimination of IPAS from PNETs with 3.0-T MRI system, which may be attributed to the fact that the IPAS has similar tissue structure and properties as the spleen which possesses the lowest ADC values among the upper abdominal viscera.

Please add to the limitations that not all IPASs were diagnosed histopathologically.

Authors response: Not all of the IPAS included in the study had histopathological confirmation. However, by combining the use of typical imaging findings and stability on imaging follow up, we achieved reasonable confidence in confirming these lesions as IPAS. We revised the limitations as suggested.

References:

1. *Bhutiani N, Egger ME, Doughtie CA, Burkardt ES, Scoggins CR, Martin RC 2nd, McMasters KM. Intrapancreatic accessory spleen (IPAS): A single-institution experience and review of the literature. Am J Surg 2017; **213**:816–820 [PMID: 27894508 DOI: 10.1016/j.amjsurg.2016]*
2. *Ishigami K, Nishie A, Nakayama T,Asayama Y, Kakihara D, Fujita N, Ushijima Y, Okamoto D, Ohtsuka T, Mori Y, Ito T, Mochidome N, Honda H. Superparamagnetic iron-oxide-enhanced diffusion-weighted magnetic resonance imaging for the diagnosis of intrapancreatic accessory spleen. Abdom Radiol 2019; **44**:3325–3335 [PMID: 31420705 DOI: 10.1007/s00261-019-02189-8]*
3. *Kang BK, Kim JH, Byun JH, Lee SS, Kim HJ, Kim SY, Lee MG. Diffusion-weighted MRI: Usefulness for differentiating intrapancreatic accessory spleen and small hypervascular neuroendocrine tumor of the pancreas. Acta radiol 2014; **55**:1157–1165 [PMID: 24259300 DOI: 10.1177/0284185113513760]*
4. *Pandey A, Pandey P, Ghasabeh MA, Varzaneh FN, Khoshpouri P, Shao N, Pour MZ, Fouladi DF, Hruban RH, O'Broin-Lennon AM, Kamel IR. Accuracy of apparent diffusion coefficient in differentiating pancreatic neuroendocrine tumour from intrapancreatic accessory spleen. Eur Radiol 2018; **28**:1560–1567 [PMID: 29134352 DOI:10.1007/s00330-017-5122-3]*
5. *Ye XH, Gao JY, Yang ZH, Liu Y. Apparent diffusion coefficient reproducibility of the pancreas measured at different MR scanners using diffusion-weighted imaging. J Magn Reson Imaging 2014; **40**:1375–1381 [PMID: 24222019 DOI: 10.1002/jmri.24492]*