

ANSWERING REVIEWERS



February 7, 2015

Dear Editor,

We sincerely appreciate the positive comments from the reviewers and editors. In accordance with the requirement of the journal and the reviewer's comments, we revised the manuscript carefully. Please find the edited manuscript in Word format (file name: 15878-revised-locked.doc). As well, the suggested revisions are highlighted in yellow in this letter.

Title: Gadolinium-ethoxybenzyl-diethylenetriamine-pentaacetic acid-enhanced magnetic resonance imaging for bile duct intraductal papillary mucinous neoplasms

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15878

The manuscript has been improved according to the suggestions of editors and reviewers:

Comments from editors:

1. The title of the article was reduced to Gadolinium-ethoxybenzyl-diethylenetriamine-pentaacetic acid-enhanced magnetic resonance imaging for bile duct intraductal papillary mucinous neoplasms.
2. An Ethics approval, Informed consent, Conflict-of-interest and Data sharing statement is added.
3. A paragraph of comments is added.
4. The article has been edited by a professional English language editing company. There are too many modified contents, so they haven't been highlighted in yellow in the manuscript. And the following paragraph is added to the end of MATERIALS AND METHODS according to AMEditor's comments.

US and PET-CT

All US studies were performed by a color ultrasound (Sequoia 512; Siemens Medical Solutions, Munich, Germany) with a 1.0- to 4.0-MHz convex probe. One patient received a whole-body PET/CT scan performed on an integrated PET/CT scanner (Biograph 16; Siemens Medical Solutions) after the injection of 350 MBq ¹⁸F-FDG.

Comments from reviewers

Reviewer-53417

Question: Gd-EOB-DTPA-enhanced MR is a new technique using double-specific contrast agent that has the consistent enhancement effects. It may delineate mucin as a filling defect surrounding hyperintense bile, and provide better imaging for the diagnosis of intraductal papillary mucinous neoplasm of the bile duct (IPMN-B). This manuscript retrospectively analyzed 5 cases of pathologically-proved IPMN-B and suggested that it was a valuable examination to be chosen. The manuscript introduced Gd-EOB-DTPA-enhanced MR to readers. There is a problem for the manuscript. The study is too specific to the readers of this journal, not to the majority of them.

Answer: With the increasing awareness of intraductal papillary mucinous neoplasm of the bile duct (IPMN-B), reports of IPMN-B are growing in number and have become a hot topic in biliary diseases clinically. However, there are still difficulties in diagnosing and determining the extent of the tumor noninvasively. The use of Gd-EOB-DTPA-enhanced MRI provides a novel imaging technique in addressing the problem as introduced by our manuscript. We believe that it will be helpful to the management of the patients with IPMN-B, if the new imaging technique can be widely applied. Therefore, we think that the readers of *WJG* journal may be interested in our study.

Reviewer-2537303

Question: Dear Authors, thank you for submitting this manuscript about the highly interesting topic of challenging diagnostic in neoplasm of the bile duct. You reported on 5 cases, but diagnostics and therapy are very heterogenous within this small group. Only one had a PET-CT and only two complete pathological investigations after surgery. Due to this strong limitations of the study any conclusions cannot be supported by the data given. Therefore I recommend to reject this manuscript, although introduction and parts of discussion are well written and reflect the situation for this rare disease. Sincerely Reviewer

Answer: With the increasing awareness of intraductal papillary mucinous neoplasm of the bile duct (IPMN-B), reports of IPMN-B are gradually growing in number. However, only few IPMN-B cases were reported to be diagnosed by Gd-EOB-DTPA-enhanced MRI, as it is difficult to collect such patients. In this study, we presented the largest series of IPMN-B cases underwent Gd-EOB-DTPA-enhanced MRI so far in the world. As for the pathological results of our cases, we added more detailed description as follows for the reader's better understanding. And the following description has been incorporated into the revised manuscript at *Study subjects* of **MATERIALS AND METHODS**.

Two cases were confirmed by surgical pathology. Three cases underwent thick-needle biopsy, and 3–5 pieces of cord-like tissue were obtained for each case; diagnoses were confirmed by two senior pathologists.

Reviewer-58510

Question: Whilst well constructed, the written English needs attention in a number of places to improve understanding. Discussion and presentation is generally of a good standard.

Answer: Our manuscript has been edited by a professional English language editing company.

Reviewer-71501

Question: Good compilation of 5 cases of intraductal papillary mucinous neoplasm of the bile duct and the diagnostic value of Gd-EOB-DTPA-enhanced MRI. The observation on findings in these cases may require large series and further study to validate the findings and its usefulness.

Answer: I fully agree with the comments from the reviewer. Actually we are collecting more IPMN-B patients who will be diagnosed by using Gd-EOB-DTPA-enhanced MRI.

Reviewer-68184

Question: This is an interesting series of intraductal papillary mucinous neoplasm of the bile duct that was evaluated by Gd-EOB-DTPA-enhanced MRI for better evaluation of the lesion and differentiation between tumor invasion and inflammation. I think the quality of manuscript is good, the English writing needs minor revision.

Answer: The manuscript has been edited by a professional English language editing company.

Reviewer-182188

Question: The article is relevant because is difficult to make an accurate diagnosis preoperatively of Intraductal papillary mucinous neoplasm of the bile duct (IPNB). The IPNB has low incidence and lack of a specific clinical manifestation and imaging findings. The diagnostic value of Gd-EOB-DTPA-enhanced MRI is an important contribution because mucin plugs or sloughed masses may be confused with stones. The manuscript has interesting information and can be published, but I have some recommendations. 1) Table 1 or 2: showing the imaging patterns according classified into five subtypes; 2) Discussion: Highlight the contribution of the findings for the differential diagnosis among the cystic lesions of biliary tract and between mucin plugs and biliary sludge and stones; 3) Figure 3 (white arrow) at T2WI (c). I think is black arrow.

Answer:

1. Thank you for the advice from the reviewer. Actually, in the manuscript, table 1 and table 2 provide clinical data and imaging parameters respectively, this is necessary information for readers to comprehend our study in general. As the imaging features have been described in details in the text for each case, we suggest keeping the table 1 and 2 as it is.
2. Thanks for the suggestion from the reviewer. We added a paragraph regarding the differential diagnosis among the cystic lesions of billiary tract and between mucin plugs and billiary sludge and stones in the revised manuscript. Please see the third paragraph in the *Discussion* section for detailed description.

Although biliary sludge and stones can also appear as filling defects in EOB-enhanced MRI, they show a low signal in T2-weighted images that can be differentiated from mucus, as shown in cases 1 and 2. Although the cystic appearance of the IPMN-B in case 2 is similar to cystadenoma or cystadenocarcinoma, these cystic lesions are not connected with the bile duct. Moreover, contrast agent can be seen in both the cystic lesion and the bile duct in case 2 during the hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI.

3. The legend in Figure 3 has been corrected according to the comments.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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