

ANSWERING REVIEWERS



March 13, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9370 -review.doc).

Title: Comparative analysis of ERCP, IDUS, EUS and CT in predicting malignant bile duct strictures

Authors: Hauke S Heinzow, Sara Kammerer, Carina Rammes, Johannes Wessling, Dirk Domagk, Tobias Meister

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 9370

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

1 Format has been updated

Please note: The title cannot be further shortened – it is 14 words long

2 Revision has been made according to the suggestions of the reviewer
Reviewer#00289448

The authors present an interesting research. The paper is well written but needs some revisions before publishing.

1- define the imaging criteria used in each modality to diagnose benign vs. malignant bile strictures.

Answer: Presence of uniform (homogeneous) echo of the tumor with smooth margins and no signs of infiltrative processes were considered as benign characteristics on IDUS or EUS. Signs of malignancy were inhomogeneous echo of the tumor with infiltration of the adjunct tissue. A double-duct-sign was also considered as a malignant charactersitic. The characterization of malignant biliary obstruction by ERCP followed the known criteria as described before (PMID: 10685746): irregularly shaped intraluminal filling defect of the bile duct, promptly and irregularly altered shape of a distal narrow segment and a proportionally dilated biliary tree proximally.

2- According to the established criteria of bile duct malignancy CT signs range from excentric thickness of the bile duct wall leading to stenosis of the bile duct lumen and proximal dilatation of the biliary tract to tumor formations mostly with hypodensic density aspects. Signs of invasion into neighbouring tissue, blurred borders, tumoral compression or blunt termination of biliary tracts and vessels as well as lymphogenic or hematogenic tumor spread are usually characteristic signs of malignancy. On the contrary, the absence of neighboring lymph node involvement and metastases as well as signs of progressive narrowing and sharply defined tissue borders or other causes of extrahepatic cholestasis like bile duct stones pleads for benign tumors.

3- MRI and MRCP are not mentioned at all though they are important imaging techniques in the workup of biliary tree pathology with better diagnostic performances than CT. Why MR techniques were not used in the patients of this study?

Answer: We agree to the reviewer's comments. In recent years, other imaging techniques like magnetic resonance cholangio-pancreatography (MRCP) have also been evaluated for their diagnostic sensitivity and specificity in biliary duct tumors. Its implementation was however beyond the scope of our study.

- 4- You should add another image This is important to demonstrate the superiority of ERCP/IDUS over those techniques.

Answer: We have added another image panel of a case showing a malignant stricture diagnosed with ERCP/IDUS that was missed or misdiagnosed by EUS and CT.

Figure 3 demonstrates that malignancy could only be observed through IDUS (Figure 3B). This pancreatic tumor could not be visualized by EUS or CT (Figures 3B and 3C).

Reviewer#00503175:

Article Comparative analysis of ERCP, IDUS, EUS and CT in predicting malignant bile duct strictures – results of a tertiary referral center with 234 patients“ by Heinzow et al. is according to my opinion, acceptable for publication with minor revisions. The authors analyzed influence of different diagnostic techniques in predicting malignant bile duct strictures. The results of this study are useful for management of patients with bile duct stricture. Major revisions: NONE

Minor revisions :

1. In Material and Methods section (Procedures) I believe that this two sentences are divide by mistake: 194 procedures included additional forceps biopsies. Endoscopic transpapillary biopsies (n= 4-8 specimens) were taken out of the biliary strictures by straight or angled endoscopic forceps.

Answer: we clarified these two sentences.

2. In section Discussion, page 14 entitiy instead of entity.

Answer: we corrected this spelling mistake.

Reviewer#00289451:

The paper is well written, nevertheless some minor revisions are still needed:

- 1.) First of all, more details about criteria for the clinical assessment should be provided for the studied imaging techniques possibly providing some insight on future quantification methodology.
- 2.) Then, the results should be presented in a more accessible way: instead of only tables and numbers some graphics summarizing the results would facilitate the reader in evaluating the presented approaches.
- 3.) Finally, some comparative considerations about invasiveness, operative difficulties, costs and exam durations should be also better detailed for a better full framework depiction of the presented conclusions.

Minor revisions :

1. We have added more details about criteria for the clinical assessment of benign and malignant bile duct stenosis (see comment to reviewer 1).

2. We have converted table 3 into a graphic figure in order o present our results in a more accessible way.

3. We thank reviewer #3 for this important comment. Costs and exam durations of the three imaging modalities was however beyond the scope of our study. Anyhow, we have added remarks on invasiveness and complication rates under the section „conclusions“ for a better full framework.

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in blue ink, appearing to read 'T. Meister', with a stylized flourish at the end.

Tobias Meister, MD, FEBG
Dept. of Medicine II
Helios Albert-Schweitzer-Hospital
Göttingen University Teaching Hospital
D-37154 Northeim
Fax: +49-5551-1420
E-mail: tobiasmeister@gmx.de