

Response to reviewers' comments

Reviewer's code: 02546581

Reviewer's country: Germany

COMMENTS TO AUTHORS

In this review manuscript, the authors evaluated the current role of EUS in liver disease. The manuscript investigates the diagnostic and therapeutic role of EUS in liver biopsy, focal hepatic lesions, portal hypertension, liver abscess and hepatic cysts. In the context of focal hepatic lesions, the sensitivity of EUS was compared to the sensitivity of CT-Scan. The advantages of EUS are shown sufficiently based on the data presented. - However, the informative value is limited by the fact, that underlying studies are old and the technological progress have not been taking into account. Current studies, e.g. „Applications of contrast-enhanced harmonic endoscopic ultrasound on biliary, focal liver lesions and vascular diseases“, published in Endosc Ultrasound Jan 2017, should be discussed. The superiority auf EUS-FNA in the diagnostic of focal hepatic lesions is sufficiently presented. Whereas the variety of major-complications should be explained in more detail, particularly with regard to gastric and duodenal perforations. The advantages over non-invasive methods should be highlighted. - The authors provide an overview of therapeutic use of EUS guided FNA. The EUS guided ethanol lavage is presented as promising approach in the therapy of simple hepatic cysts. The statement is based on a single center retrospective cohort study, that leads to methodological weaknesses. Only Seventeen patients with 19 hepatic cysts were enrolled. This should be discussed more critically in the discussion part. - The conclusions concerning the EUS guides drainage of liver abscess and portal hypertension are drawn appropriately based on the available literature. The fact, that EUS could be used for creation of an intra-hepatic portosystemic shunt is an innovative outlook. - The authors should include tables summarizing the described studies. - This is an interesting review manuscript, well written and the most recent findings of EUS in liver diseases are well discussed. Thus, the manuscript should be accepted after minor revisions.

Response

Thank you for reviewing our manuscript and for your great suggestions and comments. Please find below the response to the comments and we have incorporated the changes in the manuscript.

The reviewer mentioned the need to use newer studies to discuss the advantage of endoscopic ultrasound (EUS) over Computed tomography (CT) scan. The reviewer suggested to cite the



BAISHIDENG PUBLISHING GROUP INC

7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgooffice@wjgnet.com

<http://www.wjgnet.com>

article "Applications of contrast-enhanced harmonic endoscopic ultrasound on biliary, focal liver lesions and vascular diseases ", published in Endoscopic Ultrasound in Jan 2017. We have incorporated these changes in our manuscript and have discussed the above mentioned article under the heading "Diagnostic use of EUS, contrast enhanced harmonic EUS (CH-EUS), EUS-guided fine needle aspiration (FNA) in focal hepatic lesions". Other similar articles have also been cited to emphasize the advantages of EUS over CT scan.

Per suggestion from the reviewer, we have also incorporated the discussion on complications of EUS especially perforations.

The reviewer also raised a valid concern regarding the use of EUS guided ethanol lavage in management of simple hepatic cysts. This has also been addressed in our revised manuscript by emphasizing and discussing the limitations of the used study and reporting that a multi-center clinical trial would be needed in the future to establish validity of use of EUS guided ethanol lavage and assess its outcome.

Per recommendation from the reviewer, we have created a table (Table 1) summarizing the studies regarding EUS guided placement of intra-hepatic portosystemic shunt.

Reviewer's code: 01467102

COMMENTS TO AUTHORS

A review on this subject is a good idea nevertheless there are some problems to be corrected : - a short introduction on EUS performances, limits and usual side effects is needed at the beginning - the order of the chapters is unclear. Or you delineate clearly diagnosis (including FNA) and therapy, or for every chapter you get two sub topics : diagnosis and therapy - in the same manner you must differentiate when the use of EUS can be applied in clinical practice and when the procedure is always experimental and must be performed in trials. - diagnosis of diffuse liver diseases by liver EUS-FNB is lacking - tables must be added when possible and text shortened (ex:results of EUS-FNA of focal hepatic lesions, drainage of liver abscesses ... - in the topic : diagnostic use of EUS in focal hepatic lesions * MRI and PETscan must be cited and a table comparing the different exams and their performances included. *Add the reference : EUS-derived criteria for distinguishing benign from malignant metastatic solid hepatic masses. Fujii-Lau LL, et al Gastrointest Endosc 2015;81(5):1188-1196. *table about complications of EUS-FNA vs transcutaneous approach - it seems that some page are lacking ? or there is no conclusion ...? - in all the topics the author must underlined if EUS diagnosis or therapy has a



BAISHIDENG PUBLISHING GROUP INC

7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

real future or will only remain an exceptional way to diagnose or treat the problem. - What is considered as the future research (other applications or development of applications) must be clearly identified before the conclusion

Response

Thank you for your detailed review and valuable comments and suggestions. Per your suggestion, we have elaborated our "introduction" to incorporate the limitations, performances and side effects related to EUS.

We have also re-arranged the headings in our revised manuscript accordingly, and diagnostic aspect of EUS in liver disease has been separated from therapeutic role to provide clarity to the readers.

The reviewer highlighted the importance of including small paragraph on EUS guided liver biopsy. We have incorporated that in our revised manuscript.

We have also clarified in our revised manuscript, when the role of EUS is applicable to clinical practice versus still experimental. This has specifically been highlighted in EUS guided creation of portosystemic shunt placement.

Per suggestion from the reviewer, we have cited the reference: "EUS-derived criteria for distinguishing benign from malignant metastatic solid hepatic masses. Fujii-Lau LL, et al Gastrointest Endosc 2015;81(5):1188-1196" [reference 13] and have analyzed this important article in our revised manuscript.

In regards to complication of EUS-FNA compared with transcutaneous approach, a table has been added to the revised manuscript to summarize the complications of both procedures.

Per suggestion from the reviewer and other reviewers we have incorporated a conclusion in the end of our manuscript.



BAISHIDENG PUBLISHING GROUP INC

7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

Reviewer's code: 03475240

COMMENTS TO AUTHORS

Congratulations on the work done for this review article. Good summary of the evidence in the literature to date. You mention "We have also summarized the future research on this subject" however there wasn't very much of that. Would be nice for you to comment on what you think the future directions should be as opposed to what the papers you have summarized suggested.

Response:

Thank you for reviewing our manuscript and for your kind and encouraging comments. We have elaborated the future directions in various parts of the manuscript.

Reviewer's code: 02441041

Reviewer's country: Sweden

COMMENTS TO AUTHORS

This review provides an interesting and thorough overview over the subject EUS in liver disease. It is clear and covering the subject in a systematic way. The authors could add a conclusion about the areas with the high potential to be implemented in routine clinical care in the future.

Response:

Thank you for your comments and for taking the time for reviewing our manuscript. Per your suggestion, we have included a conclusion at the end of our revised manuscript.