

8 Dec 2015

Editor-in-Chief

World Journal of Gastrointestinal Endoscopy

Re : Oh et al. What are the Current and Potential Future Roles for Endoscopic
Ultrasound in the Treatment of Pancreatic Cancer?

Dear Editor-in-Chief

Thank you for considering this manuscript for revision. The authors feel that the reviewers' comments and concerns allow us to provide a stronger manuscript for review. Please find responses to individual reviewer's concerns below (responses highlighted in yellow) and a revised manuscript.

With regards,

Stephen Oh

1. This manuscript is an interesting review article focusing on current status and future perspective of interventional EUS in the treatment of pancreatic cancer. Its content is abundant and well written. 1. Concerning EUS-guided celiac plexus neurolysis, I recommend authors to add relation of puncture site to its efficacy; i.e. unilateral vs bilateray, and broad injection.

Please refer to the new paragraph on the central versus bilateral injection approaches and broad plexus neurolysis. One randomized trial comparing the two techniques and a Japanese study examining the utility of broad plexus neurolysis have been referenced.

2. The paper gives a comprehensive overview of future options and is highly relevant, but several reports quoted is obviously emre feasibilty studies, even though some are comparative (even randomized). The risk of interventions seems underestimated, and the limitations of EUS-interventions need further clarification.

We agree with the reviewer's comment about the risks and limitations of EUS-interventions.

- Serious but rare adverse events of EUS-guided coeliac interventions have been mentioned in the manuscript, including paralysis due to anterior spinal cord infection, necrotic gastric perforation, and celiac artery thrombosis with infarction.
- In regard to EUS-guided biliary drainage, there is a substantial failure rate of 25% with the rendezvous technique which can result in prolonged procedure time and bile leak. Transluminal stenting can also lead to stent migration, occlusion, bile leak, cholangitis and haemobilia and pneumoperitoneum. We agree with the experts' recommendation that EUS-guided biliary drainage be performed by a highly skilled endoscopist trained in both ERCP and EUS in an expert tertiary center, where surgery and radiology support is available in case of adverse events – we iterate this in our conclusion/summary.
- We refer to small case series which reported on EUS-guided gastroenteric anastomosis-related stent migration and perforation. Given the paucity of reports, however, actual complication rates are largely unknown.
- EUS-guided anti-tumor therapies have largely been reported in small case series and pilot studies. One study examining the efficacy of ONYX-015 reported serious adverse events including 2 duodenal perforations and 2 patients with sepsis.

We also emphasize in our summary/conclusion that many of these techniques (anastomosis, anti-tumor therapy, ablative therapies) are in the preliminary stage of development and therefore are not the standard in current practice.