

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6955-review.doc)

Title: Endoscopic ultrasound-guided treatments: are we getting evidence based - a systematic review

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers. We wish to thank all the reviewers for their very important comments which helped us to improve significantly our manuscript. Point-by-reply is attached below.

Reviewer 1	
<p><u>EUS-GUIDED DRAINAGE OF PFCs</u></p> <p>Consider to add a subtitle about 'endoscopic necrosectomies' and to include the following important papers about endoscopic necrosectomies where EUS was used to gain access:</p> <ul style="list-style-type: none"> - Seifert H et al. (Transluminal endoscopic necrosectomy after acute pancreatitis: a multicentre study with long-term follow-up (the GEPARD Study). Gut 2009;58:1260-1266). This multicentre study from Germany included 93 patients with necrotic PFCs. EUS was used in most of them to gain access. Clinical success, complication and mortality were 80%, 26% and 7.5% respectively. - Yasuda I et al. (Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: The JENIPaN study. Endoscopy 2013;45:627-34). Another similar multicenter study 	<p>The suggested revisions have been made. A new section and a new table "EUS-guided necrosectomy" have been added.</p> <p>However we included only original articles and systematic reviews.</p> <p>Some studies were not included because the EUS was not used in all patients and therefore it was not possible evaluate the outcomes, such as the GEPARD Study by Seifert et al. (Gut 2009) or the study by Gardner et al. (Gastrointest Endosc 2011).</p>

<p>but from Japan. This is another large cohort study that included 57 patients. Clinical success, complications and mortality were 75%, 33% and 11%.</p> <ul style="list-style-type: none"> - Jürgensen et al. (Endoscopic ultrasound-guided endoscopic necrosectomy of the pancreas: is irrigation necessary? Surg Endosc 2012; 26:1359-63). This study enrolled 35 patients from a unique center (Germany). EUS-guided internal drainage and mechanical necrosectomy without any kind of irrigation (internal or external) was done. <p>I recommend to include a systematic review about endoscopic necrosectomy of pancreatic necrosis by Haghshenas Kashani (Surg Endosc 2011; 25:3724-30). It includes the most important studies about endoscopic necrosectomies. Most of them used EUS-guided drainage in the first (or unique) session.</p>	
<p><u>Use of covered self-expandable metal stents:</u></p> <ul style="list-style-type: none"> - Consider to include (or mention) a recent state-of-art recently published by Perez-Miranda M et al (Endoscopy 2013; 45:300-304). This paper includes a table with the last (year 2012) experiences of EUS-guided drainage of PFC with SEMSs. - I recommend you to include a recent experience by using an AXIOS stent by Gornals JB et al. (Surgical Endosc 2013; 27:1428-34). This study included 19 cases of PFCs. Although, only 9 cases with FCSEMS were included, in 6 cases a new access device (specific for use with an echoendoscope, called NAVIX) was used, and the results were compared 	<p>The suggested articles have been included.</p>

<p>with 10 plastic double pigtail stents. It is described a statistically significant difference of the procedure time between both groups, (25 vs 42 minutes).</p> <ul style="list-style-type: none"> - Consider to mention or include a recent 'report on emerging technology' by DesiletsDJ (ASGE Technology Committes, Gastrointes Endosc 2013;77:835-8)specific in new devices and techniques for management of pancreatic fluid collections. Different andnew devices for us in EUS-guided drainage of collections are mentioned. - Finally, although it is notified that the literature research of articles was done up to September 2013, I would like recommend a very new specific update about PFCs and EUS published on September 2013 (Pancreatic Fluid Collection Drainage by Endoscopic Ultrasound-An update. Clinical Endoscopy 2013;46:506-514). This is a very completed and well-written update from another referent group of interventional endoscopic (Kahaleh M) 	
<p><u>EUS-GUIDED CHOLANGIOGRAPHY AND BILIARY DRAINAGE</u></p> <ul style="list-style-type: none"> - Please, consider including another recent and complete review about the <i>rendezvous</i> technique by Isayama et al (The endoscopic ultrasonography-guided rendezvous technique for biliary cannulation: atechical review. J.HepatobiliaryPancreatSci 2012). - I recommend you to add an additional paper of the InEBD Study Group just before ref. #41 (Gupta K). This paper is entitled 'Endoscopic ultrasonography guided biliary drainage: Summary of consortium 	<p>The suggested articles on EUS have been included.</p> <p>However we could not include the two papers that are dealing only with the rendezvous technique because we think they were out of the purpose of our review. s.</p>

<p>meeting, May7th, 2011, Chicago' (Kahaleh M. WJG 2013;19:137279) because there is an excellent summary and review of literature about the EUS-guided biliary drainage and can be useful for the readers interested in this technique</p> <ul style="list-style-type: none"> - Consider including a second paper by Dhir (plus ref 89) (Dhir et al. Comparison of EUS-guided rendezvous and precut papillotomy techniques for biliary access (with videos). GastrointestEndosc 2012;75:354-9), because the section of patient and methods (procedural technique) there is a complete and well-written description of their effective and particular technique of the rendezvous using a hydrophilic angled-tip short (260cm long) guidewire. - I recommend you to comment another paper by Gornals (Single-session endosonography and endoscopic retrograde cholangiopancreatography for biliopancreatic disease is feasible, effective and cost beneficial, Dig Liver Dis 2013;45:578-83). Fifty-five patients were included, and 16 EUS-guided biliary drainages were performed. A cost analysis is described. 	
Reviewer 2	
<p>Comments to authors In the present paper the authors make a very interesting challenge for a complete systematic review of all the therapeutics options of the EUS. Although is very interesting for gastroenterologist I have many concerns about the property of call "systematic review" to this paper. No figure or line in some table that summarizes the findings in certain subject evaluated (ej. PFCs, biliary drainage, CPN, etc). I believe that to be</p>	<p>The suggested revisions have been made. We have added a final line in all the tables where it was applicable to to summarize the findings and number of papers. We have included a complete description about complications in the EUS-GD of PFCs section. We have included the reference World J Gastrointest Endosc. 2013 Jun 16;5(6):297-9 in the sub-section <i>Use of covered self-expandable metal stents</i></p>

published, this work should be amended so that it contains specific values that summarize the findings in each of the subjects or figures that allow the same. In its current form the work only contains a very high number of descriptions that do not help to the clinician to make decisions as it represents only succinct "copy-paste" of the summaries of each work. Results - A complete description about complications (type of, mortality) and need of surgery after failure with EUS-GD of PFCs is needed. - The following reference must be included: World J Gastrointest Endosc. 2013 Jun 16;5(6):297-9 - Endosc Ultrasound 2013; 2(3): 153-156	We have included the reference Endosc Ultrasound 2013; 2(3): 153-156 in the sub-section <i>EUS guided CPN</i>
Reviewer 3	
To include recent articles on 1. Necrosectomies. 2. SEMS in PFC drainages 3. newer technologies/upcoming ones 4. summarize the papers viewed with results	The suggested revisions have been made. See also replies to reviewers 1 and 2.

3 References and typesetting were corrected

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

Sincerely yours,

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