To the editorial office and Reviewers' comments

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Reviewer's code: 01430761 (page 4-6) / Reviewer's code: 03262781 (page 7-9)/ Reviewer's code: 02729532 (page 10)/ Reviewer's code: 03706560 (page 11-14)/ Reviewer's code: 01489500 (page 15)

（1） To the editorial office

1) Science Editor: I suggest that the manuscript should be rejected. Summary of the peer-review report: Reviewer#01430761 thought the area lacks a strong evidence and this kind of review article but similar review articles have been published, included one by Teoh et al. (DOI: 10.1055/a-0959-5870). All three reviewers put forward that "Indications and contraindications" part of the manuscript was poorly written. The indication to perform an injective ablation of a pancreatic cyst must be carefully evaluated, and a multidisciplinary consultation should be always performed. Reviewer#03262781 English should be improved through the entire manuscript. Reviewer#03706560 also thought English review from a gastroenterology/endoscopist English native speaker is necessary. Postoperative care and follow-up topic are not good enough and evaluation methods topic need more information.

Answer

Thanks for your advice. (1) We have answered the comment of reviewer # 01430761. This area is a novel one which deserves further study. Reviewer#01430761 thought there are similar reviews, and we have answered this comment as following. There are several studies about EUS-guided ablation and a review is needed. The study by Teoh et al is a good statement, instead of a review. Pro. Enqiang Linghu is also one of the authors of this international statement, who is the corresponding author of our manuscript. This statement aims at several detailed statement, instead of the whole procedure. The international statement is more suitable for those who already have an experience of EUS-guided ablation, instead of a beginner. That statement is important, but simple. Our review demonstrated EUS-guided ablation in detailed, including "indications, contraindications, preoperative treatment, endoscopic procedure, postoperative care and follow-up, evaluation method, treatment efficiency, treatment safety, tips and tricks, current controversies and perspectives".

There are other two reviews (Ref 7 and Ref 37). Canakis et al. (An Updated Review on Ablative Treatment of Pancreatic Cystic Lesions, published on GIE) demonstrated their article based on the ablative methods. They divided to "EUS-Guided Ethanol-Induced Ablation", "Paclitaxel Ablation", and "Radiofrequency Ablation" part. Our review is much different to theirs. Attila et al. ("The efficacy and safety of endoscopic ultrasound-guided ablation of pancreatic cysts with alcohol and paclitaxel: a systematic review", published on European Journal of Gastroenterology & Hepatology) made a systematic review. Their focus was the safety and effectivess, instead of pre or post procedure treatment.

Our review is different from any other reviews published. Our review demonstrated the ablation method completely and in detailed. What's more, there are no other

related reviews published on WJG. Therefore, we believe it is a good review which is suitable for the high quality journal, namely “WJG”.
(2) As three reviewers comments, we have corrected the part of “Indications and contraindications”.
(3) About the English. We are so sorry that the English quality is not so good. We are not a native English speaker, so we sent the revised manuscript to native English editing.

2) Editorial Office Director: Recommend for transfer to the WJGE. 1. Scientific quality: I have checked the comments written by the science editor, and I don’t agree with the science editor. The topic of this manuscript is a review of EUS-guided agent ablation to treat pancreatic cystic neoplasms, and it is within the scope of the WJGE. The reviewers stated that this manuscript is a review of EUS-guided agent ablation to treat pancreatic cystic neoplasms, which is interesting. The reviewer 03767650 pointed out that this manuscript is clear and well written. However, the questions raised by the reviewers should be answered. 1 table and 2 figures. 36 references were cited, including 13 references published in the last 3 years. 3 references self-cited. 2. Language quality: 1A4B. Language editing certificate was provided by AJE. The reviewer 03262781 pointed out that the English should be improved through the entire manuscript. 3. Academic norms and rules: I have checked the documents, including the conflict-of-interest disclosure form and copyright license agreement, all of which are qualified. No academic misconduct was found in the CrossCheck investigation and the Bing search. 4 Supplementary comments: (1) Invited manuscript. (2) Without financial support. (3) The corresponding author has published 4 articles in BPG journals.

Answer

Thanks a lot. First of all, thanks for the comments of Pro. Ma. However, I think that this manuscript is pretty suitable for WJG. WJG is a well-accepted journal and it has accepted many studies of high quality, including many studies focused on endoscopic treatment. Endoscopic treatment is one kind of treatment methods to gastroenterology, so I believe the manuscript belongs to the scope of WJG. What's more, the format for review to WJG is also a manuscript related to endoscopy, named "endoscopic management of adenomatous ampullary lesions".
After received your invitation, I have read many reviews n your journal to make a better understanding for WJG. I do not want to upset you. I found there was a study named "endoscopic ultrasound-guided ethanol ablation therapy for tumors" in 2013 on WJG, and this is a pretty good topic, however it only included 5 related articles on pancreatic cystic lesions. There is no other related reviews on WJG, and reviews published on other journal were not detailed. I am glad that your journal has accepted my title last year. So, I hope that the editorial office can rethink the meaningful of this review. I do believe that WJGE is also a great journal, however I prefer WJG.

3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript

is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors.

Answer

Thanks a lot. It is our greatest honour that this manuscript has received your compliment. We have revised the manuscript as reviewers' comments. We hope that the revised manuscript is suitable for WJG.

(II) Reviewers' comments

（1）Reviewer's code: 01430761

This is a review article of EUS-guided ablation of pancreatic cystic neoplasms.

1.The area lacks a strong evidence and this kind of review article but similar review articles have been published, included one by Teoh et al. (Ref 18).

Answer

Thanks for your comments and your effort to improve our manuscript. We have made several changes as you suggested. I hope the revised manuscript will not upset you.

The study by Teoh et al is a good statement, instead of a review. Pro. Enqiang Linghu is also one of the authors of this international statement, who is the corresponding author of our manuscript. This statement aims at several detailed statement, instead of the whole procedure. The international statement is more suitable for those who already have an experience of EUS-guided ablation, instead of a beginner. That statement is important, but simple. Our review demonstrated EUS-guided ablation in detailed, including "indications, contraindications, preoperative treatment, endoscopic procedure, postoperative care and follow-up, evaluation method, treatment efficiency, treatment safety, tips and tricks, current controversies and perspectives".

There are other two reviews (Ref 7 and Ref 37). Canakis et al. (An Updated Review on Ablative Treatment of Pancreatic Cystic Lesions, published on GIE) demonstrated their article based on the ablative methods. They divided to "EUS-Guided Ethanol-Induced Ablation", "Paclitaxel Ablation", and "Radiofrequency Ablation" part. Our review is much different to theirs. Attila et al. ("The efficacy and safety of endoscopic ultrasound-guided ablation of pancreatic cysts with alcohol and paclitaxel: a systematic review", published on European Journal of Gastroenterology & Hepatology) made a systematic review. Their focus was the safety and effectivess, instead of pre or post procedure treatment.

Our review is different from any other reviews published. Our review demonstrated the ablation method completely and in detailed. What's more, there are no other related reviews published on WJG. Therefore, we believe it is a good review which is suitable for the high quality journal, namely "WJG".

2. I cannot fully agree with the indication and contraindication. SCN is a benign PCN and almost always enlarges with time. What is the definition of enlarging SCN? Are there any evidences that support to include SCN as an indication for EUS ablation? In addition, SCN typically has 6 or more locules.

Answer

Thanks for your advice. SCN is regarded as benign lesion and some experts think that it should not be treated with EUS-guided ablation or surgical resection. In our opinion, SCN that did not cause any discomfort or that with stable size can be monitored. However, if the lesion cause discomfort to patients, it should be intervened. EUS-guided ablation is preferred to surgical resection for its minimal invasion. With the size increasing, symptoms may occur and patients may feel stressful. However, we are so sorry there is no definition of enlarging SCN. If the patient is old and SCN grows slowly, imaging follow-up will be a good choice. We think it is pretty have to make a definition because there are many factors affecting the decision of the doctors,

such as the original size, patients age, patients willingness, family history and so on. Actually, except for 5 studies, 10 studies enrolled SCNs.

We are pretty agree with you that SCN usually has honeycomb appearance and some has more than 6 locules. However, we can also find oligocystic SCN. To many locules have a negative influence on treatment effectiveness. So many studies regarded 6 as a demarcation line. SCN with no more than 6 locules may response better than that with more than 6 locules. However, it does not mean that SCN with more than 6 locules can not be treated with ablation.

We hope that we have expressed our opinion well and you can agree with us.

3. Communication with PD should be included in the contraindication. Thus, I don't recommend ablation of typical SB-IPMN.

Answer

Thanks for your advice. You and other two reviewers both made a comment on this area. We authors discussed together and read related articles. We believed that your advice is pretty precious and we have changed it to "absolute contraindication". You are right that there is no one article of EUS-guided ablation enrolling MD-IPMN or mix IPMN. We authors used to hope that these cysts could be treated by ablation based on our opinion. Sorry.

About BD-IPMN, we have not done researches on the ablation of BD-IPMN, however there are many studies enrolled BD-IPMN. They revealed that EUS-guided ablation to treat BD-IPMN is safe and effective. So, BD-IPMN might be regarded as an indication.

4. The authors recommend the use of PPI. Are there any data?

Answer

Thanks for your advice. We are sorry for our statement of using PPI. It is our experience, but just as you mentioned, no other studies suggested that. We have corrected our statement as "Whether proton pump inhibitors (PPIs) should be used is controversial. Most studies did not mentioned the use of PPIs,[14, 22, 24, 30, 33] however Linghu et al.[2] intravenously administered PPI for 3 days, followed by oral PPI intake for 3 to 7 days. Whether the use of PPI can decrease the possibility of pancreatitis related to EUS-guided ablation remains unknown."

5. IPMNs have a risk of two types of cancer development; cancer derived from IPMN and concomitant PDAC (Gastroenterology. 2020 Jan;158(1):226-237.). If the authors think IPMN is the indication of EUS-guided ablation. The risk of concomitant PDAC should be discussed.

Answer

Thanks for your advice. As you suggested, we have changed MD-IPMN to "absolute contraindication". BD-IPMN is less likely to be malignant compared with MD-IPMN and mixed IPMN. Therefore, many studies enrolled BD-IPMN.

As you recommended, we have noted that "Some authors believe that the presence of an IPMN is not an optimal indication for EUS-guided agent ablation[2, 25]. Because of the communication between cyst and pancreatic duct of IPMN, the ablative agent might get out of the cyst, causing poor treatment response and higher risk of pancreatitis. In addition, IPMN larger than 3 cm has a greater malignant potential which is not suitable

for EUS-guided ablation." in "Indications and contraindications" part and "BD-IPMNs were theoretically believed to be more accessible to procedure-related pancreatitis than SCNs and MCNs; however, a study by DiMaio et al. demonstrated that EUS-guided ethanol ablation was safe in patients with BD-IPMNs, while only 1 patient (7.7%) noted postprocedure minor abdominal pain[30]" in "Safety profile" part.

If the IPMN was diagnosed with concomitant PDAC, it should be eliminated for EUS-guided ablation, and surgical resection or chemotherapy should be recommended.

（2）**Reviewer's code:** 03262781

This is a comprehensive review focusing on injective ablative treatments of pancreatic cystic lesions under EUS guidance.

(1) General comment: The topic is interesting. This manuscript could provide a rapid guide for endosonographers before the procedure. However, the manuscript should be significantly improved before being considered for publication. In particular, I have several concerns about the heading of "Indications and contraindications". Moreover, English should be improved through the entire manuscript.

Answer

Thanks for your encouragement and comments. You are so kind to make great effort to improve the quality of our manuscript. As you recommended, we have sent the revised manuscript for further English editing. We hope the revised manuscript will not upset you. We have divided your comments in separate statements and answered each individually. We hope it can make you have a better understanding of our answer.

(2) Major comments: Title: should be changed in "EUS-guided injective ablative treatments of pancreatic cystic lesions".

Answer

Thanks for your suggestion. We have changed the title as you suggested.

(3) Introduction: - You stated: "Unfortunately, it is difficult to achieve an accurate diagnosis of the type of PCN, making clinical decisions difficult". Although the diagnosis of pancreatic cystic lesions remains a challenge, new tools recently introduced have improved the diagnostic rate. For example, through-the-needle biopsy of the cystic wall has been demonstrated to reach a diagnostic yield of approximately 80% (cite Crinò SF, Bernardoni L, Brozzi L, et al. Association between macroscopically visible tissue samples and diagnostic accuracy of EUS-guided through-the-needle microforceps biopsy sampling of pancreatic cystic lesions. Gastrointest Endosc. 2019;90(6):933–943). This should be mentioned because this tool gives a full awareness of the disease and have an impact on the decision-making process.

Answer

Thanks for your suggestions. We have added related descriptions of EUS through the-needle biopsy (EUS-TTNB) in "Introduction" and "Preoperative treatment" parts. We have added "Histological accuracy could be improved by the development of techniques, such as EUS-guided fine needle biopsy (EUS-FNB), single-operator cholangioscopy (SOC), and EUS-guided through-the-needle biopsy (EUS-TTNB)[9-12]. However, these examination methods are challenging to perform, and this affects their wide application." in "Introduction" part.

(4) Indications and contraindications: In general, this part of the manuscript must be mitigated. The indication to perform an injective ablation of a pancreatic cyst must be carefully evaluated, and a multidisciplinary consultation should be always performed. Please rewrite this section using terms like "injective ablative treatment could be considered…". - This sentence "EUS-guided agent ablation is absolutely indicated for the following patients" must be mitigated. Indeed, EUS ablation is NEVER "absolutely indicated". Is a treatment option that must be considered in selected

patients, especially when surgery is indicated according to guidelines but patients refuse surgery, or the surgical risk is increased because of comorbidities.

Answer

Thanks for your advice. We pretty agree with you and have made corrections as you suggested. EUS-guided ablation is a new method compared with surgical resection. We should not use so intense words because there remains much unknown. We used to use “absolute”, aiming to make distinguish from relative. However, we failed to express our opinion well. We have changed “is absolutely indicated for” to “could be considered for”.

We have also changed the paragraph of relative indications to “The following patients were also considered for enrolment : (1) those with a presumed or confirmed diagnosis of BD-IPMN; (2) those with a multilocular cyst with more than 6 locules; and (3) those with multiple pancreatic cysts. However, the treatment response in these patients may not be as promising, and the procedure might be more challenging.”

(5) In general, it is not sufficient a diagnosis presumed or confirmed of MCN or BD-IPMN. At least worrisome features should be present in a BD-IPMN or risk features in MCN (e.g., size > 4 cm) - It should be specified that microcystic SCA cannot be treated by injective agents. - A short life expectancy cannot be considered an absolute contraindication if symptoms impacting the quality of life are referred by the patient - Number (5) is repeated 2 times. –

Answer

Thanks for your advice.

We agree with you on the “a short life expectancy” statement and we think it should be changed to the relative contraindication. We have deleted the repeated (5). Thank you.

To be honest, we are so sorry that we might have a different opinion with you on MCN and IPMN. I will appreciate it if you let us express our opinion. You believe that the MCN or IPMN with worrisome features should be treated while those without should be followed up. Long-term surveillance may not only increase the financial burden and psychological stress for patients but also result in a missed malignancy. MCN or IPMN with worrisome features has great malignant potential than that without. However, there are chances for those without. Earlier treatment might cause better prognosis. EUS-guided is a relatively novel treatment, and lesions with less chance of malignance were better indications. If the cyst was diagnosed of great possibility of malignance with many worrisome features, surgical resection should be operated according to guideline. We hope that you agree with us.

(6) How can you state that “Enrolled patients must meet the last 4 inclusion criteria while meeting either criterion (1) or (2)”? Is it your personal suggestion? - What do you mean with “an inability to eliminate pancreatic cancer or a sign of malignancy”? It is almost impossible, in a preoperative setting, to exclude malignancy in a pancreatic cyst.

Answer

Thanks for your advice. As you suggested, we have deleted “Enrolled patients must meet the last 4 inclusion criteria while meeting either criterion (1) or (2)”. The

previous statement was obscure. We are so sorry. We just want to express that MCN and SCN which meet the indication could be enrolled, however MCN belonged to (1) while SCN belong to (2). We used to be afraid to mislead readers that the lesions should be SCN and MCN (multiple cystics).

As you reminded, we have changed “an inability to eliminate pancreatic cancer or a sign of malignancy” to “a sign of malignancy”. Completely exclude malignancy without resection seems less possible.

(7) Preoperative treatment - “Enhanced EUS and fine needle biopsy (FNB) and single-operator cholangioscopy (SOC) under EUS guidance can provide useful information for diagnosing pancreatic cysts”. As suggested above, please refer also to microforceps biopsy (e.g., Tacelli M, Celsa C, Magro B, et al. Diagnostic performance of endoscopic ultrasound through-the-needle microforceps biopsy of pancreatic cystic lesions: Systematic review with meta-analysis [published online ahead of print, 2020 Jan 8]. Dig Endosc. 2020;10.1111/den.13626.)

Answer

Thanks a lot. We are so sorry that we forgot that. You also mentioned this methods in “comment 3”. We have added related researches in the manuscript as you suggested. Actually, we sometimes did microforceps biopsy, too (Linghu et al. The Diagnostic Value of the Biopsy of Small Pancreatic Cystic Neoplasms' Cystic Wall by SpyGlass Through a 19-gauge Needle EUS. Am J Gastroentrol, 2016;111:S162-S162). It is a different method from FNB.

We have read the study you suggest, it give us a better understanding of microforceps biopsy. We have added “EUS-TTNB allowed a high rate of adequate specimens to be obtained for histology with an overall histological accuracy rate of 86.7%[11].

However, its complication rate was slightly higher than that of standard EUS-FNA. It can be applied in selected patients by experienced operators. ” in the “Preoperative treatment” part.

（3）**Reviewer’s code:** 02729532

Very good systematic review. There are some minor problems with font formatting. Kindly rectify that.

Answer:

Thanks for your kindly reminder. We have changed the font formatting as you recommended.

（4）**Reviewer's code:** 03706560

Thank you for the opportunity to review your manuscript "EUS-guided agent ablation to treat pancreatic cystic neoplasms". This is a well done review. However, I have some comments:

(1) English review from an gastroenterology/endoscopist English native speaker is necessary to improve the quality of your paper (MAJOR).

Answer:

Thanks for your suggestions. I am so appreciated for everything you have done for our manuscript. We have sent the revised manuscript for English editing as you suggested.

(2-3) Introduction is good. Very easy to follow. I have just 2 MINOR concerns: - PCNs is estimated to be as high as 2%-45%. 45% is to high to be true. Please modify it. - Unfortunately, it is difficult to achieve an accurate diagnosis of the type of PCN - I do not agree. You may modify for some times achieve an accurate diagnosis is challeging...

Answer:

Thank you. Actually, there is a great range from 2% to 45%. I agree with you that 45% is too high and we changed the incidence to nearly 20% as many related articles mentioned to decrease the extreme points caused by several studies. The new sentence is “With the development of cross-sectional imaging modalities and increasing attention being paid to physical examinations, the prevalence of PCNs is estimated to be nearly 20% ”.

(4) Indication and contraindicationsis topic is also easy to follow. However, a presumed or confirmed diagnosis of MD-IPMN or mixed IPMN is an ABSOLUTE contraindication and not a relative.

Answer:

Thanks for your advice. We authors discussed together and read related articles. We believed that your advice is pretty precious and we have changed it to “absolute contraindication” as you suggested. You are right that there is no one article of EUS-guided ablation enrolling MD-IPMN or mix IPMN. We authors used to hope that these cysts could be treated by ablation based on our opinion. Sorry.

(5) "Some authors believe that the presence of an IPMN is not an optimal indication for EUS-guided agent ablation". I´m one of these authors. You cannot treat an IPMN larger than 3 cm with EUS-guided ablation --> please discuss it in your review (MAJOR)

Answer:

As you suggested, we have added related discussion on the last paragraph of “Indications and contraindications” part. The new statement is “Because of the communication between the cyst and the pancreatic duct of an IPMN, the ablative agent might escape the cyst, resulting in a poor treatment response and a higher risk of pancreatitis. In addition, IPMNs larger than 3 cm have a greater malignant potential and are not suitable for EUS-guided ablation”.

(6) Preoperative treatment is also easy to follow. However, it needs English revision.

Answer:

Sorry for our English level. We have rechecked this part for better understanding and

sent the revised manuscript to AJE for further English editing as you suggested.

(7) EUS-guided ablation procedure is also well-written and easy to follw. However, I suggest the authors to include a table with the name of the ablation solution, dose, and volume to be infused. This table will make it much easier for readers who want to start this procedure (MAJOR).

Answer:

As you recommended, we added these information in a new table (Table 1) to make a better understanding.

(8) Postoperative care and follow-up topis is not good enough and needs to be re-write. You should include how long the patient needs to stay in the hospital. 3 to 5 days of IV antibiotic? (MAJOR)

Answer:

As you suggested, we rewrite this part and added the hospital days. The new part is that "After ablation, patients should be carefully monitored to record any problems or symptoms. Complications, such as abdominal pain, abdominal distention, fever, vomiting, hypotension, hematemesis, hematochezia, and bleeding, should be recorded. Serum amylase and lipase levels and complete blood counts should be assessed the morning after the procedure. However, in some studies, the patients were discharged from the hospital only 2 hours postprocedure without any blood tests[18, 25, 26, 32]. Whether proton pump inhibitors (PPIs) should be used in these patients is controversial. Most studies have not mentioned the use of PPIs[18, 26, 28, 32, 35], however, Linghu et al.[2] intravenously administered PPI for 3 days, followed by oral PPI intake for 3 to 7 days. Whether the use of PPIs decreases the possibility of pancreatitis related to EUS-guided ablation remains unknown. In addition, there is no consensus regarding the use of antibiotics. Some studies did not use any antibiotics[5, 15, 25, 31, 32], while others included the administration of intravenous or oral antibiotics[2, 26, 35]. Octreotide was intravenously administered for at least one day until the serum amylase level returned to normal in a study of lauromacrogol[2]. Patients suffering from severe pain or suspected pancreatitis are recommended to undergo abdominal ultrasound or CT.

This procedure had a shortened hospital time of 2 hours postprocedure[18, 25, 26, 32, 34, 35], and several studies reported that patients could be discharged 2 days after the procedure if no complications were noted[5, 15, 28, 31]".

(9) Evaluation methods topic is not bad.. However, more information is needed. For example. What is the next step after PR or persistent cyst? (MAJOR)

Answer:

As you suggested, we added "Re-ablation could be considered for patients with PR, persistent cysts or progressive cysts if the cysts were larger than 1 cm. However, it remains unknown whether surgical resection should be recommended if the effectiveness of EUS-guided re-ablation is unsatisfactory. For patients who did not achieve CR, the follow-up can involve more frequent appointments and last longer" in this part.

(10) Treatment efficiency: needs English native review. Additionally, please try to

clarify the information. There is a lot of great information, however, it is not easy to follow (MINOR) - Figures 1 and 2 are great. Congratulations. - Table 1 is also an excellent table. However, you must include the results of the study (CR/PR and not effective), such as efficacy and adverse events, between diagnosis and follow-up (MAJOR).

Answer:

Thanks for your comments. We have sent the revised manuscript for English editing. We hope the quality will not upset you. We agree with you that the results such as efficacy and AEs between diagnosis and follow-up are important. Actually, there are some studies compared CR and unresolved cysts. All studies which made a comparison regarded CR as resolved cysts with others (including PR and persistent cyst) as unresolved ones. “Most studies have reported that the diagnosis of PCNs has no effect on the ablative results[2, 11, 14, 25]; however, Park et al.[12] doubted these findings. They found that patients with IPMNs were less likely to achieve CR.” was noted in our manuscript. Actually, follow-up is also important. However, related studies is few. We noted that “Park et al.[12] reported that no more than 6 months are needed for most patients undergoing EUS-guided ethanol ablation therapy to achieve CR. Another study by Oh et al reported that CR was achieved 6-12 months after ablation in 57.1% of patients[11]” in “Current controversies and perspectives” part. There is no other studies compared the efficacy and safety between follow-up time. We hope you will be agree with us that it is not suitable for us to compare between different articles in follow-up time on our own analyse. Because, there are many difference between the response evaluation method, follow-up time calculation methods (mean or median), patients and cystic characteristics.

(11) Treatment safety - Modify the title for Safety profile. - plase add the adverse events in the table.

Answer:

Thanks a lot. We have changed “Treatment safety” to “Safety profile” as you suggested. The adverse events were shown in the last line of table 2 (we named complications). The number and rate of complications are both demonstrated.

(12) Tips and Tricks: i liked it. - "Finally, the agent concentration in the cyst is roughly equal to that used in the study" --> which study?

Answer:

Thanks for your reminder. As you mentioned, this sentence is hard to understand, so we changed it to “Finally, the agent concentration in the cyst should be roughly equal to its original concentration before injected to the cyst”.

(13) Current controversies and perspectives: - "Although there are several challenges to EUS-guided agent ablation, it is a promising method to treat PCNs with minimal invasion and excellent effectiveness. The surgical resection of pancreatic lesions is extremely challenging and can severely influence patients’ quality of life, especially when lesions are located in the pancreatic head. EUS-guided agent ablation provides doctors and patients with a safer choice." --> this statment is the opposite about what you wrote in this topic. Please dele or reword this statment (MAJOR).

Answer:

Thanks for your comments. We used to many “challenge”, making the meaning of this paragraph hard to understand. We just want to express that although EUS-guided is not so simple to undergo, it seems better than surgical resection for its minimal invasion and excellent effectiveness. We have changed our statement to “Although several challenges are associated with EUS-guided injective ablation, it is a promising and minimally invasive method for treating PCNs that has excellent effectiveness. The surgical resection of pancreatic lesions can severely influence patients’ quality of life, especially when the lesions are located in the pancreatic head. Compared with surgical resection, EUS-guided injective ablation provides doctors and patients with a safer choice”.

(14) Conclusion: "EUS-guided agent ablation is a minimally invasive, effective and safe treatment for PCNs". Please include: in selected patients. Additionally, the results are not really effective and there is no long term follow-up in the literature. The safety is also a concern with rates varying from 8.5 to 21%. Therefore you cannot stated this technique is effectiveand safe!(MAJOR!!!) Again I want to congratulate the authors for this great revision abour EUS-guided ablation. I´m looking forward to see the revised version of your paper.

Answer:

Thanks you again. This is a great suggestion, and we have corrected our discussion as you suggested, “EUS-guided agent ablation is a minimally invasive, effective and safe treatment for PCNs in selected patients”.

（5）**Reviewer's code:** 01489500

This is a review of EUS-guided agent ablation treatments for pancreatic cystic neoplasms. Authors have indeed searched and reviewed all the existing studies available in the literature so far. They have analysed available data thoroughly and extensively, showing an excellent knowledge of the subject under review. They have presented their data clearly and have emphasized key points in each category of items studied. They have also proposed the appropriate method of ablation in their opinion taking into account the pros and cons of each agent studied.

Answer:

Thanks for your comments. We are so glad for your appraise. We have revised the manuscript to further update the quality of our manuscript, not only academic quality but also English level. We hope the revised manuscript will not upset you.