



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54174

Title: Endoscopic ultrasound-guided injective ablative treatment of pancreatic cystic neoplasms

Reviewer's code: 01430761

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2020-01-13

Reviewer chosen by: Ying Dou

Reviewer accepted review: 2020-03-25 09:18

Reviewer performed review: 2020-03-25 10:38

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

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). 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. 3. Communication with PD should be included in the contraindication. Thus, I don't recommend ablation of typical SB-IPMN. 4. The authors recommend the use of PPI. Are there any data? 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.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54174

Title: Endoscopic ultrasound-guided injective ablative treatment of pancreatic cystic neoplasms

Reviewer's code: 03262781

Position: Peer Reviewer

Academic degree: MD

Professional title: Assistant Professor, Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-01-13

Reviewer chosen by: Ying Dou

Reviewer accepted review: 2020-03-25 06:53

Reviewer performed review: 2020-03-25 13:57

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This is a comprehensive review focusing on injective ablative treatments of pancreatic cystic lesions under EUS guidance. 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. Major comments: Title: should be changed in “EUS-guided injective ablative treatments of pancreatic cystic lesions”. 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. 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



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



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Endoscopic ultrasound-guided injective ablative treatment of pancreatic cystic neoplasms

Reviewer's code: 02729532

Position: Editorial Board

Academic degree: MBBS, MD

Professional title: Associate Professor

Reviewer's Country/Territory: India

Author's Country/Territory: China

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Reviewer chosen by: Ying Dou

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

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



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54174

Title: Endoscopic ultrasound-guided injective ablative treatment of pancreatic cystic neoplasms

Reviewer's code: 03706560

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Assistant Professor, Postdoc, Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

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). 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 too 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 challenging... 4. Indication and contraindications 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. 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) 6. Preoperative treatment is also easy to follow. However, it needs English revision. 7. EUS-guided ablation procedure is also well-written and easy to follow. 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) 8. Postoperative care and follow-up topic is not good enough and needs to be re-written. You should include how long the patient needs to stay in the hospital. 3 to 5 days of IV antibiotic? (MAJOR) 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) 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.



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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). 11. Treatment safety - Modify the title for Safety profile. - please add the adverse events in the table. 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? 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 statement is the opposite about what you wrote in this topic. Please delete or reword this statement (MAJOR). 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 state this technique is effective and safe!(MAJOR!!!) Again I want to congratulate the authors for this great revision about EUS-guided ablation. I'm looking forward to see the revised version of your paper.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54174

Title: Endoscopic ultrasound-guided injective ablative treatment of pancreatic cystic neoplasms

Reviewer's code: 01489500

Position: Peer Reviewer

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Author's Country/Territory: China

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Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing [] Grade B: Minor language polishing [] Grade C: A great deal of language polishing [] Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) [] Accept (General priority) [] Minor revision [] Major revision [] Rejection
Re-review	[] Yes [] No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous [] Onymous Conflicts-of-Interest: [] Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

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.