

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Endoscopy*

Manuscript NO: 73867

Title: Endoscopic ultrasound diagnostic gain over computed tomography and magnetic resonance cholangiopancreatography in defining etiology of idiopathic acute pancreatitis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06148218

Position: Peer Reviewer

Academic degree: FRCP (C), MBChB, MSc

Professional title: Assistant Professor

Reviewer's Country/Territory: Kuwait

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-06 15:26

Reviewer performed review: 2022-02-09 15:54

Review time: 3 Days

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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 Grade E: Do not publish |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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 |

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|---------------------------------|---|
| Re-review | <input type="checkbox"/> Yes <input checked="" 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 |

SPECIFIC COMMENTS TO AUTHORS

This is a retrospective study that aimed at assessing the role of EUS in idiopathic acute pancreatitis (AP). The study concludes that EUS that was able to identify the etiology of AP in 79%. More importantly, EUS was able to identify the etiology of AP in 63% of patients where both CT and MRI failed to find the cause. In addition, the authors were able to identify some clinical parameters that increases the probability of certain etiologies, for example elevated liver enzymes and the risk of biliary etiology of AP.

TITLE: Appropriate for the purpose of the study **ABSTRACT:** Appropriate and summaries the main findings in clear and concise way. **INTRODUCTION:** I think this part can be summarized more. It includes some unnecessary basic information for the purpose of the study such as the definition and mechanisms of acute pancreatitis. I think the authors should include more data from the literature on idiopathic pancreatitis and the role of EUS in this scenario. There has been multiple studies assessing the role of EUS in idiopathic pancreatitis so the authors should mention this part and discuss why this study is important and how it is different from published literature. **METHODS:** Well-described, using validated and clear definitions for the exposures and the outcomes. The inclusion and the exclusion criteria were very clear. The follow up period long enough to detect most recurrent episodes (median 31.5 months). Under statistical analysis (page 14): "The continuous variables with normal distribution are described as median \pm standard deviation (SD) ". I think the authors meant "MEAN \pm standard deviation". Please correct if appropriate. **RESULTS:** Clear and well-written. The authors found that biliary etiology and chronic pancreatitis are the most underlying

causes of AP on EUS. This is in keeping with previous literature that has shown the superiority of EUS in detecting microlithiasis and early changes of chronic pancreatitis over other imaging techniques. The surprising findings (at least to me) include the superiority of EUS over MRCP in detecting pancreas divisum and ductal anomalies. Previous meta-analysis (Wan et al. GIE 2017) have shown that MRCP is superior to EUS in detecting pancreas divisum in patient presenting with idiopathic AP. Would be interesting to hear the authors perspective on this point (could be added to the discussion section). Another important finding which was highlighted by the authors is the usefulness of EUS is more among patients who did not have previous cholecystectomy (since missed biliary etiology is more likely in this sub-group). Another point that the authors discussed in the results (but I think it should be highlighted more in the discussion part) is the fact that EUS findings changed the management of patients significantly including referral to cholecystectomy, ERCP for ductal stentin/sphincterotomy and surgical referral for tumor removal. This is important to highlight since it provides even stronger argument as to why EUS should be utilized more often in patient with idiopathic AP. **DISCUSSION:** Gives a good summary of the findings. I think the authors should discuss previous literature in this field and if their findings are in keeping with previous studies (most previous studies and meta-analyses in this field agree with the study findings). Overall, nicely done and well-written study but the main limitations are the small size (81 pts), retrospective nature of the study. More importantly even though this study looks at a very important and common clinical scenario (idiopathic pancreatitis), multiple larger previous studies have been published which were summarized in a number of meta-analyses (Wan et al. GIE 2017, Umans et al. Endoscopy 2020) which came to the same conclusion as the current study. So overall, this study does not add much to the current literature.

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Peer-review model: Single blind

Reviewer's code: 03474273

Position: Associate Editor

Academic degree: MD, PhD

Professional title: Chief Doctor, Director, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

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|--------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 |

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| Re-review | <input type="checkbox"/> Yes <input checked="" 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 |

SPECIFIC COMMENTS TO AUTHORS

The study by Mazza et al. concluded that EUS is superior to CT/US/MRCP in determining the etiology of idiopathic acute pancreatitis. The topic is important, and the manuscript is well writtern. However, many studies had been published on this topic for years. Even meta-analysis on this topic has been published with 22 studies included (PMID: 32557477). Hence, the novelty is low for this study. Moreover, the sample size for this study is small and it was a single center retrospective study. In general, I recommend this study to be published in World journal of Gastrointestinal endoscopy.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05462132

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-28

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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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 |

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| Re-review | <input type="checkbox"/> Yes <input checked="" 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 |

SPECIFIC COMMENTS TO AUTHORS

This manuscript describes the role of endoscopic ultrasound in idiopathic acute pancreatitis in which the etiology could not be determined by various examinations. While there is no dispute that EUS is useful in the etiologic diagnosis of acute pancreatitis, a study of the Diagnostic gain of EUS after US, CECT or MRI would be very informative. I think this is a well-structured study. However, there is not much novelty and the sample size is small. Furthermore, it has already been summarized in a meta-analysis and has the same conclusion.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Endoscopy*

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Position: Associate Editor

Academic degree: MD, PhD

Professional title: Chief Doctor, Director, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-28

Reviewer chosen by: Li-Li Wang

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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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 |



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**Peer-reviewer
statements**

Peer-Review: ☒ Anonymous ☐ Onymous

Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

I have no further comment.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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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 |
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| 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

I would like to thank the authors for their correspondence to my previous comments. The manuscript content has been modified and improved compared to previous version. However, I think the sections are misplaced in the paper (i.e. the text under CONCLUSION is actually the introduction section, the text under DISCUSSION is actually the methods..etc). Please modify.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Author's Country/Territory: Italy

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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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |



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| | |
|-------------------------------------|---|
| Peer-reviewer statements | Peer-Review: [Y] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [Y] No |
|-------------------------------------|---|

SPECIFIC COMMENTS TO AUTHORS

I appreciate the author's response to the reviewer's comments. The manuscript is well revised compared to the previous version. However, I believe some corrections are needed for errors in sections, such as the conclusion in the "INTRODUCTION" section.