PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 84014

Title: Pancreatic cancer, autoimmune or chronic pancreatitis, beyond tissue diagnosis: Collateral imaging and clinical characteristics may differentiate them

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05601558

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Mexico

Manuscript submission date: 2023-02-20

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-03-14 04:17

Reviewer performed review: 2023-03-14 06:13

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The article discusses the challenges in accurately diagnosing pancreatic ductal adenocarcinoma (PDAC), which has a low survival rate. Other pancreatic masses such as autoimmune pancreatitis (AIP) and mass-forming chronic pancreatitis (MFCP) can be mistaken for PDAC, making it important to differentiate them due to different treatment and prognostic implications. Current diagnostic tools have limitations and may not always provide a clear diagnosis, leading to major pancreatic resections being performed unnecessarily. The article highlights disease-specific characteristics that can aid in accurate diagnosis, such as clinical, radiological, serological, and histological hallmarks. I would suggest to slightly restructure the manuscript to allow the reader efficiently catch the bulletts. Here is a possible outline for systematically reviewing the topic of accurately diagnosing pancreatic masses, including PDAC, AIP, and MFCP: I. Introduction   Background information on pancreatic masses, including PDAC, AIP, and MFCP Importance of accurate diagnosis due to different treatment and prognostic implications Overview of current diagnostic tools and their limitations II. Methods Systematic search strategy for relevant studies in multiple databases Inclusion and

exclusion criteria for studies Quality assessment of included studies III. Results Summary of studies that evaluated the accuracy of different diagnostic tools for distinguishing between PDAC, AIP, and MFCP Description of disease-specific clinical, radiological, serological, and histological characteristics that can aid in accurate diagnosis Discussion of the limitations and challenges of current diagnostic tools, including cases where major pancreatic resections were performed unnecessarily IV. Discussion   Implications of accurate diagnosis on treatment and prognosis for patients with pancreatic masses Recommendations for improving diagnostic accuracy, such as incorporating disease-specific characteristics and using multiple diagnostic tools in combination Future research directions, including the development of new diagnostic tools and the evaluation of novel biomarkers V. Conclusion   Summary of key findings and recommendations for improving diagnostic accuracy in pancreatic masses VI. Limitations   Limitations of the systematic review, such as the quality and quantity of included studies, as well as potential publication bias Suggestions for future research to address these limitations   As the authors tried to, Incorporating case reports within the review can help provide real-world examples of the challenges faced in accurately diagnosing and treating pancreatic cancer.   One approach could be to include a separate section dedicated to case reports, where a few representative cases are summarized and discussed in relation to the main themes of the review. The selected cases could highlight the difficulties in accurately differentiating pancreatic ductal adenocarcinoma (PDAC) from other pancreatic masses, the impact of genetic alterations on treatment decisions and outcomes, and the challenges posed by the tumor microenvironment in achieving effective treatment. By incorporating case reports that illustrate key points of the review, readers can gain a better understanding of the real-world implications of the challenges in diagnosing and treating pancreatic cancer. CARE (CAse REport) guidelines are a set of internationally recognized guidelines

developed to improve the accuracy, transparency, and completeness of case reports. These guidelines provide a standardized approach to writing and reporting case reports, with the aim of ensuring that all relevant information is included and that the report is of high quality. The CARE guidelines consist of a 13-item checklist covering different aspects of the case report, including the title, abstract, introduction, case description, discussion, and conclusion. The guidelines recommend that case reports include a clear description of the patient's history and presentation, details of the diagnostic evaluation, treatment, and outcomes, and any relevant ethical considerations. Previously published manuscript contributing to the understanding of pancreatic cancer and the need for accurate diagnosis and effective therapeutic strategies to improve the prognosis and survival rates of patients with this disease should be discussed. Indeed, the tumor microenvironment, which includes blood vessels, plays a crucial role in pancreatic cancer progression and immune evasion. Endothelial cells in blood vessels can act as immune checkpoints, controlling immune patrolling and affecting the response to immunotherapy. In pancreatic cancer, the tumor microenvironment is known to be immunosuppressive, making it difficult for immune cells to infiltrate and attack cancer cells. Therefore, understanding the role of blood vessels and endothelial cells in the tumor microenvironment and their relationship with key mutations (i.e. K-RAS) can help in developing effective treatment strategies for pancreatic cancer, including targeting the immune checkpoint molecules expressed by endothelial cells (PLEASE refer to PMID: 33918146 and expand accordingly).

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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

SPECIFIC COMMENTS TO AUTHORS

This article described current diagnostic limitations of diagnosis among AIP, PDAC and MFCP and highlighted the disease specific imaging, serological and histological characteristics which may play a significant role in the differentiation of pancreatic mass of uncertain diagnosis after an initial diagnostic approach. The following question should be concerns.   New Imaging Techniques in Pancreas, such as Perfusion CT, Dual-energy CT and low-voltage tube techniques, MRI elastography, etc. might provide useful information that would increase our capability to differentiate benign from malignant pancreatic masses. It is suggested to add the typical imaging of "New Imaging Techniques in Pancreas", and its disctintive radiological features of AIP. MFCP and PDAC in Table 1.

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

This article is a well-written review article which summarized the clinical methods to do the differentiation between pancreatic cancer and pancreatitis .The author lists many imaging features that can aid in diagnosis such as Double Duct Sign，Duct-penetrating sign，Calcification distribution ，Blood vessels peripheral soft tissue etc.It is helpful to distinguishing among pancreatic mass.Although this paper is good, it would be ever better if some extra data were add.   There are still some clerical error such as in Figure 6 "Penetrating duct sing(sign) "and "Double duct sing(sign)"

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD

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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have clarified several of the questions I raised in my previous review. Most of the major problems have been addressed by this revision.