Manuscript title: Age and red cell distribution width in pancreatic cystic neoplasms: A simple tool for preoperative malignancy risk stratification

(Manuscript ID number: 115078)

Dear editor and reviewers:

We sincerely thank the editor and all reviewers for their valuable comments, which we have used to improve the quality of the manuscript. Corresponding revisions have been made according to the editor and reviewer' s respected suggestions and comments. We hope that the revisions and the revised manuscript now are acceptable for approval. Point-by-point responses to the referees' comments are listed as following:

Peer-Review Report(s)

Reviewer 1#

1. Please modify statements suggesting direct clinical application (e.g., "aids in identifying high-risk patients," "optimizes clinical decision-making") to reflect its strictly hypothesis-generating status. Emphasize that validation in multicenter prospective studies is important before considering clinical implementation, particularly highlighting the need for testing in non-surgical PCN cohorts to address selection bias.

[Response] Thank you for your valuable feedback. I have revised the wording throughout the manuscript in accordance with your suggestions.

2. The mechanistic link between RDW and PCN malignancy remains highly speculative. Rather than detailing unrelated TME pathways (e.g., HCC and PDAC mechanisms cited in Section 5), focus on established RDW pathophysiology relevant to pancreatic neoplasia: its association with chronic inflammation (e.g., IL-6 mediated hepatocyte iron regulation), nutritional deficiencies (B12/folate impacting DNA repair), or erythrocyte aging in hypoxic microenvironments. Cite direct evidence linking RDW to pancreatic disease outcomes (e.g., PMID 36574524 on RDW in pancreatic cancer prognosis) to build a more coherent biological narrative.

[Response] Thank you for your insightful comments. We have revised the "RESEARCH IMPLICATIONS AND FUTURE DIRECTIONS" section in accordance with your suggestions, focusing on RDW pathophysiology relevant to pancreatic neoplasia—such as chronic inflammation, nutritional deficiencies, and hypoxic microenvironments—and have strengthened the biological coherence of the discussion.

3. To enhance translational relevance, add a comparative table or paragraph mapping this model against existing risk-stratification systems (e.g., Fukuoka consensus or AGA guidelines). Specify where RDW/age thresholds could supplement imaging/EUS criteria (e.g., for indeterminate cysts) or help prioritize biopsy in resource-limited settings. Crucially, address whether RDW adds value beyond CA19-9/NLR and how false positives might escalate unnecessary interventions given RDW's non-specificity.

[Response] Thank you for your valuable comments. We have incorporated the suggested revisions in the “RESEARCH IMPLICATIONS AND FUTURE DIRECTIONS” section to better address the translational relevance of the study.

Editorial Office’s comments

Science Editor#

1. Summary of the Peer-Review Report: The reviewer pointed out several issues that need to be addressed. (1) Please modify statements suggesting direct clinical application to reflect its strictly hypothesis-generating status; (2) The mechanistic link between RDW and PCN malignancy remains highly speculative; and (3) To enhance translational relevance, add a comparative table or paragraph mapping this model against existing risk-stratification systems.

[Response] We are grateful to the editor and the reviewer for their time and constructive feedback. We have diligently incorporated all the suggestions into our revised manuscript.

2. Manuscript Type: After verification, the manuscript type is "Letter to the Editor".

[Response] We thank the editor for the confirmation and guidance. In accordance with the manuscript type "Letter to the Editor," we have revised the text accordingly.

3. Manuscript Title: If a title contains a colon, please capitalize the first letter of the first word after the colon. For example: Unexplained fetal tachycardia: A case report.

[Response] Thanks for the editor's suggestion. I have revised the title according to the requirements.

4. The “Key Words” does not meet the requirements: The ‘Key words’ list will provide 5-10 keywords that reflect the main content of the study.

[Response] Thank you for your valuable feedback. We have now expanded the list of keywords to better reflect the core content of the article.

4. Audio Core Tip. In order to attract readers to read the full-text article, we request that the first author make an audio file describing the final core tip. This audio file will be published online, along with the article. The author can invite English language editing company to assist in resolving the language issues of Audio Core Tip.

[Response] Thanks for your guidance. We have prepared the audio file for the Audio Core Tip as requested. Please find it attached and let us know if any further adjustments are needed.

5. Reference numbers in the main text. The name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference. Example: Mandal et al[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

[Response] Thank you for your valuable feedback. I have followed the instructions and numbered the references in the main text.

6. There are issues with the references:
To ensure the accuracy of the references, please use "Edit References by Auto-Analyser" (https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx) to edit the references of the manuscript.

[Response] Thank you for your guidance. Thank you for the feedback. We have fully complied with the editorial request and have used the "Edit References by Auto-Analyser" tool to revise the references in our manuscript accordingly.

7. The WJGS article which this editorial discussed has not been listed in the references list. Please add the WJGS article which this editorial discussed into the main text and references list <Martli HF, Acehan F, Şimşek A, Şahingöz E, Sürel AA, Er S, Tez M. Preoperative malignancy risk assessment in pancreatic cystic neoplasms using clinical and laboratory parameters. World J Gastrointestinal Surgery 2025; In press>.

[Response] Thank you for your feedback. We have now added the mentioned WJGS article to the main text and included it in the reference list as requested.