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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 78250

Title: Online Calculator for Predicting the Risk of Malignancy in Patients with Pancreatic Cystic Neoplasms: A Multicenter, Retrospective Study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05947786
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-06-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-16 08:12

Reviewer performed review: 2022-06-17 02:52

Review time: 18 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

Review This study establishes a nomogram-based online calculator for predicting the risk of malignancy in patients with PCNs. I think it is meaningful for the relevant clinical practice. Here are some suggestions and questions: 1. Abstract: statistical analysis methods should be indicated in the part of method. 2.Study population: what's the "similar therapeutic approaches for PCNs"? It should be explained. 3. Method: "In this study, patients were categorized as showing low-risk (low- or intermediate-grade dysplasia) or high-risk (high-grade dysplasia or invasive carcinoma) disease on the basis of the pathological diagnosis.", is there any references for this category? 4.

Preoperative evaluation: "In accordance with the same preoperative evaluation protocol at all centers", what's the evidence about the same preoperative evaluation protocol? 5. Postoperative management: "A digestive secretion inhibitor and broad-spectrum antibiotics were administered immediately after surgery.", is there any references or guidelines about the timing of antibiotic administration in this study? 6.

Patient cohorts and clinicopathologic features: a flowchart should be used to indicate the enrolled patients and the process of inclusion or exclusion.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01588784
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor, Surgeon
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2022-06-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-16 22:32

Reviewer performed review: 2022-06-23 10:58

Review time: 6 Days and 12 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] 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	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

General comments: The authors attempted to develop a nomogram-based online calculator for predicting the risk of malignancy in patients with pancreatic cystic neoplasms (PCNs). The authors had performed established sequential analyses and validation protocols and found that their proposed nomogram showed highly accuracy in predicting the malignancy of PCNs. The inclusion and exclusion criteria were clearly defined. The statistical methods were reliable and reproducible. The predictabilities of the model were excellent, although the number of included patients were small due to the rarity of the disease which required surgical intervention. The available online calculator is easy to use. Minor points: 1.The authors suggested several limitations. Other limitations could be the relatively small number of patients included in the analyses, and possible heterogeneity in pathological diagnosis determining the grade of dysplasia or malignancy. 2. Figure 2 legends: "The nomogram had c-index values of 0.824 and 0.892", but the latter must be "0.893". 3. Figure 3: In the ROC curves, the factor "solid mass" was shown in green lines. Does that mean "tumor diameter > 40mm" according to the main text??

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06298691
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-06-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-16 17:09

Reviewer performed review: 2022-06-24 00:46

Review time: 7 Days and 7 Hours

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 [ ] Grade B: Minor language polishing [Y] 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

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

SPECIFIC COMMENTS TO AUTHORS

In this retrospective, multi-institutional study, the authors sought to develop and validate a prediction model based on clinicopathological data to predict the risk of malignancy in patients with PCNs. This report is intriguing and significant; however, the current study does not meet the publishing criteria in this journal. I raised several points to improve the content of the report. 1. The format of the abstract does not meet the requirements of the WJG. For the Retrospective cohort study, the abstract is structured and should include sections for AIM (no more than 20 words), METHODS (no more than 80 words), RESULTS (no more than 120 words), and CONCLUSION (no more than 26 words). 2. Why is preoperative imaging necessary for pathological diagnosis? If so, do preoperative images require the intervention of an imaging physician? 3. How to interpret the statement that the appearance of high-risk disease was characterized as a study endpoint? 4. The sections of surgical procedure and postoperative management can be briefly described, which is not the focus of this article. 5. How to ensure that the sample size as training cohort and validation cohort is sufficient? 6. Which R packages were used for statistical analysis in statistical analysis? 7. Recommend that the manuscript consistently use multivariable analysis. Multivariable cannot be used interchangeably with multivariate as these are different. 8. A flowchart of patient recruitment and diagnosis should be added. 9. The symbol font of "≥" should be corrected in Tables and Figures. 10. It would be preferred if you described the OR and the 95% CI of the factors, rather than just the p-value. Please do so throughout the text. 11. Please plot the ROC curve to determine the optimal cutoff value of NLR. 12. The AUC value of the prediction model and factors should provide confidence intervals.

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13. The C-index is not mentioned in the Methods section. Why use C-index in the third part and AUC in the fourth part? The C-index was 0.824 (95% CI, 0.735-0.914) and 0.893 (95% CI, 0.823-0.963) for the training cohort and the validation cohort, respectively. Was there a statistical difference in C-index between the two cohorts? 14. In the Result section, the values of AUC and C-index are the same for the training and validation cohorts. What is the difference between C-index and AUC? 15. Was there any assessment of multicollinearity or effect modification with the multivariable model? 16. How to develop the online calculator according to the nomogram? How were the factors assigned to points during the creation of the nomogram? 17. Is there a statistical difference in the AUC between the nomogram and the three factors (tumor diameter ≥ 40mm, enhancing mural nodules, and main pancreatic duct dilatation) in the training and validation cohorts? 18. How to interpret decision curve analysis and clinical impact curves? More detailed information is needed to help the reader understand the information in Figure 4 and Figure 5. 19. Whether nomogram provides more net benefits than the other three factors (tumor diameter ≥ 40mm, enhancing mural nodules, and main pancreatic duct dilatation)? 20. Rather than reporting only the AUC for comparison between the training and validation cohorts, it would be preferred for you to describe the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value with the associated 95%CI of the model performance in the training and validation cohorts, respectively. 21. All patients underwent at least two preoperative imaging examinations among ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), and 2-18F-fluoro-2-deoxy-D-glucose positron emission tomography (PET)-CT. However, how to reduce the heterogeneity between different imaging examinations? 22. The English writing of this paper needs to be greatly improved. It is strongly recommended to seek the help/service from professional English editor or company to improve this paper.

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Peer-review model: Single blind

Reviewer's code: 06196661
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Lecturer, Senior Researcher, Surgeon
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-06-16
Reviewer chosen by: AI Technique
Reviewer accepted review: 2022-06-16 03:28
Reviewer performed review: 2022-06-25 05:30
Review time: 9 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] 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

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

SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review this manuscript. The authors try to develop an Online Calculator for Predicting the Individual Risk of Malignancy in Patients with Pancreatic Cystic Neoplasms. They have used Clinicopathological data of patients in three medical centers who were pathologically confirmed to have PCNs. They finally concluded that the proposed calculator demonstrated optimal predictive performance for identifying the risk of malignancy in patients with PCNs. There are several major issues within the work need be addressed: 1- Methodology: authors excluded some other types of cystic lesions, How can clinicians decided to use/ or not use the proposed calculator during clinical practice? How would it affect the efficiency of the model? How to avoid selection bias? Please explain 2- Methodology: no details about steps of creating the online calculator 3- Methodology: Why did not you use machine learning algorisms rather than simple multivariate nomogram model 4- Methodology: The study focusses on the developing and validation a nomogram, why to add preoperative, surgical and postoperative details? "Please move it to a supplementary document" 5- Methodology: AUC is not enough for discriminatory performance assessment. Please add other more in-depth statistical techniques. 6- Results: the authors stated" In the training cohort, the nomogram achieved a C-index of 0.824 for predicting the risk of malignancy. The predictive ability of the model was validated in an external cohort (C-index: 0.893)". Is it logic that model performance on the external validation dataset surpassed the model performance during training?? Please this point must be explained in detail. 7- Results, DCA and CICA is poorly interpreted. Normal readers should have more details explanations. 8- Discussion: more comparisons with

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advanced machine learning models should be extensively discussed.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 78250

Title: Online Calculator for Predicting the Risk of Malignancy in Patients with Pancreatic Cystic Neoplasms: A Multicenter, Retrospective Study

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06298691
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2022-06-16
Reviewer chosen by: Jia-Ru Fan
Reviewer accepted review: 2022-07-28 09:46
Reviewer performed review: 2022-08-12 01:17
Review time: 14 Days and 15 Hours

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

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

SPECIFIC COMMENTS TO AUTHORS

After the author's revision, my comments were addressed and I think this article can be accepted by WJG.