

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 74843

Title: A simple model established by blood markers predicting overall survival after radical resection of type II and type III AEG

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05079313

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2022-02-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-13 06:40

Reviewer performed review: 2022-03-16 07:08

Review time: 3 Days

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 Grade E: Do not publish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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 checked="" 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

1- All abbreviations showed be clarified when mentioned for the first time. 2- The manuscript requires linguistic and grammatical corrections, the sentences are too long. 3- Page 4, line 9: please remove the word “important” all organs are important, there is no important and not important organ. 4- Page 4, line 11: “1) Previous malignant tumors or various primary tumors”. Please rewrite this sentence; it is not clear. 5- Page 4, line 20, remove the word “so on” and add all the data required. 6- Please add the significance of the ROC curve for both TNM and nomogram scoring. 7- There is significant plagiarism between this manuscript and <https://doi.org/10.3389/fonc.2020.00583> “A Simple Model Established by Blood Markers Predicting Overall Survival After Radical Resection of Pancreatic Ductal Adenocarcinoma” So the manuscript should be totally modified. 6- in page 6 line 17: “the area under the curve (AUC) of the nomogram was sharply larger than the TNM stage,” the difference cannot be described as a “sharply”, as it is [0.630 and 0.720]. 8- The abstract is not informative enough. 9- Tumor location was included in the multivariate analysis though it did not achieve significant value in the univariate analysis

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Title: A simple model established by blood markers predicting overall survival after radical resection of type II and type III AEG

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06250974

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor, Instructor, Lecturer, Staff Physician, Teacher

Reviewer's Country/Territory: Thailand

Author's Country/Territory: China

Manuscript submission date: 2022-02-11

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-19 04:33

Reviewer performed review: 2022-03-27 07:10

Review time: 8 Days and 2 Hours

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 checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review this work. This is a study which the authors aimed to establish a clinical prediction model including blood biomarkers to predict overall survival after radical resection of AEG (Type II and Type III). Detailed comments about this manuscript are as follows:

-1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes

-2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? -Timeframe of this study should be mentioned as a prospective or retrospective study. -In the result, statistical values should be reported according to its 95% confidence intervals such as AUC. -In the result, the authors reported as "The new prognostic nomogram could effectively enhance the predictive value of the TNM stage system." It seems to be the authors' opinion; therefore, it should be moved to the conclusion section rather than being in the result section. Because the result should inform only outcomes that the study found. -Please state the full term of the abbreviation in the first place, for example, "NLR," and "BMI" in the result subheading.

-3 Key words. Do the key words reflect the focus of the manuscript? Some keywords could not be found in the Medical Subject Headings (MeSH) (available from <https://meshb.nlm.nih.gov>): "Adenocarcinomas of the esophagogastric junction," "neutrophils to lymphocytes ratio," and "platelets to lymphocytes ratio." Changing to the appropriate term may be suitable.

-4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes

-5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? -It is unclear whether as prospective or retrospective design because the authors reported

as “patients were analyzed retrospectively during the research.” and “The patients enrolled had prospective follow-up.” in the method. However, the authors informed that “Each patient signed an informed consent form.” in ethics approval and consent to participate section. How was the informed consent to participate in the study obtained from all patients in the retrospective design, if so? -Why did exclude the patient with a previous malignant tumor? Did this study exclude the patient with a previous malignant tumor and success cure it with a low rate of recurrent? Because some malignant tumors might not be affecting the biomarkers of AEG. Exclusion might be potential for selection bias. Please give more detail on which tumors along with the timing (where applicable) were exclusion criteria. -Why did exclude the patient who died within 30 days after surgery? This study planned to use surviving analysis in which the timing of death is essential. Excluding those patients might be selection bias as well. Was this exclusion a run-in period? Please give more reasons why did exclude them. -Please avoid the term “and so on” in “The data of patients’ demographic and clinicopathological features were gathered through the medical record room of our hospital, including age, gender, BMI, tumor size, differentiation grade and so on.” Please mention all of the variables that planned to collect the data. Also, same as in “The routine laboratory data are listed below: neutrophil, lymphocyte, platelet, prealbumin, albumin, hemoglobin etc.” -Please check the typo of the unit in “total lymphocyte count (10⁹/L).” The authors presented as “10⁹/L” without superscript of the 10⁹ cells per liter; therefore, it should be changed to “10⁹/L” where the 10 power 9 of the cells per liter is superscript form. -Please define the unit of BMI in “BMI was divided into 3 groups: <18.5 (low group), 18.5 to 24.9 (normal group), and ≥25 (high group).” -Please clearly mention the censoring in the analysis. -6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? -Please give the 95%CI of the C-index in “The C-index of the model was

0.697, indicating this model is reliable.” -The authors stated that “To further validate the performance of the new score system, the ROC curve was plotted for the nomogram and TNM stage (Figures 4, 5), and the area under the curve (AUC) of the nomogram was sharply larger than the TNM stage, which indicated that the constructed nomogram was a reliable scoring system.” How did the authors ensure whether the ROC curve or AUC of the new proposed model is sharply larger than the TNM staging curve? Please provide the statistical testing (such as using the statistical package to compare two ROC curves) or 95% CI to ensure the AUC of the new proposed model is statistically significantly greater than the AUC of the TNM staging. -Please clearly mention in case the total score of the nomogram is 58. Because the author stated that “In addition, we divided the patients into two groups according to the total score of the nomogram (low risk: <58 and high risk: >58).” In which not include the “58.” -7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper’s scientific significance and/or relevance to clinical practice sufficiently? -Please use the scientific name style (use italic or underline) in case to indicate the organism such as *Helicobacter pylori*. -8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? -In the header row of Table 1, “N(percentage) or Median(25%-75%)” might be changed to the other word and moved the old one to the table caption and using the symbol to indicate it. Also, “25%-75%” should be changed to the 25th percentile or 75th percentile or changed to the IQR (interquartile range) as needed. -In Table 1, it may be suitable to report the data as classified by the primary outcome (overall survival). Therefore, please divide the column as surviving or death. -In Table 1, the authors presented a

continuous variable as a categorical variable. This might lose the detail and trending of the data. It should be reported as median or mean as appropriate along with categorical as needed. For example, the authors presented “ages” as “<60” vs “≥60”, this might be presented as mean or median as well. Also, same as tumor size, and BMI. -In Table 1, please check the typo of the unit. The authors presented as “BMI(kg/m²)” without superscript of the meter unit; therefore, it should be changed to “BMI(kg/m²)” where the squared form of the meter unit is superscript form. -In Table 2, please change the term “gender (men/women)” into a clear word that described what variable is to be the reference of the comparison. For example, men have the HR 1.081 in comparison to women. -Please choose the word “β” (symbol in Table 1) or “beta” (in Table 2) and rewrite it into the same word for consistency. Also, the authors might be defined the full term of the beta such as “coefficient,” or “log-hazard.” -In Table 2, please check the hazard ratio of the albumin variable (hazard ratio = 0.479, 95% CI 0.557 to 1.008) because the hazard ratio is out-of-range of its 95% CI. -In Tables 2 and 3, please explain the asterisk symbol (*) in the table caption. -In Table 3, please check the 95% CI of “Tumor location” because the 95% CI seems wide and the upper bound seems higher than usual (hazard ratio = 0.922, 95% CI 0.695 to 1222). -In Figure 1, the nomogram format quality should be improved such as overlapping of the text “3-years Survival Probability,” and “5-years Survival Probability” and their scales, respectively. -In the legend of Figure 1, please explain how to use the nomogram (step-by-step). Also, the authors might incorporate Table 4 and Figure 1 into the same Figure for easy-to-use purposes. -In Figures 2, and 3, please adjust the scale of both axes of the calibration curves to the probability of survival to 1.0. -In Figures 4, and 5, please provide the 95% CI of ROC. -In Figure 6, please provide shading of the 95% CI for each curve. -According to the general table or figure style should be standalone by itself, some abbreviations should be defined the full term in the table caption or figure legend, such as “NLR,” “PLR,” and

“PNI” in Tables 1, 2, 3, and 4, Figure 1. -The authors might consider presenting the study flow diagram for clarity as a supplementary file. -9 Biostatistics. Does the manuscript meet the requirements of biostatistics? -According to the clinical prediction design, the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) reporting guideline suggested that an internal validation is a necessary part of model development. Please add the internal validation method and an optimistic estimate of performance in the method section and also report it in the result section. (Ann Intern Med. 2015;162:W1-W73. doi:10.7326/M14-0698 mentioned as “Studies developing new prediction models should therefore always include some form of internal validation to quantify any optimism in the predictive performance (for example, calibration and discrimination) of the developed model and adjust the model for overfitting. Internal validation techniques use only the original study sample and include such methods as bootstrapping or crossvalidation. Internal validation is a necessary part of model development.”) -How did the authors handle the missing data? Please describe the method of handling. Whether exclude the patient having incomplete data from the study, if so, please mention in the exclusion criterion section. If the authors included the patient having missing data, please report the missing rate of the data in the results. -Please provide the detail on how to check whether a violation of the proportional hazard assumption. -Please provide more detail of the statistical software. For example, IBM SPSS Statistics version 16 (IBM Corp., Armonk, NY, USA). Moreover, it might give the special package of the statistical software used in the analysis for reproducibility. -The author stated that “P values of variables less than 0.05 in univariate analysis were included in the multivariate analysis.” According to the TRIPOD reporting guideline, those method seems faulty. TRIPOD stated the following “Predictor Selection During Modeling. One approach to predictor selection is to fit a model by choosing predictors on the basis of the strength of their



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unadjusted (univariable) association with the outcome that is to be predicted, or to preselect predictors before the multivariable modeling. The reasoning is that predictors with limited predictive value, based on nonsignificant univariable predictor–outcome association, can be dropped. Although quite common, that strategy is ‘not recommended’ as a basis for selecting predictors, because important predictors may be rejected owing to nuances in the data set or confounding by other predictors. Thus a nonsignificant (unadjusted) statistical association with the outcome does not necessarily imply that a predictor is unimportant. However, if done, univariable predictor–outcome analyses should be reported, including the selection criteria (for example, significance level), and sample size (including the number of events) for each of the univariable analyses, because it is a form of predictor selection.” -Please explain how to select the variables in the full multivariable model to be in the reduced (final) model including backward elimination or forward selection (where applicable). -Please provide the sample size estimation in the method. -Please state the level of statistical significance in each statistical analysis such as a p-value of less than 0.05 is considered statistically significant. -10 Units. Does the manuscript meet the requirements of use of SI units? Yes -11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Please recheck about reference format. -Reference 1 “Kumamoto T, Kurahashi Y, Niwa H, et al. True esophagogastric junctionadenocarcinoma: background of its definition and current surgical trends. *SurgToday*. 2020;50(8):809-814.” The journal abbreviation is not having the space between the words. It should be “Surg Today.” -12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? English style and grammar should be improved throughout a manuscript. Please state

the full term of the abbreviation in the first place, for example, “BMI” in the method section. -13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? -According to the clinical prediction design, the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) reporting guideline should be followed. Please state that this manuscript conforms to the TRIPOD guideline (where applicable) in the method section. -14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 74843

Title: A simple model established by blood markers predicting overall survival after radical resection of type II and type III AEG

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06250974

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor, Instructor, Lecturer, Staff Physician, Teacher

Reviewer's Country/Territory: Thailand

Author's Country/Territory: China

Manuscript submission date: 2022-02-11

Reviewer chosen by: Meng-Tian Li

Reviewer accepted review: 2022-05-11 13:38

Reviewer performed review: 2022-05-11 14:58

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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

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

SPECIFIC COMMENTS TO AUTHORS

Thank you for the author's responses and the revised manuscript. I think the manuscript deserves publication after minor revision as following comments as I mentioned in previous reviewer's comment. 1. English style and grammar should be improved. For example, "355 patients who underwent curative AEG at ..." in the abstract that please consider spelling out the number at the beginning of this sentence. In Result, "The The baseline characteristics of 355 patients are presented in Table 1." In Discussion, "Early detection of AEG is often difficult, owing to the limitations of diagnostic techniques, resulting in a poor prognosis." Please check the word "owning." In Study flow (file name: additional figure1.jpg in 74843-Image-File-revision.zip), "417 patients with compelte clinical data." Please correct the word "compelte." 2. In Study flow (file name: additional figure1.jpg in 74843-Image-File-revision.zip), the authors mentioned "417 patients with compelte clinical data." However, the authors reported "In accordance with the inclusion criteria, 440 patients with AEG were included in the study" in the main text. Please recheck the number of the patients. 3. In Abstract, "355 patients who underwent curative AEG at ... from January 2014 to June 2015 were retrospectively included in this study." However, "...who were hospitalized at ... between January 2018 and June 2018." in the main text. Please recheck the period. 4. In Reference 5, "Yuan Y, Chen X, Hu J, Chen L. Zhonghua Wei Chang Wai Ke Za Zhi. 2019;22(2):101-106." There was no title of the article.