

Peer Review File

Article information: <https://dx.doi.org/10.21037/tcr-23-2023>

Reviewer A

- **Comment:** It is an article on a topic that has gained relevance in recent years: early-onset colon cancer. The manuscript is well-structured, the methodology is adequate, and the results are appropriately discussed. I recommend its acceptance without any changes.

- **Reply:** Thank you for your positive feedback and recommendation. While you suggested no changes, we made some minor adjustments to enhance clarity and accuracy. We hope you understand and anticipate your satisfaction with the final manuscript.

-**Changes in the text:** Not applicable (NA)

Reviewer B

- **Comment 1:** Low technical quality because of typos and repetitions of words and acronyms (line57, line 60, 61,70,269, 271)

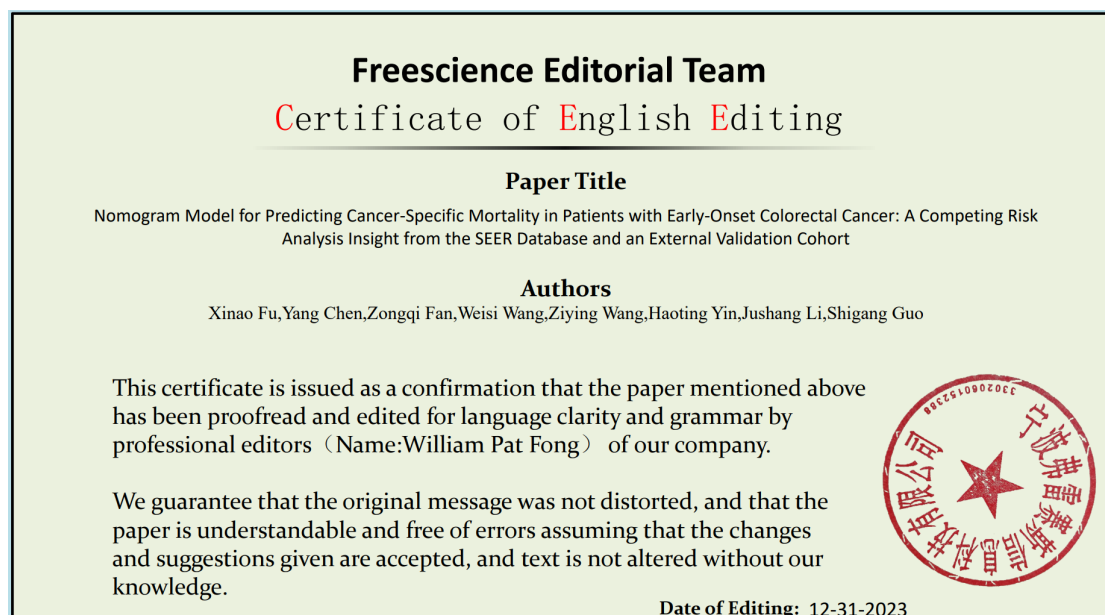
- **Reply:** Thank you for your thoughtful observations. We have dedicated considerable effort to addressing language issues, including typos, acronyms, and word repetitions. The changes made are extensive, and while we won't list them individually. The following are some of the major revisions, please see the manuscript for details. Additionally, we have invited a professional editor to refine the language. The certificate of English editing of the institution is demonstrated as following.

-**Changes in the text:** Typos and incorrect grammar: tumours → tumors (Page 7, line 116) , internal→internally, external →externally (Page 15, line 275-276) , the study aims to develop a nomogram for predicting→the study aimed to develop a

nomogram predicting (Page 2, line 26), partitioned→divided (Page 2, line 32),
using→at (Page 2, line 33), A nomogram visualize →A nomogram was generated
to visualize (Page 2, line 35-36), demonstrated→demonstrating (Page 2, line 35-
36) , were validated internally and externally, respectively → underwent internal and
external validation. (Highlight Box Page 4, line 58) , Delays in diagnosis in...
affecting→ Delayed diagnosis in ...affects (Page 5, line 79-80) , using nomograms,
whichparameters, offers→employs nomograms, which integrate multiple
parameters, offering (Page 6, line 84) , of EOCRC →of the EOCRC (Page 6, line
97) investigate→investigated (Page 6, line 99) Excluding cases comorbid
other→The exclusion criteria were cases involving (Page 7, line 115) ,
encompassed surgical status→ encompassed the surgical status (Page 8, line 128) ,
Tumor→ The tumor (Page 8, line 135) , from SEER cause →from SEER's cause
(Page 9, line 150) , Marital→marital (Page 13, line 236) , who receive→who
received (Page 13, line 242) , against→of (Page 13, line 246) , who were →above
(Page 14, line 258) ,see Figure 7A-7F in Appendix.2.→ See Figure 7A-7F in
Appendix.2 (Page 14, line 259) ,Based on the specific characteristics ...yields→Each
variable....which yield (Page 14, line 268) ,The presented curve
demonstrates...yield→The curve demonstrated ...yielded (Page 15, line 289) , is not
yet fully understood →remains incompletely understood (Page 16, line 312) , as
in→compared to (Page 17, line 317) , to have→exhibiting (Page 19, line 370) ,
There is a ...suggesting →A suggests (Page 20, line 383) , Our study findings..
indicate→Our study results corroborated indicating (Page 20, line 389-390) , for →of

(Page 20, line 393) , only provides→summarized radiotherapy (Page 21, line 405) , literature to identify→literature were analyzed to (Page 21, line 413) , we excluded this variance.→this variance was excluded. (Page 21, line 418) , but did not→but no (Page 23, line 446) .

Repetitions of words and acronyms : patients with EOCRC→EOCRC patients. (Page 2, line 29; Page 3, line 51; Page 10, line 173; Page 12, line 215; Page 13, line 237; Page 14, line 245; Page 14, line 258; Page 14, line 263; Page 18, line 338 et al.) , colorectal cancer (CRC) patients →CRC patients (Page 5, line 76; Page 16, line 298; Page 20, line 384; Page 20, line 387; Page 21, line 402) , Early-Onset Colorectal Cancer (EOCRC)→EOCRC (Page 14, line 271; Page 16, line 295) .



- **Comment 2:** There are no logical flow of arguments with poor writing structure.
- **Reply:** We have recognized the problems of illogical arguments and poorly structured writing. In order to address these issues, we have made efforts to strengthen the coherence and structure of the manuscript , and the following are some of the changes that have been made.

-Changes in the text: Paragraph Organization: Switched the position of paragraphs: Paragraph “EOCRC typically affects the left;” and paragraph “The etiology of EOCRC.....” prior to paragraph “When analyzing survival data,” (Page 16-17, line 306-323) . Add the paragraph “When analyzing survival” (Page 17, line 324-336)

Argumentative logic : however, because the majority→Nonetheless, the majority (Page 5, line 76) , **Bring the sentence "Notably, EOCRC patients exhibit...." to the beginning of the paragraph. (Page 5, line 74) , Add “However, in our multifactorial analysis... Furthermore, studies” to “the survival time and quality of life of patients with advanced metastatic disease have significantly improved“ and “studies have demonstrated ” (Page 20, line 393-397)** Cardiovascular complicationscancer patients. However→Cardiovascular in CRC patients. In contrast, (Page 21, line 401-402) It is important to acknowledge that our study possesses certain limitations.→Nevertheless, the limitations of the study should be acknowledged. (Page 22, line 435) .

Modify incongruent sentences to make them more logical: There are a total of 3 table and 7 figures included in the manuscript.→A total of 3 tables and 7 figures are included in the manuscript. (Page 1, line 17-18) , Patients with EOCRC were drawn→Data from EOCRC patients were collected (Page 2, line 29) , this study included patients→EOCRC patients were also included in the study (Page 2, line 31-32) , This study has effectively developed→a competing risk model for CSM was developed in EOCRC patients. (Page 3, line 50-51) , Established nomogram to predict→ A nomogram predicting cancer-specific mortality was established (Highlight Box Page 4, line 58) , Healthcare professionals can now have a

more→The findings of this study enable a more precise understanding (**Highlight Box Page 4, line 58**) , there have been notable advancements in our comprehension→Recent studies have contributed to deepening our understanding of CRC, which has triggered (**Page 5, line 65-67**) the majority of studies the prognosis.....compared to→the majority of studies indicated ... compared to that of older CRC patients (**Page 5, line 74-76**) , we gathered and performed....China Medical University→patient data obtained from were also analyzed (**Page 7, line 109-111**) , Surgical status→In addition, the surgical (**Page 8, line 142**) , Furthermore, data fromafter excluding→Furthermore, data fromwere collected, among which 76 patients were included for external validation (**Page 10, line 172-174**) , a multivariate Cox regression analysis was performed in order to→The identified factors were then subjected to a multivariate Cox regression analysis to determine independent risk factors. (**Page 12, line 210-212**) , The prevalence of EOCRC is increasing .As evidenced by the rising prevalence in multiple countries, including the United States→EOCRC is increasingly prevalent worldwide, including countries such as the United States (**Page 16, line 295-297**) , but this trend did not show a significant difference in the CSM→but this trend was not observed for CSM (**Page 19, line 366-368**) , we conducted a screening of patients with EOCRC to identify prognostic factors.→EOCRC patients from the SEER database were screened to identify prognostic factors. (**Page 19, line 338-339**)

- **Comment 3:** Very poor clarity of presentation especially the discussion section. The authors

keep repeating their introduction instead of highlighting what is new in their research and discussing the meaning of their results.

- Reply: We acknowledge the noted clarity issues, particularly in the discussion section. We have revised the text to focus on highlighting the novelty of our research and providing a more meaningful discussion of the results, avoiding unnecessary repetition of the introduction. The following modifications were made.

-Changes in the text: Remove duplicate content: ~~Single-center studiescolorectal cancer(22,23).~~ (Page 16, line 299-305) , add a discussion of the significance of new research findings: When analyzing survival data, we often encounter situations where the endpoint event is notendpoint measure (22,23).

(Page 17, line 324-336) , add a discussion of the significance of the new research findings: This factor indeed has the highest contribution coefficient in our nomogram. (Page 19, line 370-371) , add a discussion of the significance of the new research findings: However, currently, due to a lack of sufficient.....an approach (29). (Page 19, line 373-378) , add a discussion of the significance of the new research findings: in our multifactorial analysis at a later stage. Furthermore,

(Page 20, line 393-396) , Switched the position of paragraphs: Paragraph “EOCRC typically affects the left;” and paragraph “The etiology of EOCRC.....” prior to paragraph “When analyzing survival data,” (Page 16-17, line 306-323) .

- **Comment 4:** This research lacks translational impact in the clinical settings.

- Reply: Thank you for your insightful feedback on our study. We appreciate your concern about the lack of translational impact in clinical practice. While our study may not have explicitly highlighted clinical applications, we believe it provides valuable insights into the broader understanding of EOCRC and has implications for future prognostic and therapeutic approaches.

In future work, we plan to improve the accuracy of the model while enhancing its clinical utility by incorporating dynamic nomograms and exploring machine learning methods for statistical analysis. Thank you for your guidance. We appreciate the opportunity to discuss the implications of the model for clinical

translation.

-Changes in the text: Not applicable (NA)

Reviewer C

- **Comment 1:** Overall impressive study. Solid methodology. Intriguing results. No criticism of methodology.

- **Reply:** Thank you for your positive assessment of our study's methodology and results.

-Changes in the text: Not applicable (NA)

- **Comment 2:** But I cannot get past all of the typos, inconsistent spacing and capitalization, and incongruent sentences. The authors need to revise the manuscript so that it reads easier. Multiple times I had to go over a sentence several times to try to understand what was being implied. There are too many instances for me to succinctly point them out.

- **Reply:** We appreciate your constructive feedback on the readability issues, including typos, inconsistent spacing, and incongruent sentences. We acknowledge these concerns and will diligently revise the manuscript to ensure a smoother and more comprehensible flow. Your feedback is invaluable, and we are committed to enhancing the overall readability of the document. In addition, we sought the expertise of a native English-speaking medical professional to review the manuscript, and we trust that the revisions will enhance its readability for you! The following are some of the major revisions, please see the manuscript for details.

-Changes in the text: Typos and incorrect grammar: tumours → tumors (Page 7, line 116) , internal→internally, external →externally (Page 15, line 275-276) , the study aims to develop a nomogram for predicting→the study aimed to develop a nomogram predicting (Page 2, line 26) , partitioned→divided (Page 2, line 32) ,

using→at (**Page 2, line 33**), A nomogram visualize →A nomogram was generated to visualize (**Page 2, line 35-36**), demonstrated→demonstrating (**Page 2, line 35-36**), were validated internally and externally, respectively → underwent internal and external validation. (**Highlight Box Page 4, line 58**), Delays in diagnosis in... affecting→ Delayed diagnosis in ...affects (**Page 5, line 79-80**), using nomograms, whichparameters, offers→employs nomograms, which integrate multiple parameters, offering (**Page 6, line 84**), of EOCRC →of the EOCRC (**Page 6, line 97**) investigate→investigated (**Page 6, line 99**) Excluding cases comorbid other→The exclusion criteria were cases involving (**Page 7, line 115**), encompassed surgical status→ encompassed the surgical status (**Page 8, line 128**), Tumor→ The tumor (**Page 8, line 135**), from SEER cause →from SEER's cause (**Page 9, line 150**), Marital→marital (**Page 13, line 236**), who receive→who received (**Page 13, line 242**), against→of (**Page 13, line 246**), who were →above (**Page 14, line 258**),see Figure 7A-7F in Appendix.2.→ See Figure 7A-7F in Appendix.2 (**Page 14, line 259**), Based on the specific characteristics ...yields→Each variable....which yield (**Page 14, line 268**), The presented curve demonstrates...yield→The curve demonstrated ...yielded (**Page 15, line 289**), is not yet fully understood →remains incompletely understood (**Page 16, line 312**), as in→compared to (**Page 17, line 317**), to have→exhibiting (**Page 19, line 370**), There is a ...suggesting →A suggests (**Page 20, line 383**), Our study findings.. indicate→Our study results corroborated indicating (**Page 20, line 389-390**), for →of (**Page 20, line 393**), only provides→summarized radiotherapy (**Page 21, line 405**),

literature to identify→literature were analyzed to (**Page 21, line 413**), we excluded this variance.→this variance was excluded. (**Page 21, line 418**), but did not→but no (**Page 23, line 446**)

Modify incongruent sentences to make them more logical: There are a total of 3 table and 7 figures included in the manuscript.→A total of 3 tables and 7 figures are included in the manuscript. (**Page 1, line 17-18**), Patients with EOCRC were drawn→Data from EOCRC patients were collected (**Page 2, line 29**), this study included patients→EOCRC patients were also included in the study (**Page 2, line 31-32**), This study has effectively developed→a competing risk model for CSM was developed in EOCRC patients. (**Page 3, line 50-51**),

Established nomogram to predict→ A nomogram predicting cancer-specific mortality was established (**Highlight Box Page 4, line 58**), Healthcare professionals can now have a more→The findings of this study enable a more precise understanding (**Highlight Box Page 4, line 58**), there have been notable advancements in our comprehension→Recent studies have contributed to deepening our understanding of CRC, which has triggered (**Page 5, line 65-67**) the majority of studies the prognosis.....compared to→the majority of studies indicated ... compared to that of older CRC patients (**Page 5, line 74-76**), we gathered and performed....China Medical University→patient data obtained from were also analyzed (**Page 7, line 109-111**), Surgical status→In addition, the surgical (**Page 8, line 142**), Furthermore, data fromafter excluding→Furthermore, data fromwere collected, among which 76 patients were included for external validation (**Page 10, line 172-174**), a multivariate Cox regression analysis was performed in order to→The identified

factors were then subjected to a multivariate Cox regression analysis to determine independent risk factors. (Page 12, line 210-212) , The prevalence of EOCRC is increasing .As evidenced by the rising prevalence in multiple countries, including the United States→EOCRC is increasingly prevalent worldwide, including countries such as the United States (Page 16, line 295-297) , but this trend did not show a significant difference in the CSM→but this trend was not observed for CSM (Page 19, line 366-368) , we conducted a screening of patients with EOCRC to identify prognostic factors.→EOCRC patients from the SEER database were screened to identify prognostic factors. (Page 19, line 338-339)

Reviewer D

- **Comment 1:** Overall, this is a useful paper on an important clinically relevant topic. Writing is good. Methodology sound, interpretations reasonable. Data presentation good. I am choosing "accept" as I see no major flaws and these are data that need to be seen by the scientific community.

- **Reply:** Thank you for your positive evaluation of our paper on this clinically relevant topic. We appreciate your compliments on the writing, sound methodology, reasonable interpretations, and effective data presentation. Your decision to "accept" is greatly appreciated, and we are honored to contribute valuable data to the scientific community.

-**Changes in the text:** Not applicable (NA)

- **Comment 2:** One piece of advice for future research along these lines - the "Others" category in the racial background really needs to be broken down further. Hispanic, East Asian, South Asian, Native American, etc. could all have different characteristics that influence EOCRC.

- **Reply:** We also appreciate your insightful advice for future research, particularly

regarding the need to further break down the "Others" category in the racial background. We will consider this suggestion for more comprehensive analysis in future studies.

-Changes in the text: Not applicable (NA)