Dear Editor and Reviewers,

Thank you for thoroughly reviewing our manuscript. We appreciate your time and helpful suggestions. Please see our point-by-point responses to your suggestions and comments below.

Reviewer 1

1. Upon examining Table 1, a notable inconsistency emerges between the rT and the pT across the same cohort, particularly concerning the proportion of T4 cases. Such discrepancies are critical as they could significantly impact the nomogram's predictive accuracy and clinical utility. It is crucial to ensure the accuracy of both rT and pT staging to maintain the integrity of the study's findings. I would recommend a thorough validation of the data presented. If discrepancies persist, a detailed investigation into the pathology department's assessment procedures may be warranted to rule out systemic errors or misclassification in T staging.

Response:Thank you very much for your suggestion. Based on your advice, we conducted a thorough review of the data, and the current results are correct. From this result, we performed an analysis and identified two potential causes. Firstly, the small density difference between the layers of the colon wall makes it difficult for CT scans to differentiate and display these layers, thus hindering accurate assessment of the tumor invasion depth in early-stage colon cancer without significant wall thickening. For distinguishing T2 and T3 stages, CT primarily relies on whether the outer edge of the colon wall is smooth and whether the density of the surrounding fat spaces is blurred, but both tumors and inflammation can cause these fat spaces to blur, leading to discrepancies. The second reason is that there is a significant difference between rT and pT in T3 and T4 stages. This discrepancy can be explained by the fact that TNM does not provide a clear definition of what is covered by the umbrella term "structures" in their classification of T4b disease as "any tumour with invasion of another organ or structure."[1]. Therefore, the extent and degree of invasion identified in imaging and pathology are inconsistent, inevitably leading to discrepancies. Although the above results lead to differences in staging, considering that pT and rT are not independent risk factors in our current study, these discrepancies will not affect our results.

1.Zhou C, Lu L, Huang Q, et al. Current controversies in TNM for the radiological staging of rectal cancer and how to deal with them: results of a global online survey and multidisciplinary expert consensus. European Radiology (2022) 32:4991–5003.

2. In the manuscript, ctLNM is highlighted as an independent prognostic factor for colon cancer, distinct from traditional pathology-related metrics like pN and MLN-number. However, the surprising non-independence of pN, typically a robust predictor of OS, necessitates a detailed discussion within the manuscript to elucidate potential underlying reasons. To strengthen the study, it is advisable to introduce a binary pathological feature that mirrors ctLNM's approach by simply indicating the metastatic status of lymph nodes. This addition would allow for direct comparisons through further univariate and multivariate analyses, providing a clearer picture of how ctLNM and this new pathologic metric independently contribute to OS predictions. Such enhancements will ensure a more comprehensive evaluation of the nomogram's effectiveness, offering valuable insights for clinical application in assessing prognosis in colon cancer patients.

Response:We greatly appreciate this valuable suggestion and have included a discussion about pN in our paper: "However, unlike previous studies, pN in this paper is not an independent influencing factor. And I believe there are two possible reasons for this. Firstly, the limited data collected may introduce some bias in the results; additionally, the number of lymph nodes evaluated in resected specimens may vary among patients, surgeons, pathologists, and tumor or treatment-related factors[16], which could also lead to discrepancies in the statistical results. Although pN is not an independent prognostic factor for colon cancer in this paper, univariate analysis results indicate that pN might be an important factor affecting the prognosis of colon cancer($P < 0.05$). In the future, increasing the data size could allow for further analysis of pN." (see revised pages 9).

In this study, ctLNM is a binary variable, where (-) represents no lymph node metastasis and (+) represents lymph node metastasis. It reflects the status of lymph nodes through whether there is metastasis observed on the CT scan, thus predicting the prognosis of colon cancer. Indeed, introducing new binary pathological features can further improve the prediction of OS (overall survival). However, the current features in the study already include the number and region of lymph node metastases, which indirectly reflect the status of the lymph nodes and have yielded good results. We have also included relevant discussions in the limitations section: "The features

currently introduced are not comprehensive enough, and more features such as lymph node related pathological features will be included in the future to enhance the effectiveness of the model and ensure the comprehensiveness and effectiveness of the model."(see revised pages 11).

16.Manilich EA, Kiran RP, Radivoyevitch T, et al. A novel data-driven prognostic model for staging of colorectal cancer. J Am Coll Surg2011; 213:579-588.

3. In the current model, mucinous carcinoma is incorrectly classified under 'differentiation,' which traditionally assesses the extent to which tumor cells resemble their normal counterparts, rather than representing a distinct pathologic type. Mucinous carcinoma, however, is a specific tumor type in pathology known for its unique clinical behavior and prognosis. To rectify this categorization error and enhance the model's accuracy in predicting outcomes, it is recommended that mucinous carcinoma be removed from the 'differentiation' category. Instead, a new feature titled ' pathologic tumor classification ' should be introduced to include mucinous carcinoma. This adjustment will not only correct a critical methodological oversight but will also better represent the prognostic variations associated with different pathologic types of colon cancer.

Response:Thank you very much for your criticism and correction. "Differentiation" is an evaluation of the degree to which tumor cells resemble normal cells, and it indeed does not encompass mucinous adenocarcinoma. However, since mucinous adenocarcinoma is a very important pathological type that affects the prognosis of colon cancer patients, tumors are classified into mucinous adenocarcinoma and other non-specific adenocarcinomas. Among other non-specific adenocarcinomas, they are further divided into poorly differentiated adenocarcinoma, moderately differentiated adenocarcinoma, and well-differentiated adenocarcinoma. Therefore, based on your suggestion, "differentiation" will be removed and the new term "tumor classification" will be introduced, which includes poorly differentiated adenocarcinoma, moderately differentiated adenocarcinoma, well-differentiated adenocarcinoma, and mucinous adenocarcinoma.

4. The study primarily utilizes data from a single institution, which might limit the generalizability of the findings to broader clinical settings. To enhance the robustness and applicability of the nomogram, I strongly advocate for the inclusion of a multicenter study design. By training the model with datasets from

your institution and validating it with independent data from other institutions, you can assess the model's performance across diverse clinical environments.

Response:Thank you for your valuable suggestions. I will further discuss this issue in the discussion section: "Although this is a single-center study, it utilized a moderate sample size and yielded very valuable results. In the future, we will conduct multi-center studies to better validate the effectiveness of the model."(see revised pages 11).