

## Peer Review File

Article information: <https://dx.doi.org/10.21037/tcr-24-1030>

### Reviewer A

Comment 1: The authors introduce the topic appropriately and discuss the relevance of PNI and current adjuvant therapies. The paper would benefit from further clarity on exact hypothesis and aims of this study separated from the introductory text.

Reply 1: Thank you for your kind advice. We have made it clear that we will investigate whether there is an influence of PNI on the outcomes of CCRP in T4 CC patients.

Changes in the text: We have modified our text as advised (see Page 4, line 76-79).

Comment 2: The discussion highlights the main findings and presents their relevance to the current literature. My main comment is with the discussion falling short of future research recommendations. How do the authors envisage their nomogram becoming a routine part of care? I presume this is for use at treatment planning stage and to guide adjuvant therapy. How will the research group take these findings forward? Further detail on how this may be trialled to show significance in patient outcomes should be added. Addition of these details will strengthen the relevance of these findings.

Reply 2: Thank you for your positive response to our work and the kind advice. We have added the use of our nomogram and our plan for next phase of our research in our discussion.

Changes in the text: We have modified our text as advised (see Page 8, line 265; Page 9, line 310-316).

### Reviewer B

Please see the attached PDF.

Comment 1(line 22): Colon cancer standard of care does not include radiation as an adjuvant therapy? clarify that assessment's relevance

Reply 1: Thank you for your question. According to our reference 15, adjuvant radiotherapy can only be considered in several clinical scenarios, such as positive margins or advanced local disease (pT4). The SEER database includes cases with radiotherapy after radical surgery; therefore, we incorporated it as a variable for analysis.

Changes in the text: -

Comment 2(line29): can remove certain

Reply 2: We agree with the reviewer. We have deleted it in our revised manuscript.

Changes in the text: We have modified our text as advised (see Page 3, line 48).

Comment 3(line29): because concurrent chemo/xrt is not the standard of care does not

include XRT and are you sure whether the XRT was offered in the adjuvant setting?  
not standard of care

Reply 3: Thank you for your question. The SEER database indicates that radiotherapy was administered after radical surgery, however, the relationship of radiotherapy with chemotherapy remains unclear. We have discussed this as a limitation in our discussion.  
Changes in the text: We have modified our text as advised (see Page 9, line 310-316).

Comment 4(line 58): consider to remove this word, cause validation can happen when other people cite your work or it gets proven in a clinical trial

Reply 4: Thank you for your advice. We have deleted it in our revised manuscript.  
Changes in the text: We have modified our text as advised (see Page 4, line 80).

Comment 5(line82-83): can be rephrased for coherence, if they have a 2nd primary tumor

Reply 5: Thank you for your advice. We have revised it in our revised manuscript.  
Changes in the text: We have modified our text as advised (see Page 4, line 104-105).

Comment 6(line83): clarify, is it disease specific survival or overall survival?

Reply 6: Thank you for your question. We have revised it in our revised manuscript.  
Changes in the text: We have modified our text as advised (see Page 4, line 105).

Comment 7(line83): incomplete or variable?

Reply 7: Thank you for your question. We have revised it in our revised manuscript.  
Changes in the text: We have modified our text as advised (see Page 4, line 106).

Comment 8(line 144): Clarify what high means here

Reply 8: Thank you for your advice. It means higher T and N stage. We have revised it in our revised manuscript.  
Changes in the text: We have modified our text as advised (see Page 6, line 167).

Comment 9(line 179): it's confusing whether racial disparities were something which were checked, because this statement shows that white other races everyone has lower colon cancer specific cancer rates

Reply 9: Thank you for your kind advice. We have deleted "other races" in our revised manuscript, due to the high diversity of ethnic groups included in this category, it is challenging to ascertain whether a specific ethnicity constitutes a risk factor.  
Changes in the text: We have modified our text as advised (see Page 7, line 205).

Comment 10(line181-182): are these separate groups for each category?

Reply 10: Thank you for your question. All these variables were included in the multivariable competing risk analysis.  
Changes in the text: -

Comment 11(line 193-195): This part can be removed because it's quite obvious that

patients who were treated with any therapy would do better than patients without any treatment, especially because there were multiple clinical trials done to establish the standard of care

Reply 11: Thank you for your kind advice. Although the conclusions have been repeatedly validated, we still present this section to ensure the completeness of the subgroup analysis for patients with or without PNI.

Changes in the text: -

Comment 12(line 203-205): hence this not a new finding that your study brought to light, this sentence needs to be rephrased

Reply 12: We agree with the reviewer. We have revised the “confirm” in the manuscript to "validated".

Changes in the text: We have modified our text as advised (see Page 7, line 229).

Comment 13(line 214): what's the general populations prevalence of PNI?

Reply 13: Thank you for your question. According to reference 4, 33% of patients with colorectal cancer exhibit PNI.

Changes in the text: -

Comment 14(line 218): can be rephrased, sounds very vague

Reply 14: Thank you for your kind advice. We have revised it in our revised manuscript.

Changes in the text: We have modified our text as advised (see Page 8, line 245).

Comment 15(line 248-249): clarify what this means

Reply 15: Thank you for your question. In order to phrase our meaning more carefully, we have revised the “discrepancies” in the manuscript to "difference in HR".

Changes in the text: We have modified our text as advised (see Page 8, line 277).

Comment 16(line256): can be removed

Reply 16: Thank you for your advice. We have deleted it in our revised manuscript.

Changes in the text: We have modified our text as advised (see Page 8, line 285).

Comment 17(line 266): is it adjuvant radiation therapy? does the SEER data shows the timing of XRT whether it was adjuvant vs palliative?

Reply 17: Thank you for your question. The SEER database demonstrates that the timing of radiotherapy was after radical surgery, however, it is acknowledged that in some cases, the role of radiotherapy as an adjuvant treatment may not be definitive, and its relationship with chemotherapy is not well-established. We have added this part in the discussion section.

Changes in the text: We have modified our text as advised (see Page 9, line 309-315).

Comment 18(line 280): if the radiation timing and intent is not defined in the SEER data it should be mentioned in the limitations section

Reply 18: Thank you for your advice. The SEER database demonstrates that the timing

of radiotherapy was after radical surgery, however, it is acknowledged that in some cases, the role of radiotherapy as an adjuvant treatment may not be definitive, and its relationship with chemotherapy is not well-established. We have added this part in the discussion section.

Changes in the text: We have modified our text as advised (see Page 9, line 309-315).

Comment 19(line 286-287): this conclusion might be showing up as an outlier and slight deviation from the overall study, consider removing it, because higher T stage is a high-risk factor but them getting benefit is not logical

Reply 19: Thank you for your advice. According to our reference 15, adjuvant radiotherapy can only be considered in several clinical scenarios, such as positive margins or advanced local disease (pT4). Patients in stage T4 without PNI may indicate a more localized tumor, thereby potentially benefiting from radiotherapy.

Changes in the text: -