Peer Review File

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Reviewer comment-Reviewer A

1) First, the title needs to indicate the clinical research design of this study, i.e., a retrospective comparative cohort study.

Reply 1: We have modified our text as advised.

Changes in the text: We have added research types to the title. We have modified our text as advised (see Page 1, Line5).

2) Second, the abstract is not informative and not standardized and needs further revisions. The background did not indicate the clinical needs for comparing nICT and nCRT and what its knowledge gap is. The results need to describe the inclusion of subjects, the assessment of baseline clinical factors, and follow up procedures. The results need to quantify the findings by providing detailed outcome values of the two groups and accurate P values for the comparisons. The conclusion should not repeat the main findings again, please have comments for the clinical implications of the findings.

Reply 2: According to your suggestions, we have revised our abstract.

Changes in the text: We added background information on nCRT. For the result part, we give detailed P values. Finally, according to the research results, we gave the clinical application value of neoadjuvant immunotherapy.

We have modified our text as advised (see Page 2, Line39 to 41, Line 46 to 47. Page3, Line 61, Line 63, Line 67 to 70).

3) Third, in the introduction of the main text, the authors cannot described no comparisons between nICT and nCRT, so they compared nICT with nCRT. The authors need to clearly indicate the clinical needs and clinical significance of such comparison and analyze why no studies compared the two. It is very likely that such comparison has very little clinical significance, so the authors must provide adequate rationale for this study.

Reply 3: Thank you very much for your comments. We have noticed that we used the wording incorrectly and have revised it. Due to the late application of neoadjuvant immunotherapy in the treatment of esophageal malignancies, there are few studies on the comparison between neoadjuvant immunotherapy plus chemotherapy and neoadjuvant chemoradiotherapy. However, currently more and more centers are conducting research on the discussion of neoadjuvant immunotherapy combined with chemotherapy.

Change in the text: Page 4, Line 104.

We have modified our text as advised (see Page 4, Line 104).

4) Fourth, in the methodology of the main text, please correctly describe the clinical research design of this study, ethical approval, sample size estimation, assessment of baseline clinical factors including demographics, and, importantly, in the authors' real-world clinical practice, how the two treatments, nICT and nCRT, were assigned to the patients. In statistics, please first describe the test of baseline comparability of the clinical factors of the two groups and consider to do adjustment analysis when the baseline is not comparable. Please ensure $P<0.05$ is two-sided.

Reply 4: The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethical Committee of Gaozhou People's Hospital (No. GYLLPJ - 2022104). Individual consent for this retrospective analysis was waived.In this study, patients receiving neoadjuvant therapy in Gaozhou People's Hospital from January 1, 2019 to September 1, 2022 were included and divided into two groups, nCRT and nICT, according to different neoadjuvant therapy regiments. Clinical data, including demographics of the two groups were compared at baseline, showing no statistical difference.
In actual work, we will select neoadjuvant therapy through multidisciplinary discussion of esophageal cancer and combined with patients' treatment wishes.
Changes in the text: Page 4, Line 110 to 113.
We have modified our text as advised (see Page 4, Line 110 to 113).

5) Finally, please consider to cite the below related papers: 1. Yu Y, Wang W, Qin Z, Li H, Liu Q, Ma H, Sun H, Bauer TL, Pimiento JM, Gabriel E, Birdas T, Li Y, Xing W. A clinical nomogram for predicting tumor regression grade in esophageal squamous-cell carcinoma treated with immune neoadjuvant immunotherapy. Ann Transl Med 2022;10(2):102. doi: 10.21037/atm-22-78. 2. Li C, Li B, Yang Y, Liu J, Zhang M, Zhang H, Tan L, Shen X, Li Z. Stratified treatment of localized cervical esophageal squamous cell carcinoma induced by neoadjuvant immunotherapy plus chemotherapy (SCENIC). J Thorac Dis 2022;14(9):3277-3284. doi: 10.21037/jtd-22-402. 3. Li J, Chen B, Wang X, Xu C, Chen D, Zhu K, Jin Z, Qiu H, Shen J, Ye M. Prognosis of patients with esophageal squamous cell carcinoma undergoing surgery versus no surgery after neoadjuvant chemoradiotherapy: a retrospective cohort study. J Gastrointest Oncol 2022;13(3):903-911. doi: 10.21037/jgo-22-296. 4. Yu Y, Xu L, Chen X, Li H, Liu Q, Zhang R, Xie H, Chen Y, Yuan L, Tan B, Li Y, Xing W. Neoadjuvant therapy combined with surgery is superior to chemoradiotherapy in esophageal squamous cell cancer patients with resectable supraclavicular lymph node metastasis: a propensity score-matched analysis. Ann Transl Med 2022;10(6):349. doi: 10.21037/atm-22-577.

Replay 5: Thanks for providing these studies, we have studied them in detail and cited related papers based on our research.
Changes in the text: In the references, Page 11 to 14, Line 334 to 406.
We have modified our text as advised (see Page 4, Line 110 to 113).

Reviewer comment-Reviewer B

1. The sample size of the two groups is relatively small. Does it cause a big deviation to the statistical results?

Reply 1: Thank you very much for your opinion. Before starting this study, we collected the information of our clinical cases. We also noticed that our sample size was small, so we adopted different statistical methods according to the actual cases (see details on page 6-7, lines 170-182), hoping to draw a more appropriate conclusion. We also plan to further expand the sample size in subsequent studies to further explore the practical clinical application value of nICT in the treatment of esophageal cancer.

2. Improve the flow chart.
Reply 2: We have modified our text as advised.
Changes in the text: Page 15, Line 435 to 455.

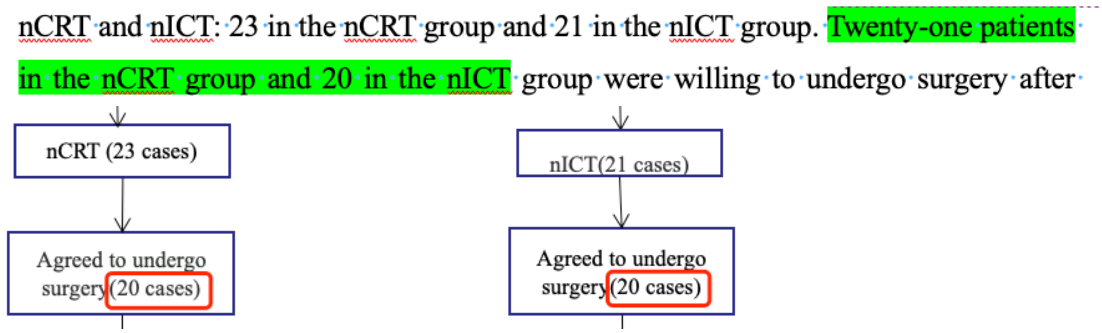
3. It is suggested to add the prognosis analysis of the patients and compare the long-term survival of the

two groups.
Reply 3: Thank you for your suggestion. Due to the short follow-up time between the two groups, the comparison of survival or disease-free survival between the two groups was not listed in this study. We will make comparison in the follow-up study.

4. The clinical significance and innovation of the paper are insufficient.
There is not enough evidence to draw a conclusion. The study needs additional data and trials.
Reply4: Thank you for your comments. This study is a retrospective analysis, and we strictly implement the research strategy and requirements of retrospective analysis. Based on the small sample size and retrospective analysis, our preliminary conclusion suggests that nICT is a potentially feasible and effective clinical treatment measure. We plan to use a multi-center study with a large sample size in the follow-up studies, and even design some prospective studies to further explore the clinical therapeutic value of nICT.

Reviewer comment-Reviewer C

1. Figure 1
Please check the legend and figure, the data should be the same.



Reply: Thank you, the number should be twenty-one. We had corrected it.
Change in the text: Figure1
We have modified our text as advised (Figure1).

2. Table 1
Please explain SD in the table footnote.
Reply: We inserted footnotes to the SD in Table 2 and Table 3.

3. References/Citations
a) Please check if the author's name matches with the citation.

250 Yan et al. (10) reported a 50% PCR rate and a 75% major pathologic response (MPR)

Reply: We corrected "Yan" to "Yang".
Change in the text: Page 8 Line 235.
We have modified our text as advised (Page 8 Line 235).

b) References 13 and 15 are the same, please delete one of them and revise both the citation in main text and reference list's order.
Reply: We have amended the reference of the 15th.
Change in the text: Page 13 Line 398.The 15th in the list of references.
We have modified our text as advised (See Page 13 Line 398 to 401).

c) Please double-check if citations should be added as you mentioned "studies".

243 → There are a growing number of clinical studies of neoadjuvant immunotherapy in
244 treating locally advanced resectable ESCC[13]. Considering the short clinical

Reply: We add articles 8, 9 and 11 from the list of citations to the citations.
Change in the text: Page 8, Line229.
We have modified our text as advised (See Page 8, Line 229).