

List of Responses

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "The critical prognostic value of the log odds of negative lymph nodes/tumor size in rectal cancer patients"(Manuscript NO.: 60753). Those comments are all valuable and very helpful for revising and improving our paper as well as the important guiding significance to our researches. We have studied comments carefully and have made correction using Microsoft Word Track Changes. which we hope meet with approval. Revised portions are marked in red in the paper. The main corrections in the paper and the responses to the reviewer's comments are as flowing:

Responds to the reviewer's comments: Reviewer #1:

1. In my opinion, it is totally unclear why this analysis is restricted to rectal cancer - the remaining colon would deliver an ideal either additional or control group.

Response: The reason is that we considered that colon cancer and rectal cancer have different biological behaviors, surgical approaches and the number of examined lymph nodes^[1-3]. The most important is the number of lymph nodes that can be retrieved varies with the site, and previous studies^[1, 2] have shown that the number of lymph nodes examined in colon cancer was significantly more than that in rectal cancer(Table 1). Therefore, we hypothesized that the optimal cut-off value of LONS was different in different site. Thus, to get an accurate cut-off value of LONS, this study was limited to rectal cancer. Of course, this is a very good suggestion. We will study colon cancer and compare it with rectal cancer in our next work.

Table 1 ^[2] Site affecting the number of lymph nodes examined

Stage II	<i>P</i>	Stage III	<i>P</i>
Number of lymph nodes examined		Number of lymph nodes examined	
(mean±standard deviation)		(mean±standard deviation)	

Tumor size		0.001	0.002
Right colon	19.12±11.23		19.27±10.94
Left colon	14.92±11.57		16.26±11.219
Rectum	13.40±9.93		14.73±9.08

2. Why is the distribution of the training cohort versus validation cohort so uneven?

Response: We allocate cases according to 7:3 mainly based on the followed two reasons. On the one hand, we referred to the previous studies^[4, 5]. On the other hand, The larger the sample size in the training cohort was, the more accurate the result was. At the same time, if the result was also stable in small sample size, the conclusion would be more convincing.

3. Please cite a suited work to proof that the relative degree of LND can be quantified by comparing pure numbers of dissected LNs with the tumor size

Response: To our knowledge, this is the first study that we combined the number of examined lymph nodes and tumor size to quantify the relative degree of lymph node dissection. Because previous studies have suggested that examined lymph nodes, negative lymph nodes and tumor size were associated with survival of rectal cancer. Our study only combined the advantages of negative lymph nodes and size by mathematical converting. Therefore, Our hypothesis is reasonable.

4. In general, the manuscript must be carefully checked concerning typos and style. Similarly, the Figures should be checked - for example Figure 2: the left lower graph is too high.

Response: We have carefully checked concerning typos and style and have corrected them using Microsoft Word Track Changes. Revised portions are marked in red in the paper. Figures have been adjusted as required.

5. I found no “Author contribution” section. Please provide the author contributions

In fact, we put Author contribution in the Footnotes section , but now we have added it in the title page.

6. I found the authors did not provide the approved grant application form

We have upload the funding agency copy of any approval document(s).

7. I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor

We have prepare and arrange the figures using PowerPoint.

8. I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text.

We have added the “article highlights” section at the end of the main text.

References:

- 1 Bilimoria KY, Palis B, Stewart AK, Bentrem DJ, Freel AC, Sigurdson ER, Talamonti MS, Ko CY. Impact of Tumor Location on Nodal Evaluation for Colon Cancer. DIS COLON RECTUM 2008; 51(2): 154-161.
- 2 Sarli L, Bader G, Iusco D, Salvemini C, Mauro DD, Mazzeo A, Regina G, Roncoroni L. Number of lymph nodes examined and prognosis of TNM stage II colorectal cancer. EUR J CANCER 2005 2005-01-01; 41(2): 272-279.
- 3 Tamas K, Walenkamp AM, de Vries EG, van Vugt MA, Beets-Tan RG, van Etten B, de Groot DJ, Hospers GA. Rectal and colon cancer: Not just a different anatomic site. CANCER TREAT REV 2015 2015-09-01; 41(8): 671-679.
- 4 Cai D, Huang ZH, Yu HC, Wang XL, Bai LL, Tang GN, Peng SY, Li YJ, Huang MJ, Cao GW, Wang JP, Luo YX. Prognostic value of preoperative carcinoembryonic antigen/tumor size in rectal cancer. World J Gastroenterol 2019 2019-09-07; 25(33): 4945-4958.
- 5 Chen S, Liu Y, Yang J, Liu Q, You H, Dong Y, Lyu J. Development and Validation of a Nomogram for Predicting Survival in Male Patients With Breast Cancer. FRONT ONCOL 2019 2019-01-20; 9: 361.