

## ANSWERING REVIEWERS

October 2, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11147-edited.doc).

**Title:** The ratio of metastatic lymph nodes is more important for rectal cancer patients treated with preoperative chemoradiotherapy

**Author:** In Ja Park, Chagn Sik Yu, Seok-Byung Lim, Yong Sik Yoon, Chang Wook Kim, Tae Won Kim, Jong Hoon Kim and Jin Cheon Kim

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 13144

The manuscript has been improved according to the suggestions of reviewers:

### **1 Format has been updated**

### **2 Revision has been made according to the suggestions of the reviewers comment**

*Reviewer 70191;* In this study the prognostic impact of the LNR in rectal cancer patients with metastatic lymph nodes after radical resection was evaluated. It is found that the lymph node ratio (LNR) is an important prognostic predictor of RFS in rectal cancer patients especially treated with PCRT. 1. The errors in alignment of tables should be corrected. 2. Language needs minor revision

**(Answer)** Thank you for your nice comment.

1. We corrected alignment of tables.

2. We check manuscript by English editor.

*Reviewer 182276;* This article is very important because it underlines the impact of neoadjuvant radiochemotherapy of rectal cancer and moreover can predict recurrence free survival . It would be useful to check these patients data according to tumor regression grade as well.

**(Answer) 2.** Thank you for comment. As you pointed out tumor regression grade was very important point in patients treated with PCRT. In this manuscript, however, we tried to show the importance and efficacy of LNR comparing PCRT and No-PCRT patients. Therefore, it is hard to use tumor regression grade as an additional analysis. We checked tumor regression grade in PCRT patients and add in Result section.

**Reviewer 503612;** appreciate the opportunity to review your manuscript looking at LNR following neoadjuvant chemoXRT for rectal cancer. A few comments/questions 1. You should consider adding some more specific raw data of outcomes to the abstract to give the reader an idea of the major points that you found. 2. The bottom line is this is a fine paper, but I disagree with the major premise that it "is unclear whether the impact of the LNR on prognosis differs between rectal cancer patients treated with PCRT and those treated with upfront surgical resection". This study has been several times before looking at LNR in the preoperative group with TME for rectal cancer. Please clarify what you mean by unclear, or novel in this series other than it is your series.

**(Answer)** Thank you for reviewers comment.

1. We didn't understand what you mean by "more specific raw data of outcomes". But, we checked data to find more information.

2. The prognostic value of the LNR has also been demonstrated in colon and rectal cancer for several times [Rosenberg R, Friederichs J, Schuster T, Gertler R, Maak M, Becker K, Grebner A, Ulm K, Hofler H, Nekarda H, Siewert JR. Prognosis of patients with colorectal cancer is associated with lymph node ratio: a single-center analysis of 3,026 patients over a 25-year time period. *Ann Surg* 2008; **248**: 968-978, Kim YS, Kim JH, Yoon SM, Choi EK, Ahn SD, Lee SW, Kim JC, Yu CS, Kim HC, Kim TW, Chang HM. lymph node ratio as a prognostic factor in patients with stage III rectal cancer treated with total mesorectal excision followed by chemoradiotherapy. *Int J Radiat Oncol Biol Phys* 2009; **74**: 796-802, Peschaud F, Benoist S, Julie C, Beauchet A, Penna C, Rougier P, Nordlinger B. The ratio of metastatic to examined lymph nodes is a powerful independent prognostic factor in rectal cancer. *Ann Surg* 2008; **248**: 1067-1073]. These previous studies have shown that the LNR can be used not only as a prognostic indicator, but also as a parameter for a more accurate stratification system than the metastatic LN absolute number-based staging system in colon and rectal cancer. Also, LNR might have usefulness for prognostication in patients who receive preoperative chemoradiotherapy (PCRT). Because number of harvested lymph nodes might be decrease after PCRT. Consequently, the number of LNs examined could be below the recommended number in patients with rectal cancer. Therefore, for patients with rectal cancer treated with PCRT, a complementary LN metastasis stratification

method may be needed than for those treated with upfront surgery. Hypothetically, LNR could be useful in PCRT setting than upfront surgery setting. However, there have been few studies comparing role of LNR for prognostication between PCRT and No-PCRT patients directly. We mean this situation by “it is unclear whether the impact of the LNR on prognosis differs between rectal cancer patients treated with PCRT and those treated with upfront surgical resection”. And it is main hypothesis of this study.

### **3. References and typesetting were corrected**

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Chang Sik Yu

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