
ANSWERING REVIEWERS

29th of January 2013

Dear Editor,

On behalf of my co-authors, we would like to thank the reviewer for her/his insightful and constructive comments on our manuscript. We have modified the manuscript substantially in this revised version to address the reviewers' comments. Revisions are marked with tracked changes. We have also included a point-by-point response to the reviewer. We hope you find the revised manuscript acceptable for publication in the World Journal of Gastrointestinal Oncology.

Title: Long-term outcomes and prognostic factors for patients with esophageal cancer following radiotherapy

Author: Chuangzhen Chen

Manuscript No: ESPS-389

Point-to-point responses.

1. It is difficult to understand how many patients received what kind of treatment. Please prepare a patient flow chart to clearly illustrate the allocation of treatment.

We have added a patient flow chart in the section of materials and methods as suggested.

Change: 15th line of 2nd paragraph of method section.

2. Gender, median age, and the number of patients according to primary tumor location should be described in the Results section.

According to the reviewer's comment, we have shifted these data from methods section to results section, including gender, median age, and tumor location.

Change: 1st Line of 1st paragraph of result section.

3. In addition to point 2 above, the number of patients according to TNM clinical stage should also be included in the Results section to facilitate understanding of the disease stage of the study group.

We could not provide the accurate data of T stage in this study, since most patients were evaluated with enhanced CT, instead of endoscopic ultrasound. It is difficult to differentiate T₃ from T₂, or T₂ from T₁. However, we can identify T₄ stage, N stage and M stage based on comprehensive assessments. In this study, the majority of patients were with locoregionally advanced stage (57.5% of patients had invasion to adjacent structures and 64.1% of patients were found with positive

regional lymph nodes metastases). We have included these data in the result sections.

Change: 6th line of 1st paragraph of result section.

4. The definition of N+ in Table 2 was not based on RECIST version 1.1. What is the reason for this?

Compared with RECIST 1.1, peri-esophageal lymph node with longest diameter of ≥ 5 mm was also defined as positive lymph node in this study. There are two main reasons. Firstly, the risk of cancer metastasis from esophagus to the peri-esophageal region through lymphatic vessels is extremely high. Therefore, lymph nodes at this region should be considered as positive generally, even though the diameter might not be greater than 10mm. More importantly, histomorphologic studies had showed that the average size of metastatic nodes was less 10 mm, and only a small portion of metastatic nodes were >10 mm in diameter^[1]. When the criterion of 5 mm was used, the sensitivity, specificity, and accuracy for CT to detect lymph node metastases were 68, 92, and 87%, respectively^[2]. Any nodule arising at the peri-esophageal region should be regarded as positive lymph node^[3]. In this study, these small peri-esophageal lymph nodes were treated with radical radiation dose according to the institutional guidelines.

1. Schröder W, Baldus SE, Mönig SP, Beckurts TK, Dienes HP, Höltscher AH. Lymph node staging of esophageal squamous cell carcinoma in patients with and without neoadjuvant radiochemotherapy: histomorphologic analysis. *World J Surg.* 2002 May;26(5):584-7.

2. Mizowaki T, Nishimura Y, Shimada Y, Nakano Y, Imamura M, Konishi J, Hiraoka M. Optimal size criteria of malignant lymph nodes in the treatment planning of radiotherapy for esophageal cancer: evaluation by computed tomography and magnetic resonance imaging. *Int J Radiat Oncol Biol Phys.* 1996 Dec 1; 36(5):1091-8.

3. Gu YJ, Wang JH, Xiang JQ, Ma LF. A study on clinical value of CT features of tracheoesophageal groove lymph node metastasis of thoracic esophageal carcinoma. *Chinese Journal of Radiology.* 2002, 36(2): 139-141.

5. The abbreviation “LCAH” in Table 2 should be defined. All abbreviations and acronyms in the text and tables should be defined at the point of first mention.

We apologize for our negligence and have added the definition of “LCAH” in table 2.

6. The authors should discuss the degree of concordance between Y diameter, a new prognostic factor found in this study, and T category of the TNM classification.

We acknowledge that it is meaningful to discuss the degree of concordance between Y diameter and T category of TNM classification. However, it could not be done in this study due to the limited power of CT in T staging.

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

Sincerely yours,

Chuangzhen Chen