Peer Review File

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Reviewer Comments

This work contains a large number of cases treated and those from SEER database. It is informative.
Some issues should be addressed:
1. The therapeutic protocol should be disclosed in detail: chemotherapy regimens and treatment duration ... etc., as well as the radiation dose.

Reply 1：We thank the reviewer for the suggestion to add more details of therapeutic protocol, which we have modified our text as advised (see page 9, line 183-186, Table 1) in revised manuscript.

Changes in the text: All patients received long-course NCRT with a total dose of ~40-50 Gy (median 50 Gy) administered in 20 to 28 fractions during a five-week period, concurrently with capecitabine (825 mg/m^2, bis in die) with or without oxaliplatin (infusion 50 mg/m^2, weekly).

2. Pathological features such as differentiation, intra-vascular and perineurial invasion should be listed and analyzed for their clinical significance.

Reply 2：We add some data (see table 1) and the results section of 3.1 has been modified (see page 11, line 228-232).

Changes in the text: After NCRT, the majority of the patients were found to have moderately differentiated tumors: 62 patients (13.9%) had perineurial invasion, and 20 patients (4.5%) had intra-vascular invasion. The prognosis was worse for the patients who exhibited perineurial invasion or vascular invasion.

3. The status of positive nodes should be differentiated based on the size of metastatic deposits.

Reply 3: We would like to express our heartfelt thanks to referee for his thorough reading of our manuscript and for his very useful suggestions. First of all, we have modified our text as advised and added a detailed description of the pathological assessment (see page 10, line 192-199). Tumor regression grade (TRG) after neoadjuvant therapy, determined based on the degree of fibrosis in proportion to the number of residual cancer cells, reflects therapeutic response. Similarly, after neoadjuvant therapy, metastatic lymph nodes also had a therapeutic response (lymph node regression, LRG). LRG of lymph node was categorized by a change in the presence of tumor cells to the evidence of regression determined by the presence of fibrosis or mucous lakes with the same protocol as the primary tumor (Tetsuro Tominaga et al. Surgery. 2019 Dec;166(6):1061-1067; Haizeng Zhang et al. Cancer Medicine. 2020 Dec;9(24):9373-9384). Therefore, we consider lymph nodes to be positive as long as there are residual tumor cells in them.

Changes in the text: Standard hematoxylin-eosin and saffron staining of each paraffin block was performed for histologic examination. All slices were re-evaluated by two professional gastrointestinal pathologists. We reevaluated the depth of tumor invasion (ypT), the total number of lymph nodes harvested, the number of metastatic lymph nodes (If there is residual live tumor cells, even rare residual tumor cell in the lymph node), perineural invasion, vascular invasion, circumferential resection margin (CRM), and tumor regression grade (TRG). The TRG was evaluated according to the TRG system proposed by Mandard et al.