



Dec 10, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format.

**Title:** Clinical Significance of Lymph Node Metastasis from Gastric Cancer

**Author:** Deng J and Liang H

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

**ESPS Manuscript NO:** 6573

**Reviewer 01558238:**

**Q1)** The most recent western publications agreed with D2 dissection. Therefore, the author should describe more about the concept of D2 dissection than present version.

**Answer:** We have added the more contents to describe the concept of the extended lymph node dissection as follows: "Primary tumors were resected en bloc with limited or extended lymphadenectomy (D1 or D2-3 according to the Japanese Gastric Cancer Association (JGCA) 19). Limited lymphadenectomy (D1) entails the removal of the perigastric nodes only, whereas extended lymphadenectomy (D2 or D3) involves the removal of both perigastric and extragastric nodes".

**Q2)** Although both UICC staging system and the most recent Japanese classification system are using the number of positive nodes as a key staging factor, clinical significance of extent of positive node should be described more precisely.

**Answer:** We added the contents to describe the clinical significance of extent of positive node more precisely as follows: "The first category of metastatic lymph nodes originated from Japan in 1980s, which defined the status of lymph node metastasis by the location of positive lymph nodes relative to the primary tumor according to the JCGC. Once extragastric lymph node metastasis is identified, the probability of systemic dissemination of cancer cells significantly increases in theory. In our latest study, we demonstrated that extragastric lymph node was an important factor associated with the dismal prognosis of patients, even undergoing the extended lymphadenectomy".

**Q3)** On page 6, the author cited their own previous publication on "VEGF-D expression". Such topics were not matched to present form of review. Other review on "molecular staging" or "molecular diagnosis" could be fine, if the author preferred to cite such topics.

**Answer:** We agree with your suggestion and delete these sentence about the "VEGF-D expression" on the page 6.

**Q4)** I agreed with that "negative node" and "minimum number of dissected node" were also important issue for discussion. However, recent topics, such as "micro-metastases" and/or "sentinel node navigation" should be noted as an important topic.

**Answer:** We agree with your opinion. Actually, we have described the micro-metastasis in lymph node on the page 12 and 13. Besides, we added the contents of sentinel node navigation research on the page 13 as follows: "Recently, the sentinel node navigation was demonstrated to be an important factor for influence the diagnosis and

treatment of lymph node metastasis from gastric cancer, especially to the early stage patients [106]. Clinical application of the sentinel node navigation in the gastric cancer is still restricted in the early gastric cancer patients, owing to the complexities of the lymphatic drainage pathways of the stomach. The results of two noted random control trails (JCOG0302 and SNNS) of the sentinel node navigation in Japan failed to demonstrate that the detection of sentinel lymph node could exactly predict the status of lymph node metastasis in operation, which implied the lymphadenectomy should be irreplaceable for the elimination of nodal metastasis”.

**Q5)** “CONCLUSION” part seems not to be a most recent fashion on this topics.

**Answer:** We think the “conclusion” is only brief of summary of this paper.

**Reviewer 00504418**

**Q1)** Could you inform how to decide the diagnosis of positive or negative lymph node in frozen specimen?

**Answer:** We think it need to rely on routine biopsy under a microscope detection.

**Q2)** How many cut sections does pathologists make to diagnosis?

**Answer:** No less than 4-5 sections.

**Q3)** Micrometastasis depends on the number of cut sections. Is the number of cut section common all over the world?

**Answer:** The diagnosis of micrometastasis of lymph node needs the immunohistochemical examination. The number of cut sections is no less than 4-5 sections. There is not a consensus of the number of cut sections in the world.

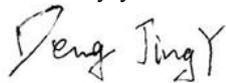
**Reviewer 02570440:**

**Q1)** Language polish needed.

**Answer:** We have edited the language by the special editing corporation.

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

Sincerely yours,



Department of Gastric Oncology Division,  
Tianjin Medical University Cancer Hospital and City Key Laboratory of Tianjin Cancer  
Center, National Clinical Center of Cancer, Tianjin 300060, China

Fax: +86-22-23359904

E-mail: dengery@126.com