

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5687-review.doc).

**Title:** Analysis of prognostic outcomes of gastric cancer in younger patients: A case control study using propensity score methods

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

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

1 Format has been updated and the Language has been edited by BioMed Proofreading, LLC Company.

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer 00183059

1) In the conclusion section of abstract, author mentioned that extensive lymph node dissection improved the prognosis and patient survival. It is hard to say from this study.

: Thanks for your opinion. So we delete a sentence of extensive LN dissection in the conclusion

2) In this study, case samples were selected using propensity score. It would be better to refer the previous article about propensity score. In addition, if the author shows clinicopathological feature of the patients in unmatched group (unmatched group, 112 vs 1555), it would be more persuasive.

Thanks for your opinion. Initially, we analyzed the clinicopathological features of patients in unmatched group (unmatched group, 112 vs 1555). But there were many reports which analyzed the data by large scale. Our purpose for this study was on the comparison between the younger and older group in the case matched state. That's why we haven't described the comparison in the large scale in this study.

3) If the author would like to reduce bias in this study, the background of lymph node dissection has to be same. And the author might see more clear difference in prognosis between younger and elder patient's group.

As you can see, this study aimed at the prognostic differences between the younger and older age groups. And the study was carried out with parameters of the age and operation types (subtotal and total) in both groups. We intended to see as in other reports that the younger age group had a poorer prognosis by the analysis of these two parameters. If we had added other parameters such as disease stage and lymph node dissection for the study, we suggest it wouldn't have shown the aggressive patterns of younger age group. This study tried to elucidate, nevertheless, that if the surgery guarantees the curative resection, the prognosis of the younger age group would be as good as that of the older group.

(2) Reviewer 00503549

- 1) Despite their conclusion, difference in two survival curves, those for younger and older groups, appears relatively large both in overall cases and in the cases with advanced gastric cancer. The risk of death at 5 years after surgery was about 50% higher in younger patients than in older patients overall, and the risk was about 42% higher in younger patients than in older patients in the cases at advanced stages. This reviewer is reluctant to conclude that this kind of large difference could be of no difference.

Dear reviewer, we are sorry that we cannot fully understand your opinion.

- 2) The authors did not show the data of adjuvant chemotherapy.

We do not carry out chemotherapy for stage I gastric cancer. We carried out chemotherapy for the patients in Stage IIA or more by Chemotherapy. Generally, in Korea, recommendations of adjuvant chemotherapy are for the patients above Stage II. (Korean Clinical Practice Guideline for Gastric Cancer, 2012, Korean Academy of Medical Sciences)

We added this comment in the section of patients and methods and in table.

- 3) In Abstract, line 12-13, "advanced stage gastric cancer ( $p = 0.045$ )" should be "advanced T stage gastric cancer ( $p = 0.045$ ).

We corrected

(3) Reviewer 00182538

- 1) As the authors mentioned, the diffuse type is usually more prevalent in the younger group which usually occupy the two thirds of the stomach or the whole stomach. In Table 1, the gastric cancers in the young patients located at the one third of the stomach except 2 cases (2%) which did not show any significant difference from the elder patient group. The authors should show their speculations about this concern in the Discussion.

; Thanks for your reply. Generally, diffuse type may involve 2/3 of the stomach or sometimes whole stomach. Lauren classification shows that intestinal type usually occurs at the distal stomach, while diffuse type may also occur in high frequency at middle or upper stomach as well as distal area. However, there have been no data reported that most of diffuse type involve 2/3 or whole stomach. In our data, we had 72 cases of diffuse type in the younger group and 34 cases in the older group. But there were only 2 cases which involved the whole stomach from both groups. For your reference, we attach 2 theses below for this topic.

1. Quiñones J, Portanova M, Yabar A. Relationship between histologic type and location of gastric adenocarcinoma in the Rebagliati Hospital. Rev Gastroenterol Peru. 2011;31(2):139-45. [PMID: 21836654]
  2. Adachi Y, Yasuda K, Inomata M, Sato K, Shiraishi N, Kitano S. Pathology and prognosis of gastric carcinoma: well versus poorly differentiated type. Cancer. 2000;89(7):1418-24. [PMID: 11013353]
- 2) Table 2 showed that 69 younger patients (70%) underwent over D2 lymphadenectomy. D2 lymphadenectomy is supposed to be sufficient for the regional cancer control. What lymph node stations were removed for over D2 in this study? Couldn't it be too invasive for them? Did the authors have any evidence in which over D2 lymphadenectomy improved the prognosis for the gastric cancer patients? The authors should discuss about this concern.

; We performed D2 lymph node dissection according to 7<sup>th</sup> edition guideline in our institute. As for the nodes of 14v, 14a, 13, 16, we believe it is a general rule in Korean that when they are found in preoperative CT or grossly found in operative

fields, they are to be dissected.

- 3) The authors should show the proportion of the patients who underwent adjuvant chemotherapy in the two groups in the Results. Although the authors concluded that carefully curative resection with extensive lymph node dissection improved the prognosis and patient survival, I believe the adjuvant chemotherapy is more likely to extend their survival. Again, do the authors have any evidence in which extensive lymphadenectomy improved the prognosis for the gastric cancer patients?

; We also see that extensive lymph node dissection would make no significant difference in prognosis. We will remove the comments on the extensive lymph node dissection. We also added the comments on the prognostic change with chemotherapy in the text and the table as the reviewer had mentioned.

- 4) The authors should use age-adjusted survival curves and analysis in Figure 1, because the younger patients without recurrence have a longer survival than those in the elder patients group.

; There were some errors with p-values of survival curve. We corrected the p-value in Figure 1. We added age-adjusted survival curve in Figure and described in patients and methods and in results (Figure 2).

(4) Reviewer 00183459

This is an interesting study aimed at analyzing the prognostic outcomes of gastric cancer in younger patients compared to older subjects using propensity score methods. The manuscript is well written and the results are interesting.

: Thanks for your reply.

3 References and typesetting were corrected

4 Figure was updated

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

Sincerely yours,

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