

ANSWERING REVIEWERS



July 8, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11085- review.doc).

Title: Lymph node micrometastasis on prognosis of gastric carcinoma: A meta-analysis

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11085

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 reviewer

(1) The words "cohort trials" or "trials" alone are used throughout the manuscript to indicate "cohort studies". The reader can be misled, as these words usually stand for "randomized clinical trials". We are so sorry about this.

Response: Thank you for your meaningful concerns. We had used "cohort studies" instead of "cohort trials".

(2) "OS was defined as the time from randomization to death from any cause". Is there randomization in any of the studies examined ?

Response: We fully agree with you. There is no randomization in cohort studies and we made the correction. We used numbers of patient died in five years to evaluate the survival condition of patients instead of OS.

(3) You used cut-offs of $p \leq 0.1$ and $I^2 \geq 50\%$ to adopt random model. In my experience a random model is usually adopted when $p < 0.05$ and $I^2 > 30\%$. You should also mention that p value refers to "a test of heterogeneity".

Response: We fully agree with you and we made correction in the paragraph of Statistical Analysis accordingly. Hopefully, this addresses your concern.

(4) The Odds ratio is suited for case-control, while in cohort studies the Relative risk must be used.

Response: Thank you for your meaningful concerns. We had used Relative risk in cohort studies instead of Odds ratio accordingly. We hope this addresses your concern.

(5) Funnel plots are used to detect small study effects, such as publication bias or small series effect. In small studies, an inexperienced pathologist could have failed to identify micrometastases. In addition, a

test of significance (such as Egger's test) should be used. Also the INTERPRETATION of the results is not satisfactory. Geographic area (Asia vs. Europe/Australia) modifies the association between lymph node micrometastasis and prognosis. This effect modification is quite important and should be clearly presented in the Abstract and thoroughly discussed in the Discussion section. For instance, can it be attributed to the higher number of retrieved nodes in Eastern Asia (average 22-41.9) with respect to the Italian, German and Australian studies (average 18-23.7)? Does the remarkable difference in survival between the East and the West play a role ?

Response: Thank you for your concerns. We had used Egger's test and there is a relatively small publication bias ($P=0.184$). It's relatively harder to have a satisfied number of retrieved lymph nodes in patients in the West than in patients in the East for the reason likes patients in the West have larger BMI generally. We found that there were higher number of retrieved lymph nodes in studies of Eastern Asia (average 22-41.9) than studies of Italian, German and Australian (average 18-23.7). Considering the situation that average number of retrieved lymph nodes were more than 15 but several number of retrieved lymph nodes were fewer than 15 in individual patients could exist in these studies and the fewer the number of retrieved lymph nodes was, the more possible an inexperienced pathologist could have failed to identify micrometastases in these small studies we referred, so a higher number of retrieved lymph nodes studies' results could be more reliable relatively. What's more, only three cohort trails were referred in Europe and Australia group, there could be publication bias. For the total numbers of patients of the available evidence from three cohort trails in Europe and Australia group is 528, and there were no randomization in cohort studies, all mentioned above could effect on the difference of numbers of patients died in 5 years for Asia vs. Europe/Australia. We had rewritten the Discussion section about this. Hopefully, this may address your concern.

(6) The ENGLISH is POOR. See for instance: Abstract, Methods: "We searched electronic databases included including ..." Abstract, Results: "Lymph node micrometastases in patients with gastric carcinoma significant have significantly higher recurrence rate Abstract, Conclusion: "in the clinical setting" Introduction, 1st line "during the past 10 years of data" Introduction, 2nd page, 5th line and Discussion, 4th page, last line: "in size which is often common" Materials and Methods, 2nd page, last line: "and exclusion criteria was were designed". Results, page 4: "no statistically significant difference in" is repeated twice.

Response: We fully agree with you and we made correction in the paragraph mentioned accordingly. And according to the Revision Policies of BPG for Article, we had asked professional English language editing company for editing our English language. We are so sorry about that.

3 References and typesetting were corrected

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

Sincerely yours



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