

ANSWERING REVIEWERS

Dear Editor,

Thank you for your constructive review and comments. By addressing these concerns, we believe that the manuscript is significantly strengthened and is now acceptable for publication. All changes have been highlighted in yellow in the revised manuscript.

Please find enclosed the edited manuscript in Word format (file name: 15774- revised.doc).

Title: Diagnostic performance of magnifying narrow-band imaging for early gastric cancer: a meta-analysis

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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

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

Reviewed by 02440526

(1) Comment 1: The main limit of the paper is the absence of an appropriate reference to the cost of the method also comparing it with the cost of histopathology (Takeuchi Y1, Hanafusa M, Kanzaki H, Ohta T, Hanaoka N. Proposal of a new 'resect and discard' strategy using magnifying narrow band imaging: pilot study of diagnostic accuracy. *Dig Endosc.* 2014 Apr;26 Suppl 2:90-7. doi: 10.1111/den.12248.) Therefore, at least a paragraph about it should be included.

Response: We are grateful for your valuable advice. This referred to the comparison of cost-effectiveness between ME-NBI and histopathology. There were several reasons for not comparing their cost-effectiveness. First, although ME-NBI has been applied in the diagnosis of EGC, it's difficult to reveal the pathological type of EGC compared with colorectal neoplasm. Second, as the enrolled studies were from different regions, the costs of ME-NBI or histopathology would be considerably different. At last, the absence of the comparison of cost-effectiveness between them were indeed the main limit of our paper, so we included this related content in Discussion section as follows: Second, the cost-effectiveness of ME-NBI was not reported, as well as the comparison with that of histopathology. Recently, Y. Takeuchi et al^[34] proposed that "a new resect and discard strategy" with ME-NBI in colorectal cancer screening might reduce the costs of histopathology. (Page 16)

Reviewed by 01588319

(2) Comment 2: In "Abstract" section, the diagnostic odds ratio for ME-NBI diagnosis of EGC is 102.75 (95% CI, 48.14-219.32), what it means? Please explain it in clinical application.

Response: Thanks for your comments. The diagnostic odds ratio [DOR = (TP/FN)/(FP/TN), TP/FP/TN/FN mean numbers of true-positive, false-positive, true-negative and false-negative cases] of a test is the ratio of the odds of positivity in the disease group relative to the odds of positivity in the control group. The value of a DOR ranges from 0 to infinity, with higher values indicating better discriminatory test performance (Reference: A.S. Glas et al / *Journal of Clinical Epidemiology* 56 (2003) 1129–1135). A value of 1 means that a test does not discriminate between patients with the disorder and those without it. In our study, the

diagnostic odds ratio for ME-NBI diagnosis of EGC was 102.75, meaning that the odds for positivity of ME-NBI among EGC lesions was 102.75 times higher than the odds for positivity among non-cancerous lesions, which indicated a high discriminatory performance of ME-NBI.

- (3) Comment 3: The definition of "EGC" is not clear, please clarify it!

Response: EGC is defined as gastric cancer which is limited to the mucosa or submucosa layer, regardless of lymphatic metastasis (Reference: Gann Monogr Cancer Res1971;11:53–5). The enrolled studies used "The revised Vienna classification Categories 4 and 5" and "The Vienna classification Categories 4 and 5", which were applied as pathological reference standard to define EGC, including high grade intraepithelial neoplasia and infiltration into the mucosa or submucosa.

- (4) Comment 4: In the "Materials and Methods" section, the authors mentioned about TP/FP/TN/FN, however, we only see the statement "In addition, the positive predictive value (PPV) and negative predictive value (NPV) of ME-NBI were 85.0% and 96.3%." in the "Diagnostic performance of ME-NBI" of the "Results" section. Please explain it.

Response: We are grateful for your cautious review. TP/FP/TN/FN could be applied to calculate $PPV(TP/(TP+FP))$ and $NPV(TN/(TN+FN))$, which was not mentioned in the "Materials and Methods" section. The positive predictive value (PPV) of ME-NBI was 85.0%, meaning that there were 85 percents of positive results of ME-NBI to be correctly diagnosed as EGC. The negative predictive value (NPV) of ME-NBI was 96.3%, meaning there were 96.3 percents of negative results of ME-NBI to be accurately diagnosed as non-cancer. In the "Materials and Methods" section, we didn't refer to PPV or NPV, because they were not what we focused on and other methods were used to evaluate the accuracy of ME-NBI in EGC diagnosis. If you agree, we'd like to remove these contents to make our manuscript more organized.

- (5) Comment 5: This manuscript will be more valuable if the resolution of all the figures can be improved.

Response: We have improved the resolution of all figures.

Reviewed by 00044980

- (6) Comment 6: Authors mention that diagnostic sensitivity of ME-NBI in depressed lesions is lower than that in not depressed ones. However, most depressed lesions were less than 10 mm in this study. Authors should mention this point in the Discussion section.

Response: Thanks for valuable reminding. The diagnostic performance of ME-NBI for depressed type EGC was one of our concentrations, so we included this essential point in the Discussion section as follows: "Noteworthy, the size of most depressed lesions was less than 10 mm in enrolled studies, thus the diagnostic performance for depressed type lesions is representative of these lesions with diameter less than 10 mm. As for the depressed type lesions with diameter more than 10 mm, we failed to find relevant studies, and further researches might be required in the future." (Page 13)

- (7) Comment 7: Please correct 'simple size' to 'sample size'.

Response: We apologize for the spelling mistakes. We have carefully checked the manuscript and correct "simple size" to "sample size".

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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