

Point-by-point revision

Manuscript number: World Journal of Clinical Cases, No.55672

Manuscript title: Clinical applicability of gastroscopy with narrow-band imaging for the diagnosis of *Helicobacter pylori* gastritis, precancerous gastric lesion, and neoplasia

Dear Editor:

Thank you for your meticulous review of our manuscript and valuable comments. We answered the reviewer`s comments. The enclosed is the point-by-point reply to the comments. In the revised manuscript, the changes were highlighted by using red-colored text.

Sincerely yours,

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Reviewer #1

1. Overall a good review, however some clarifications needed: In Table 2, "VS" is not clarified in the legend.

Answer: As you mentioned, we made “vessel plus surface” as a footnote of “VS” in Table 2.

2. Use of the term "small" gastric cancer is ambiguous: should this be termed "early" gastric cancer instead?

Answer: Thank you for your important comment. Usually, small gastric cancer is defined as early gastric cancer less than 10 mm. Most studies enrolled the small lesion for magnifying NBI endoscopic diagnosis of early gastric cancer. We described the “(≤ 10 mm)” beside the word “small” in the section of early gastric cancer.

3. The sentence "The sensitivity and specificity of magnifying endoscopy for H. pylori infection are 93.8% to 100% and 82.2% to 96.2%, respectively" needs a citation.

Answer: As you commented, we made reference numbers of the sentence as below.

The sensitivities and specificities of magnifying endoscopy for H. pylori infection are 93.8% to 100% and 82.2% to 96.2%, respectively^[13-15].

4. In the abstract it is stated "Rather than pathologic examination by mucosal biopsy, it may be ideal to individually evaluate the extent and severity of GIM by advanced endoscopic imaging". However, it needs to be made more obvious what the detrimental aspects of mucosal biopsy are, to justify engaging endoscopists in such complex endoscopic diagnostic training with M-NBI, with such a difficult learning curve. Similarly, in the introduction, it is stated "Although pathologic diagnosis is the gold standard, accurate endoscopic prediction is important to minimize the number of biopsies and prevent post-biopsy bleeding". What is the evidence that post-biopsy bleeding is a significant enough worldwide problem to justify moving away from biopsy? Or are there other reasons that the authors should include in the introduction to justify moving away from biopsy?

Answer: Thank you for your careful comment. We deleted the sentence of "Rather than pathologic examination by mucosal biopsy, it may be ideal to individually evaluate the extent and severity of GIM by advanced endoscopic imaging" in the abstract. However, endoscopic biopsy may not be representative of the entire lesion due to its superficiality and sampling errors. In a study by Lee et al, up to 64.5% of gastric lesions with indefinite pathology were upgraded to dysplasia and cancer after endoscopic submucosal dissection^[1]. Repeated biopsy can make the subsequent endoscopic treatment to be difficult due to submucosal fibrosis^[2]. Meanwhile, antiplatelets or direct oral anticoagulants (DOAC) are widely prescribed for elderly patients with cardiovascular and thromboembolic risks. Although diagnostic endoscopy including mucosal biopsy sampling is low risk procedure, there is no sufficient data about post-biopsy bleeding in patients taking the DOACs. These are the reasons why we should use an advanced endoscopic imaging for diagnosis of gastric lesions in clinical practice. In a study by Dias-Silva et al, a web-based video system was useful for learning NBI endoscopic classification precancerous gastric lesions^[3].

- [1] Lee H, Kim H, Shin SK, et al. The diagnostic role of endoscopic submucosal dissection for gastric lesions with indefinite pathology. Scand J Gastroenterol. 2012; 47: 1101-1107.
- [2] Kim CG. Tissue acquisition in gastric epithelial tumor prior to endoscopic resection. Clin Endosc. 2013; 46: 436-440.
- [3] Dias-Silva D, Pimentel-Nunes P, Magalhaes J, et al. The learning curve for narrow-band imaging in the diagnosis of precancerous gastric lesions by using Web-based video. Gastrointest Endosc. 2014; 79: 910-920.

5. The most salient improvement needed in this article is more clarity about the number of pathological conditions are going to be discussed. The title states "precancerous gastric lesion and neoplasia". However this does not encompass the manuscript's discussion of H pylori infection, which is not itself a precancerous gastric lesion. The abstract also mentions atrophic gastritis, intestinal metaplasia but does not mention dysplasia.

Answer: Thank you for your valuable comment. We changed the manuscript's title for adding *H. pylori* infection. In the abstract, the sentences about atrophic gastritis and gastric dysplasia were written. Please check the revised manuscript.

In this manuscript, gastric neoplasia mean gastric dysplasia and cancer. According to the revised Vienne classification, low and high grade dysplasia (category 3 and 4.1) is considered as gastric epithelial neoplasia (Dixon MF, *Gut* 2002; 51: 130-1). In WHO classification of gastric tumors, adenoma/dysplasia is categorized into non-invasive neoplasia (WHO Classification of Tumours. Lyon: IARC Press; 2000). We think that precancerous lesions are known to be atrophic gastritis and intestinal metaplasia.

Table 1 The revised Vienna classification of gastrointestinal epithelial neoplasia

Category	Diagnosis	Clinical management
1	Negative for neoplasia	Optional follow up
2	Indefinite for neoplasia	Follow up
3	Mucosal low grade neoplasia Low grade adenoma Low grade dysplasia	Endoscopic resection or follow up*
4	Mucosal high grade neoplasia 4.1 High grade adenoma/dysplasia 4.2 Non-invasive carcinoma (carcinoma in situ) 4.3 Suspicious for invasive carcinoma 4.4 Intramucosal carcinoma	Endoscopic or surgical local resection*
5	Submucosal invasion by carcinoma	Surgical resection*

*Choice of treatment will depend on the overall size of the lesion; the depth of invasion as assessed endoscopically, radiologically, or ultrasonographically; and on general factors such as the patient's age and comorbid conditions. For gastric, oesophageal, and non-polypoid colorectal well and moderately differentiated carcinomas showing only minimal submucosal invasion (sm1) without lymphatic involvement, local resection is sufficient. Likewise, for polypoid colorectal carcinomas with deeper submucosal invasion in the stalk/base but without lymphatic or blood vessel invasion, complete local resection is considered adequate treatment.

6. The introduction states "(1) detection of H. pylori gastritis, (2) endoscopic finding of GIM, (3) magnifying NBI endoscopy for diagnosis of small gastric cancer, and (4) determination of the horizontal extent of EGC" but does not mention atrophic gastritis (which can be a separate entity to H pylori infection) or dysplasia. The main text, at various points, mentions 5 key conditions: 1) H pylori infection, 2) atrophic gastritis, 3) intestinal metaplasia, 4) gastric dysplasia and 5) early gastric cancer/neoplasia. I think the title should therefore include H pylori gastritis. I think the abstract and introduction should clearly list these 5 key conditions that are going to be discussed separately. I think the main text should be separated in 5 sections that discuss each of these key conditions in that order (I do not see a need for separate section about the diagnosis of EGC/neoplasia and estimating the horizontal margins of EGC/neoplasia: this can be part of the same section).

Answer: Thank you for your valuable comment. We changed the titles of sections as below.

INTRODUCTION

PRINCIPLE OF NARROW-BAND IMAGING WITH MAGNIFICATION

HELICOBACTER PYLORI GASTRITIS

ATROPHIC GASTRITIS

GASTRIC INTESTINAL METAPLASIA

GASTRIC DYSPLASIA

EARLY GASTRIC CANCER

- Differential diagnosis between focal gastritis and small depressed cancer

- Determination of the horizontal extent of early gastric cancer before endoscopic submucosal dissection

7. Similarly it is unclear why Figure 5 is cited at the end of a paragraph regarding early gastric cancer, as Figure 5 is discussing gastric dysplasia, not neoplasia. Similarly, it is unclear where Figure 6 regards neoplasia or dysplasia. It is labelled "NBI endoscopy for determining the horizontal margin of gastric dysplasia before endoscopic submucosal dissection". However in the manuscript Figure 6 is cited in a paragraph about EGC, which is neoplasia. The legend for Figure 6A states "Conventional chromoendoscopy using indigo carmine is useful for determining the horizontal margin of gastric neoplasia". However the legend for Figure 6C states that this is a tubulovillous adenoma, which is dysplasia. Can the authors please introduce some consistency?

Answer: Thank you for your important comment. The Figures you mentioned were changed to be cited in a newly written section of gastric dysplasia.

Editorial comments

The "Author Contributions" section is missing. Please provide the author contributions.

Answer: We provided the author contributions in the revised manuscript.

The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Answer: According to the policy of our institute, the grant approval document is not

provided. Please keep this funding information with newly added grant number (No.20200004).

The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

Answer: We uploaded the original images using PowerPoint.