

Answering reviewers

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Title: OLGA stage is an appropriate predictor of early gastric cancer

Authors: Ying Zhou, Hai Yan Li, Jing Jing Zhang, Xiao Yu Chen, Zhi Zheng Ge and Xiao Bo Li

Question 1: The main remark is that it is unclear how patients were recruited: screening program, symptomatic individuals, all individuals referred to endoscopic unit? Indeed, the frequency of patients with gastric neoplasms in this study was very high (71 EGC on a total number of 227 esophagogastroduodenoscopy performed in a 2-year period). How do the Authors explain the high rates of GC cases? Were some strict selection criteria adopted, besides those reported in Methods?

Answer: The selection criteria has been changed to “Consecutive patients, ranging in age from 40-years-old to 80-years-old, with diagnosis of functional dyspepsia or suspicion of EGC and who underwent esophagogastroduodenoscopy were recruited to the study”. As Shanghai Ren Ji Hospital has a large-scale endoscopic treatment center for early gastrointestinal cancers including EGC, numerous patients with suspicious or diagnosed EGC come here for further treatment. On the other hand, only patients with functional dyspepsia were enrolled, patients who undergo esophagogastroduodenoscopy for follow-up or screening program did not meet the selection criteria. In addition, in order to eliminate the interobserver agreement of three methods (EGA classification, OLGA/OLGIM stages), enrolled patients were all examined and treated by one highly experienced endoscopist, patients examined by other endoscopists were not involved. The above three reasons may lead to the high rates of GC cases in this study.

Question 2: In the selection criteria, patients with “severe systemic diseases” were excluded. Please clarify this point.

Answer: This point has been clarified.” severe systemic diseases (*e.g.* a severe cardiac condition, serious infection, or renal failure).”

Question 3: Discussion is too long and with many numerical data to be omitted, please discuss mainly the most important results in light of current literature, potential clinical implications, strengths and weaknesses of the

study.

Answer: In the discussion part, several changes have been made according to the peer-reviewer's comments.

1. "With the development of endoscopic techniques, such as ME-NBI, EMR and ESD, more GCs were diagnosed and treated at an early stage." was deleted.

2. "As for EGC, atrophic gastritis and IM are rarely detected in people younger than 40 years old, the present study investigated the characteristics of background mucosa of EGC by using EGA classification, OLGA and OLGIM stage in patients of 40-80 years." was deleted.

3. "56.4% cases were staged consistently using either OLGA or OLGIM criteria. For the 43.6% cases staged inconsistently" was deleted.

4. "Marcos-Pinto^[16]*et al.* performed a modified OLGA/OLGIM-staging system with exclusion of the biopsy of the incisura, they showed a downgrade of stages in comparison with standard OLGA stages, however the downgrade in high-risk stages was relatively less prominent" was replaced by "Marcos-Pinto *et al*^[16] applied a modified OLGA/OLGIM staging system, with exclusion of biopsy of the incisura, and showed a downgrade of stages in comparison with standard OLGA stages."

5. "The interobserver agreement of OLGA/OLGIM by expert pathologists was reported higher than EGA (kappa value for OLGA 0.41-0.64, for OLGIM 0.80-0.87) [9, 24]." was replaced by "The interobserver agreement of OLGA/OLGIM by expert pathologists was reportedly higher than that for EGA"

6. As *H. pylori* infection was not the main point we focus on in our study, the whole paragraph of *H. pylori* "*H. pylori* was classified as a type I carcinogen of GC by the International Agency for Research on Cancer (IARC) in 1994^[25]. A previous study claimed that the pooled relative risk (RR) of GC was 3.0 for *H. pylori* seropositive patients compared with seronegative patients ^[26]. In our study, the *H. pylori* infection rate of EGC group was higher than that of non-EGC group, but the difference was not remarkable (70.4% vs. 61.5%, $p=0.195$). In regard to the association of *H. pylori* infection with other risk factors of EGC, Nam^[27]*et al.* analyzed 632 subjects who underwent esophagogastroduodenoscopy for GC screening, the result showed that *H. pylori* infection was an independent risk factor for high-risk OLGA/OLGIM stages (OR= 8.46 vs. OR= 5.89). The present study also found that *H. pylori* infection was related to high-risk OLGA/OLGIM stages. Moreover, *H. pylori*

infection was significantly related to moderate-to-severe EGA in our study, which suggested the importance of early *H. pylori* eradication in preventing the progression to high risk stages and thus reducing GC risk.

"was deleted and replaced by "In addition, since *H. pylori* infection is considered high risk for GC^[25, 26] and has been demonstrated as significantly related to high-risk OLGA/OLGIM stages^[27] and to moderate-to-severe EGA (the present study), we emphasized the importance of *H. pylori* infection in the detection of EGC."

7. "In contrast, Yoshihara^[28] *et al.* suggested that patients with extensive atrophic gastritis or IM obtain follow-up every year. In addition, some researchers from Japan recommended that *H. pylori*-infected patients with moderate atrophic gastritis should receive follow-up every 2 years, those with none-to-mild every 3 years^[29]" was replaced by " In contrast, some researchers from Japan have suggested that patients with extensive atrophic gastritis or IM obtain follow-up every 1 year, those with moderate atrophic gastritis every 2 years, and those with none-to-mild every 3 years^[28, 29]."

8. When came to the strengths and weaknesses of the study, one weakness "In addition, because our data were from a highly prevalent area of *H. pylori* infection and GC, our results may not be appropriate for Western countries where the risk of GC is much lower." was replaced by the strengths" However, to the best of our knowledge, this is the first study to identify that OLGA stage is more appropriate for predicting EGC than OLGIM stage and EGA classification, which can further help in establishment of a thorough surveillance program for EGC."

Question 4: some spelling should be corrected ("Diagnosises")

Answer: The language of this manuscript has been modified by editors of Filipodia Publishing with the Certificate of Service.