

Format for ANSWERING REVIEWERS

March 25, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 16413-review.doc).

Title: Changes in the spectrum of gastric polyps in the Chinese population

Author: Nan-Nan Fan, Jing Yang, Gang Sun, Zhong-Sheng Lu, En Qiang Ling Hu, Xiang-Dong Wang, Yun Sheng Yang

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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 reviewers

- (1) There are many grammatical mistakes and I think the manuscript needs a major language revision, mainly the discussion section (E.g. : line 147: "an" must be changed with "a"; line 232 "we" with "We", line 271 "conduced" with "conducted", line 274 "not a" must be erased). (Reviewer NO-3026822)

Answer: Thank you very much for your good comments and your recommendation for our work. These grammatical mistakes in this paper including those you mentioned have been completely corrected.

- (2) It is very interesting the association found between fundic gland polyps (FGPs) and prolonged PPI use. In the results section authors mention a hypothetical association between reflux esophagitis and fundic gland polyps. I think it should be stressed in the discussion section as well. Is it the use of PPI that, treating reflux esophagitis, represents a risk factor for FGPs, or FGPs are more frequent in patients with severe reflux esophagitis not responsive to PPI?

(Reviewer NO-3026822)

Answer: Thank you very much for your good comments. I has stated my views on our finding as your advised on this subject in the third paragraph of the **discussion section**. In

our study, it is interesting that there was significant differences in the incidence of reflux esophagitis under endoscopy in patients with FGPs relative to the overall patient population and those with HPPs. Moreover, the incidence of reflux esophagitis in patients with gastric polyps overall has increased year by year, which coincides with the increasing detection rate of FGPs. This finding may suggest a positive association between FGPs and reflux esophagitis, but this association was defined based on observations. With respect to this, although whether PPIs play a positive role in the genesis of FGPs remains controversial, in recent studies, PPIs have been reported to be associated with FGPs. These patients with reflux esophagitis tend to use PPIs for prolonged periods, given a possible positive role of PPIs in FGPs, hence, we considered that increasing incidence of reflux esophagitis may result in the change of polyp spectrum. However, we could not gain information on the use of PPIs in this retrospective study, and our observations cannot define a clear correlation between PPIs and reflux esophagitis and FGPs. So, your consideration that FGPs may be more frequent in patients with severe reflux esophagitis not responsive to PPI may be another explanation to our findings, which suggest that further investigations on this issue and the role of PPIs in the genesis of sporadic FGPs are needed.

(3) The male/female ratio of 3.69/1 is quite interesting. Are there any anthropological motivations, e.g. different eating habits in Chinese populations, that could explain this epidemiological finding? (Reviewer NO-3026822)

Answer: Thank you very much for your good comments. I have reviewed many published similar studies, no study has investigated whether the gender is a risk factor associated with gastric polyps. There are different eating habits between Western countries and China, and the diet of the former is usually rather low in fiber and high in fat and refined carbohydrates compared with the diet of people living in China. We have noted an interesting phenomenon in our clinical work that individuals from the Inner Mongolia which is a province of China tend to have polyps in EGD and colonoscopy, as food intake of people living in this area contain much meat and products such as beef and mutton. There might be other potential factors associated with adenomas, such as genetics related to gender, which needs further studies to be confirmed.

- (4) This interesting paper describes the changing prevalence of gastric polyps in China. An obvious limitation is the retrospectivity of the design. As a minor comment: in the result section of the abstract, 2.6% should be written near to 4043 cases in the second line.(Reviewer NO-3024915)

Answer: Thank you very much for your good comments and your time. I has corrected 2.6% to be written in the form of 4043/157 902 in the third line of the abstract. The present study is a retrospective study, although these characteristics such as large-scale, patients from different geographic areas and data from a top tertiary hospital center over a long period of time which ensures that the figures obtained represent largely the status of the entire nation. However, it is not a screening study based on an asymptomatic population undergoing EGD, hence, all findings from the study should be interpreted with the inevitable limitations of retrospective studies. The current data on the prevalence of gastric polyps shown in these studies can not actually represent the true incidence in the entire population. And further prospective studies related to this issue should be encouraged.

- (5) For what concerns materials and methods, there is a good description of number of patients, method of recruitment, inclusion and exclusion criteria, even though it could be useful to add anamnesis information about patients' therapies at time of EGD, especially addressing any therapy with Proton pump Inhibitors. Moreover it could be advisable to add other anamnesis information about reason of the exam, if present any signs and symptoms such as epigastric pain, anemia etc. One more suggestion about methods, could be the description of polyps management, in terms of number of polyps biopsied and number of polyps removed by polypectomy.(Reviewer Dr.de'Angelis)

Answer. Thank you very much for your good comments and spending much time in reviewing my paper. Although PPIs has been reported to be associated with FGPs, the associations between PPIs and FGPs remains an controversial subject in recent series of studies. Further anamnesis information about patients' therapies at time of EGD, especially addressing any therapy with Proton pump Inhibitors will be useful to illustrate the associations between PPIs and FGPs, and these information from patients with reflux esophagitis are more important, because these patients tend to be chronic users of proton pump inhibitors (PPIs). However, when we retrospectively

recalled these reports of patients in the endoscopic database, these useful information can not be available in all patients, such as reasons of EGD exam, therapies at time of EGD. And your excellent advices on the design of the present study will promote to improve our management of clinical information of the patients undergoing EGD exam, and we will add more information about therapies at time of EGD and clinical symptoms bringing patients to EGD exam as you advised in our further study.

I have added the polyps management including biopsy and polypectomy to the method in the abstract. It is very useful for improving our work with respect to your suggestion that the description of polyps management could be added to method in terms of number of polyps biopsied and number of polyps removed by polypectomy. In this retrospective study, we enrolled 4043 patients with gastric polyps, and these 4043 EGD endoscopic procedures were performed by different gastroenterologists. Although information about the location of polyps, polyps management and pathologic diagnosis were gained by recalling these procedures, the accurate number of removed polyps was not available. Thus, in this study, the patient with one and more gastric polyps diagnosed by pathology was defined as a polyp case. However, your excellent suggestions will be taken into consideration in our further study.

- (6) All the results are clearly exposed and appropriate to their referrals in tables. Even data exposed in tables are clear and readable. Maybe it could be useful to represent data about detection rate with graphics rather than with tables, because they could be more immediate for the reader. (Reviewer Dr.de'Angelis)**

Answer. Thank you very much for your good advices. As you advised, graphaics are more immediate for readers to understand the dynamic change of information provided by our data. Thus, i have made three graphics (Figure 1, Figure 2 and Figure 3 in the results) to represent data about several detection rates, which included detected rate of various types of gastric polyps (Shown in Figure 2), *H. pylori* infection rate, incidence of reflux esophagitis(Shown in Figure 1), and regional distribution of gastric polyps (Figure 3) in the past 10 years. Thank you so much.

- (7) References are quite up-to-date, even though in latest months some other articles have been published, including epidemiological data about gastric polyps by Sonnenberg A**

on Dig Liver Dis. 2015, specific characterization of specific polypoid lesion by Lemmers A and Markowski AR, respectively on United European Gastroenterol J. 2014 and Gastroenterol Rep (Oxf). 2014, among more recent others. (Reviewer Dr.de'Angelis)

Answer. Thank you very much for spending much time in reviewing so many literatures related to gastric polyps. I have reviewed these recent published articles, especially these three articles, which are very useful to provide more data for my paper, and I have updated related data in the table titled "Spectra of gastric polyps in previous and current studies" listed in the section of the result.

3 References and typesetting were corrected

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

Sincerely yours,

Nan Nan Fan

NanNan Fan, MD, PhD

Institute of Digestive Diseases, Chinese PLA General Hospital,

Beijing 100853, China.

Nankai University School of Medicine,

Tianjin 300071 , China

Fax: +86-10-68212267

E-mail: nkfan1986@163.com