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### Format for ANSWERING REVIEWERS

September 29, 2016

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 27944-revised manuscript.doc).

**Title:** Clinical Features of Upper Gastrointestinal Serrated Lesions: an Endoscopy Database Analysis of 98,746 Patients

**Author:** Hailong Cao, Wenxiao Dong, Mengque Xu, Yujie Zhang, Sinan Wang, Meiyu Piao, Xiaocang Cao, and Bangmao Wang

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 27944

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

#### **Reviewer 1:**

The manuscript called "Clinical Features of Upper Gastrointestinal Serrated Lesions: an Endoscopy Database Analysis of 98,746 Patients" is a descriptive study focused on the evaluation of upper gastrointestinal serrated lesions as a negative prognostic marker of colorectal cancer. Although the prevalence of serrated lesions in UPGI was very low, the authors analyzed an exceptionally large cohort of patients who underwent esophagogastroduodenoscopy and precisely described the target group of patients. Minor comment: Cox proportional hazard model would enhance the validity of the presence of UPGI serrated lesions as an independent negative prognostic marker for CRC.

**Response:** We appreciate the Reviewer for pointing out this important issue. As rarity of serrated lesions in UPGI, we think it is difficult to perform a Cox proportional hazard model to enhance the validity of the presence of UPGI serrated lesions as an independent negative prognostic marker for CRC, so we need more clinical and endoscopic data to perfect it.

#### **Reviewer 2:**

The Authors present a study on serrated polyps of the upper digestive tract. To my knowledge is the largest study on this topic I ever read. They found on a very large sample study of 98,746 patients who underwent EGDS study only 21 (0,02%) patients with serrated polyps of UPGI demonstrating "per se" the rarity of these lesions. Moreover the Authors try to find an association between the serrated polyps of the UPGI and colorectal adenoma. Major comment I have some concerns about the statistics of this study. It is not clear the random selection of the so called "control group". How was this group selected?



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I think that for the purpose of this study the Authors should perform a propensity score matching method. Alternatively they should compare the rate of adenoma detection to the cumulative incidence of colorectal adenoma in the whole sample study or they should refer to the literature data. Moreover as suggested by the wide 95% CI of the OR of adenoma and advanced adenoma detection rate, the interpretation of these findings could result in a type II error because of a small sample size.

**Response:** We appreciate the Reviewer to point out this issue. We select the control group: In case of UPGI serrated lesions were histologically confirmed, colonoscopy was required simultaneously or within six months. Each patient was compared with two randomly selected age- and gender-matched controls without serrated lesions who also underwent colonoscopy in the same period (Gut Liver. 2011, 5(4):432-6; PLoS One. 2015 Apr 13;10(4):e0122996) (Page 6).

As rarity of serrated lesions in UPGI, it is difficult to perform a propensity score matching method, so we need more clinical and endoscopic data to perfect it. It is a good advice to compare the rate adenoma detection to the cumulative incidence of colorectal adenoma in the whole sample study, we will complete this section after long time follow up.

### Reviewer 3:

“Important concept. However, needs to be extensively re-written preferably by an expert in English.”

**Response:** We appreciate the Reviewer for the positive comment. For the English writing we have revised the manuscript carefully and also delivered it to a professional English language editing companies.

### Reviewer 4:

In this study, authors select the upper gastrointestinal (UPGI) serrated lesions as study topic. Through retrospective study, authors analyzed the clinical and pathological features of serrated lesions in UPGI and also evaluated the colonoscopy findings at same time. Although the serrated lesions in UPGI are rare in the population, it is very important to understand its clinical and pathological features as such lesions maybe related to invasive carcinoma in UPGI exhibited.

Furthermore, authors found in this study that the serrated lesions in UPGI are associated with higher colorectal adenoma detection rate. Therefore, the manuscript is good for the readership of WJG. The format of manuscript including the cited literatures should be modified according to the request of the Journal.

#### SPECIFIC COMMENTS:

Title: The title accurately reflects the major topic and contents of the study.

Abstract: The description of aim, material and methods, result and conclusion sections is Ok.

Introduction: It is well written.

Material and methods:

1, Section of Design and patients is ok.

2, In section of Endoscopic procedure, only procedure of colonoscopy is mentioned, however the procedure of EGD is not mentioned. In fact, this study focus on UPGI serrated lesions, therefore the procedure of EGD is very important.

3, Section of Pathological evaluation. Is the biopsy or the resected lesions taken by EGD? If yes, the procedure should be mentioned.

4, Section of Statistical analysis is ok.

5, In relation to the groups of the study, author should unify the name of groups throughout the manuscript, such as control group or average group.

Results: This section clearly described the results obtained from the study.

Discussion: The discussion is well written.

References: The references are appropriate, relevant, and updated.

Tables and figures: Figure and tables are appropriately presented.

**Response:** We appreciate the Reviewer for pointing out these important issues. We totally accept your advice. We add this section in our article: All collected specimens from biopsy or the resected lesions **under EGD** were fixed in 10% formalin within 1h of removal and then fixed for a minimum of 4h. All haematoxylin and eosin-stained sections used for pathological assessment and classification were evaluated by experienced pathologists. Serrated lesions in UPGI are clinically and molecularly diverse changes that have common features as crypt luminal morphology characterized by glandular serration (Page 6). Risks of colorectal neoplasia between patients with serrated lesions in UPGI and the **control group** in our database were compared by Chi-square test or Fisher exact test (Page 7).

#### Minor comments

1, Page 2, line 10 "...these patients which underwent colonoscopy simultaneously or within six months..." should read as "...these patients who underwent colonoscopy simultaneously or within six months..."

2, Page 2, line 21 "...in the duodenum intramucosal carcinoma." should read as "in the intramucosal carcinoma of duodenum."

3, Page 3, line 9 "...and sessile serrated adenoma/polyp are divided," should read as "and sessile serrated adenoma/polyp have been divided,"

4, Page 3, line 12 "UPGI nonconventional adenomatous and nonadenomatous type of dysplasia," should read as "UPGI nonconventional adenomatous and nonadenomatous types of dysplasia".

5, Page 8, last line of table 2: About >10 mm, please indicate what lesion is over 10 mm.

**Response:** We appreciate the Reviewer for scientific and rigorous attitude. We have corrected the irregular terms seriously based on the comments.

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

Sincerely yours,

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