

## Round-1

### Dear editor:

Many thanks for your email of Oct 2020, regarding the revision and advice of the paper 58661. Overall, the comments have been fair, encouraging and constructive. We have learned much from it. After carefully studying the reviewer' comments and your advice, we have made corresponding changes to the paper. Our response of the comments is enclosed. Response to Specific Points.

Response to Reviewer #2:

**Question 1:** how did the authors quantify treatment success or aggravation based on a telephone follow up? How many patients were lost to follow up? What was the median follow up? Was the number/percentage lost to follow up different amongst the histological subtypes?

**Answer:** We evaluated the treatment effect through re-examination of biopsy; all 2248 cases in this study underwent biopsy re-examination, and the cases lost to follow-up were not included in this study; the median follow-up time was 2 years; 205 cases of simple type accounted for 9.1%; 654 cases of hyperplastic type Accounted for 29.1%; 1132 cases of Intestinal epithelialization accounted for 50.4%; 257 cases of IEN phenotype accounted for 11.4%. All biopsy reviews.

**Question 2:** Table 1. the percentages do not add up to 100%.

**Answer:** Thank you very much for careful review of the article. I have modified the corresponding part of the article.

Table 1. Age statistics for each type of CAG, cases (%)

Type	Less than 40 years old	41–50 years old	51–60 years old	61–70 years old	>70 years old	Total
Simple	4 (2.0)	20 (9.8)	53 (25.9)	94 (45.9)	34 (16.6)	205
Hyperplasia	37 (5.7)	251 (38.4)	213 (32.6)	97 (14.8)	56 (8.6)	654
Intestinal metaplasia	85 (7.5)	447 (39.5)	414 (36.6)	95 (8.4)	91 (8.0)	1132
Intraepithelial neoplasia	9 (3.0)	34 (13.2)	69 (26.8)	87 (33.9)	58 (22.6)	257

**Question 3:** Table 2 is confusing. Why are there three columns under each histological subtype? How did the authors confirm treatment success?

**Answer:** Thank you very much for the reviewer's careful review, I have modified the Table 2. It is through the follow-up, the biopsy review sample is compared with the sample before the follow-up, found the different of morphology.

Group	Simple type (205 cases)			Hyperplasia type (654 cases)			Intestinal epithelial metaplasia type (1132 cases)			Intraepithelial neoplasia type (257cases)		
	cured	slightly changed	Aggravated	cured	slightly changed	Aggravated	cured	slightly changed	Aggravated	cured	slightly changed	Aggravated
1-3 months		3	1	32	94	11	16	187	14	2	28	6
4-6 months	2	47	14	91	149	67	31	435	75	10	113	27
7-12 months	7	99	32	50	96	94	40	229	105	1	56	15
Total (%)	9 (4.4%)	149 (72.7%)	47 (22.9%)	173 (37.9%)	339 (51.8%)	142 (21.7%)	87 (7.7%)	851 (75.2%)	194 (17.1%)	13 (5.1%)	197 (76.7%)	48 (18.7%)

Table 2. Comparison of follow-up time and prognosis of CAG

**Question 4:** Since the goal/aim of the manuscript is to define new histopathological classifications for CAG, the authors need a figure with the characteristics and accompanying images for each histological subtype.

**Answer:** Our article divides CAG into 4 subtypes, and each subtype was defined and illustrated with drawings.

Response to Reviewer #3:

**Question i):** sentences in Results subsection of Abstract should be past tense rather than present tense;

**Answer:** Thanks to the experts for such pertinent questions. We have revised all the grammatical problems in the text.

**Question ii):** some general information given in Results subsection of Abstract are inappropriate;

**Answer:** We have checked the manuscript and revised it according to the comments.

**Question iii):** although the authors have been stated about treatment throughout the text, there is no any treatment modality rather than follow-up; i

**Answer:**

**Question v):** although the have been stated that "We have also discussed the histological

criteria for the diagnosis of CAG and its differential diagnosis, as well as the appropriate follow-up time and treatment period.”, there is no any discussion about differential diagnosis, the appropriate follow-up time and treatment period;

**Answer:** This study mainly analyzes histomorphology. As the research progresses, more cases will be added, and the treatment plan will be discussed with clinicians to further track the treatment effect.

**Question iv):** although the have been stated that “We have also discussed the histological criteria for the diagnosis of CAG and its differential diagnosis, as well as the appropriate follow-up time and treatment period.”, there is no any discussion about differential diagnosis, the appropriate follow-up time and treatment period;

**Answer:** This part was a translation error and has been modified to “we discussed the histological diagnostic criteria of CAG in order to target the follow up time, accurate treatment time, improve the detection rate of early gastric cancer and reduce the incidence of gastric cancer.”

**Question iv):** a reference(s) could be added for citation of further classification systems stated in Introduction;

**Answer:** This part of the content has been explained in the quotation: “Chronic atrophic gastritis (CAG) in gastric mucosal biopsy is a common lesion in gastric biopsy and it is mostly divided into light, medium and heavy levels in clinical pathologic examination.” In our study, we analyzed the clinical manifestations, biopsy site of 2248 CAG cases from four hospitals, and then divided them into four type, simple type, hyperplasia type, Intestinal epithelialization and intraepithelial neoplastic type.

## **Round-2**

### **Dear editor:**

Many thanks for your email of Feb 2021, regarding the revision and advice of the paper 58661. Overall, the comments have been fair, encouraging and constructive. We have learned much from it. After carefully studying the reviewer' comments and your advice, we have made corresponding changes to the paper. Our response of the comments is enclosed. Response to Specific Points.

**Question 1:** Methods: “We divided” is not necessary, You need to describe the methods better. The “Results” is not a discussion. Review this, this is abstract!

**Answer:** we revised the “Method” and “Results” part according to the reviewers comments. The details can be seen in main text.

**Question 2:** Core tip: “In conclusion” this is not a conclusion! Review the newspaper's rules.

**Answer:** we rewrote the “Core tip” part according to the reviewer's comments. The details can be seen in main text.

**Question 3:** “In our study, we analyzed the clinical manifestations, biopsy site of 2248 CAG cases from four hospitals, and then divided them into four type, simple type, hyperplasia type,

IM type and IEN type. In addition, we discussed " This is an introduction, not a result. It needs to be redone.

**Answer:** This is an introduction to our research methods and results.

**Question 4:** "2248 cases that diagnosed in Feb 2014 to July 2018" Why is the database so old and does not cover 2019 and 2020?

**Answer:** Our study is from 2014, the cases were followed up a long time, so the latest specimens were not used.

**Question 5:** "There were 1251 male cases and 997 female cases, divided into five groups by age, less than 40 years old, 41-50 years old, 51-60 years old, 61-70 years old and over 71 years old. The lesion sites contained angular notch, pylorus, gastric body, cardia and fundus were observed. " These are results, not methods.

**Answer:** This part was deleted in here, and add in "result" part.

**Question 6:** "MUC-1, MUC-2 MUC-5AC and MUC-6" do not use acronyms without first mentioning them.

**Answer:** The revised abstract contained these antibodies, and the full names are marked.

**Question 7:** "2248 CAG patients were treated" treated with what?

**Answer:** During the follow-up process, the treatment status was not asked, and it will be added in future studies.

**Question 8:** "In addition to the degree of atrophy, CAG also has the type of tissue morphology, such as whether the glands have dilated and / or branched changes, whether there is an increase or decrease in mucous secretion in the glandular cavity, the mucus in the glandular cavity is neutral mucus or acidic mucus, Helicobacter pylori infection and degree, the type and extent of inflammatory cell infiltration; References?

**Answer:** references 16, 17

**Question 9:** "Because the intestinal epithelial metaplasia has a brush margin that does not secrete mucus and a brush margin of goblet cells and absorption cells with acidic mucin" References?

**Answer:** References 18,19

**Question 10:** ". Hyperplasia type mostly happens between 40-60 years old " Reference?

**Answer:** References 20

**Question 11:** ". Commonly, lesions are limited to quantitative changes with increased mucus secretion. But the lesions can be alleviated or cured after positive treatment. " References?

**Answer:** References 21

**Question 12:** "The cases of the IM type increases with the age, especially among those over 50 years old." References?

**Answer:** References 22

**Question 13:** "Mucus secretion has not only a quantitative change but also a qualitative change, containing varying degrees of salivary acid mucus and (or) sulfuric acid mucus." References?

**Answer:** References 23

**Question 14:** ". Intraepithelial neoplastic type is commonly developed from the previous several types " References?

**Answer:** References 23

**Question 15:** "Decrease of mucus secretion is an essential marker for the precancerous lesion. Endoscopic Submucosal Dissection (ESD) is recommended. " References?

**Answer:** References 24

**Question 16:** Summary of discussion: There is no discussion. There is no comparison with the current literature, a text completely without references. It needs to be completely redone. Conclusion: The conclusion only answers the objective of the study and only that. Its conclusion practically repeats the text and that is not how it is done. It needs to improve a lot.

**Answer:** The "Conclusion" and "ARTICLE HIGHLIGHTS" part was rewritten followed the comments. The details can be seen in main text. The modified part was marked in red.