

## Response to the reviewers

### Reviewer 1

*This is a well-conducted retrospective cohort study that investigates the incidence of gastric cancer based on the endoscopic Kyoto classification of gastritis. The study suggests that the Kyoto classification can be used to assess GC risk and that a high total Kyoto score ( $\geq 4$ ) is associated with GC incidence. The study is well designed and its findings are relevant to clinical practice. My comments are as follows:*

*1. Can we assume a normal distribution for the number of EGD per person and Kyoto classification score? Would it be better to use median and IQR to present this information?*

We would like to thank for your precious comments that have improved our manuscript. As you pointed out, we can not assume a normal distribution for the number of EGD per person and the Kyoto classification score. We corrected the presentation of the entire manuscript from the mean (SD) to the median (IQR), including the Abstract and Results. Revised Table 1 is shown with the median and IQR. Since it is difficult to understand the difference in EF score between the GC and non-GC groups, Supplementary Table 2 is added and shown with the mean and standard deviation.

**Revised Table 1. Demographic characteristics and endoscopic findings of the patient at baseline.**

All	Gastric	Non-gastric	P
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		cancer		cancer	value <sup>1</sup>
<b>No.</b>	6718	34		6684	
<b>Age, median (IQR), yr</b>	54 (46-64)	69.5 (57.8-73.8)		54 (46-64)	< 0.001
<b>Male sex, no. (%)</b>	2969 (44.2)	17 (50.0)		2956 (44.2)	0.49
<b><i>H. pylori</i> status, no. (%)</b>					< 0.001
<b>Uninfected</b>	3754 (55.9)	5 (14.7)		3749 (56.1)	
<b>Eradicated</b>	2264 (33.7)	20 (58.8)		2244 (33.6)	
<b>Currently infected</b>	700 (10.4)	9 (26.5)		691 (10.3)	
<b>Duration of follow up, median (IQR), yr</b>	2.56 (1.74-3.64)	1.03 (0.85-1.78)		2.57 (1.76-3.64)	< 0.001
<b>No. EGD per patient, median (IQR)</b>	2.95 ± 1.27	2.85 ± 1.73		2.95 ± 1.27	
<b>Kyoto classification score, median (IQR)</b>					
<b>Atrophy</b>	0 (0-1)	2 (1-2)		0 (0-1)	< 0.001

<b>Intestinal metaplasia</b>	0 (0-0)	2 (0-2)	0 (0-0)	< 0.00 1
<b>Enlarged folds</b>	0 (0-0)	0 (0-0)	0 (0-0)	< 0.00 1
<b>Nodularity</b>	0 (0-0)	0 (0-0)	0 (0-0)	0.91 6
<b>Diffuse redness</b>	0 (0-0)	1 (1-1)	0 (0-0)	< 0.00 1
<b>Total Kyoto</b>	0 (0-2)	5 (4-5)	0 (0-2)	< 0.00 1

<sup>1</sup> *P* values were calculated using binomial logistic regression model.

IQR: interquartile range; EGD: esophagogastroduodenoscopy.

**Supplementary Table 2. Demographic characteristics and endoscopic findings of the patient at baseline with mean and standard deviation.**

	<b>All</b>	<b>Gastric cancer</b>	<b>Non-gastric cancer</b>
<b>No.</b>	6718	34	6684
<b>Age, yr</b>	55.0 ± 12.4	66.3 ± 11.9	54.9 ± 12.4
<b>Male sex, no. (%)</b>	2969 (44.2)	17 (50.0)	2956 (44.2)

***H. pylori* status, no. (%)**

<b>Uninfected</b>	3754 (55.9)	5 (14.7)	3749 (56.1)
<b>Eradicated</b>	2264 (33.7)	20 (58.8)	2244 (33.6)
<b>Currently infected</b>	700 (10.4)	9 (26.5)	691 (10.3)
<b>Duration of follow up, yr</b>	2.60 ± 1.17	1.46 ± 1.12	2.61 ± 1.16
<b>No. EGD per patient</b>	2.95 ± 1.27	2.85 ± 1.73	2.95 ± 1.27
<b>Kyoto classification score</b>			
<b>Atrophy</b>	0.585 ± 0.776	1.559 ± 0.705	0.580 ± 0.773
<b>Intestinal metaplasia</b>	0.284 ± 0.645	1.324 ± 0.912	0.279 ± 0.640
<b>Enlarged folds</b>	0.039 ± 0.193	0.176 ± 0.387	0.038 ± 0.192
<b>Nodularity</b>	0.026 ± 0.161	0.029 ± 0.171	0.026 ± 0.161
<b>Diffuse redness</b>	0.312 ± 0.590	1.000 ± 0.696	0.309 ± 0.587
<b>Total Kyoto</b>	1.247 ± 1.811	4.088 ± 2.021	1.232 ± 1.798

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EGD: esophagogastroduodenoscopy.

*2. According to your opinion, as the association between nodularity and the risk of developing GC is still debated, should nodularity be listed separately when reporting Kyoto score to emphasize its value in predicting gastric cancer? For example, should the Kyoto classification score for A1IM1H1N1DR0 be reported as 3+1 instead of 4?*

Thank you for your very insightful comments. We added the content you pointed out to the Discussion as the following:

As the association between nodularity and the risk of developing GC is still debated, nodularity might be listed separately. For example, the total Kyoto

classification score for atrophy 1, IM 0, EF 1, nodularity 1, and DR 1 might be reported as 3+1 instead of 4.

Reviewer 2

*Assessment of the risk of developing gastric cancer in patients with chronic gastritis and other underlying diseases of the stomach is important, as it makes it possible to detect this serious complication at an early stage or, in some cases, even prevent the development of gastric cancer. The authors analyzed the results of a study of 6,718 patients with gastritis and, based on the large clinical material, confirmed the possibility of stratifying patients with chronic gastritis into risk groups depending on atrophy, intestinal metaplasia, enlarged folds, nodularity, diffuse redness, and total Kyoto scores. Thus, the data obtained are of practical importance and should be taken into account when assessing the risk of developing gastric cancer in patients with chronic gastritis. A few notes to which the authors should pay attention.*

*ABSTRACT 1. It is desirable to clarify the period during which patients were under observation.*

We would like to thank you for your valuable comments that have improved our manuscript. We added the duration of the observation to the Abstract as the following:

During the follow-up period (max 5.02 years; median 2.56 years), GC developed in 34 patients.

*RESULTS and DISCUSSION 1. (p. 9, pp. 22-23). The sentence “The annual incidence*

*rates of GC increased with the total Kyoto score (0.05%, 0.07%, 0.47%, and 1.27% for the total Kyoto scores of 0-1, 2-3, 4, and 5-8, respectively). » Specify that we are talking about the average frequency of cases per year. This is important, because according to Figures 1-3, the highest incidence of gastric cancer is observed between 4 and 5 years for almost all studied factors. This remark also applies to other sentences where the authors talk about "annual incidence rates".*

Thank you for your very insightful comments. The term “the annual incidence rate of GC” was corrected to “the average frequency of GCs per year” for the entire manuscript including the Abstract, Methods, Results, Discussion, and Figure legends.

2. (p. 9, pp. 24-25). *Perhaps the authors did not mean “subsequent”, but “previous” studies.*

We corrected from “subsequent” to “previous”, as you pointed out.

*Table 1. 1. It is desirable to indicate the significance of differences between groups (significance level) In general, the manuscript is written in good English, well structured. Tables improve the perception of text. I believe that after minor corrections the manuscript can be published.*

Thank you for your precious comment. The difference between the two groups in Table 1 was analyzed by binomial logistic regression model. We added

the information to the Methods as the following:

Baseline characteristics were compared between GC and non-GC groups using binomial logistic regression model.

We added the *P* values to the revised Table 1 as the following:

**Revised Table 1. Demographic characteristics and endoscopic findings of the patient at baseline.**

	All	Gastric cancer	Non-gastric cancer	<i>P</i> value <sup>1</sup>
<b>No.</b>	6718	34	6684	
<b>Age, median (IQR), yr</b>	54 (46-64)	69.5 (57.8-73.8)	54 (46-64)	< 0.001
<b>Male sex, no. (%)</b>	2969 (44.2)	17 (50.0)	2956 (44.2)	0.495
<b><i>H. pylori</i> status, no. (%)</b>				< 0.001
<b>Uninfected</b>	3754 (55.9)	5 (14.7)	3749 (56.1)	
<b>Eradicated</b>	2264 (33.7)	20 (58.8)	2244 (33.6)	
<b>Currently infected</b>	700 (10.4)	9 (26.5)	691 (10.3)	

<b>Duration of follow up,</b>	2.56 (1.74-3.64)	1.03 (0.85-	2.57 (1.76-	<
<b>median (IQR), yr</b>		1.78)	3.64)	0.00
				1
<b>No. EGD per patient,</b>	2.95 ± 1.27	2.85 ± 1.73	2.95 ± 1.27	
<b>median (IQR)</b>				
<b>Kyoto classification</b>				
<b>score, median (IQR)</b>				
<b>Atrophy</b>	0 (0-1)	2 (1-2)	0 (0-1)	<
				0.00
				1
<b>Intestinal metaplasia</b>	0 (0-0)	2 (0-2)	0 (0-0)	<
				0.00
				1
<b>Enlarged folds</b>	0 (0-0)	0 (0-0)	0 (0-0)	<
				0.00
				1
<b>Nodularity</b>	0 (0-0)	0 (0-0)	0 (0-0)	0.91
				6
<b>Diffuse redness</b>	0 (0-0)	1 (1-1)	0 (0-0)	<
				0.00
				1
<b>Total Kyoto</b>	0 (0-2)	5 (4-5)	0 (0-2)	<
				0.00
				1

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<sup>1</sup> *P* values were calculated using binomial logistic regression model.

IQR: interquartile range; EGD: esophagogastroduodenoscopy.