

Comment

This study aims to determine the gastric adenocarcinoma (GAC) occurrence rate and related factors by evaluating the follow-up results of patients who received endoscopic resection for gastric dysplasia. The topic is clinically important since both EMR and ESD have become the most important treatment modalities for gastric premalignant lesion or early gastric cancer and the long-term outcomes of these treatment modalities deserve comprehensive studies.

Generally speaking, this study is well-written and has a relatively large sample size with a long follow-up period. The results are concise and easy to understand. However, before reaching the final conclusions for future citations and references, the reviewer has a few comments as follows:

Major concern:

1. Since this study has a retrospective design as has been listed by the authors as one major limitation, the authors may want to further discuss the influence of patients who were lost to follow-up. The number may be significant and thus may underestimate the occurrence rate of GAC. The flow chart of figure 1 may start from the initial 1273 patients who received resection for gastric dysplasia.
2. Intestinal metaplasia (IM) and gastric atrophy are both important variables in the present study. Inter-observer variation may need to be considered since the severity of gastric atrophy and presence of IM in each patient was endoscopically evaluated by three endoscopists. In addition, what is the timing of determining the presence of IM and atrophy? prospective (reported in the initial resection) or retrospective (review of the stored images or video clips) ?
3. The authors have arbitrarily categorized all analyzed subjects into three groups: control, synchronous and metachronous. How did the authors categorize patients who were found to have both synchronous and metachronous lesions?
4. In Table 2, what comparison does the p value stand for?
5. Since the histology of gastric lesion is also an important risk factor for metachronous lesions as reported in previous studies, the authors are suggested to include the information of histology, esp the percentage of poorly differentiated type.
6. The Discussion Section is a little lengthy without further division into paragraphs, which makes the reading difficult. The authors have cited many importance reference but there is lacking on the comparison of their results with other studies, ex role of Hp infection, histology.
7. Among the demographics, there are other common risk factors of gastric

dysplasia not included, such as tobacco smoking and alcohol consumption.

8. How did the multivariate analysis performed for table 3-5? What factors have been controlled?

April 3 2017

To: Editorial Board of World Journal of Gastroenterology

ESPS manuscript NO: 33562

Title: Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia: retrospective, single-center study

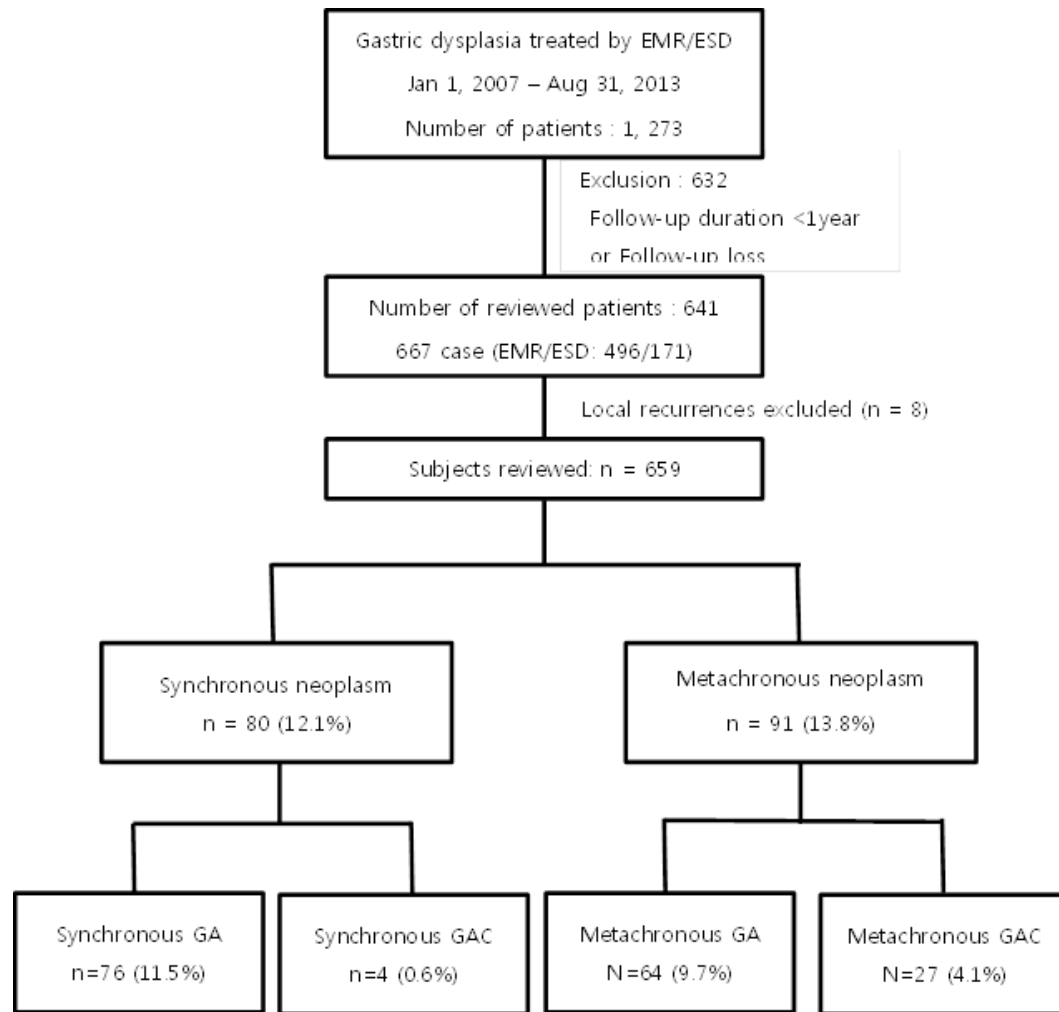
We would like to express our appreciation to the reviewers and editor for spending time and effort to improve our manuscript. Your suggestions were valuable to help us strengthen our work.

1. Since this study has a retrospective design as has been listed by the authors as one major limitation, the authors may want to further discuss the influence of patients who were lost to follow-up. The number may be significant and thus may underestimate the occurrence rate of GAC. The flow chart of figure 1 may start from the initial 1273 patients who received resection for gastric dysplasia.

: We agree with your comment. Of the initial 1273 patients who underwent resection for gastric dysplasia, 632 were not followed up. Gastric dysplasia is not a malignancy; therefore, we think that patients' recognition of their disease had an effect on the necessity of follow-up. In addition, surveillance at another hospital (e.g., at the hospital where the diagnosis was first made) is possible. Your comment regarding the possibility of underestimation of the occurrence rate of GAC is reflected in the Discussion section as follows:

Finally, about half of the patients were not followed up, and the occurrence rates of synchronous and metachronous lesions could be underestimated.

In addition, as you pointed out, we have revised the flowchart of Figure 1.



2. Intestinal metaplasia (IM) and gastric atrophy are both important variables in the present study. Inter-observer variation may need to be considered since the severity of gastric atrophy and presence of IM in each patient was endoscopically evaluated by three endoscopists. In addition, what is the timing of determining the presence of IM and atrophy? prospective (reported in the initial resection) or retrospective (review of the stored images or video clips) ?

: We have revised the sentence in the Definitions section as follows, reflecting your comment:

Three experienced endoscopists (HS Moon, JK Sung, and HY Jeong) performed all the procedures, and all data were saved as images. The records of all the patients were reviewed retrospectively, and the severity of gastric atrophy and presence of IM in each patient was decided after discussion among the three experts.

3. The authors have arbitrarily categorized all analyzed subjects into three groups: control, synchronous and metachronous. How did the authors categorize patients who were found to have both synchronous and metachronous lesions?

: We classified the three groups according to lesion, not patient.

4. In Table 2, what comparison does the p value stand for?

: The P value indicates the difference between the three groups after the χ^2 test. And we have modified the sentence

Male gender, open-type atrophic gastritis, and intestinal metaplasia were significantly different among the three groups.

5. Since the histology of gastric lesion is also an important risk factor for metachronous lesions as reported in previous studies, the authors are suggested to include the information of histology, esp the percentage of poorly differentiated type.

: We have included your comment and revised the sentence in the RESULTS section as follows:

The degree of differentiation of metachronous gastric cancer was as follows: moderately differentiated cancer in 20 patients, well-differentiated cancer in 5 patients, and poorly differentiated cancer in 2 patients.

6. The Discussion Section is a little lengthy without further division into paragraphs, which makes the reading difficult. The authors have cited many importance reference but there is lacking on the comparison of their results with other studies, ex role of Hp infection, histology.

: We have revised the Discussion section in accordance with your comments

7. Among the demographics, there are other common risk factors of gastric dysplasia not included, such as tobacco smoking and alcohol consumption.

: This was a retrospective study. Therefore, we could not confirm the exact smoking and alcohol consumption status in all the patients. In addition, we had difficulty

distinguishing current smokers from past smokers and in quantifying the alcohol consumption objectively.

8. How did the multivariate analysis performed for table 3-5? What factors have been controlled?

: Significant values obtained from the univariate analysis were analyzed by using a multivariate analysis. We have revised Tables 3–5 by applying the control factors.

Once again, we appreciate the time that the reviewer and the editor have spent in bringing these points to our attention. We believe that the manuscript is now much improved, and we hope that the response has been adequate. We again appreciate your consideration for publishing this manuscript in World Journal of Gastroenterology.

Sincerely,

Hee Seok Moon