A Doctoral Dissertation

Clinical implications and risk factors for high-grade dysplasia or carcinoma in biopsy-proven gastric regenerative atypia

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(Supervised by professor Jin Won Hyun)

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ABSTRACT

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Background and Objectives: Tissue biopsies are routinely performed during gastroscopy, however, the clinical implications and therapeutic strategies of lesions identified as regenerative atypia (RA) remain unclear. This study analyzed the clinical implications and risk factors for high-grade adenoma or carcinoma in patients with biopsy proven gastric RA.

Subjects and Methods:

Between January, 2015, and December, 2016, 296 patients were diagnosed as RA after initial forceps biopsy performed during gastroscopy at Jeju National University Hospital. We retrospectively reviewed medical records, pathologic reports, and endoscopic findings.

Results: The detection rate of RA was 1.46% (296/20,271) among patients who underwent gastroscopy. Of 96 RA lesions that met eligibly criteria, 23 (24.0%) were

neoplasia according to the final diagnosis; 14 (14.6%) were high-grade dysplasia or carcinoma, and 9 (9.4%) were low-grade dysplasia. Surface nodularity, surface redness, corporal lesions, and intestinal metaplasia were identified as risk factors in the univariate analysis. Multivariate analysis adjusted for age and sex showed that only surface nodularity among endoscopic findings was a statistically significant independent risk factor for high-grade dysplasia or carcinoma ($p = 0.01$; odds ratio, 6.4; 95% confidence interval, 1.5-26.4).

Conclusion: Most patients initially diagnosed as RA were finally diagnosed with benign lesions such as gastritis and low-grade dysplasia. However, RA has potential that can be changed and upgraded to high-grade adenoma or carcinoma in the final diagnosis. Close follow-up observation is needed in the presence of risk factors such as surface nodularity.

Key words: Biopsy; Stomach neoplasms; Gastritis

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IFND, indefinite for neoplasia/dysplasia

AG, atypical gland/cellular atypia

RA, reactive/regenerative atypia

MALToma, mucosal-associated lymphoid tissue lymphoma

OR, odds ratio

CI, confidence interval

INTRODUCTION

Gastric cancer is the most common gastrointestinal tumor in East Asia including Korea.[1,2] A National Cancer Screening Program for adults over 40 years old was implemented in Korea because of the high prevalence of gastric cancer.[3] The increase in the number of screening endoscopies has increased the rate of early diagnosis of gastric cancer and pre-cancerous lesions. A biopsy is usually performed during endoscopy in lesions suspicious for adenoma or carcinoma. However, the histologic diagnosis based on forceps biopsy is not always consistent from resected specimens. Although biopsy is the most reliable diagnostic method, it is often insufficient for a confirmed diagnosis.[4,5] When endoscopists perform an acute forceps biopsy, the probability of a diagnosis of gastric cancer is 81.3% for the first biopsy, 94.9% for the second biopsy, and 98.3% for the third biopsy.[6] In some cases showing cellular architectural distortion and/or nuclear atypia, it is difficult to discriminate reactive changes from neoplasia. These lesions are classified as Category 2 (indefinite for neoplasia/dysplasia, IFND) according to the revised Vienna classification.[7]

IFND can be subcategorized into atypical gland/cellular atypia (AG) or reactive/regenerative atypia (RA) in pathologic reports.[8,9] In general, AG is similar to dysplasia, whereas RA resembles inflammatory changes. However, there is no clear boundary between the two categories. Clinical guidelines recommend re-biopsy in cases classfified as IFND in the pathologic report.[7] A re-biopsy needs to be performed within 3-6 months based on the endoscopic and pathologic findings and through close communication between the pathologist and the endoscopist.[10]

Gastric adenoma is a precancerous lesion that can show various clinical courses. Certain lesions develop into gastric carcinoma, whereas other lesions remain stable and do not show changes for a long time.[11] High-grade adenoma/dysplasia is likely to coexist with carcinoma or tends to develop into carcinoma, and complete endoscopic or surgical resection is recommended in these cases.[11-14] The predictive risk factors for carcinoma in

gastric IFND were reported previously.[10,15-19] A recent study analyzed gastric AG to identify predictive risk factors for malignancy.[20] In clinical practice, RA is a more frequent finding than AG. However, there are analyzing the clinical implications of RA. The aim of this study was to analyze the clinical implications and risk factors for high-grade adenoma or carcinoma in patients with biopsy-proven gastric RA.

METHODS

Subjects

The study included patients who underwent biopsy for suspected gastric neoplasia duing endoscopy and were diagnosed as RA at Jeju National University Hospital between January, 2015, and December, 2016. Patients who were referred from outside clinics were diagnosed as RA based on the review of biopsy results by pathologists at Jeju National University Hospital. The final diagnosis of RA was confirmed based on results of follow-up endoscopy and biopsy performed before December, 2018. The baseline characteristics of the patients and the endoscopic and pathologic reports leading to the diagnosis of RA were obtained by review of electronic medical records and endoscopic images.

Exclusion criteria were as follows: 1) no definite findings of RA in the pathologic review (atypical glands, adenoma, and gastritis, etc.); 2) lost to follow-up; 3) no re-biopsy during follow-up endoscopy; 4) biopsy of the post-gastrectomy anastomosis site; 5) biopsy of the previous endoscopic resection site; 6) surgery for synchronous malignancy during the diagnosis of RA; and 7) insufficient medical records and/or endoscopic imagnes.

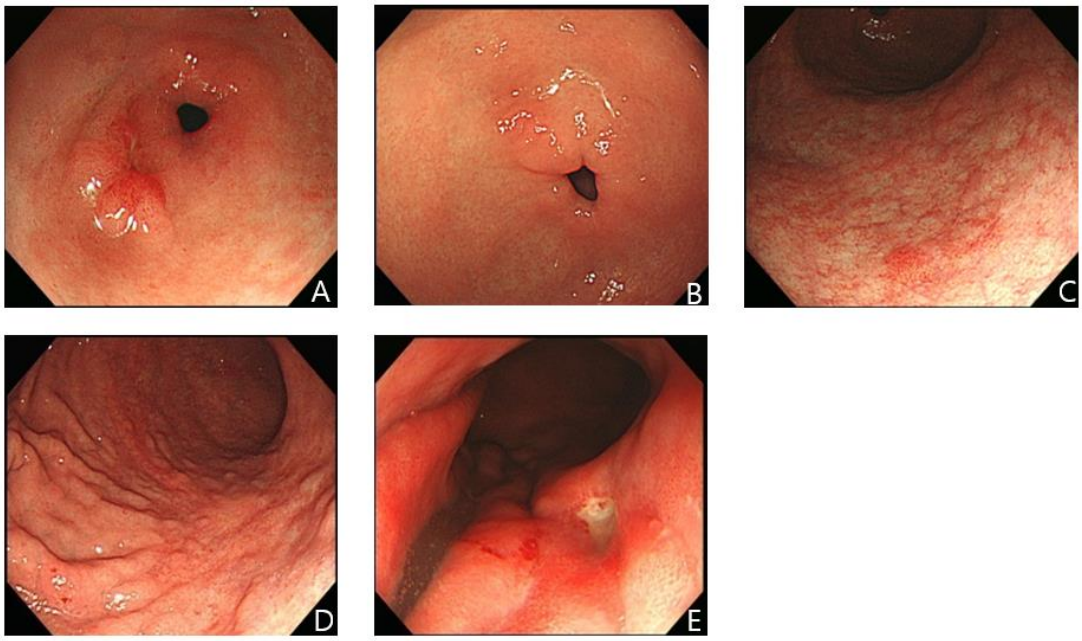
This study was approved by the Institutional Review Board of Jeju National University Hospital (IRB No. 2019-07-024) and was performed according to the Declaration of Helsinki. Patient consent was omitted because of the retrospective nature of the study.

Endoscopic factors

Three endoscopes were used during the study period (GIF-Q260/H290/HQ290; Olympus Optical Co., Ltd., Tokyo, Japan). One endoscopist (SY Na) with 10 years of endoscopic experience who performed >1,000 gastroscopies reviewed the endoscopic images. The endoscopist reviewed the images three times to minimize intra-observer variation.

Endoscopic findings included the size and characteristics of the lesions. The variables of the endoscopic findings included size, gross types, mucosal redness, mucosal nodularity, erosion, ulceration, scar, and location of the lesions (Fig. 1). Gross types were classified according to the Paris classification as elevated (type 0-I, 0-IIa), flat (type 0-IIb), and depressed (type 0-IIc, 0-III).[21] Redness was defined as a red color change of the mucosal surface, and nodularity was defined as an irregular or nodular shape of the mucosal surface.[22] The location of the lesion was divided into the upper portion (1/3), the middle portion (1/3), and the lower portion (1/3).[23]

Figure 1. Endoscopic findings of regenerative atypia. (A) Nodularity. (B) Redness. (C) Erosion. (D) Ulcer. (E) Scar.



Histopathological factors

The classification of epithelial neoplasia was performed following the revised Vienna classification, and Category 2 (IFND) was subcategorized into RA and AG (Table 1).[10,20] Reactive changes show features similar to dysplasia such as mucin depletion, nuclear hyperchromasia, and pseudostratification due to inflammation.[24] The balance between the degree of atypia and inflammation is important. RA was defined as inflammation that was similar to, or higher than, the degree of atypia. AG was defined as atypia exceeding the degree of inflammation (Fig. 2).[24]

Variables of histopathologic findings included the degree of atrophy (-, 1+, 2+, and 3+), degree of intestinal metaplasia (-, 1+, 2+, and 3+), and presence of *Helicobacter pylori* (-, 1+, 2+, and 3+). *Helicobacter pylori* infection was detected by Giemsa staining.

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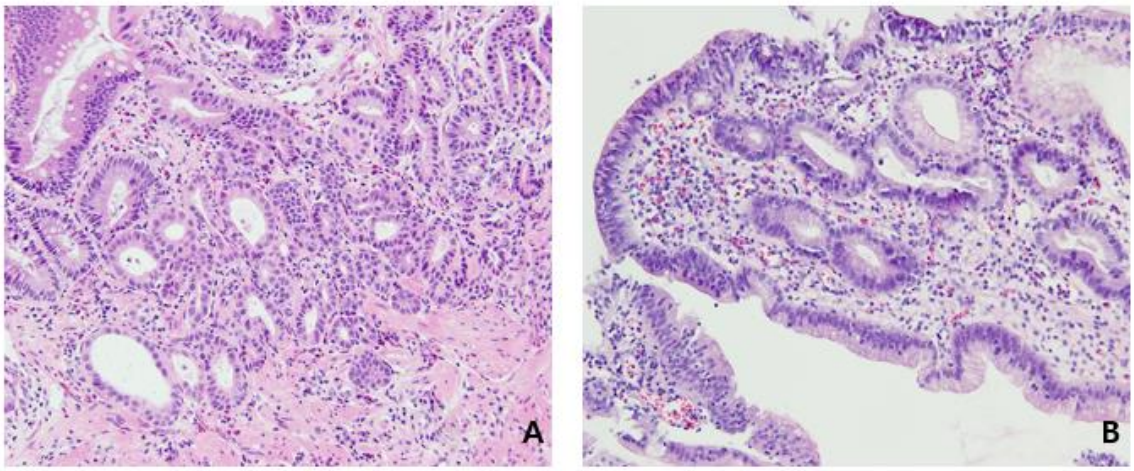
Table 1. Modified classification of gastric epithelial neoplasia according to the revised Vienna classification[7]

Category	Diagnosis
1	Negative for neoplasia
	Indefinite for neoplasia
2	Reactive/regenerative atypia
	Atypical gland/cellular atypia
3	Mucosal low grade neoplasia (low grade adenoma/dysplasia)
	Mucosal high grade neoplasia
	High grade adenoma/dysplasia
4	Non-invasive carcinoma (carcinoma in situ)
	Suspicious for invasive carcinoma
	Intramural carcinoma
5	Submucosal invasion by carcinoma

Figure 2. Typical pathologic findings of atypical gland and regenerative atypia in cases indefinite for neoplasia/dysplasia. (A) Atypical gland showing findings similar to those of dysplasia with well differentiated type. (B) Regenerative atypia predominantly shows inflammatory infiltration rather than dysplastic features.



Statistical analyses

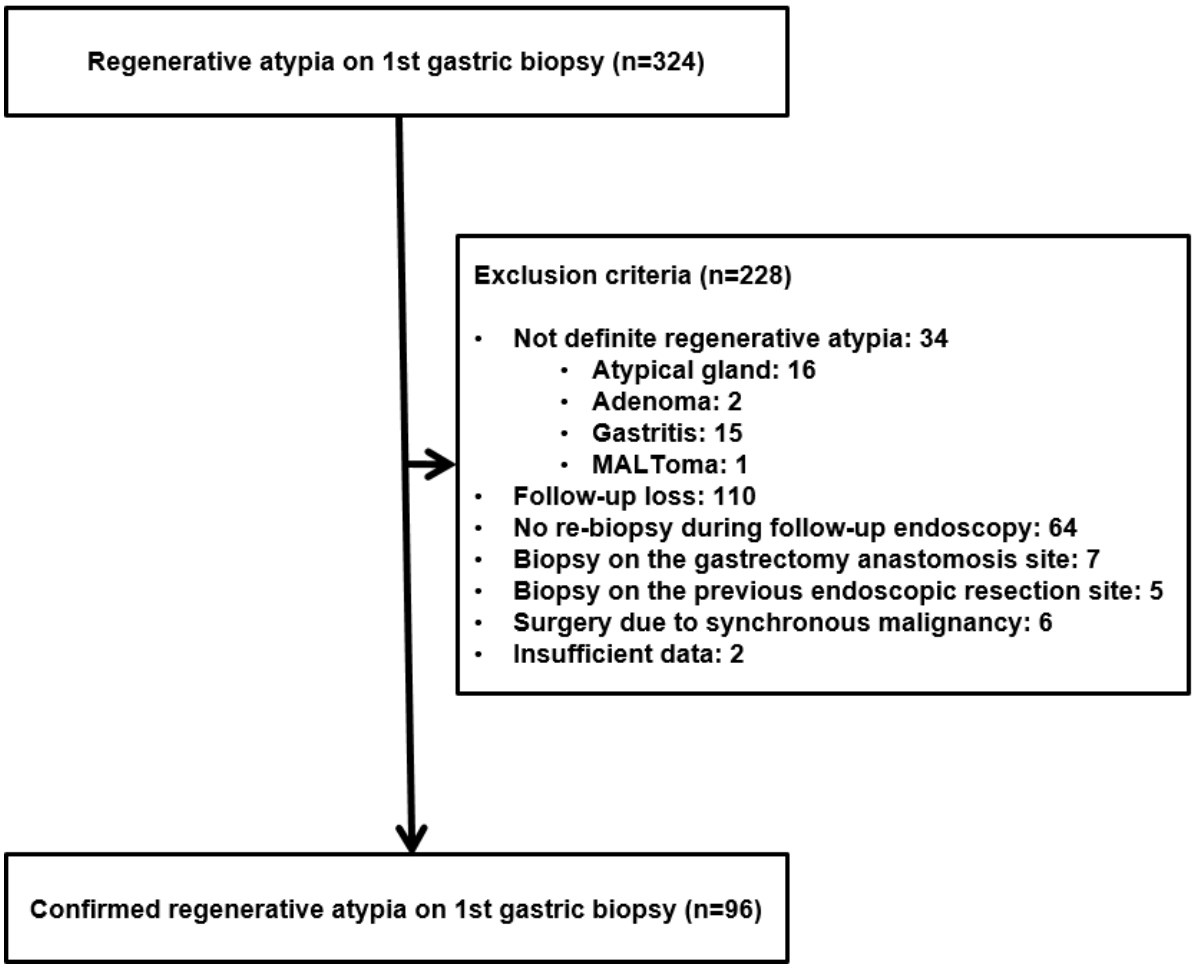
To identify risk factors for high-grade dysplasia or carcinoma of RA, the lesions were divided into two subgroups according to the final diagnosis and the revised Vienna classification as follows: the high-grade dysplasia/carcinoma (category 4/5) group and the benign lesions (category 1/3) group. The chi-square test, Fisher's exact test, and Student's t-test were used to identify significant variables in the univariate analysis. Multiple logistic regression analyses were used for the multivariate analysis including age, sex, and variables confirmed as $p < 0.05$ in the univariate analysis. Statistical analyses were performed using SPSS 18.0 (IBM Corp., Armonk, NY, USA). A p value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

During the study period, 20,271 gastroscopic examinations were performed at Jeju National University Hospital; 54.4% (11,026/20,271) of the patients were men. Of these, 324 lesions were reported as RA in 296 patients (1.46%), and 67.9% (201/296) of them were men. A total of 232 lesions were excluded from the pathologic review, including 34 cases of AG/dysplasia/gastritis/mucosa-associated lymphoid tissue lymphoma, 110 cases of follow-up loss, 64 cases who underwent endoscopy but no biopsy, 7 cases of biopsy at the post-gastrectomy anastomosis site, 5 cases of biopsy at the previous endoscopic resection site, 6 cases of surgery for synchronous malignant lesions when RA was diagnosed, and 2 cases of insufficient medical records and/or endoscopic images. Finally, 96 lesions diagnosed as RA were analyzed (Fig. 3).

Figure 3. Flowchart of the study subjects. MALToma, Mucosal-associated lymphoid tissue lymphoma.



The endoscopic and pathologic results of 96 lesions examined until December, 2018, were included in the study. The median time to the second biopsy was 137 days (range, 14–1268 days). Endoscopy and re-biopsy were serially performed when the second biopsy result was reported as IFND. Most of the RA cases identified in the first biopsy received a definitive diagnosis on the second biopsy; however, 11.5% (11/96) of cases required more than three follow-up endoscopies and re-biopsy because of persistent IFND pathologic findings (Fig. 4). None of the patients underwent diagnostic endoscopic resection or surgery. The final diagnosis was high-grade dysplasia or carcinoma in 14 patients, low-grade dysplasia in 9 patients, and gastritis in 73 patients (Fig. 5).

Figure 4. Flowchart of the final diagnosis of 96 patients with regenerative atypia.

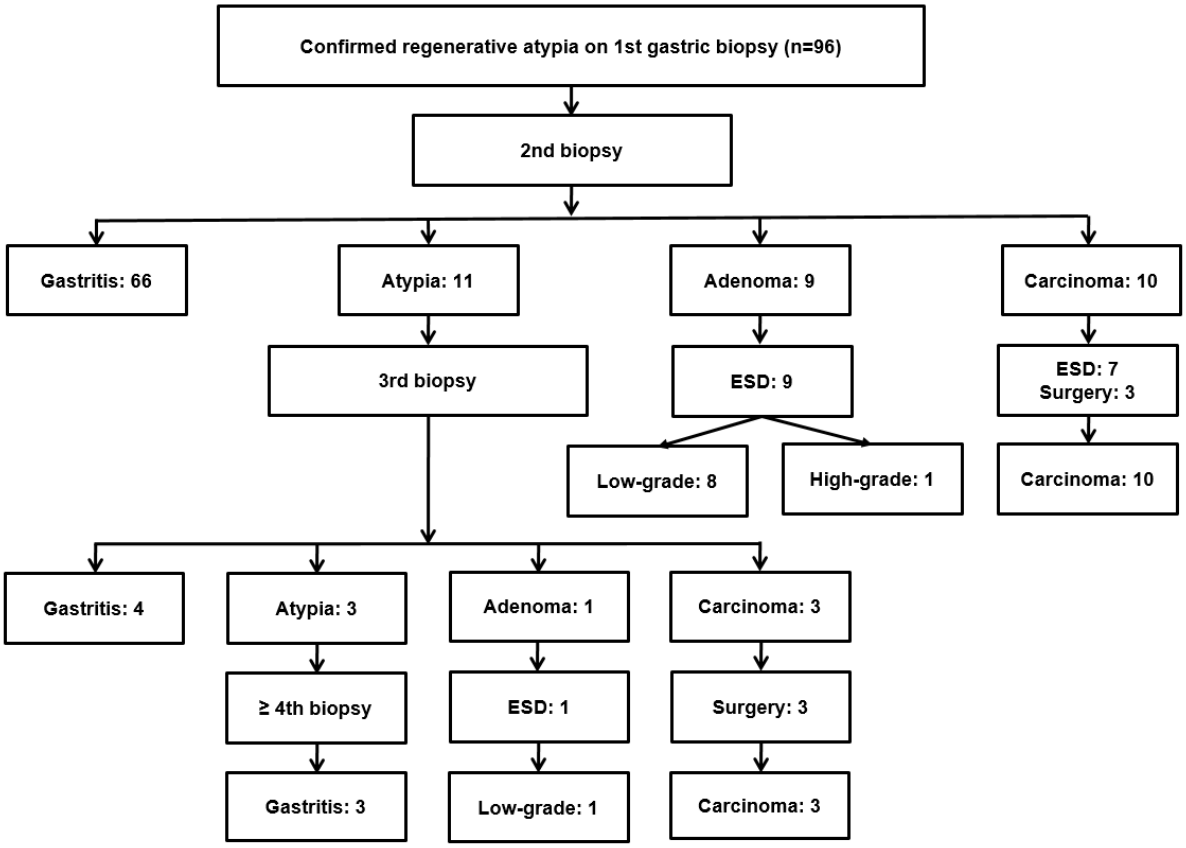
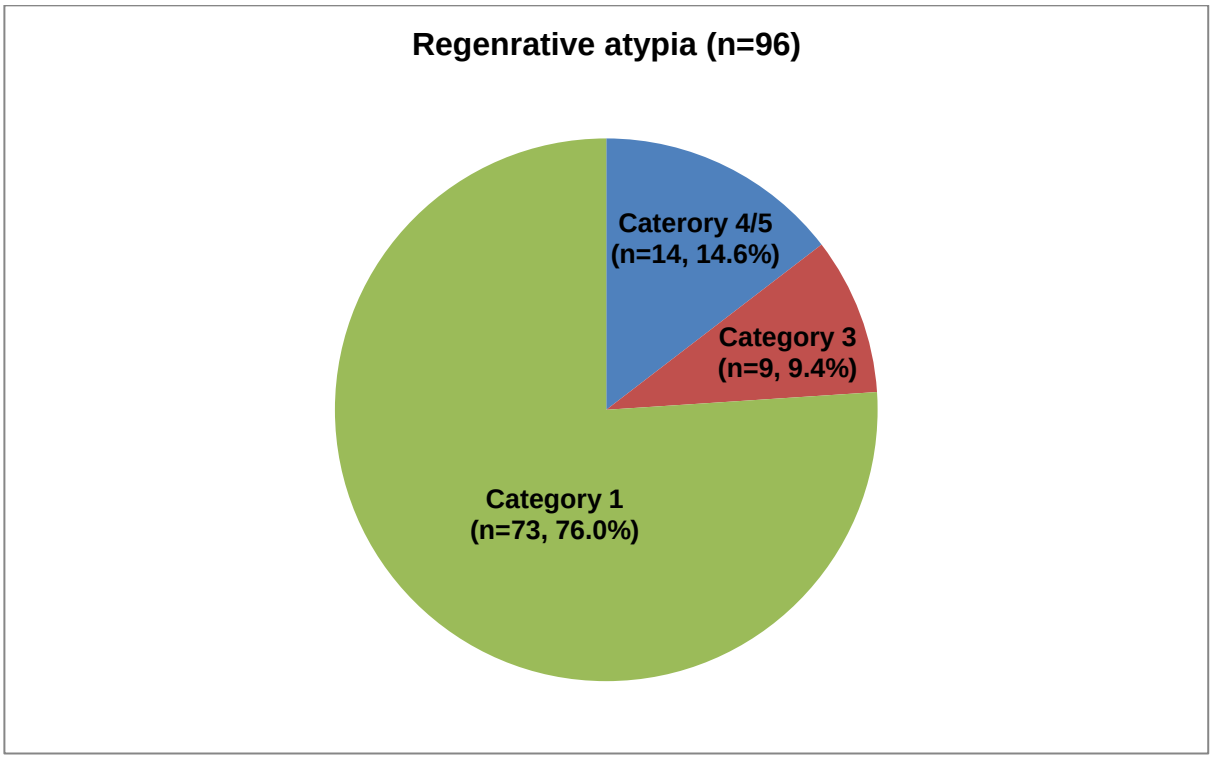


Figure 5. Final diagnosis according to the revised Vienna classification. Category 5, submucosal invasion by carcinoma; Category 4, high-grade dysplasia; Catero3, low-grade dysplasia; and Category 1, negative for neoplasia.



The mean age of the three groups at the time of the final diagnosis was 63.5 ± 11.7, 63.6 ± 13.3, and 60.9 ± 11.3 years, and there was no significant difference between the three groups. The mean size of the lesions was 9.6 ± 5.1, 10.0 ± 6.0, and 9.2 ± 6.7 mm in each of the groups, and there was no significant difference between the three groups. The most common gross type was depressed morphology, accounting for 56.3% of cases, and the most common location of the lesion was the lower portion, accounting for 66.7% of cases. In 81.2% (78/96) of the lesions, the endoscopic features detected were redness, nodularity, erosion, ulcer, and scar. The most common finding was redness, which was observed in 45.8% of patients. Most lesions showed atrophic changes (80.2%), and intestinal metaplasia was detected in 51.0% of cases according to the pathologic reports. Giemsa staining was positive for *Helicobacter pylori* in 30.2% of the patients (Table 2).

Table 2. Baseline characteristics of patients with regenerative atypia according to the final diagnosis and the revised Vienna classification. Category 5, submucosal invasion by carcinoma; Category 4, high-grade dysplasia; Catero3, low-grade dysplasia; and Category 1, negative for neoplasia.

Characteristics	Category 4/5 (n=14)	Category 3 (n=9)	Category 1 (n=73)	Total (n=96)
Age, years	63.5±11.7	63.6±13.3	60.9±11.3	61.6±11.7
Male sex	12 (85.7%)	9 (100.0%)	48 (65.8%)	69 (71.9%)
Lesion size, mm	9.6±5.1	10.0±6.0	9.2±6.7	9.4±6.4
Gross type				
Elevated	1 (7.7%)	4 (40.0%)	22 (29.3%)	26 (27.1%)
Flat	4 (30.8%)	2 (20.0%)	11 (14.7%)	16 (16.7%)
Depressed	6 (46.2%)	4 (40.0%)	25 (33.3%)	54 (56.3%)
Nodularity	9 (69.2%)	4 (40.0%)	10 (13.3%)	23 (24.0%)
Redness	9 (69.2%)	5 (50.0%)	30 (40.0%)	44 (45.8%)
Erosion	1 (7.7%)	3 (30.0%)	20 (26.7%)	24 (25.0%)
Ulcer	5 (38.5%)	0	23 (30.7%)	28 (29.2%)
Scar	2 (15.4%)	1 (10.0%)	8 (10.7%)	11 (11.5%)
Location				
Lower third	4 (30.8%)	5 (50.0%)	56 (74.7%)	64 (66.7%)
Middle third	7 (53.8%)	5	17 (22.7%)	28 (29.2%)
Upper third	2 (15.4%)	0	2 (2.7%)	4 (4.2%)
Gastric atrophy	9/10 (90%)	9/10 (90%)	58/72 (80.6%)	77 (80.2%)
Intestinal metaplasia	12 (92.3%)	7 (70.0%)	32 (42.7%)	49 (51.0%)
H. pylori positive	3 (23.1%)	2 (20.0%)	24 (32.0%)	29 (30.2%)

Risk factors for high-grade dysplasia or carcinoma in regenerative atypia

The baseline characteristics of the 14 patients with high-grade dysplasia or carcinoma and the features of RA lesions were analyzed. Univariate analysis identified the following significant risk factors for high-grade dysplasia or carcinoma: nodularity [odds ratio (OR), 8.7; 95% confidence interval (CI), 2.5–30.1; p = 0.001], redness (OR, 3.5; 95% CI, 1.02–2.2; p = 0.046), upper third portion lesion (OR, 4.6; 95% CI, 1.4–15.2; p = 0.012), and intestinal metaplasia (OR, 16.6; 95% CI, 2.1–133.0; p = 0.008) (Table 3). Age, sex, and size of lesions were not show statistically significant factors. In age and sex adjusted multivariate analyses, only nodularity was identified as a significant risk factor (OR, 6.4; 95% CI, 1.5–26.4; p = 0.01) (Table 4).

Table 3. Risk factors for gastric high-grade dysplasia or carcinoma in cases of regenerative atypia.

Characteristics	High-grade dysplasia or carcinoma (n=14)	Benign lesions (n=82)	p-value
Age (≥ 65 years)	7 (50.0%)	30 (36.6%)	0.34
Male sex	12 (85.7%)	57 (69.5%)	0.34
Lesion size (≥ 10 mm)	6 (42.9%)	27 (32.9%)	0.47
Gross type			0.14
Elevated	1 (7.1%)	25 (30.5%)	
Flat	4 (28.6%)	12 (14.6%)	
Depressed	9 (64.3%)	45 (54.9%)	
Nodularity	9 (64.3%)	14 (17.1%)	<0.001
Redness	10 (71.4%)	34 (41.5%)	0.046
Erosion	1 (7.1%)	23 (28.0%)	0.18
Ulcer	5 (35.7%)	23 (28.0%)	0.56
Scar	2 (14.3%)	9 (11.0%)	0.66
Location			0.008
Antrum	5 (35.7%)	59 (72.0%)	
Body	9 (64.3%)	23 (28.0%)	
Gastric atrophy	13 (92.8%)	64 (78.0%)	0.199
Intestinal metaplasia	13 (92.9%)	36 (43.9%)	0.001
H. pylori positive	3 (21.4%)	26 (31.7%)	0.54

Table 4. Risk factors for gastric high-grade dysplasia or carcinoma in cases of regenerative atypia identified by univariate and multivariate analyses.

Risk factors	Univariate analysis		Multivariate analysis	
	p-value	OR (95% CI)	p-value	OR (95/5 CI)
Nodularity	0.001	8.7 (2.5 - 30.1)	0.01	6.4 (1.5 - 26.4)
Redness	0.046	3.5 (1.02 - 2.2)	0.33	2.1 (0.5 - 9.1)
Corporal lesion	0.012	4.6 (1.4 - 15.2)	0.29	2.4 (0.5 - 11.7)
Intestinal metaplasia	0.008	16.6 (2.1 - 133.0)	0.07	8.1 (0.8 - 83.4)

DISCUSSION

An endoscopic biopsy is performed to obtain a definitive diagnosis in cases of suspected neoplasm detected during gastroscopy. Although tissue biopsy is the most reliable diagnostic method during endoscopy, it does not always provide a definitive diagnosis. Diagnostic discrepancies occur for the following reasons: First, biopsy samples do not represent the entire lesion, which may show various pathologic features depending on its location. Second, obtaining adequate samples consistently is difficult because the status of the patient and the position, depth, and shape of the lesion affect biopsy sampling during endoscopic examination. Finally, the amount of biopsy tissue collected can affect the pathologic results.[25] Therefore, biopsy results are often reported as IFND, which indicates a failure to clearly distinguish a benign lesion from a malignant lesion. AG and RA are subcategories of IFND that describe a benign lesion such as gastritis or a neoplasm such as dysplasia or carcinoma that cannot be distinguished. Distinguishing between neoplasm and gastritis is difficult when a small-volume tissue sample is obtained during biopsy because the pathologic features of the lesion cannot be evaluated completely.[23,26] Although IFND is an indication for re-biopsy, there is no clear consensus on this issue.[7] Kwon et al. suggested that a follow-up endoscopic re-examination should be performed at 3–6 months in cases of IFND.[10] In this study, the second follow-up endoscopy with re-biopsy was performed at a median period of 3–4 months following general recommendations.

In this study, RA was diagnosed in 1.46% of the subjects, and the mean age was 61.6 years. In a previous study, 1.04% of patients who underwent gastric endoscopic biopsy were diagnosed with IFND including both AG and RA, and the median age was 59 years, which is consistent with the present results.[10] Although IFND is not a common clinical finding, it indicates the possibility of adenoma/dysplasia or carcinoma; therefore, a diagnosis of IFND needs to be followed-up with caution. However, many endoscopists overlook this result, as indicated in the present study, in which approximately one-third of patients did not undergo

follow-up endoscopy. The clinical implications of AG and RA remain to be established. Although AG and RA show similar features, inflammation is more common in RA than in AG. A Spanish single center study reported the microscopic and histopathologic results of the atypical gastric epithelium. Of 44 patients, 3 (2.7%) received a final diagnosis of early gastric cancer, and most of them were intestinal metaplasia.[27] However, several recent Korean studies reported that approximately 25% of subjects with IFND are diagnosed as carcinoma.[10,15-19] Another study reported that approximately 75% of IFND patients are diagnosed with carcinoma including only AG.[20] Despite the variability in the reported risk of carcinoma in cases of IFND, which may be attributed to differences in methodology, AG is associated with a higher risk of malignancy than RA. To the best of our knowledge, there are no studies addressing RA alone, and its clinical implications have not been clarified until now. In this study, neoplasm was diagnosed in approximately 25% of patients with RA, and two-thirds of these cases were high-grade adenoma or carcinoma. A biopsy does not provide a final diagnosis, and in cases with insufficient biopsy specimens, a definitive diagnosis is difficult. In this study, the pathologists' tendency, intuition, and experience may be responsible for upgrading in one-quarter of the lesions. Approximately one-third of the patients who were initially diagnosed with RA did not undergo follow-up endoscopy, which can be attributed to the patient’s compliance or the physician’s decision. However, most of the patients who did not undergo re-biopsy during the follow-up endoscopy had lesions that showed improvement or were less likely to require biopsy. Thus the probability of neoplasm among patients with RA is lower in the clinical setting than that observed in the present study. In this study, 15% of patients with RA received a final diagnosis of neoplasm including patients who underwent follow-up endoscopy but not biopsy, and 9% of patients with RA were diagnosed with high-grade adenoma and carcinoma. However, differences in the probability of neoplasm do not affect the analysis of risk factors for high-grade adenoma or carcinoma according to endoscopic or pathologic findings.

Endoscopic findings are important when they are interpreted as IFND according to

pathology. The risk factors for malignant tumors in IFND include size >1 cm, depressed gross type, redness, nodularity, isolated lesion, old age, and spontaneous bleeding.[10,17,18] Lesion size >1 cm, depressed gross type, and nodularity are risk factors for malignant tumors in AG.[20] Pathologic variables such as atrophy, metaplasia, and *H. pylori* are not risk factors for adenocarcinoma. In this study, among endoscopic findings, nodularity was the only significant risk factor for high-grade dysplasia or carcinoma in RA. Consistent with previous studies, none of the pathologic variables was identified as a significant risk factor. Endoscopic findings are important for identifying malignant tumors in patients diagnosed as IFND. However, lesion size was not a significant factor in the present study, which differs from previous findings. This may be associated with the large size of benign ulcerative lesions in RA when a biopsy is performed during the course of healing (regeneration). Small-sized type IIc lesions, which appear to be simple erosions or ulcerated type III lesions, have both low positive and negative predictive values for carcinoma. Therefore, close communication between endoscopists and pathologists is important for the interpretation of serial biopsies in cases of suspected carcinoma based on endoscopic findings when the pathologic interpretation is IFND.

Limitations

First, this study had a retrospective design, which may be associated with selection bias. However, because the detection rate of RA is low and not all patients require follow-up endoscopy, prospective studies with a long-term follow up and a large number of patients are difficult to perform.

Second, inter-observer variation between endoscopists and pathologists may have occurred. However, one endoscopic specialist reviewed the endoscopic findings three times and one pathologist reviewed the first pathologic findings without knowledge of the final pathologic results to minimize inter-observer variation.

Third, endoscopic findings were analyzed using conventional endoscopic methods. Analysis of the endoscopic findings using narrow-band or chromoendoscopic imaging may have improved the results.

Finally, histopathological findings were based on hematoxylin and eosin staining, and immunohistochemical staining was not performed. A pathological study from Japan reported that positivity for p53 and Ki67 in biopsy samples from patients with IFND was indicative of carcinoma.[28]

CONCLUSION

Biopsy is the most reliable method for diagnosing lesions during endoscopy. However, biopsy samples do not represent the entire lesion, which may lead to discrepancy with the final diagnosis, and gastric IFND is associated with the risk of malignant lesions. The detection rate of RA in screening gastroscopy was 1.5% in our study, despite the fact that RA is more common than AG in the clinical setting. However, results need to be interpreted with caution because RA can develop into high-grade adenoma or carcinoma. Although most cases diagnosed as RA in the first biopsy were finally diagnosed as gastritis, approximately 25% of cases were diagnosed as neoplasms, of which two-thirds were high-grade adenoma or carcinoma. Approximately one-third of the RA cases in the present study population were not followed up. The present results suggest that in RA lesions with nodularity, patient follow-up and a timely second biopsy are important. On the other hand, in cases of RA without risk factors, a second biopsy can be performed after a longer interval.

IMPLICATIONS FOR INTERNAL MEDICINIE

A diagnosis of IFND in the pathologic report raises concerns regarding the need for follow-up endoscopy and serial biopsy as well as their timing. In cases diagnosed as AG, endoscopists usually recommend follow-up because AG has a relatively high malignant potential. However, in cases of RA, establishing a follow-up or therapeutic plan is difficult because the clinical implications are not clear. This study is expected to help endoscopic physicians understand the clinical implications of RA to design an appropriate therapeutic strategy in cases diagnosed as RA based on biopsy results.

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국 문 요 약

배경 및 연구목적: 비록 위 내시경 검사 동안 많은 조직 검사가 이루어 지고 있지만, 재생성 비정형으로 확인 되는 경우 그 임상적 의미와 치료적 계획에 대해서는 아직까지 보고된 바가 없다. 본 연구는 검진 내시경에서 생검 겸자를 이용하여 시행한 조직검사에서 재생성 비정형으로 판독 된 경우 그 임상적 의미와 고등급 선종 또는 선종에 대한 위험 인자를 분석하고자 한다.

대상 및 방법: 2015년 1월부터 2016년 12월까지 2년 동안 제주대학교병원에서 시행한 위 내시경 조직 검사에서 재생성 비정형으로 판독된 296명의 환자를 대상으로 하였다. 이들 병변에 대해 후향적으로 의무기록, 병리 소견, 내시경 소견 등을 분석하였다.

결과: 전체 내시경 시행 환자에서 재생성 비정형의 진단율은 1.46% (296/20,271)였다. 최초 조직검사에서 재생성 비정형으로 진단된 330 개의 병변 중 최종 96 개의 병변을 분석하였다. 최종 진단에서 신생물은 약 1/4 이었다. 고등급 선종과 선암이 14 명(14.6%)이었고, 저등급 선종이 9 명(9.4%)이었다. 단변량 분석에서는 결절성 표면, 발적성 표면, 위체부 병변, 장상피 화생이 고등급 선종 또는 선종의 의미있는 위험인자였다. 성별과 나이를 보정한 다변량 분석에서는 오직 결절성 표면만이 의미 있는 위험인자로 확인 되었다 ($p = 0.01$; odds ratio, 6.4; 95% confidence interval, 1.5–26.4).

결론: 대다수 재생성 비전형의 최종 진단은 위염 또는 저등급 선종의 양성

병변이었다. 하지만, 재생성 비전형은 최종적으로 고등급 선종 또는 선암으로 진단이 바뀔 가능성이 있기 때문에 주의가 필요하다. 특히 결절성 표면과 같은 위험인자를 가지고 있는 재생성 비전형에서는 더욱 계획적이고 주의 깊은 추적 관찰이 요구된다.

중심단어: 생검; 위 신생물, 위염