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Follow-up for Patients with Intestinal Metaplasia Restricted to the Antrum

Antrumda Sınırlı İntestinal Metaplazisi Olan Hastaların Takibi

Deniz Öğütmen Koç[1], Sadettin Hülagü[2], Yeşim Saliha Gürbüz[3], Altay Çelebi[2], Ali Erkan Duman[2], Tanyeli Güneyligil Kazaz[4]

[1]University of Health Sciences Turkey, Gaziosmanpaşa Training and Research Hospital, Clinic of Gastroenterology, İstanbul, Turkey
[2]Kocaeli University Faculty of Medicine, Department of Gastroenterology, İzmit, Turkey
[3]İstinye University Faculty of Medicine, Department of Pathology, İstanbul, Turkey
[4]Gaziantep University Faculty of Medicine, Department of Biostatistics, Gaziantep, Turkey

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ABSTRACT

Objective: Guidelines recommend endoscopic surveillance for patients with extensive atrophy/intestinal metaplasia (IM), but follow-up is not recommended for patients with atrophy/IM restricted to the antrum. We evaluated the risk of neoplastic lesions in patients with antrum-restricted IM to determine whether surveillance endoscopy is necessary.

Methods: Overall, 117 patients with antrum-restricted IM diagnosed within the past 10 years underwent surveillance endoscopy. The gastric biopsy specimens were evaluated for atrophy, IM, and dysplasia.

Results: We enrolled 117 patients. Surveillance endoscopy was performed at a median (interquartile range) of 7.2 years (5.9-8.7 years) after the initial diagnosis of IM. On surveillance endoscopy, 27.4% of patients exhibited progression in their IM grade, whereas 25.6% had atrophy progression, and 33.3% had dysplasia progression. High-grade dysplasia and gastric cancer (GC) were detected in four and two patients, respectively. The annual incidence of GC in patients with antrum-restricted IM was 0.17%. IM grade and type regressed in 29.9% and 38.5% of patients, respectively. Most patients with progressive IM grade, IM type, and dysplasia on surveillance endoscopy had Operative Link on Gastritis Assessment (OLGA) stage 3-4 (p=0.0001, p=0.008, and p=0.0001, respectively), and most patients with progressive atrophy and dysplasia had Operative Link on Gastric IM (OLGIM) stage 3-4 (both p=0.001).

Conclusion: Patients with IM restricted to the antrum are at risk for neoplastic lesions and require endoscopic surveillance, contrary to existing recommendations. Premalignant lesions can exhibit both progression and regression. Therefore, a patient-specific surveillance program based on OLGA and OLGIM might be appropriate.

Keywords: Gastric cancer, intestinal metaplasia, surveillance endoscopy

ÖZ

Amaç: Kılavuzlar, yaygın atrofi/intestinal metaplazisi (İM) olan hastalar için endoskopik sürveyansı önermektedir, ancak antrumla sınırlı İM/atrofisi olan hastalar için takip önerilmemektedir. Bu çalışmada, antrum kısıtlı İM olan hastalarda sürveyans endoskopisinin gerekli olup olmadığını belirlemek için neoplastik lezyon riskini değerlendirdik.

Yöntemler: Son 10 yıl içinde antrum kısıtlı İM tanısı alan 117 hastaya sürveyans endoskopisi yapıldı. Mide biyopsi örneklerinde İM, atrofi, ve displazi değerlendirildi.

Bulgular: Çalışmamıza 117 hastayı dahil ettik. Sürveyans endoskopi, İM'nin ilk tanısından sonra medyan (çeyrekler arası aralık) 7,2 (5,9-8,7 yıl) sonra yapıldı. Gözetim endoskopisinde, hastaların %27,4'ü İM grade ilerlemesi gösterirken, %25,6 atrofi ilerlemesi ve %33,3 displazide ilerleme gösterdi. Dört hastada yüksek dereceli displazi ve iki hastada mide kanseri (MK) saptandı. Antrum kısıtlı İM olan hastalarda yıllık MK insidansı %0,17 idi. İM grade

ORCID IDs of the authors: D.Ö.K. 0000-0003-2738-625X; S.H. 0000-0001-6659-1286; Y.S.G. 0000-0002-4278-8241; A.Ç. 0000-0003-2864-7124; A.E.D. 0000-0002-7093-2503; T.G.K. 0000-0002-4191-1244.

Corresponding Author/Sorumlu Yazar: Deniz Öğütmen Koç, E-mail: drdenizkoc@gmail.com

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ÖZ

ve tipi hastaların sırasıyla %29,9 ve %38,5'inde geriledi. Sürveyans endoskopisinde progresif İM grade, İM tip ve displazisi olan hastaların çoğunluğu OLGA evre 3-4 (sırasıyla; p=0,0001, p=0,008 ve p=0,0001) ve progresif atrofi ve displazili hastaların çoğunluğu OLGİM evre 3-4'e sahipti (her ikisi de; p=0,001).

Sonuç: Antrumla sınırlı İM'li hastalar neoplastik lezyon gelişimi açısından risk altındadır ve önerilerin aksine endoskopik gözetim gerektirir. Premalign lezyonlar hem ilerleme hem de gerileme gösterebilir. OLGA ve OLGİM'ye dayalı hastaya özel bir gözetim programı uygun olabilir.

Anahtar kelimeler: Mide kanseri, intestinal metaplazi, surveyans endoskopi

INTRODUCTION

Gastric cancer (GC) is one of the most common cancers globally and has a poor prognosis, especially in the advanced stages of the disease. Nevertheless, screening and monitoring patients at risk of GC can facilitate early detection and treatment and reduce mortality (1).

Intestinal-type gastric adenocarcinoma is the final stage of a multi-stage disease process known as the Correa cascade, which includes inflammation, atrophy, intestinal metaplasia (IM), dysplasia, and carcinoma (2). IM is a precancerous lesion characterized by replacement of the epithelium in the oxyntic or antral mucosa with intestinal epithelium. IM is classified as complete (small-intestine type) or incomplete (colonic type; thought to be the most advanced stage of IM) based on the histologic characteristics and type of mucinous material secreted (3). Notably, patients with gastric IM, along with other precancerous gastric lesions, are better monitored in Asia than in Europe (4). New guidelines for screening programs were published recently in Western countries (5,6). However, a study conducted in the United States revealed that 78% of endoscopists were not aware of the guidelines for the surveillance and management of IM (7). Notably, the best strategy for reducing mortality in patients at high risk of GC is diagnosis and surveillance of precancerous gastric lesions (8,9). The recently presented guidelines recommend endoscopic surveillance for patients with extensive atrophy and/or IM (5,6,10). However, no scheduled endoscopic and histologic surveillance was recommended for patients with antrum-restricted IM and atrophy (6,11). However, to the best of our knowledge, no comprehensive study has been conducted regarding the follow-up of patients with premalignant gastric lesions restricted to the antrum.

Our study evaluated the risk of neoplastic lesions in patients with antrum-restricted IM to determine whether surveillance endoscopy is necessary.

METHODS

For this single-center study, we invited patients with antrum-restricted IM that had been histologically confirmed with untargeted biopsy sampling in the past 10 years to undergo targeted biopsy sampling during surveillance endoscopy. We selected patients with at least 4 years between the initial and surveillance endoscopies. Overall, 607 patients were identified. We excluded patients with peptic ulcers, Barrett's esophagus, GC, other cancers, and prior gastric resection. In addition, we excluded patients whose initial gastric biopsy did not meet the minimum quality criteria (e.g., paraffin block for a reassessment of the antrum mucosa) and those who could not be reached by telephone. We called up 182 patients and invited them to undergo surveillance endoscopy; of these, 117 agreed and were included in the study. During the appointment, patients were asked about their smoking history, use of non-steroidal anti-inflammatory drugs (NSAIDs), use of proton pump inhibitors (PPIs), diagnosis and treatment of *Helicobacter pylori (H. pylori)* infection, and family history of GC. For consistency, all esophagogastroduodenoscopy and biopsy procedures were performed by a single physician (D.O.K.).

For optimal assessment of the severity and distribution of premalignant gastric lesions, biopsies were obtained from five standardized intragastric locations during surveillance endoscopy according to a predetermined protocol (12) (Figure 1). Overall, the following 12 biopsies were obtained: 4 from the pylorus 2-3 cm proximal to the antrum, 2 from the opposite walls of the incisura angularis, 2 from the corpus minor curvature, 2 from the corpus greater curvature, and 2 from the cardia. Additional targeted biopsies were obtained of visible abnormalities and lesions in the stomach, if present.

IM was graded according to the visual analog scale of the updated Sydney system (0: absent; 1: mild; 2: moderate; 3: marked). Mucosal atrophy score was evaluated on a four-level scale [no atrophy (0%) score=0; mild atrophy (1-30%) score=1; moderate atrophy (31-60%) score=2; and severe atrophy (>60%) score=3] (3).

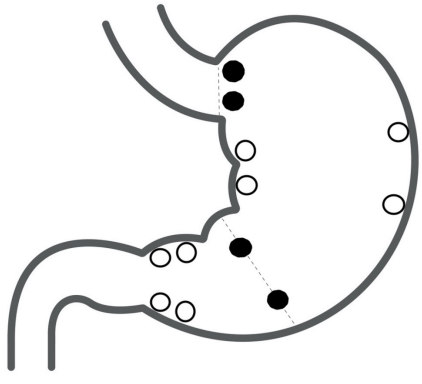

Figure 1: Biopsy sites (adapted from reference 12)

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In addition, the Vienna system was used to classify dysplasia as low- or high-grade neoplasia (13). For histopathologic examination, preparations were stained with hematoxylin-eosin and Alcian blue-periodic acid Schiff (pH 2.5). Giemsa staining was performed to identify *H. pylori* infection. The biopsy samples obtained during the first endoscopy were re-evaluated by the same pathologist (Y.S.G.), independent of any subsequent biopsy. Because different lesion grades often coexist in pathologic specimens obtained from the same patient, the highest grade lesion observed in any biopsy specimen was used to grade the disease in each patient. IM was subclassified, based on the morphologic characteristics, as "complete" (presence of mature brush border absorptive cells, sialomucin-secreting goblet cells and, occasionally, Paneth cells) or "incomplete" (few absorptive cells, secretion of sulfomucin by intermediate cells, secretion of sialomucin and/or sulfomucin by goblet cells, and marked glandular distortion and branching in the metaplastic glands) (14).

The Operative Link on Gastritis Assessment (OLGA) staging system was used to determine the disease status according to the antrum and corpus scores. The disease was graded on a scale ranging from stage 0 (none) to stage 4 (severe) (15). For the Operative Link on Gastric Intestinal Metaplasia (OLGIM) system, IM was evaluated instead of atrophy, and the severity and distribution of IM were classified on a scale ranging from stage 0 (none) to stage 4 (severe) (16). Patients with stage 3-4 disease on OLGA and OLGIM were considered at high risk of GC.

This study was approved by the Kocaeli University Faculty of Medicine Local Ethics Committee (approval number: 48, date: 2010). Informed consent was obtained.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA). We used the Shapiro-Wilk test to determine if numerical variables followed a normal distribution. The Wilcoxon test was used to evaluate the dependent numerical variables that were not normally distributed. The relationship between categorical variables was determined using the chi-square analysis. Relationships between numerical variables were tested using the Spearman's rank correlation coefficient. Numerical variables are expressed as mean and standard deviation, and categorical variables are expressed as numbers and percentages. A p-value <0.05 indicated statistical significance.

RESULTS

Baseline Characteristics at Initial Endoscopy

The study included 117 patients with IM restricted to the antrum, with or without atrophy on initial endoscopy, which was performed at the Department of Gastroenterology, Kocaeli University Faculty of Medicine. The median [interquartile range (IQR)] age of patients at the time of surveillance endoscopy was 59 years (49-67 years), and 57.3% of patients were women. At baseline, 95 patients (81%) had a histologic diagnosis of atrophy, 79 (67.5%) had incomplete IM, 38 (32.5%) had complete IM, and 19 (16.2%) had low-grade dysplasia (LGD). On initial endoscopy, 41.0% of patients had *H. pylori* infection, of which 44.8% had undergone *H pylori* eradication therapy after initial endoscopy. Overall, 51.7% of patients were smokers, 36.8% were using NSAIDs, and 69.2% were on PPIs at initial endoscopy. One-quarter (25.0%) of patients had a family history of GC. Nevertheless, no relationship was noted between history of GC and IM type (p=0.301) or IM grade (p=0.929) (Table 1).

Table 1. Baseline characteristics of the 117 patients

Age, mean (± SD), y	58.26±11.2
Sex	
Male	50 (42.7)*
Female	67 (57.3)*
IM type	
Complete	38 (32.5)*
Incomplete	79 (67.5)*
IM grade	
Mild	48.0 (41.0)*
Moderate	48.0 (41.0)*
Marked	21 (18.0)*
Atrophy	
None	22 (18.8)*
Mild	65 (55.5)*
Moderate	26 (22.2)*
Marked	4 (3.4)*
Dysplasia	
None	31 (26.5)*
Indefinite	67 (57.3)*
Low grade	19 (16.2)*
Helicobacter pylori	
Negative	69 (59)*
Positive	48 (41)*
Family history of gastric cancer	
Yes	29 (25.0)*
No	87 (75.0)*
NSAIDs	
Yes	43 (36.8)*
No	74 (63.3)*
Proton pump inhibitors	
Yes	81 (69.2)*
No	36 (30.8)*
Smoking	
Yes	60 (51.7)*
No	56 (48.3)*
Alcohol consumption	
Yes	13 (11.2)*
No	103 (88.8)*

*(n, %), IM: intestinal metaplasia, NSAIDs: non-steroidal anti-inflammatory drugs, SD: standard deviation

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Surveillance Endoscopy

Surveillance endoscopy was performed at a median (IQR) of 7.2 years (5.9-8.7) after the initial diagnosis of IM. On initial endoscopy, 22 patients had antrum-restricted IM with atrophy, and 95 patients had no atrophy. On surveillance endoscopy, the rates of dysplasia were similar between patients with and without atrophy (p=0.339). IM was absent in 22 patients (18.8%) on surveillance endoscopy. Among the 95 patients with IM, 58.9% of patients had IM present in only the antrum or incisura angularis, 4.2% in the corpus, and 36.8% had in both regions.

Surveillance endoscopy revealed high-grade dysplasia (HGD) in four patients (3.4%) with previous indefinite dysplasia and gastric adenocarcinoma in two patients (1.7%) with previous LGD. The annual incidence of GC in patients with antrum-restricted IM was 0.17%. In the first patient with gastric adenocarcinoma, diffuse gastric carcinoma was detected in the incisura angularis 4.6 years after the initial endoscopy, and surgery was performed. In the second patient, an intestinal-type early gastric carcinoma was detected 4.7 years after onset, and endoscopic submucosal dissection was performed.

Progression and Regression of Premalignant Lesions

On surveillance endoscopy, 11.1% of patients exhibited progression of IM type, 27.4% had progression of IM grade, 25.6% had progression of atrophy, and 33.3% had progression of dysplasia compared with the results of the initial endoscopy. Compared with the findings on initial endoscopy, IM type regressed in 38.5% of patients, and IM grade regressed in 29.9%. Notably, IM type and grade were stable in 50.4% and 42.7% of patients, respectively. Similarly, atrophy regressed in 35.0% of patients, and atrophy was stable in 39.3% based on surveillance endoscopy; dysplasia regressed in 23.1% of patients, and dysplasia was stable in 43.6% (Table 2). Among patients with incomplete metaplasia on initial endoscopy, 54.0% had incomplete IM on surveillance endoscopy, 25.3% had complete IM, and 20.3% did not have IM. Among the patients with complete IM on initial endoscopy, 34.2% progressed to incomplete metaplasia, and 23.7% did not have IM.

On surveillance endoscopies, a positive correlation was observed between the progression of the IM grade and the progression of the IM type (r=0.59, p=0.001), atrophy (r=0.52, p=0.001), and dysplasia (r=0.55, p=0.001). Likewise, as IM type progression, both atrophy (r=0.22, p<0.05) and dysplasia progressed (r=0.41,

Table 2. Progression and regression of premalignant gastric lesions on surveillance endoscopy

	Surveillance endoscopy n (%)		
	Progression	**Regression**	**No change**
Baseline endoscopy			
IM types	13 (11.1)	45 (38.5)	59 (50.4)
IM grade	32 (27.4)	35 (29.9)	50 (42.7)
Atrophy	30 (25.6)	41 (35)	46 (39.3)
Dysplasia	39 (33.3)	27 (23.1)	51 (43.6)

IM: intestinal metaplasia

Table 3. Comparison of patients at low and high risk for gastric cancer on surveillance endoscopy according to histologic characteristics on initial endoscopy

Dysplasia on surveillance endoscopy, n (%)						
Baseline endoscopy	**GC (n=2)**	**HGD (n=4)**	**LGD (n=32)**	**Indefinite (n=38)**	**None (n=41)**	**p**
IM grade						
Marked	0	0	10 (31.3)	7 (18.4)	4 (9.8)	-
Moderate	2 (100)	4 (100)	14 (43.8)	14 (36.8)	14 (34.1)	0.002*
Mild	0	0	8 (25)	17 (44.7)	23 (56.1)	-
IM type						
Incomplete	2 (100)	4 (100)	24 (75)	25 (65.8)	24 (58.5)	0.070
Complete	0	0	8 (25)	13 (34.2)	17 (41.5)	-
Atrophy						
Marked	0	0	1 (3.1)	0	3 (7.3)	-
Moderate	2 (100)	0	13 (40.6)	4 (10.5)	7 (17.1)	-
Mild	0	4 (100)	13 (40.6)	28 (73.7)	20 (48.8)	0.019*
None	0	0	5 (15.6)	6 (15.8)	11 (26.8)	-

*p<0.05 indicates significance.
GC: gastric cancer, HGD: high-grade dysplasia, IM: intestinal metaplasia, LGD: low-grade dysplasia

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p=0.001). Moreover, as atrophy progressed, dysplasia progressed too (r=0.53, p=0.001).

Progression to Dysplasia in Premalignant Lesions

A statistically significant difference was observed between IM grade on the initial biopsies and the distribution of dysplasia in subsequent biopsies (p=0.002) and between atrophy status on the initial biopsies and the distribution of dysplasia in subsequent biopsies (p=0.019). Fourteen patients (43.8%) who had LGD on surveillance endoscopy, as well as all four patients with HGD (100%) and two patients with GC (100%), had moderate IM on initial endoscopy. However, 23 patients (56.1%) without dysplasia and 17 (44.7%) with indefinite dysplasia had mild IM on initial endoscopy (p=0.002). Likewise, 13 patients (40.6%) with LGD and 2 patients (100%) with GC had moderate atrophy scores on the initial biopsies. Moreover, 20 patients (48.8%) without dysplasia and 28 patients (73.7%) with indefinite dysplasia had mild atrophy scores on the initial biopsies (p=0.019). No significant relationship was noted between IM type on the initial biopsies and the distribution of dysplasia on subsequent biopsies (p=0.070) (Table 3). However, 24 of 32 patients (75%) who had LGD on surveillance endoscopy had incomplete IM on initial endoscopy, and in all 4 patients (100%) with HGD and both patients (100%) with GC on surveillance endoscopy, incomplete IM was noted on initial endoscopy.

Risk Factors

The rate of *H. pylori* infection was significantly higher on surveillance endoscopy compared with initial endoscopy (p=0.001). Notably, including the 23 patients who received eradication therapy before initial endoscopy, 53 patients (76.8%) without *H. pylori* infection had positive *H. pylori* results on surveillance endoscopy.

Nevertheless, no correlation was noted between the progression and regression status of premalignant lesions and possible risk factors, such as age, sex, smoking history, alcohol use, PPI and NSAID use, and *H. pylori* infection (all p>0.05).

OLGA and OLGIM Stage

On surveillance endoscopy, 32.8% of patients had OLGA stage 1 disease, 24.1% had stage 2, 10.3% had stage 3, and 1.7% had stage 4. No significant relationship was observed between IM grade (p=0.064), IM type (p=0.593), atrophy (p=0.222), or dysplasia distribution (p=0.138) on initial endoscopy and the OLGA stages on surveillance endoscopy. However, on surveillance endoscopy, OLGA stage 3-4 disease was noted in most patients who had progression of IM grade (p=0.0001), IM type (p=0.008), and dysplasia (p=0.0001).

On surveillance endoscopy, 19 patients (16.2%) had OLGIM stage 1, 41 (35%) had stage 2, 22 (18.8%) had stage 3, and 14 (12%) had stage 4. Furthermore, with the increase in IM grade, IM type, atrophy, and dysplasia on initial endoscopy, an increase in OLGIM stage was observed on surveillance endoscopy. Most patients with OLGIM stage 2-4 disease had incomplete IM, and LGD, or indefinite dysplasia on initial endoscopy, whereas most OLGIM stage 1 patients had complete IM (p=0.044) and no dysplasia (p=0.009) (Table 4).

Table 4. Evaluation of OLGIM stages on surveillance endoscopy according to histology diagnoses on baseline endoscopy

OLGIM on surveillance endoscopy, n (%)						
Baseline endoscopy	**Stage 4**	**Stage 3**	**Stage 2**	**Stage 1**	**None**	**p**
IM grade						
Marked	6 (42.9)	7 (31.8)	5 (12.2)	1 (5.3)	2 (9.5)	-
Moderate	6 (42.9)	9 (40.9)	22 (53.7)	3 (15.8)	8 (38.1)	0.001*
Mild	2 (14.3)	6 (27.3)	14 (34.1)	15 (78.9)	11 (52.4)	-
IM type						
Incomplete	12 (85.7)	19 (86.4)	26 (63.4)	9 (47.4)	13 (61.9)	0.044
Complete	2 (14.3)	3 (13.6)	15 (36.6)	10 (52.6)	8 (38.1)	-
Atrophy						
Marked	0 (0.0)	1 (4.5)	0 (0.0)	1 (5.3)	2 (9.5)	-
Moderate	5 (35.7)	5 (22.7)	11 (26.8)	0 (0.0)	5 (23.8)	0.043
Mild	8 (57.1)	11 (50.0)	25 (61.0)	13 (68.4)	8 (38.1)	-
None	1 (7.1)	5 (22.7)	5 (12.2)	5 (26.3)	6 (28.6)	-
Dysplasia						
High-grade	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
Low grade	4 (28.6)	6 (27.3)	5 (12.2)	1 (5.3)	3 (14.3)	0.009*
Indefinite	9 (64.3)	11 (50.0)	29 (70.7)	6 (31.6)	12 (57.1)	-
None	1 (7.1)	5 (22.7)	7 (17.1)	12 (63.2)	6 (28.6)	-

*p<0.05 indicates significance.
IM: intestinal metaplasia , OLGIM: Operative Link on Gastric Intestinal Metaplasia

Regarding the OLGIM stage of premalignant lesions on surveillance endoscopy, moderate atrophy was noted in most patients with OLGIM stages 3 (59.1%) and 4 (50.0%); stage 2 was seen in most patients (56.1%) with mild atrophy, and atrophy was not observed in most patients with stage 1 (63.2%) (p=0.001). Incomplete IM was observed in most patients with OLGIM stages 2 (51.2%), 3 (86.4%), and 4 (85.7%), and complete IM was observed in most patients with stage 1 (73.7%) (p=0.001). Regarding dysplasia, LGD was noted in most patients with stages 3 (50.0%) and 4 (57.1%), and nearly half (48.8%) of patients with indeterminate dysplasia had stage 2. Typically, dysplasia was not observed in patients with stage 1 (p=0.001).

Furthermore, most patients whose atrophy progressed on surveillance endoscopy had OLGIM stages 3 (45.5%) and 4 (42.9%) (p=0.001), and those whose dysplasia progressed were OLGIM stages 3 (50.0%) and 4 (64.3%) (p=0.001).

DISCUSSION

In this study, patients with antrum-restricted IM on untargeted biopsies obtained during initial endoscopy were re-evaluated after a median of 7.2 years. Based on our results, patients with antrum-restricted IM are at risk of neoplastic lesions and require endoscopic surveillance. In addition, it has been observed that premalignant lesions can both progress and regress during clinical surveillance.

Delayed diagnosis of GC is associated with a high mortality rate. Therefore, it is imperative to screen for premalignant lesions in high-risk groups (17). Moreover, an uneven IM distribution might cause sampling errors, making the detection of premalignant gastric lesions challenging. Therefore, the best approach is to use diagnostic endoscopy with a gastric mapping protocol. The updated Sydney system is a widely applied biopsy protocol (7). However, studies have reported that this protocol does not fully reflect the actual state of IM (18,19). Therefore, in our study, we used a biopsy protocol to obtain specimens from all stomach regions to optimally assess the severity and distribution of premalignant gastric lesions (12). Most premalignant gastric lesions were observed in the antrum, followed by throughout the stomach and the corpus. In Western countries and other populations, 50% of precancerous gastric lesions were noted in the antrum, 17.7% in the corpus, and 15% in both regions (20,21).

Notably, the prevalence of GC varies significantly among different geographic regions (22,23). Guidelines recommend surveillance endoscopy for patients with extensive IM and atrophy, and also for patients with gastric IM who are at high risk for GC owing to their ethnicity or family history (5,6,10,11). European guidelines recommend an interval of 3 years and more more intensive surveillance for those with extensive gastric IM and atrophy, whereas the guidelines of the American Gastroenterological Association recommend a 3- to 5-year surveillance period (5,6). Nonetheless, these guidelines do not recommend follow-up for patients with antrum-restricted gastric IM and atrophy. However, in our study, 27.4% of patients with antrum-restricted IM on initial endoscopy had progression of the IM grade, whereas 25.6% had progression of atrophy and 33.3% had progression of dysplasia on surveillance endoscopy. In addition, HGD and GC were detected in four and two patients, respectively. For the two patients with GC, the mean time between initial endoscopy and GC diagnosis was 4.65 years. In our series, the annual incidence of GC was 0.17% among patients with antrum-restricted IM. In one study, the 10-year incidence of GC was 0.8% among patients with atrophic gastritis, while that of patients with IM was 1.8% (8). Therefore, it might not be appropriate to use the same follow-up period for patients with atrophic gastritis and IM. However, per another study, no patients with atrophic gastritis or complete IM on their initial biopsies developed HGD or GC during the 3-year follow-up period, with only less than 10% of cases progressing to LGD (24). Nevertheless, the annual endoscopic follow-up might not be appropriate for all patients with IM because some will not develop GC. Therefore, a better approach would be to devise a patient-individualized follow-up strategy.

Although the US guidelines on surveillance endoscopy consider patients with incomplete IM as high risk, the European guidelines and the study of Dinis-Ribeiro et al. (11) do not consider IM type (5,6,12). Gonzalez et al. (25) revealed that the risk of GC is three times higher in patients with incomplete IM than those with complete IM. In another study from Spain, 16 of 21 patients with adenocarcinoma had incomplete IM at a mean of 12.8 years after the initial diagnosis, and 1 patient had complete IM; the risk of GC was highest among patients with incomplete IM, and a family history of GC (26). In our study, all four patients with HGD and two with GC, diagnosed on surveillance endoscopy, had incomplete metaplasia on the initial endoscopy. Dinis-Ribeiro et al. (11) suggested using IM grade instead of IM subtype. However, we determined a positive correlation between IM type and grade in our study. Notably, with the progression of IM type, the IM grade and dysplasia also progressed. Therefore, contrary to recommendations, patients with complete IM in the antral mucosa, a history of smoking, a family history of GC, or incomplete IM restricted to the antrum would require endoscopic surveillance (27).

While some precancerous gastric lesions show progression, others may remain stable, or exhibit true regression or show false regression according to the characteristics of the biopsy sampling site or interpretation of histologic grades (21,28). Our data indicated that premalignant lesions might exhibit both progression and regression on clinical surveillance. In our series, based on the findings of the initial endoscopies, 38.5% of patients had IM type regression, and 29.9% had IM grade regression. Nevertheless, IM type remained stable in 50.4% of patients, and IM grade remained stable in 42.7. Similarly, 35% of patients had atrophy regression, and 39.3% had persistent atrophy, whereas 23.1% of patients had dysplasia regression, and 43.6% had persistent dysplasia. Studies have revealed that the location, severity, and extent of precancerous lesions, particularly IM, reflect the likelihood of progression to GC (29). Contrary to some studies stating that IM

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does not regress, recent studies have demonstrated that IM can be reversible (30,31). When Akbari et al. (28) used a random-effects model to review 20 studies on patients with IM, they reported that the IM regressed in 31.8%, whereas it remained stable in 43.4%. When the results of 10 studies were combined, 32.2% of patients had atrophy regression, and 38.8% had persistent atrophy (28). In addition, the characteristics of LGD and regenerative changes exhibit a large overlap, which could complicate the diagnosis of LGD (32,33). Nevertheless, a study that followed up patients with dysplasia for more than 2 years noted that among patients with LGD, 21% had progression and 36% had spontaneous regression, and in those with moderate-grade dysplasia, 33% had progression, and 27% had spontaneous regression. In addition, 43% of cases with severe dysplasia remained stable, 47% progressed to GC, and 0% regressed (34). Strikingly, den Hoed et al. (19) revealed that 67% of cases of LGD regressed to IM, and the remaining third had regression to atrophic gastritis and even normal mucosa on surveillance endoscopy.

In our study, the severity and extent of premalignant lesions detected on initial endoscopy were not associated with OLGA stage but were associated with OLGIM stage. On initial endoscopy, we observed that, as the severity of IM grade, IM type, atrophy, and dysplasia increased, so did the OLGIM stage on surveillance endoscopy. In addition, patients whose premalignant lesions exhibited progression on surveillance endoscopy had OLGA and OLGIM stages 3-4. Some experts recommend using a combination of OLGA and OLGIM to stage chronic gastritis (35). In addition, for patients with extensive atrophy/IM in both the antrum and corpus, histopathologic staging systems, such as OLGA and OLGIM, could be useful for defining patient subgroups based on the risk of progression to GC (11). Our results suggest that the OLGA and OLGIM staging systems can be used in the follow-up programs for premalignant gastric lesions.

Study Limitations

Nonetheless, our study had some limitations. Although premalignant lesions might develop into neoplastic lesions over the long term, we cannot be definitive regarding the likelihood of this transition, owing to our limited number of patients. In addition, because precancerous lesions have multifocal involvement, we cannot exclude sampling error and misclassification. Another limitation of our study was that we used regular white-light endoscopy at both baseline and surveillance. Although recent guidelines recommend the use of narrow-band imaging to detect premalignant gastric lesions (11), we use white-light endoscopy in our daily practice. Nevertheless, the strength of this study was that the biopsy specimens were obtained by a single physician to ensure consistency. Moreover, analysis of these biopsy samples by a single experienced pathologist ruled out interobserver variability.

CONCLUSION

Patients with antrum-restricted IM are at risk of neoplastic lesions and require endoscopic surveillance, contrary to the existing recommendations. Moreover, instead of using a single surveillance program to evaluate all patients, a more appropriate approach would be to use a patient-specific follow-up program and use OLGA and OLGIM criteria to determine follow-up intervals. Our data revealed that premalignant lesions might exhibit both progression and regression during clinical surveillance. In addition, our study indicated that the IM subtype, along with IM grade, is a useful marker in identifying patients at risk for GC.

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