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White ring sign is useful for differentiating between fundic gland polyp and gastric adenocarcinoma of fundic gland type

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Abstract:
Background: Gastric adenocarcinoma of fundic gland type (GA-FG) is characterized by an elevated lesion with vessel dilation exhibiting branching architectures (DVBA). However, this feature is also found in fundic gland polyp (FGP), posing a challenge in their differentiation. In this study, we aimed to investigate the clinicopathological features of gastric elevated lesions with DVBA and assess the efficacy of the white ring sign (WRS) as a novel marker for distinguishing between FGP and GA-FG.
Methods: We analyzed 159 gastric elevated lesions without DVBA and 51 gastric elevated lesions with DVBA, further dividing the latter into 39 in the positive-WRS group and 12 in the negative-WRS group. The clinicopathological features, diagnostic accuracy, and inter-rater reliability were analyzed.
Results: Univariate and multivariate analyses for gastric elevated lesions with DVBA identified the histological type consistent with FGP and GA-FG, along with the presence of round pits in the background gastric mucosa, as independent predictors. FGPs were present in 92.3% (36/39) of the positive-WRS group and GA-FGs were observed in 50.0% (6/12) of the negative-WRS group. Positive- and negative-WRS exhibited high diagnostic accuracy, with 100% sensitivity, 80.0% specificity, and 94.1% accuracy for FGP, and 100% sensitivity, 86.7% specificity, and 88.2% accuracy for GA-FG. Kappa values of WRS between experts and nonexperts were 0.891 and 0.841, respectively, indicating excellent agreement.
Conclusions: Positive- and negative-WRS demonstrate high diagnostic accuracy and inter-rater reliability for FGP and GA-FG, respectively, suggesting that WRS is a useful novel marker for distinguishing between FGP and GA-FG.

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Introduction

The prevalence of *Helicobacter pylori* (*H. pylori*)-negative gastric cancer (HpNGC) has been reported to be approximately 0.42%–5.4%, and it is anticipated to increase due to the decreasing incidence of *H. pylori* infection [1,2]. Gastric adenocarcinoma of the fundic gland type (GA-FG), which falls under the umbrella of HpNGC, has recently been proposed as a rare gastric adenocarcinoma variant [3]. Despite their small tumor size, GA-FGs often exhibit submucosal invasion, necessitating endoscopic resection [4–6]. The endoscopic feature of GA-FG is characterized by an elevated lesion with dilated vessels exhibiting branching architectures (DVBA) in the non-atrophic background mucosa [3,7]. However, a challenge arises when distinguishing GA-FGs from fundic gland polyps (FGP), as both commonly present as elevated lesions with DVBAs [8]. FGP is the most frequently encountered type of gastric polyp during esophagogastroduodenoscopy (EGD), accounting for approximately 77% of all gastric polyps [9,10]. The prevalence of FGPs has been increasing owing to the growing population of *H. pylori*-negative individuals and chronic users of proton pump inhibitors (PPI) [9]. Therefore, establishing a proper differential diagnosis between FGP and GA-FG during EGD is crucial. This study focuses on the ring-shaped white zone surrounding the elevated lesion, designated as the white ring sign (WRS), in narrow band imaging (NBI) observations. Herein, we investigated the clinicopathological features of gastric elevated lesions with DVBAs and assessed the effectiveness of the WRS as a novel marker for distinguishing between FGP and GA-FG.

Materials and methods

Study patients

A total of 1228 consecutive cases, examined by EGD using a magnifying endoscope at Asahikawa Medical University Hospital and Harada Hospital from August 2019 to January

2023, were retrospectively analyzed. These cases were extracted based on medical records and endoscopic images, and the extraction process was conducted by K.T. We included gastric elevated lesions evaluated through magnifying endoscopy with NBI (ME-NBI) and subjected to histological examination. Exclusions comprised lesions with a flat or depressed type, advanced gastric adenocarcinomas, and those lacking ME-NBI images for analysis. This study was reviewed and approved by the Institutional Review Boards of Asahikawa Medical University and Harada Hospital under approval number 21011 on May 20th, 2021. Informed consent was obtained using an opt-out method for this retrospective study.

Endoscopic equipment and procedure

Using an upper gastrointestinal endoscope, magnifying endoscopy was performed (Olympus Medical Systems, Tokyo, Japan), specifically the GIF-H260Z, GIF-H290Z, or GIF-HQ290 models. The second-generation NBI system was used with an electronic endoscopy system (EVIS LUCERA ELITE; Olympus Medical Systems, Tokyo, Japan). By setting the B8 level, the ME-NBI observation was performed. Elevated lesions with DVBAs were initially identified by the endoscopists using white light imaging and then the lesions were observed using ME-NBI. Biopsy, cold snare polypectomy (CSP), and endoscopic submucosal dissection (ESD) specimens were obtained by endoscopists and diagnosed by pathologists at each institution. The magnifying endoscopy was performed by 21 endoscopists at our hospitals.

Assessment of ME-NBI findings

We defined the WRS as the ring-shaped white zone surrounding the elevated lesion on NBI observation. Positivity was confirmed when more than three-quarters of the lesional margin was observed (**Figure 1**), while those with less than three-quarters of the lesional margin was

diagnosed as negative (**Figure 2**). In addition to WRS assessment, other characteristic ME-NBI findings of GA-FG were also evaluated, including an indistinct demarcation line (DL), dilation of crypt opening (CO), dilation of the intervening part (IP), and poor irregularity of the microvascular pattern (IMVP) [11]. To assess inter-rater reliability, four endoscopists to whom the pathological diagnosis was masked assessed the ME-NBI images. Two of these endoscopists are experts with more than 5 years of ME-NBI experience, while the other two are nonexperts with less than 3 years of experience. Kappa coefficients were used to assess the inter-rater reliability between experts and nonexperts.

Statistical analyses

All statistical examinations were conducted using the R Project for Statistical Computing version 4.0.5 software. Student's *t test* was used to compare continuous variables, and Fisher's exact probability test was used to compare nominal scale data. To assess the strength of each variable's influence, odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. Selected variables with p-values <0.05 in the univariate analysis were included in the multivariate analysis. Kappa coefficient values of <0.20, 0.21–0.40, 0.41–0.60, 0.61–0.80 and >0.80 are considered to indicate poor, fair, moderate, good, and excellent agreement, respectively. Statistical significance was set at a P value of <0.05.

Results

Among 1228 consecutive cases examined by EGD using a magnifying endoscope, 472 lesions of gastric abnormalities underwent examination using ME-NBI and histological examination. From these lesions, we identified and extracted 210 elevated gastric lesions, excluding 241 lesions with flat or depressed types, 20 lesions with advanced gastric adenocarcinoma, and 1 lesion lacking ME-NBI images for analysis. Then, we analyzed 159

gastric elevated lesions without DVBAs and 51 gastric elevated lesions with DVBAs (**Figure 3**).

The clinicopathological features of the non-DVBA and DVBA groups are presented in **Table 1**. In the non-DVBA group, there were 145 patients with 159 lesions, including 1 FGP, 102 early gastric adenocarcinomas, 8 gastric adenomas, 8 foveolar-type gastric neoplasias, 1 gastric carcinoma with lymphoid stroma, 1 gastric adenocarcinoma of fundic gland mucosa type, 2 neuroendocrine tumors, 3 malignant lymphomas, 7 hyperplastic polyps, 2 lesions classified as Group 2, and 24 lesions classified as Group 1 according to the Japanese classification of gastric carcinoma [12]. In the DVBA group, there were 44 patients with 51 lesions, including 35 FGPs, 1 FGP with dysplasia, 6 GA-FGs, 2 early gastric adenocarcinomas, and 7 lesions classified as Group 1 according to the Japanese classification of gastric carcinoma [12]. In the DVBA group, the average age was significantly younger than that of the non-DVBA group (61.2 ± 11.6 years vs. 71.9 ± 11.0 years). The elevated lesions with DVBA were observed in the middle to upper third region, accompanied by mild atrophy (C-0 and C-1 according to the Kimura-Takemoto classification), and round pits in the background gastric mucosa were identified through ME-NBI. These lesions exhibited a higher prevalence of sharing the same color as the background mucosa, smaller lesion size (6.6 ± 3.4 mm vs. 15.2 ± 12.3 mm), and a histological type consistent with FGP and GA-FG compared to the non-DVBA group. The results of univariate and multivariate analyses for DVBA-associated factors are presented in **Table 2**. The univariate analysis identified significant factors including age under 65 years, mild atrophy, the presence of round pits in the background gastric mucosa, tumor located in the upper third, same color as background mucosa, tumor size < 10mm, and a histological type consistent with FGP and GA-FG. The multivariate analysis revealed that the presence of round pits in the background gastric mucosa (OR 13.90, 95% CI 1.95-98.60, $p < 0.05$) and a histological type consistent with FGP

and GA-FG (OR 244.00, 95% CI 25.00-2390.00, $p < 0.001$) were identified as independent predictors of DVBA.

Then, we analyzed the 51 gastric elevated lesions with DVBAs, dividing them into 39 lesions in the positive-WRS group and 12 lesions in the negative-WRS group. The clinicopathological features of the positive- and the negative-WRS groups are presented in **Table 3**. In the positive-WRS group, FGPs and FGP with dysplasia were found in 92.3% (36/39) of cases, while in the negative-WRS group, GA-FGs were found in 50.0% (6/12) of cases. Regarding the diagnostic accuracy of WRS, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of positive-WRS for FGP were 100%, 80.0%, 92.3%, 100%, and 94.1%, respectively, while those of the negative-WRS for GA-FG were 100%, 86.7%, 50.0%, 100%, and 88.2%, respectively. The lesions in the positive-WRS group were diagnosed through 36 biopsies, one CSP, and two ESDs, whereas in the negative-WRS group, four biopsies and eight ESDs were used to establish diagnosis. The pathological features are shown in **Figure 4**. The positive-WRS gastric lesions occurred at a higher rate of mild atrophy compared to the negative-WRS lesions (89.7% vs. 58.3%; $p < 0.05$). No significant differences were found for age, sex, use of PPI or potassium competitive acid blocker (P-CAB), history of *H. pylori* eradication, tumor location, lesional color, estimated tumor size, and morphology between the positive-WRS group and negative-WRS groups.

Table 4 presents the incidence rate and Kappa coefficient values for ME-NBI findings, including the WRS, indistinct DL, CO dilation, IP dilation, and poor IMVP. In FGP lesions, the incidence rates of positive-WRS, indistinct DL, CO dilation, IP dilation, and poor IMVP were 100% (36/36), 0% (0/36), 27.8% (10/36), 30.6% (11/36), and 77.8% (28/36), respectively. In GA-FG lesions, the incidence rates of negative-WRS, indistinct DL, CO dilation, IP dilation, and poor IMVP were 100% (6/6), 33.3% (2/6), 66.7% (4/6), 100% (6/6),

and 50.0% (3/6), respectively. The kappa values for WRS, indistinct DL, CO dilation, IP dilation, and poor IMVP between experts were 0.891, 0.628, 0.507, 0.508, and 0.664, respectively. For nonexperts, the kappa values for WRS, indistinct DL, CO dilation, IP dilation, and poor IMVP were 0.841, 0.346, 0.079, 0.280, and 0.356, respectively. The inter-rater reliability for WRS between experts and nonexperts demonstrated excellent agreement levels, while the reliability for indistinct DL, CO dilation, IP dilation, and poor IMVP showed poor to good agreement levels.

Discussion

This is the first report demonstrating the characteristics of gastric elevated lesions with DVBA and the efficacy of WRS in distinguishing between FGP and GA-FG. Our results showed that the gastric elevated lesions with DVBAs primarily included GA-FGs and FGPs, characterized by the presence of round pits in the background gastric mucosa. The round pit reportedly indicates normal oxyntic glands without atrophy, suggesting that both GA-FGs and FGPs occur in non-atrophic fundic glands [13]. When differentiating gastric elevated lesions with DVBAs endoscopically, positive-WRS serves as a reliable indicator for FGPs, suggesting no need for further evaluation and treatment. Concerning the optical observations, NBI light scatters upon entering the marginal crypt epithelium, resulting in the appearance of a whitish edge along the margin of the crypt epithelium [14]. Figure 4a showed that the CSP specimen of FGP with positive-WRS exhibited a curved margin with hyperplasia of the crypt epithelium. The continuous alignment of the crypt epithelium along the curved margin was responsible for the visualization of the WRS on NBI observation (**Figure 4b, 4c**).

In gastric elevated lesions with DVBAs, a negative-WRS suggests the possibility of GA-FGs, necessitating further evaluations, such as endoscopic ultrasonography and

endoscopic resection. The tumor glands of GA-FGs primarily proliferate in the middle and deep layers of the gastric mucosa, and the normal foveolar epithelium covers the superficial layer [15,16]. This pathological feature causes a gradual elevation without a curved margin, termed subepithelial tumor-like, and is responsible for CO dilations and a negative-WRS on NBI observation **(Figure 4d, 4e, 4f)**. The previous study showed that a characteristic ME-NBI finding of GA-FG is an indistinct DL [11]. While both indistinct DL and negative-WRS are endoscopic features observed at the margin of GA-FG, the negative-WRS showed higher kappa coefficient values than indistinct DL. This suggests the priority of WRS as a diagnostic marker for differentiating between FGPs and GA-FGs. Regarding microsurface pattern (MSP) and microvascular pattern (MVP), CO dilation, IP dilation, and poor IMVP have also been reported as characteristic ME-NBI findings of GA-FG [11]. However, our study revealed that CO dilation, IP dilation, and poor IMVP were observed in 27.8%, 30.6%, 77.8% of FGPs. Additionally, the kappa coefficient values of these features ranged from moderate to good agreement levels in experts and poor to fair agreement levels in non-experts. Therefore, the primary consideration in distinguishing GA-FGs and FGPs is to determine the presence or absence of WRS. Subsequent diagnosis should focus on MSP and MVP features, including CO dilation, IP dilation, and poor IMVP.

Regarding gastric lesions other than FGP and GA-FG, the negative-WRS group included two gastric adenocarcinomas in our study. Distinguishing gastric adenocarcinoma from GA-FG is generally possible by observing the MSP or MVP using ME-NBI. Specifically, GA-FGs exhibit regular MSP and regular MVP, whereas gastric adenocarcinomas display irregular MSP and/or irregular MVP [17,18]. In addition, the background gastric mucosa of gastric adenocarcinomas was surrounded by chronic atrophy

and exhibited non-pit type observed by ME-NBI, resulting in a higher rate of severe atrophy in the negative-WRS group than in the positive-WRS group. On the other hand, the background gastric mucosa of GA-FGs was surrounded by mild atrophy and exhibited a round pit type observed by ME-NBI. These indicate that the difference in background mucosa contributes to the differentiation between gastric adenocarcinomas and GA-FGs.

This study has limitations. First, our study may have a selection bias because it is a retrospective study and limited to gastric elevated lesions with DVBAs that were observed by ME-NBI and examined by histopathology. Second, most pathological examinations of FGPs were performed on biopsy specimens. This is because endoscopists believe that benign tumors such as FGPs were unsuitable for endoscopic resection, while a pathological diagnosis was possible using specimens obtained through biopsy. Third, the histopathological examination methods vary, including biopsy, CSP, and ESD. These diagnostic methods may affect the accuracy of gastric lesion assessment. Fourth, gastric lesions other than FGP and GA-FG were diagnosed as normal fundic gland mucosa using biopsy specimens. These lesions have the possibility of changing the diagnosis to another condition like GA-FG when diagnosed by ESD specimens.

In conclusion, WRS showed a high diagnostic accuracy and a high inter-rater reliability for differentiating FGP from GA-FG, suggesting that WRS is a novel useful marker for diagnosing gastric elevated lesions with DVBAs. If a positive-WRS with a regular MSP and regular MVP is present, further evaluation and treatment may not be necessary. However, a negative-WRS requires additional evaluations, such as endoscopic ultrasonography and endoscopic resection.

Declarations

Ethics approval and consent to participate

The study was reviewed and approved by the Institutional Review Boards of Asahikawa Medical University and Harada Hospital. We used the patient opt-out consent method for participation in this study. We retrospectively reviewed the anonymized clinical data after each patient received standard management. Individuals cannot be identified based on the data presented.

Consent for publication

Not applicable

Availability of data and material

The datasets supporting the conclusions of this article can be made available upon request.

Disclosures

Mikihiro Fujiya received lecture fees from Olympus Corporation. The remaining authors have no conflict of interest to declare.

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Authors' contributions

KT and MF conducted the study and wrote the initial manuscript. SM, RH, YK, and NU independently assessed the ME-NBI images for inter-rater reliability. TS, ST, YS, AK, KA, and HT performed the EGD procedures. SK and KM contributed to the analysis and data interpretation. KT, KH, and TO participated in the data collection and interpretation. SY and SI provided pathological diagnoses and critically reviewed the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table 1. Clinicopathological features of the non-DVBA and DBVA groups

	Non-DVBA group	DVBA group	P value
Numer of patients/lesions, n	145 / 159	44 / 51	
Age (years, mean ± SD)	71.9 (11.0)	61.2 (11.6)	<0.001
Sex, n (%) Male Female	 96 (66.2) 49 (33.8)	 29 (65.9) 15 (34.1)	0.86
PPI/P-CAB use, n (%)	66 (45.5)	19 (43.2)	0.86
No history of Hp eradication, n (%)	97 (67.4)	35 (79.5)	0.14
Extent of atrophic gastritis, n (%) Mild (C-0 and C-1)	 26 (16.4)	 42 (82.4)	<0.001

Moderate (C-2 to C-3)	45 (28.3)	6 (11.8)	
Severe (O-1 to 0-3)	80 (50.3)	3 (5.9)	
Gastric remnant	8 (5.0)	0 (0)	
Round pit , n (%)	35 (22.0)	48 (94.1)	<0.001
Location, n (%)			<0.001
Lower third	52 (32.7)	0 (0)	
Middle third	70 (44.0)	31 (60.8)	
Upper third	29 (18.2)	20 (39.2)	
Gastric remnant	8 (5.0)	0 (0)	
Color, n (%)			<0.001
Reddish	79 (49.7)	6 (11.8)	
Same as background mucosa	29 (18.2)	30 (58.8)	
Whitish	51 (32.1)	15 (29.4)	
Estimated tumor size, mm, mean (SD)	15.2 (12.3)	6.6 (3.4)	<0.001
Morphology, n (%)			0.08
Protruded	47 (29.6)	11 (21.6)	
Semipedunculated	3 (1.9)	4 (7.8)	
Superficial elevated	109 (68.6)	36 (70.6)	
Pathology, n (%)			<0.001
FGP and FGP with dysplasia	1 (0.6)	36 (70.6)	
GA-FG	0 (0)	6 (13.7)	
Gastric neoplasm	125 (78.6)	2 (3.9)	
Gastric non-neoplasm	33 (20.8)	7 (13.7)	

PPI: proton pump inhibitor; P-CAB: potassium competitive acid blocker; FGP: fundic gland polyp; GA-FG: gastric adenocarcinoma of fundic gland type

Table 2. Univariate and multivariate analyses for factors of DVBA

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
Age < 65	6.59	3.17-14.07	<0.001	1.04	0.20-5.37	0.96
Mild atrophy	23.34	9.78-61.58	<0.001	1.53	0.24-9.64	0.65
Round pit	55.37	16.36-292.20	<0.001	13.90	1.95-98.60	<0.05
Upper third	2.88	1.35-6.08	0.004	0.63	0.12-3.30	0.59

Same color	6.33	3.04-13.50	<0.001	2.18	0.48-9.93	0.31
Tumor size < 10mm	4.96	2.29-11.52	<0.001	1.89	0.35-10.30	0.46
FGP and GA-FG	661.65	94.93-16384.00	<0.001	244.00	25.00-2390.00	<0.001

Table 3. Clinicopathological features of the positive-WRS and negative-WRS groups

	Positive-WRS group	Negative-WRS group	P value
Numer of patients/lesions, n	33 / 39 lesions	11 / 12 lesions	
Age years, mean (SD)	60.2 (11.9)	65.9 (11.8)	0.16
Sex, n (%)			0.72
Male	20 (60.6)	8 (72.7)	
Female	13 (39.4)	3 (27.3)	
PPI/P-CAB use, n (%)	14 (42.4)	6 (54.5)	0.51
No history of Hp eradication, n (%)	4 (12.1)	4 (36.4)	0.09
Extent of atrophic gastritis, n (%)			<0.05
Mild (C-0 and C-1)	35 (89.7)	7 (58.3)	
Moderate (C-2 to C-3)	4 (10.3)	2 (16.7)	
Severe (O-1 to 0-3)	0 (0)	3 (25.0)	
Round pit , n (%)	37 (94.9)	11 (91.7)	0.56
Location, n (%)			>0.99
Lower third	0 (0)	0 (0)	
Middle third	24 (61.5)	7 (58.3)	
Upper third	15 (38.5)	5 (41.7)	
Color, n (%)			0.19
Reddish	3 (7.7)	3 (25.0)	
Same as background mucosa	25 (64.1)	5 (41.7)	
Whitish	11 (28.2)	4 (33.3)	
Estimated tumor size, mm, mean (SD)	6.3 (2.6)	7.8 (5.2)	0.17
Morphology, n (%)			0.87
Protruded	8 (20.5)	3 (25.0)	
Semipedunculated	3 (7.7)	1 (8.3)	
Superficial elevated	28 (71.8)	8 (66.7)	
Diagnostic method, n (%)			<0.001
Biopsy	36 (92.3)	4 (33.3)	

Cold snare polypectomy	1 (2.6)	0	
ESD	2 (5.1)	8 (66.7)	
Pathology, n (%)			<0.001
FGP	35 (89.7)	0 (0)	
FGP with dysplasia	1 (2.6)	0 (0)	
GA-FG	0 (0)	6 (50.0)	
Gastric adenocarcinoma	0 (0)	2 (16.7)	
Normal fundic gland mucosa	3 (7.7)	4 (33.3)	

Table 4. Incidence rate of ME-NBI findings and Kappa coefficient values

	Incidence rate of ME-NBI findings		Kappa coefficient values	
	FGP, n (%)	GA-FG, n (%)	Expert	Non-expert
Positive-WRS	36/36 (100)	0/6 (0)	0.891	0.841
Indistinct DL	0/36 (0)	2/6 (33.3)	0.628	0.346
Dilation of CO	10/36 (27.8)	4/6 (66.7)	0.507	0.079
Dilation of IP	11/36 (30.6)	6/6 (100)	0.508	0.280
Poor IMVP	28/36 (77.8)	3/6 (50.0)	0.664	0.356

ME-NBI: magnifying endoscopy with narrow band imaging; GA-FG: gastric adenocarcinoma of the fundic gland type; FGP: fundic gland polyp; DL: demarcation line; CO: crypt opening; IP: intervening part; IMVP: irregularity of the microvascular pattern

Figure legends

Figure 1. Positive white ring structure (WRS) observed on white light imaging (WLI) and magnifying endoscopy with narrow band imaging (ME-NBI).

An elevated lesion with DVBAs was observed in the non-atrophic background mucosa (a). NBI clearly highlighted the presence of WRS surrounding the margin of the elevated lesion (yellow arrow) (b). The DVBAs appeared reddish in white light, while they appeared cyane in tone under NBI. The lesion was diagnosed as FGP.

Figure 2. Negative white ring structure observed on WLI and ME-NBI.

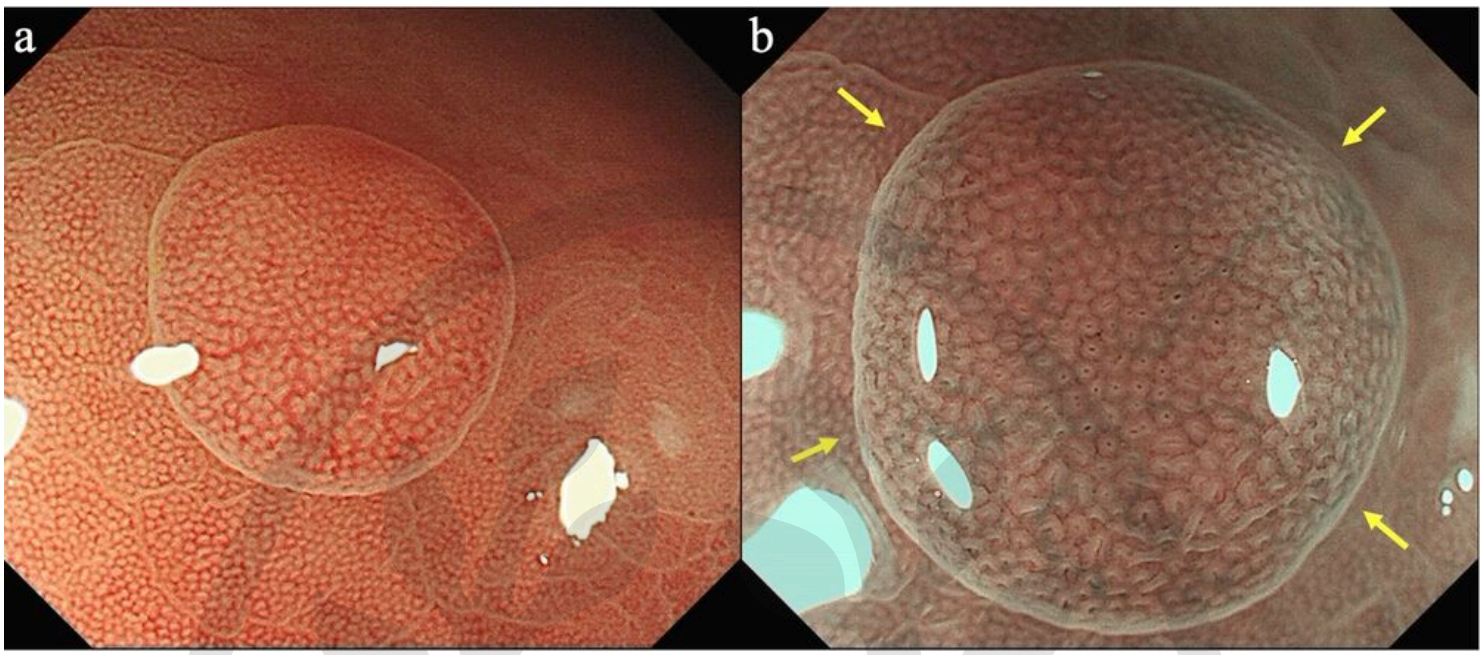
An elevated lesion with DVBAs was observed in the non-atrophic background mucosa (a). The absence of WRS was noted at the lesional margin under middle-range magnification with NBI (b). The high-range magnification with NBI showed dilation of the CO, dilation of the IP, and poor IMVP (c). The lesion was diagnosed as GA-FG.

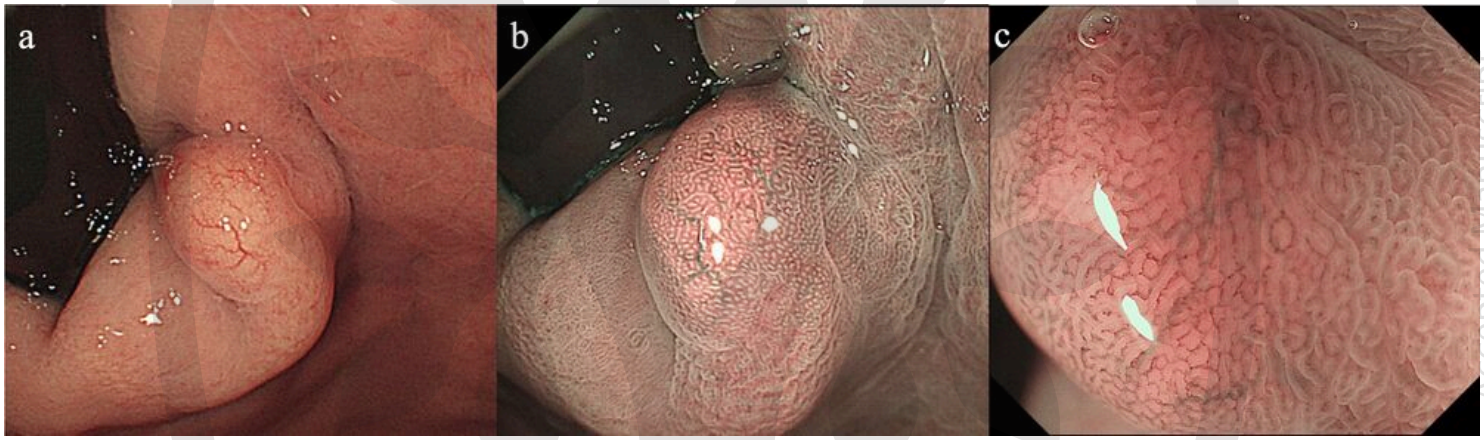
Figure 3. Study flow chart of this study

Among 1228 cases examined by EGD using a magnifying endoscope, 472 lesions of gastric abnormalities underwent examination using ME-NBI and histological examination. From these lesions, we identified and extracted 210 elevated gastric lesions, excluding 241 lesions with flat or depressed types, 20 lesions with advanced gastric adenocarcinoma, and 1 lesion lacking ME-NBI images for analysis. Then, we analyzed 159 gastric elevated lesions without DVBAs and 51 gastric elevated lesions with DVBAs.

Figure 4. The pathological findings of positive- and negative-WRS lesions.

In the positive-WRS lesion of the FGP, the CSP specimen exhibited a curved margin with hyperplasia of the crypt epithelium (a). Under high magnification, the continuous alignment of crypt epitheliums along the curved margin was observed (red line) (b). NBI light scatters upon entering the curved marginal crypt epithelium, resulting in the visualization of the WRS on NBI observation (c). In the negative-WRS lesion of the GA-FG, the ESD specimen showed gradual elevation at the lesional margin (d). In the high-power field, a normal foveolar epithelium without the curved margin was observed (red arrow)(e). NBI light scatters upon entering the each marginal crypt epithelium, resulting in CO dilations with a white zone and a negative-WRS on NBI observation (f).





1228 cases examined by EGD using a magnifying endoscope

472 gastric lesions examined by ME-NBI and histopathology

Excluded;
241 lesions with flat or depressed types
20 lesions with advanced gastric adenocarcinoma
1 lesion lacking ME-NBI images for analysis

210 gastric elevated lesions

159 gastric elevated lesions without DVBA

51 gastric elevated lesions with DVBA

39 positive-WRS lesions

12 negative-WRS lesions