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The white ring sign is useful for differentiating between fundic gland polyps and gastric adenocarcinoma of the fundic gland type

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ABSTRACT

Background and study aims Gastric adenocarcinoma of the fundic gland type (GA-FG) is characterized by an elevated lesion with vessel dilation exhibiting branching architecture (DVBA). However, this feature is also found in fundic gland polyps (FGPs), 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 FGPs and GA-FGs.

Methods We analyzed 159 gastric elevated lesions without DVBA and 51 gastric elevated lesions with DVBA, further dividing the latter into 39 in the WRS-positive group and 12 in the WRS-negative 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 FGPs and GA-FGs, 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 WRS-positive group and GA-FGs were observed in 50.0% (6/12) of the WRS-negative group. WRS positivity and negativity exhibited high diagnostic accuracy, with 100% sensitivity, 80.0% specificity, and 94.1% accuracy for FGPs, and 100% sensitivity, 86.7% specificity, and 88.2% accuracy for GA-FGs. Kappa values for WRS between experts and nonexperts were 0.891 and 0.841, respectively, indicating excellent agreement.

Conclusions WRS positivity and negativity demonstrate high diagnostic accuracy and inter-rater reliability for FGPs and GA-FGs, respectively, suggesting that WRS is a useful novel marker for distinguishing between FGPs and GA-FGs.

Introduction

The prevalence of *Helicobacter pylori*-negative gastric cancer (HpNGC) has been reported to be approximately 0.42% to 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 size, GA-FGs often exhibit submucosal invasion, necessitating endoscopic resection [4, 5, 6]. On endoscopy, GA-FG is characterized by an elevated lesion with dilated vessels exhibiting branching architecture (DVBA) in the non-atrophic background mucosa [3, 7]. However, a challenge arises when distinguishing GA-FGs from fundic gland polyps (FGPs), because both commonly present as elevated lesions with DVBAs [8]. FGP is the type of gastric polyp most frequently encountered during esophagogastroduodenoscopy (EGD), accounting for approximately 77% of all gastric polyps [9, 10]. Prevalence of FGPs has been increasing, owing to the growing population of *H. pylori*-negative individuals and chronic users of proton pump inhibitors (PPIs) [9]. Therefore, establishing a proper differential diagnosis between FGP and GA-FG during EGD is crucial. This study focused on the ring-shaped white zone surrounding the elevated lesion, designated as the white ring sign (WRS), in narrow-band imaging (NBI) observations. 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.

Patients 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 20, 2021. 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. Informed consent was obtained using an opt-out method for this retrospective study.

Endoscopic equipment and procedure

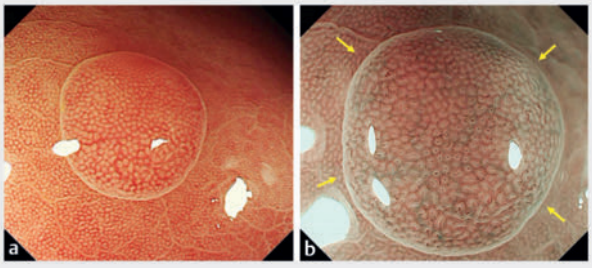
Using an upper gastrointestinal endoscope, magnifying endoscopy was performed (Olympus Medical Systems, Tokyo, Japan), specifically with the GIF-H260Z, GIF-H290Z, or GIF-HQ290 models. The second-generation NBI system was used with an electronic endoscopy system (EVIS LUCERA ELITE; Olympus Medical Systems, 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. Magnifying endoscopy was performed by 21 endoscopists at our hospitals.

Assessment of ME-NBI findings

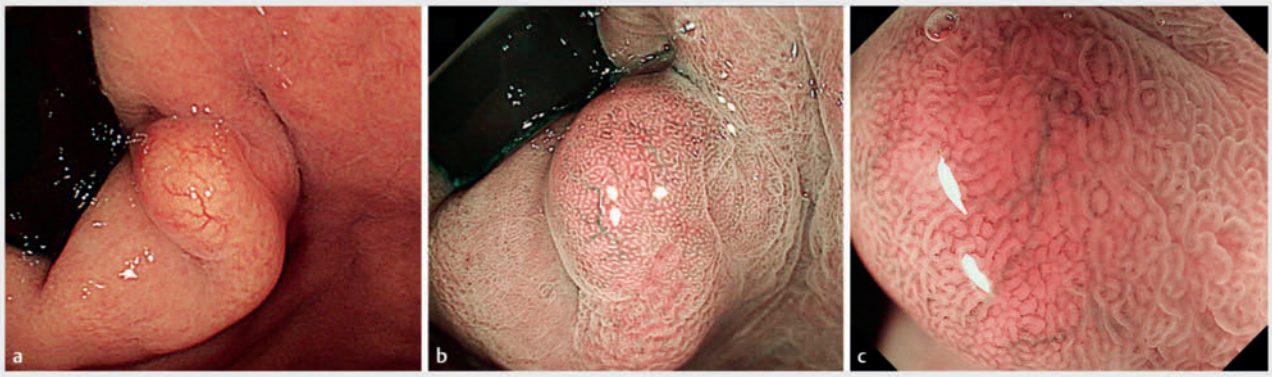
We defined the WRS as the ring-shaped white zone surrounding the elevated lesion on NBI observation. Positivity was confirmed when more than three-quarters of the lesion margin was observed (▶ **Fig. 1**), while those with less than three-quarters of the lesion margin were diagnosed as negative (▶ **Fig. 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 the 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 non-experts with less than 3 years of experience. Kappa coefficients were used to assess the inter-rater reliability between experts and non-experts.

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 (CIs) were calculated. Selected variables with $P<0.05$ in the univariate analysis were included



▶ **Fig. 1** Positive WRS observed on white-light imaging (WLI) and magnifying endoscopy with narrow-band imaging (ME-NBI). **a** An elevated lesion with DVBAs was observed in the non-atrophic background mucosa. **b** NBI clearly highlighted the presence of WRS surrounding the margin of the elevated lesion (yellow arrow). The DVBAs appeared reddish in white light, while they appeared cyan in tone under NBI. The lesion was diagnosed as FGP. DVBA, dilated vessels exhibiting branching architecture.



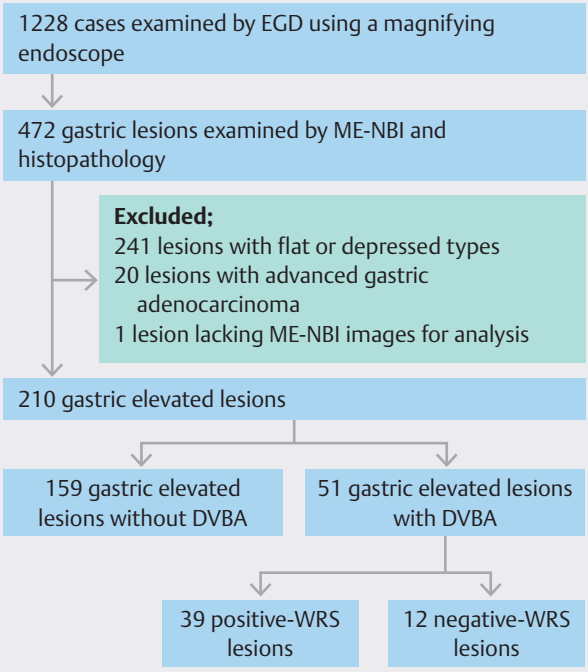
▶ **Fig. 2** Negative WRS observed on WLI and ME-NBI. **a** An elevated lesion with DVBAs was observed in the non-atrophic background mucosa. **b** Absence of WRS was noted at the lesion margin under middle-range magnification with NBI. **c** High-range magnification with NBI showed dilation of the CO, dilation of the IP, and poor IMVP. The lesion was diagnosed as GA-FG. WLI, white-light imaging; ME-NBI, magnifying endoscopy with narrow-band imaging; DVBA, dilated vessels exhibiting branching architecture; WRS, white ring sign; CO, crypt opening; IP, intervening part; IMVP, irregularity of microvascular pattern; GA-FG, gastric adenocarcinoma of the fundic gland type.

in the multivariate analysis. Kappa coefficient values of <0.20, 0.21 to 0.40, 0.41 to 0.60, 0.61 to 0.80 and >0.80 are considered to indicate poor, fair, moderate, good, and excellent agreement, respectively. Statistical significance was set at $P<0.05$.

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 one lesion lacking ME-NBI images for analysis. Then, we analyzed 159 gastric elevated lesions without DVBAs and 51 gastric elevated lesions with DVBAs (▶ **Fig. 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 one FGP, 102 early gastric adenocarcinomas, eight gastric adenomas, eight foveolar-type gastric neoplasias, one gastric carcinoma with lymphoid stroma, one gastric adenocarcinoma of fundic gland mucosa type, two neuroendocrine tumors, three malignant lymphomas, seven hyperplastic polyps, two 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, one FGP with dysplasia, six GA-FGs, two early gastric adenocarcinomas, and seven 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 in 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 muco-



▶ **Fig. 3** Study flow chart. Among 1228 cases examined by EGD using a magnifying endoscope, 472 lesions from 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 one lesion lacking ME-NBI images for analysis. Then, we analyzed 159 gastric elevated lesions without DVBAs and 51 gastric elevated lesions with DVBAs. EGD, esophagogastroduodenoscopy; ME-NBI, magnifying endoscopy with narrow-band imaging; DVBA, dilated vessels exhibiting branching architecture.

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

	Non-DVBA group	DVBA group	*P* value
Number of patients/lesions, n	145/159	44/51	
Age (years, mean ± SD)	71.9 (11.0)	61.2 (11.6)	<0.001
Sex, n (%)			0.86
▪ Male	96 (66.2)	29 (65.9)	
▪ Female	49 (33.8)	15 (34.1)	
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 (%)			<0.001
▪ Mild (C-0 and C-1)	26 (16.4)	42 (82.4)	
▪ 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)	
▪ Semi-pedunculated	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)	

DVBA, dilated vessels exhibiting branching architecture; SD, standard deviation; PPI, proton pump inhibitor; P-CAB, potassium competitive acid blocker; FGP, fundic gland polyp; GA-FG, gastric adenocarcinoma of fundic gland type.

sa 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 with 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 <65 years, mild atrophy, presence of round pits in the background gastric mucosa, tumor located in the upper third, same color as background mucosa, tumor size <10 mm, and a histological type consistent with FGP and GA-FG. Multivariate analysis revealed that the presence of round pits in the

▶ **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 <10 mm	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

DVBA, dilated vessels exhibiting branching architecture; OR, odds ratio; CI, confidence interval; FGP, fundic gland polyp; GA-FG, gastric adenocarcinoma of the fundic gland type

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 WRS-positive group and 12 lesions in the WRS-negative group. The clinicopathological features of the WRS-positive and -negative groups are presented in ▶ **Table 3**. In the WRS-positive group, FGPs and FGPs with dysplasia were found in 92.3% of cases (36/39), while in the WRS-negative group, GA-FGs were found in 50.0% of cases (6/12). Regarding the diagnostic accuracy of WRS, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of WRS positivity for FGP were 100%, 80.0%, 92.3%, 100%, and 94.1%, respectively, while those for WRS negativity for GA-FG were 100%, 86.7%, 50.0%, 100%, and 88.2%, respectively. Lesions in the WRS-positive group were diagnosed through 36 biopsies, one CSP, and two ESDs, whereas in the WRS-negative group, four biopsies and eight ESDs were used to establish diagnosis. Pathological features are shown in ▶ **Fig. 4**. The WRS-positive gastric lesions occurred at a higher rate of mild atrophy compared with the WRS-negative lesions (89.7% vs. 58.3%; *P* <0.05). No significant differences were found for age, sex, use of PPIs or potassium competitive acid blockers (P-CABs), history of *H. pylori* eradication, tumor location, lesion color, estimated tumor size, or morphology between the WRS-positive group and -negative 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 for WRS positivity, 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 for WRS negativity, 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 non-experts, 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 non-experts demonstrated excellent agreement levels, while the reliability for indistinct DL, CO dilation, IP dilation, and poor IMVP showed poor to good agreement levels.

Discussion

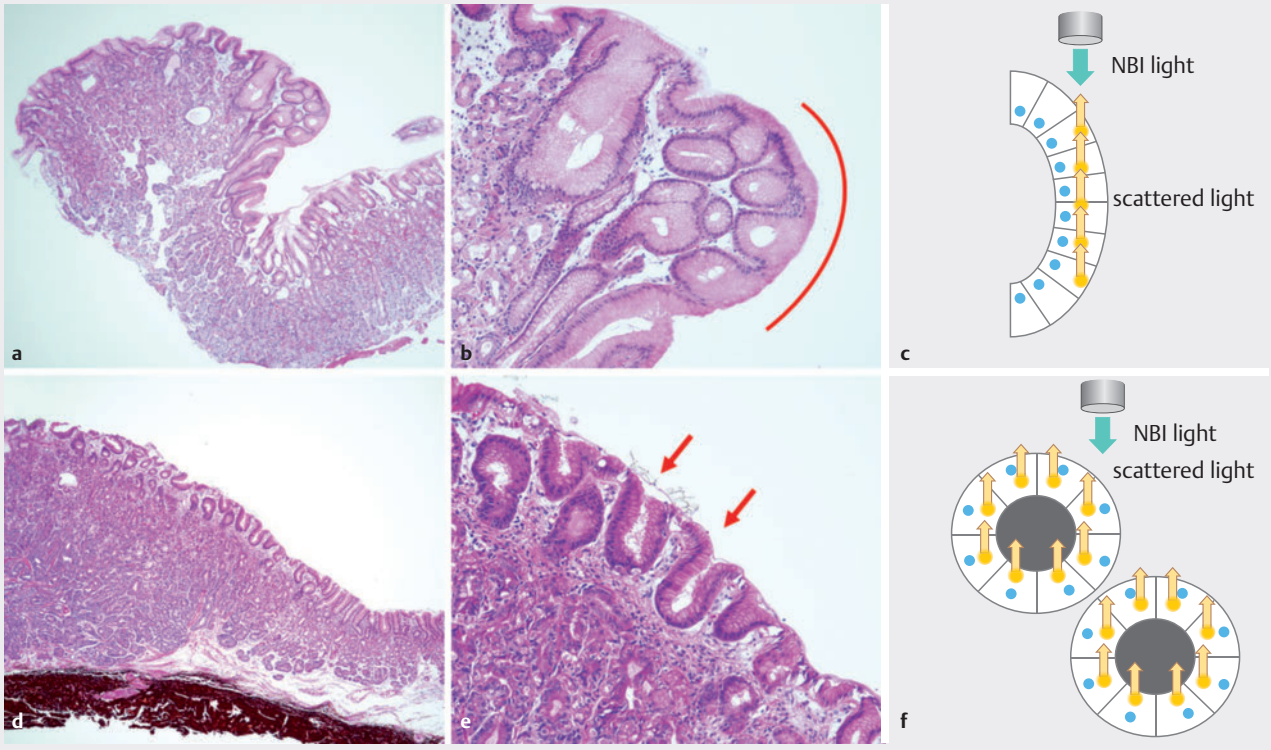
This is the first report demonstrating the characteristics of gastric elevated lesions with DVBA and the efficacy of WRS in distinguishing between FGP and GA-FG. Our results showed that the gastric elevated lesions with DVBAs primarily included GA-FGs and FGPs, characterized by presence of round pits in the background gastric mucosa. A 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, WRS positivity 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]. ▶ **Fig. 4a** shows that the CSP specimen of FGP with WRS positivity 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 (▶ **Fig. 4b**, ▶ **Fig. 4c**).

In gastric elevated lesions with DVBAs, WRS negativity 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 WRS negativity on NBI observation (▶ **Fig. 4d**, ▶ **Fig. 4e**, ▶ **Fig. 4f**). The previous study showed that a characteristic ME-NBI finding of GA-FG is an indistinct DL [11].

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

	WRS-positive group	WRS-negative group	*P* value
Number 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)	
▪ Semi-pedunculated	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)	

WRS, white ring sign; SD, standard deviation; PPI, proton pump inhibitor; CAB, competitive acid blocker; Hp, Helicobacter pylori; ESD, endoscopic submucosal dissection; FGP, fundic gland polyp; GA-FG, gastric adenocarcinoma of the fundic gland type.



▶ **Fig. 4** Pathological findings of WRS-positive and -negative lesions. **a** In the WRS-positive lesions of the FGP, the CSP specimen exhibited a curved margin with hyperplasia of the crypt epithelium. **b** Under high magnification, the continuous alignment of crypt epitheliums along the curved margin was observed (red line). **c** NBI light scatters upon entering the curved marginal crypt epithelium, resulting in visualization of the WRS on NBI observation. **d** In the WRS-negative lesion of the GA-FG, the ESD specimen showed gradual elevation at the lesion margin. **e** In the high-power field, a normal foveolar epithelium without the curved margin was observed (red arrow). **f** NBI light scatters upon entering each marginal crypt epithelium, resulting in CO dilation with a white zone and WRS negativity on NBI observation. WRS, white ring sign; FGP, fundic gland polyp; CSP, cold snare polypectomy; NBI, narrow-band imaging; GA-FG, gastric adenocarcinoma of the fundic gland type; ESD, endoscopic submucosal dissection; CO, crypt opening; NBI, narrow-band imaging.

While both an indistinct DL and WRS negativity are endoscopic features observed at the margin of GA-FG, the WRS negativity showed higher kappa coefficient values than indistinct DL. This suggests prioritization 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%, and 77.8% of FGPs, respectively. In addition, 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 WRS-negative 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 WRS-negative group than in the WRS-positive 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 differentiation between gastric adenocarcinomas and GA-FGs.

Our study has limitations. First, it may have a selection bias because it was retrospective 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 was because endoscopists believed that benign tumors such as FGPs were unsuitable for endoscopic resection, whereas a pathological diagnosis was possible using specimens obtained through biopsy. Third, the histopathological examination methods varied, including biopsy, CSP, and ESD. These diagnostic methods may have affected the accuracy of gastric lesion assessment. Fourth,

▶ **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
WRS-positive	36/36 (100)	0/6 (0)	0.891	0.841
Indistinct DL	0/36 (0)	2/6 (33.3)	0.628	0.346
CO dilation	10/36 (27.8)	4/6 (66.7)	0.507	0.079
IP dilation	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 microvascular pattern.

gastric lesions other than FGPs and GA-FGs were diagnosed as normal fundic gland mucosa using biopsy specimens. These lesions have the possibility of changing the diagnosis to another condition such as GA-FG when diagnosed by ESD specimens.

Conclusions

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 and useful marker for diagnosing gastric elevated lesions with DVBAs. If WRS positivity with a regular MSP and regular MVP is present, further evaluation and treatment may not be necessary. However, WRS negativity requires additional evaluations, such as endoscopic ultrasonography and endoscopic resection.

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Data availability statement

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

Conflict of Interest

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

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