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Research Article

Validity of low-magnification narrow-band imaging in annual endoscopy screening for gastric neoplasms: A case-control study

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ABSTRACT

Previously, I have reported the efficacy of whole stomach observation using magnifying narrow-band imaging at low magnification (LM-NBI) after routine white-light imaging (WLI). LM-NBI can detect lesions overlooked by WLI. However, the effectiveness of annual examinations remains unexplored. I conducted this case-control study at a single institution. In LM-NBI group, patients with chronic gastritis underwent a LM-NBI scan, defined as the minimal magnification offering maximal visual field coverage to unveil to the microsurface pattern of gastric mucosa, of the whole stomach following WLI. Historical control was used as the conventional magnifying endoscopy (CE) group. In both groups, index endoscopy, which equalizes the status, was performed first, and subsequently annually endoscopies up to five times were conducted. The first annual examination was performed from April 2019 to March 2020 in LM-NBI group and from April 2015 to March 2016 in CE group. The detection of gastric neoplasia was analyzed according to medical records. Among 388 patients in the LM-NBI group, and 381 in the CE group, 15 and 5 patients with gastric neoplasia were respectively identified. Except for one mucosa-associated lymphoid tissue lymphoma, all were epithelial neoplasias. All endoscopic examinations were performed safely without complications which needed additional medical interventions. Through a Cox proportional hazards model, the hazard ratio of 2.78 (95% CE, 1.01–7.64) was determined. Kaplan–Meier analysis ($p = 0.039$, log-rank test) revealed superior efficacy of annual LM-NBI over CE in detecting gastric neoplasia. This is the first study to report the efficacy of annual endoscopy using LM-NBI.

1. Introduction

Helicobacter pylori infection is recognized as a significant risk factor for gastric cancer.[1] Consequently, regular screening for early detection is crucial in regions with a high prevalence.[2] Although advances in endoscopy facilitates the resection of substantial neoplasms, smaller lesions are preferred. Nonetheless, identifying faint epithelial neoplasms is challenging.

Effective methods for accurately diagnosing gastric neoplasias include narrow-band imaging (NBI), one of image-enhanced endoscopies, and magnifying endoscopy.[3,4] Additionally, magnifying NBI (M-NBI) has displayed promising outcomes within this context. The diagnostic algorithm for conventional magnifying endoscopy (CE) was established using an evidence-based approach.[5] Initial steps of this approach involve identifying suspicious lesions using white light imaging (WLI), followed by magnifying endoscopy. Presently, image-enhanced endoscopies surpass WLI in the detection of gastric neoplasms,[6,7] making them pivotal tools for endoscopic surveillance.

In a recent report, the efficacy of utilizing low-magnification NBI (LM-NBI) for comprehensive stomach observation following routine WLI[8] was demonstrated. LM-NBI can detect minute lesions overlooked during WLI, especially those situated in regions of map-like redness or atrophic/metaplastic mucosa within the stomach. Such lesions account for approximately one-quarter of all newly diagnosed small neoplasms. The utilization of LM-NBI in endoscopic screening presents a promising avenue. However, there exists a gap in studies that validate the efficacy of periodic LM-NBI examinations in comparison with CE. Therefore, the objective of this case-control study is to evaluate the efficacy of annual

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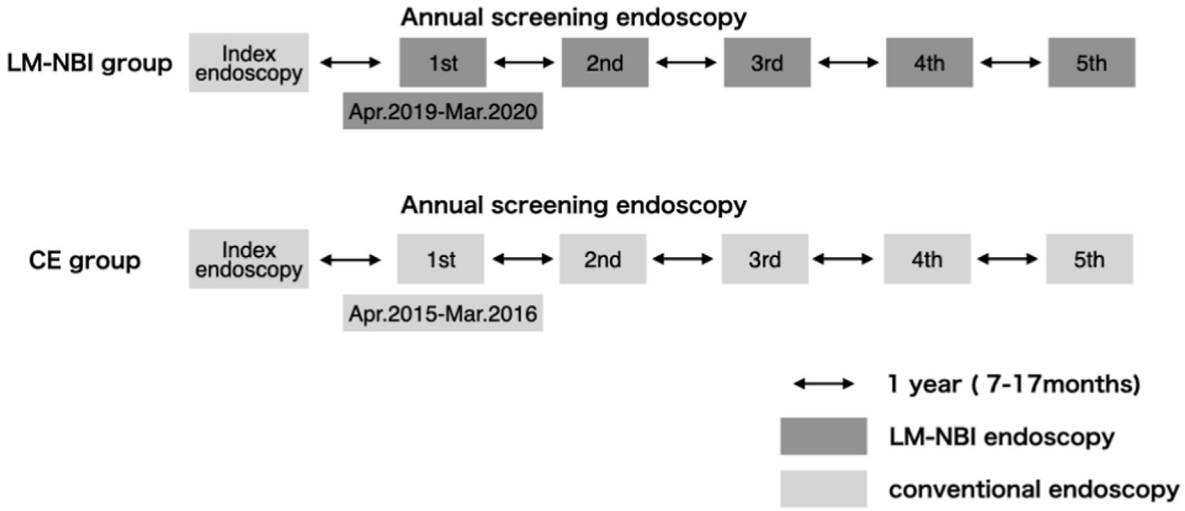

Fig. 1. Study design
All endoscopic examinations were performed within a 1-year (7–17 months) time frame. LM-NBI, low-magnification narrow-band imaging; CE, conventional magnifying endoscopy.

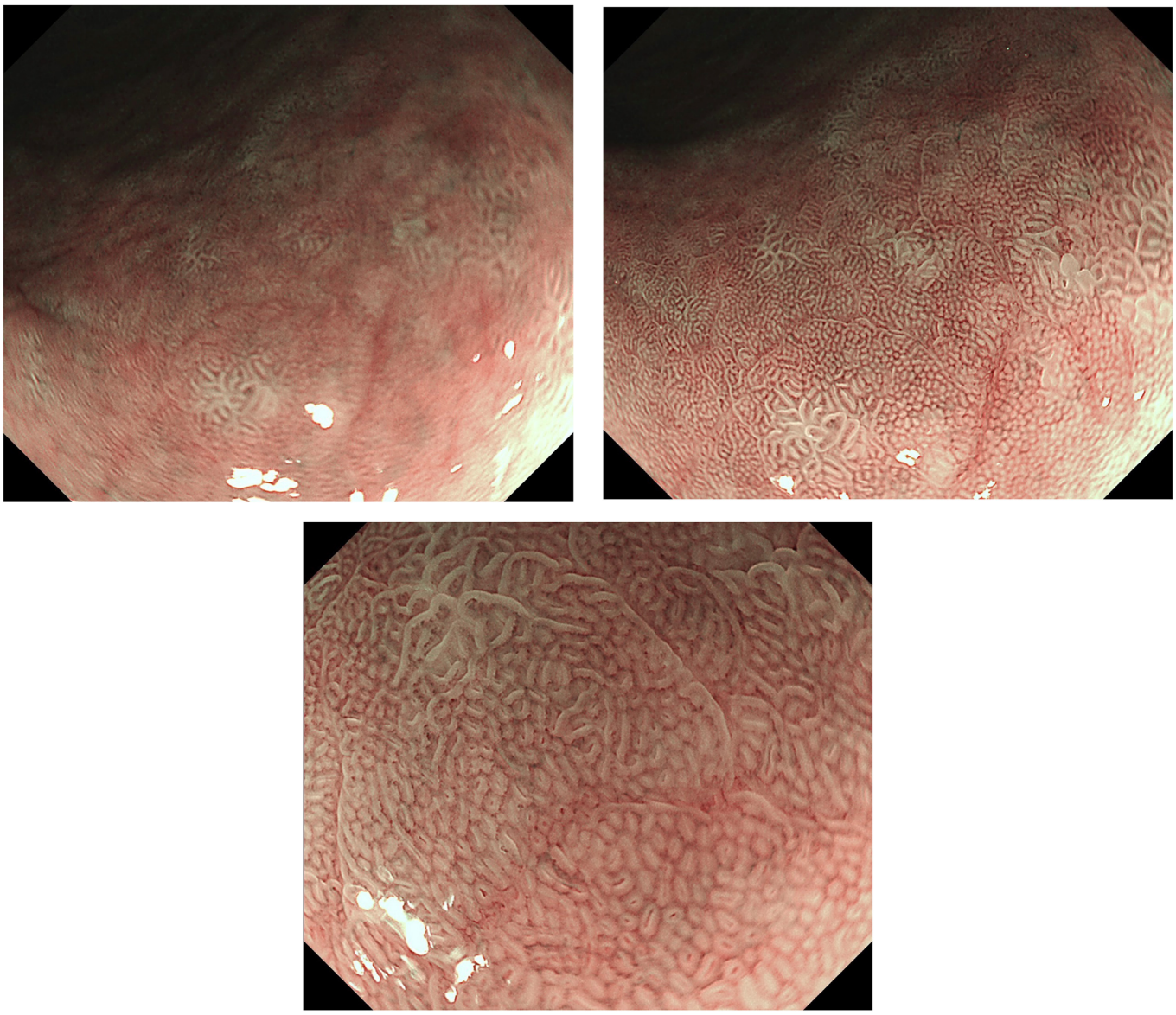

Fig. 2. LM-NBI
A, Close-up view of the antral mucosa of the stomach. Near focus exhibits a lack of sharpness. B, LM-NBI of the same angle.revealing a fine microsurface pattern. C, Higher magnification depicts minute structure narrows the field of view. LM-NBI, low-magnification narrow-band imaging.

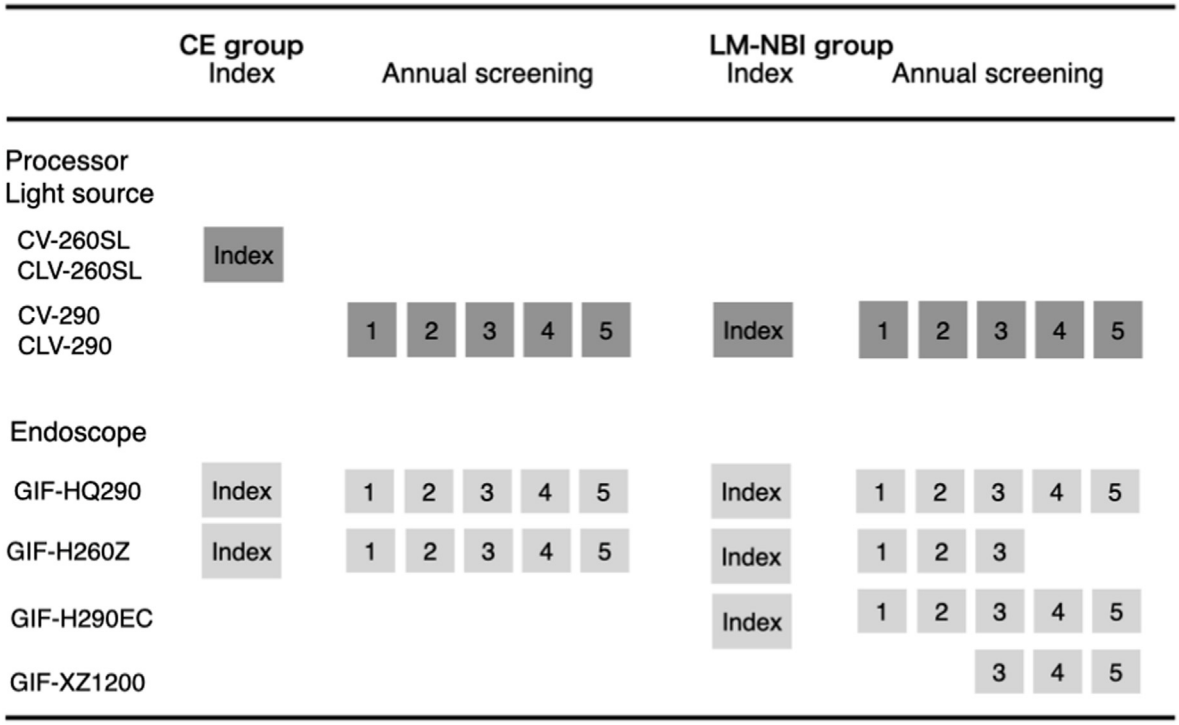

Fig. 3. Endoscopes and video endoscopic systems
LM-NBI: low-magnification narrow-band imaging. CE, conventional magnifying endoscopy.

endoscopic examinations utilizing LM-NBI for the entire stomach following WLI, aiming to detect gastric neoplasms.

2. Material and methods

2.1. Study design

This case-control study was performed at Nagashima Clinic, located in Yamagata City, the capital of Yamagata Prefecture, in Northern Japan. Given the evident efficacy of LM-NBI from a prior study,[8] ethical considerations made it difficult to establish a group without LM-NBI. Consequently, a retrospective approach was employed owing to the extended timeline needed for a new prospective study. The historical control group was included. The study design is illustrated in Fig. 1. Patients in the LM-NBI group underwent an LM-NBI scan of the entire stomach after a conventional WLI endoscopic examination between April 2019 and March 2020, classified as the first-annual LM-NBI. LM-NBI was initiated on 1st March 2019, with a 1-month incubation period. Clinical medical records were reviewed, and patients who underwent CE within a year (7–17 months in this study) were enrolled. The first CE was defined as the index endoscopy, that equalized the status of the stomach. Subsequent annual endoscopies up to five times were analyzed. Patients were included regardless of completing the full five annual endoscopies. The historical control group comprised patients from a period predating LM-NBI use. The control group encompassed patients who underwent their first annual CE screening between April 2015 and March 2016. Index endoscopy, and subsequent annual examinations were evaluated.

The study involved patients visiting Nagashima Clinic for checkups or routine follow-ups for chronic gastritis. Patient demographics and clinical characteristics were sourced from medical records. Patients with autoimmune gastritis or remnant stomach were excluded. Written informed consent for future studies using their clinical medical records was obtained from all patients. Details about the case-control study and the option to opt-out were provided on the website and premises of the clinic.

2.2. LM-NBI

Fig. 2A displays a close-up view of the microsurface pattern appearing blurry, and the magnifying function enabling to focus on the structure is illustrated in Fig. 2B. Higher magnification reveals minute structures, but narrows the visual field, as depicted in Fig. 2C. To minimize time-consuming tasks, LM-NBI was defined as the minimal magnification offering maximal visual field coverage to unveil to the microsurface pattern of gastric mucosa. Actual LM-NBI moving image were documented in a previous report.[8]

2.3. Endoscopic procedure

Endoscopic examinations took place between March 1, 2014 and January 14, 2023, under the expertise of an endoscopist with over 25 years of experience, having conducted approximately 30,000 examinations in the past 20 years. The video endoscopies and systems employed in this study are shown in Fig. 3. Processors and light sources comprised a video processor (Evis Lucera Elite CV-260SL or CV-290; Olympus Medical Systems, Tokyo, Japan) and a light source (Evis Lucera Elite CLV260SL or CLV-290; Olympus Medical Systems). All systems were equipped for NBI. CV-260SL and CVL260SL were used only for index endoscopy in the CE group. No incubation period was required for this transition as the new system did not require further expertise. GIF-HQ290, GIF-H260Z, GIF-H290EC, and GIF XZ1200 (Olympus Medical Systems) with magnifying functions, were utilized randomly.

Endoscopic examinations were performed via the oral route to observe the pharynx, esophagus, stomach, and duodenum. If sedation was required, 1% propofol was administered intravenously at an appropriate dose. To suppress peristalsis, 0.8% L-menthol was sprinkled on the stomach. After washing with a water-jet (Olympus Medical Systems), the gastric mucosa was observed under WLI. In the CE group, M-NBI was only performed upon detecting potentially suspicious neoplastic lesion.

In contrast, LM-NBI was routinely performed after WLI in the LM-NBI group. Suspicious lesions were examined with high-magnification NBI,

Table 1
Patient characteristics at index endoscopy.

Variables	LM-NBI group (n = 388)	CE group (n = 381)	*P*-value
Median age, years (IQR)	68 (61-75)	68 (61-76)	.84
Sex			.25
Male	178	191	
Female	210	190	
Helicobacter pylori status			<.01
Present infection	31	64	
Past infection	356	311	
Not tested	1	6	
Atrophic gastritis			<.01
Mild	140	100	
Moderate	94	72	
Severe	154	209	
Neoplastic lesions at index endoscopy			.67
Gastric adenoma	4	1	
Gastric cancer	2	2	
History of gastric neoplasia			.72
Gastric adenoma	11	15	
Gastric cancer	20	22	
Gastric lymphoma	2	1	
History of malignant neoplasia			>.5
Esophageal cancer	3	3	
Colorectal cancer	9	11	
Gallbladder cancer	2	2	
Lung cancer	5	3	
Breast cancer	5	6	
Thyroid cancer	2	2	
Rhinolaryngeal cancer	1	2	
Gynecological cancer	3	5	
Prostatic cancer	7	9	
Kidney-Bladder cancer	6	6	
Skin cancer	2	2	
Hematopoietic neoplasia	3	2	
History of smoking			.80
Smoker	25	29	
Ex-smoker	56	52	
Non-smoker	307	300	

IQR, interquartile range; CE, conventional magnifying endosocopy; LM-NBI, low-magnification narrow-band imaging.

Table 2
Characteristics of lesions detected in the stomach.

	Detection	Pathology	Diameter	Location	Back ground
					Mucosa
LM-NBI group					
#1	LM-NBI	LG adenoma	2 mm	Antrum	AM
#2	LM-NBI	LG adenoma	5 mm	Antrum	AM
#3	LM-NBI	LG adenoma	5 mm	Antrum	AM
#4	LM-NBI	LG adenoma	10 mm	Antrum	AM
#5	LM-NBI	LG adenoma	16 mm	Angle	MR
#6	LM-NBI	HG adenoma	5 mm	Body	
#7	LM-NBI	NI carcinoma	15 mm	Body	MR
#8	LM-NBI	MALT lymphoma	5 mm	Cardia	
#9	WLI	LG adenoma	5 mm	Antrum	AM
#10	WLI	LG adenoma	5 mm	Antrum	AM
#11	WLI	LG adenoma	13 mm	Antrum	AM
#12	WLI	HG adenoma	10 mm	Antrum	MR
#13	WLI	NI carcinoma	5 mm	Cardia	
#14	WLI	NI carcinoma	15 mm	Cardia	
#15	WLI	NI carcinoma	15 mm	Antrum	AM
CE group					
#1	WLI	LG adenoma	2 mm	Antrum	AM
#2	WLI	LG adenoma	3 mm	Antrum	AM
#3	WLI	HG adenoma	7 mm	Antrum	AM
#4	WLI	HG adenoma	20 mm	Body	
#5	WLI	NI carcinoma	6 mm	Antrum	

LG, low-grade; HG, high-grade; NI, non-invasive; AM, atrophic/metaplastic mucosa; MR, map-like redness; MALT, mucosa-associated lymphoid tissue; CE, conventional magnifying endoscopy; LM-NBI, low-magnifying narrow-band imaging.

defined as that at non-limited magnification, to clarify its characteristics in both groups. Biopsies were performed as required after the lesions were measured. Endoscopic examinations were recorded as fully moving and still images (GT Finder, Medical Image Communication System; A-Z, Sendai, Japan) with the duration of endoscopic observations measured using an embedded timer.

2.4. *H. pylori* status

H. pylori infection was determined using the ^{13}C-urea breath tests (UBit; Otsuka, Tokyo, Japan). Patient status was categorized as follows: those who tested positive on the ^{13}C-urea breath test were deemed to have a "present infection", whereas those with a history of successful eradication or no eradication history alongside negative ^{13}C-urea breath tests and atrophic changes in the gastric mucosa were classified as "past infection".

2.5. Endoscopic and pathologic criteria

According to the Kimura–Takemoto classification of atrophic gastritis,[9] atrophic status was evaluated and categorized as follows: C-1 and C-2, mild; C-3 and O-1, moderate; and O-2 and O-3, severe.

Neoplastic lesions were pathologically diagnosed based on the revised Vienna Classification of Gastrointestinal Epithelial Neoplasia (rVC)[10] as follows: rVC 3, low-grade adenoma; rVC 4.1, high-grade adenoma; and rVC4.2, non-invasive carcinoma.

2.6. Statistical analysis

Patient demographics comparisons at index endoscopy employed the Mann–Whitney *U* test with two-sided p-values for continuous variables and Fisher's exact probability test for categorical variables. An event was defined as the detection of neoplasia in the stomach, and Kaplan–Meier analysis was performed to summarize time-to-event variables. Cumulative incidence ratios were plotted, and the log-rank test facilitated comparisons. The stratified hazard ratio from the Cox proportional hazards model was utilized for estimating the hazard ratio between the groups. Statistical analyses were performed using EZR,[11] a modified version of R commander.

3. Results

A total of 388 and 381patients were enrolled in the LM-NBI and CE groups, respectively. Table 1 outlines patient demographics at index endoscopy. Patients in the control group tended toward gastric neoplasia development, including *H.pylori* infection ($p<0.01$) and severe atrophic gastritis ($p<0.01$). No significant differences were observed regarding age, sex, gastric neoplasia, history of malignant neoplastic lesions, or smoking history between the groups.

All endoscopic examinations were performed safely without complications which needed additional medical interventions including hospitalization. Observation times during first annual endoscopies were compared. The median observation time in the LM-NBI group was 491 s (interquartile range [IQR] 387–576 s), whereas 395 s (IQR, 310–437 s) in the CE group, ($p < 0.01$). LM-NBI necessitated approximately100 s more than CE. During observations, sedation was administered in 311 of the 388 patients in the LM-NBI group, and 268 of the 381patients in the CE group ($p < 0.01$).

Fifteen cases of neoplasia were identified in the LM-NBI group, whereas five cases found in the CE group. Among the LM-NBI group, 8 out of 15 cases were identified using LM-NBI. Table 2 lists all lesions, except for one mucosa-associated lymphoid tissue lymphoma; the rest included epithelial neoplasms such as adenomas or non-invasive tubular adenocarcinomas, all with diameters <20 mm. Several lesions were found in the antrum of the stomach. Endoscopically, these lesions were characterized by atrophic/metaplastic mucosa, or a background map-like

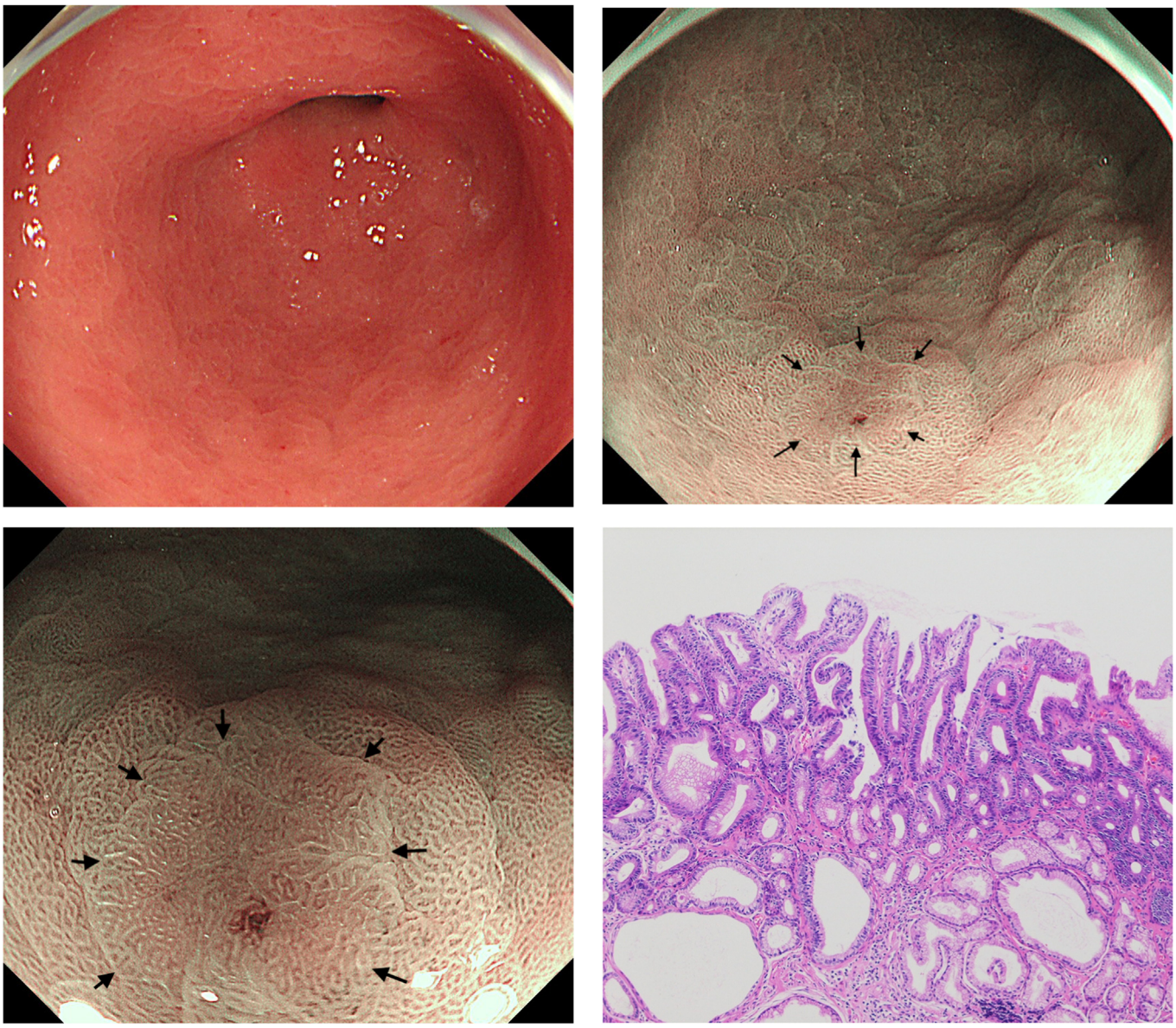

Fig. 4. Case #1
A, White light images of the antrum of the stomach, which the lesion barely visible. B, LM-NBI observation displays a small brownish area on the greater curvature (arrows). C, Higher magnification reveals the microsurface pattern of the lesion, with mild irregularity and an evident demarcation line (arrows). D, Pathological finding of the lesion reveals low-grade adenoma, characterized by tubular proliferation of glands with low atypia. LM-NBI, low-magnification narrow-band imaging.

redness, commonly observed after the successful eradication of *H.pylori*,[12]– a well-known source of gastric neoplasia. Still images of Case #1 are showcased in Fig. 4, depicting the smallest lesion discovered in this study. LM-NBI effectively detected this diminutive lesion, which was overlooked by CE.

The median follow-up duration was 31 months (interquartile range [IQR], 14 –47 months) in the LM-NBI group, and 29 months (IQR, 14 – 46 months) in the CE group. There was no significant inter-group difference ($p = 0.22$, Mann–Whitney *U* test).

Fig. 5 presents the cumulative incidence ratios, demonstration the superiority of annual LM-NBI observations in detecting gastric tumors (hazard ratio, 2.78; 95% confidence interval, 1.01–7.64; $p = 0.039$, log-rank test) when compared with CEs.

4. Discussion

This historical case-control study demonstrates the capacity of annual LM-NBI, subsequent to WLI, for detecting neoplastic lesions in the stomach at a rate approximately three times higher than CE. To the best of our knowledge, this is the first study to substantiate the efficacy of annual endoscopy employing LM-NBI for detecting gastric neoplasms.

The strengths and limitations of this study are closely tied to the fact that a single endoscopist conducted all the endoscopies at a single clinic. Given that the endoscopist was substantially experienced, each endoscopic examination was executed uniformly and methodically, devoid of bias, although control endoscopies were performed over 5 years prior to the case series examination. However, these findings may not be universally applicable to other institutions.

Further limitations emerged from the comparison between cases and controls. The control group included more patients with *H. pylori* infection and severe cases of chronic gastritis than the case series group. As these are significant risk factors for gastric cancer,[1] neoplasia prevalence was surmised to be higher in the CE group than in the LM-NBI group. Nevertheless, a substantial number of neoplasms were detected in the

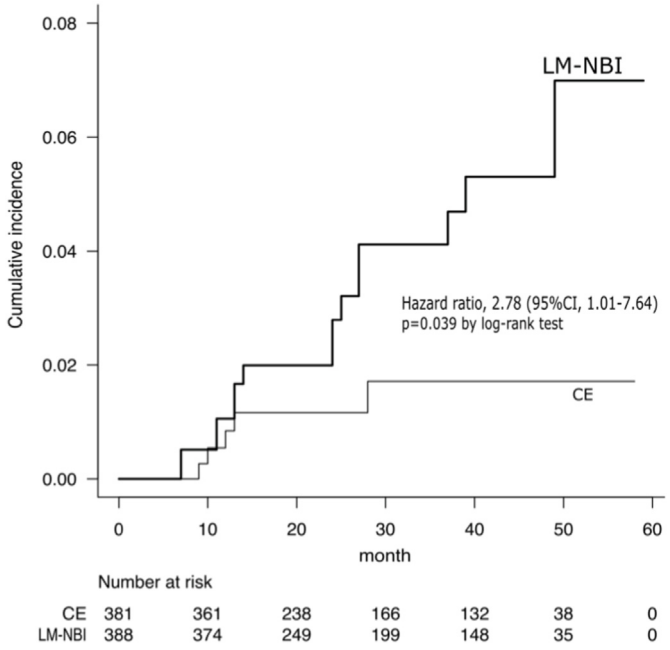

Fig. 5. Cumulative incidence of gastric neoplasms
LM-NBI: low-magnification narrow-band imaging. CE, conventional magnifying endoscopy.

case group. These disparities did not undermine the competence of LM-NBI; instead they bolstered the conclusions of this study. During LM-NBI, two novel endoscopy devices were introduced: GIH-H290EC and GIF-XZ1200. These endoscopies have prominent magnifying powers, but average image quality in the distant or middle view in combination with the processor CV-290. The endoscopies provide an accurate diagnosis of lesions at magnification, but were neutral in detecting mucosal changes in conventional observation. Therefore, parity in visualization was preserved in this study.

LM-NBI required an additional 100 s in examination compared with CE; nevertheless, there were no complications associated with this extension. Given that many patients (approximately 80%) undergoing LM-NBI required sedation, this extension can be deemed acceptable. The author has routinely performed this extended observation period to date without any major complications.

A recent report has demonstrated that LM-NBI was able to detect lesions overlooked by WLI, especially those situated in regions of map-like redness or atrophic/metaplastic mucosa of the stomach.[8] The same tendency was observed in the present study. However, it is essential to note that this study does not seek to directly compare lesions between LM-NBI and WLI, as elucidated in the earlier report featuring moving images.[8]

Unfortunately, diffuse-type carcinomas were not detected during these endoscopic examinations. Consequently, the potential of additional LM-NBI procedures in detecting these lesions remains uncertain. We might not expect much since M-NBI reportedly has limitations in diagnosing signet ring cell carcinomas.[13]

The author posits that exclusive reliance on LM-NBI for endoscopic examination is not prudent, given the risk of overlooking lesions where WLI holds superiority. Owing to inherent features in imaging systems, observers are inclined to focus on color changes in WLI. In contrast, we inspect the surface structures closely in NBI,[3,4] of course in LM-NBI. Previous reports have shown that tandem examinations involving both WLI and NBI tend to detect more lesions than either method used individually.[14] It is thus imperative to leverage reciprocal functions for comprehensive detection.

The set surveillance period of 1 year aligns with the prevalent practice of annual and biennial screenings in Asia.[2] Neoplasias have consistently surfaced during annual observations, with a recent report emphasizing the efficacy of 1-year surveillance using WLI and NBI.[15] This annual interval appears appropriate for screening patients with chronic gastritis.

Further clarification is needed to establish the superiority of LM-NBI over other image-enhanced endoscopies, such as blue laser imaging-bright[6] and linked color imaging.[7] Consequently, further studies are warranted.

5. Conclusion

This study extensively evaluated the effectiveness of annual endoscopic examinations using LM-NBI. The findings provide robust support for the routine incorporation of LM-NBI in endoscopic screening practices.

Ethics approval and consent to participate

This study was reviewed and approved by the Ethics Board of the Yamagata Prefecture branch of the Japan Medical Association (approval reference number:17). All analyses were conducted in accordance with the relevant guidelines and regulations.

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None.

Availability of data and material

The datasets analyzed in the current study are available from the author upon reasonable request.

Declaration of competing interest

The author have no conflicts of interest or financial ties to disclose.

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