Comparison between Narrow Band Imaging Technology and Methylene Blue Chromoendoscopy in Early Detection of Barrett's Esophagus

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Abstract

Background: Gastroesophageal reflux disease (GERD) is a chronic lower esophageal disorder with a variant global prevalence. Barrett's esophagus (BE) represents the replacement of the normal squamous epithelium lining of the lower esophagus by a specialized columnar epithelium and is a forerunner of esophageal adenocarcinoma (EAC). The EAC prevention paradigm relies on endoscopic monitoring of BE to identify dysplastic changes and deliver effective endoscopic treatment.

Objectives: are an assessment of the diagnostic effectiveness of narrow-band imaging-targeted (NBI) and methylene blue chromoendoscopy-targeted biopsies (MBCE) using high-resolution upper gastrointestinal endoscopy (HR-UDIE) compared to four-quadrant biopsies, using conventional upper gastrointestinal endoscopy (C-UGIE) as the gold standard for comparison.

Patients and methods: Fifty patients were clinically evaluated and underwent C-UGIE using a video endoscopy system, Olympus GIF 240, to obtain four-quadrant biopsies from any salmon-colored mucosa or visible suspicious lesion extending for ≥1 cm proximal to the gastroesophageal junction. Six weeks later, all patients were re-examined using HR-UGIE (EVIS X1), and biopsy taking was performed using either NBI or MBCE.

Results: Pathological examinations of the four-quadrant biopsies obtained by the C-UGIE detected variant pathological diagnoses, including BE with different degrees of dysplasia, and three patients had EAC. Pathological diagnoses of biopsies obtained by NBI or chromoendoscopy were comparable (P = 0.939). The diagnostic performance of NBI and MBCE for BE and EAC was comparable and matched with the result of the gold standard method.

Conclusion: Both NBI and MBCE can be effectively applied for BE screening in patients with chronic GERD.

Keywords: Gastroesophageal reflux disease (GERD); Barrett's esophagus; Esophageal adenocarcinoma; Narrow-band imaging (NBI); Chromoendoscopy.

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Gastroesophageal reflux disease (GERD), a chronic lower esophageal disorder, presents a complex pathophysiological challenge. Still, the underlying mechanisms for the development of GERD were not fully understood **(Chen et al., 2025)**.

Globally, the prevalence of GERD is variable across countries, but a high frequency of GERD was observed in countries that are accustomed to eating Western diets in conjunction with obesity, high consumption of alcohol, excessive tobacco smoking, obesity and frequent gestation **(Shen et al., 2025)**.

Barrett's esophagus (BE) represents the replacement of the normal squamous epithelium lining of the lower esophagus by a specialized columnar epithelium and is a forerunner of esophageal adenocarcinoma (EAC). The global prevalence of BE, based on risk factors for various populations, ranges from 0.4 to 20% **(Rashidian et al., 2025)**. Barrett's esophagus with indefinite dysplasia is a pathological diagnostic challenge and is associated with a higher hazard probability for progressing to neoplasia **(Angerilli et al., 2025)**

The endoscopic detection of EAC usually happens late in disease progression, which is often linked to poor prognosis and high mortality rates. This highlights the need for improved technologies for earlier detection **(Li et al., 2025)**. Early diagnosis and management of esophageal precancerous lesions are connected to significantly higher 5-year survival rates, increasing from 10% to 98% **(Hicheri et al., 2024)**.

The EAC prevention paradigm relies on endoscopic monitoring of BE to identify dysplastic changes and deliver effective endoscopic treatment. However, the subtle appearance of dysplasia, noncompliance with endoscopic tracking, and inherent sampling error all diminish the effectiveness of surveillance protocols **(Lyer & Chak, 2023)**. Several endoscopic modalities are used for diagnosing and monitoring GERD, including conventional white-light and high-resolution endoscopies, image-enhanced endoscopies, chromoendoscopy, and narrow-band imaging **(Simadibrata et al., 2023)**. Nonetheless, the differences among these modalities regarding biopsy feasibility, number of biopsies, pathological accuracy, and diagnostic performance for BE and EAC remain uncertain **(Young et al., 2025)**.

The study aimed to assess the diagnostic effectiveness of narrow-band imaging-targeted biopsies (NBI) and methylene blue chromoendoscopy-targeted biopsies (MBCE) using high-resolution upper gastrointestinal endoscopy (HR-UDIE) compared to four-quadrant biopsies, using conventional upper gastrointestinal endoscopy (C-UGIE) as the gold standard for comparison.

Patients and methods

Design: Prospective randomized clinical trial.

Setting: Department of Internal Medicine, Faculty of Medicine, in collaboration with Experimental and Clinical Internal Medicine, and Pathology Departments, Medical Research Institute, Alexandria University, Alexandria, Egypt.

Trial Registration: The Ethical Committee, Alexandria University, following the Helsinki Declaration rules, approved the study protocol with the IRB number: 0106969.

Ethical considerations: The study protocol was explained to patients who attended the Alexandria University hospital, from June 2023, and were complaining of manifestations of chronic GERD before scheduling for UGIE, and those who agreed to participate in the study were evaluated for the study enrolment criteria and signed a written consent before enrollment.

Inclusion criteria: Refractory GERD, defined as the occurrence of symptoms ≥3

times weekly, and unresponsive to a double dose of proton-pump inhibitors for 2–3 months, with or without at least two risk factors for BE or EAC, including history of BE or EAC in a first-degree relative, male gender, age older than 50 years, current or ex-smoking, and obesity, were the inclusion criteria.

Exclusion criteria: Chronic GERD for >5 years of complaining, and was previously confirmed by UGIE, age younger than 18 years, the presence of esophageal varices, coagulopathy, previous upper gastrointestinal surgeries, pregnancy, maintenance on non-steroidal anti-inflammatory drugs, and uncontrolled medical disorders that hamper UGIE, were the exclusion criteria.

Sample size calculation

Canto et al., (2000) compared cancer surveillance in BE patients using methylene blue-directed biopsies to using a "jumbo" random biopsy technique in a study comprising 43 BE patients. **Hamamoto et al., (2004)** also tried to evaluate the diagnostic yield of NBI for BE compared to conventional endoscopy in a study that included 11 patients with previously diagnosed BE. The sample size was calculated using G*Power software version 3.1.9.2 **(Faul et al., 2007)**. Setting α-error at 0.05 and power at 80%, assuming a difference in cancer detection rate was insignificant, but was significant versus the conventional endoscope, corresponding to an effect size (F) of 0.35, produced a sample size of 25 patients in each group (50 total), considering the exclusion rate.

Randomization and Grouping

Randomization was performed using a computer-generated random sequence to allocate patients into two study groups in a 1:1 ratio. Group NBI (n = 25) and the Group MBCE (n = 25). Allocation concealment was ensured by sequentially numbered, sealed, opaque envelopes prepared by a research assistant, not an author. Both patients and the endoscopists were blinded to group assignments to minimize performance and detection bias.

Pre-procedural evaluation

Clinical evaluation entailed the collection of demographic data, the presence of risk factors for BE or EAC, and a history of previous GI manipulation or surgeries. Clinical history taking for typical symptoms, which include heartburn, regurgitation, esophageal chest pain, and atypical manifestations, including belching, chronic cough, and asthma. A full clinical examination and laboratory workup were then performed.

Upper Gastrointestinal Endoscopy (UGIE) procedures

UGIE was undertaken under propofol sedation that was provided by an anesthetist, who was not included as an author. All patients underwent C-UGIE using a video endoscopy system, Olympus GIF 240, Japan, to ensure GERD diagnosis and obtain conventional four-quadrant biopsies from every 2 cm of any salmon-colored mucosa or visible suspicious lesion that extended≥1 cm proximal to the gastroesophageal junction (GEJ), based on the ASG recommendation protocols for BE surveillance **(Shaheen et al., 2016)**. Patients were given an appointment after 6 weeks to be re-examined using the HR-UGIE, using a video endoscopy system, Olympus EVIS X1, Japan **(Olympus, 2020)**, and biopsy taking according to the technique assigned for each group. All biopsy specimens taken from any suspicious lesions were placed in separate specimen jars and sent for pathological examination.

Statistical analysis

Data normality was assessed using the Kolmogorov–Smirnov test and normal Q–Q plots. Continuous variables were shown as mean and standard deviation, and the significance of differences was assessed

using the unpaired t-test. Qualitative variables were presented as frequencies and percentages, and Chi-square or Fisher's exact tests with Bonferroni correction were applied to define the significance of differences. Statistical analyses were performed using IBM® SPSS® Statistics, version 22 (IBM Corp., Armonk, NY, USA). A two-sided P-value < 0.05 was considered statistically significant.

Results

Preliminary evaluation included 63 patients; 7 patients were excluded, and 56 patients were randomly divided into two study groups. Six patients of those who had conventional endoscopy did not attend to undergo the full protocol of endoscopic assessment and were excluded from the analysis (**Fig. 1**).

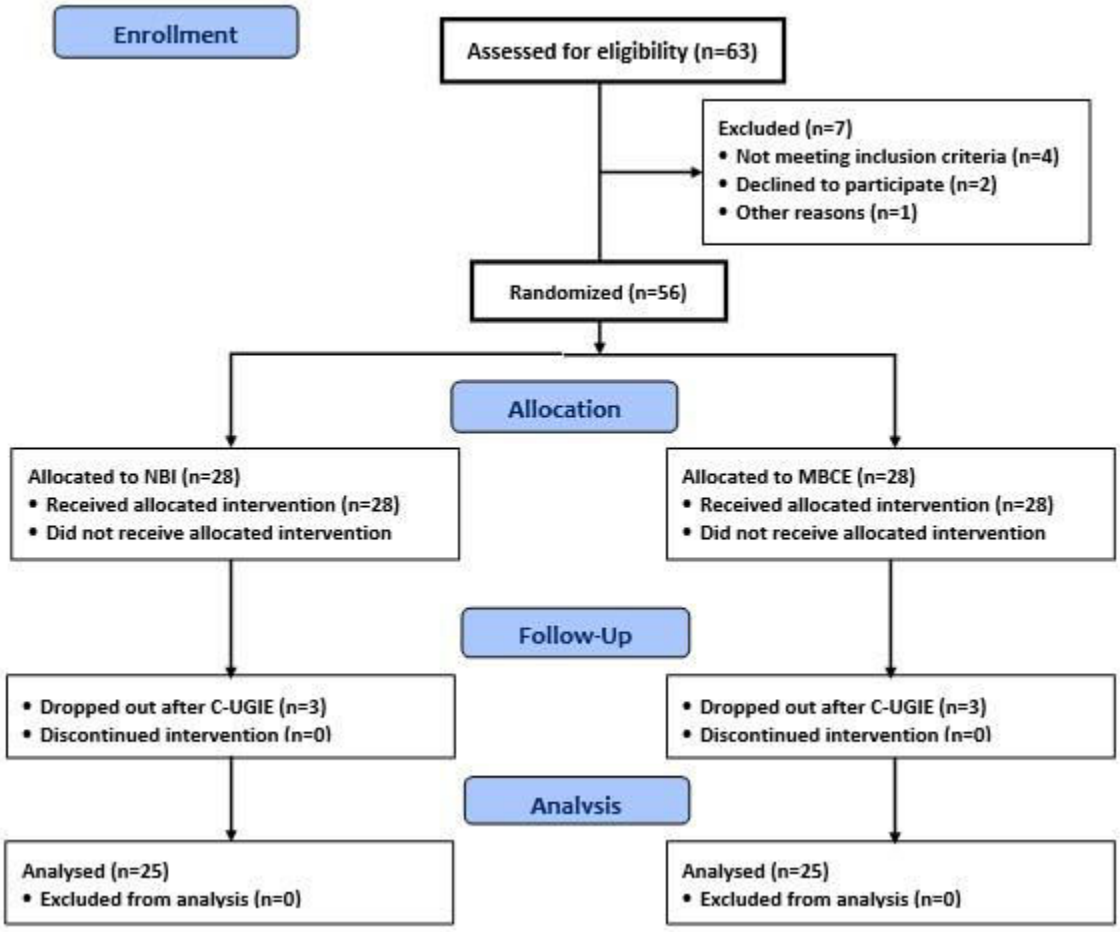

Fig.1. Consort Flowchart.

The demographic data showed insignificant intergroup differences (**Table.1**). Pathological examinations of the four-quadrant biopsies obtained by the Conventional endoscopy detected variant pathological diagnoses, including normal stratified squamous epithelium, esophagitis, BE with different degrees of dysplasia, and three patients had EAC. Targeted biopsies from suspicious lesion in gastroesophageal junction using NBI imaging technique (**Fig.2**). Targeted biopsies from suspicious lesion in gastroesophageal junction using high resolution endoscopy and methylene

blue chromoendoscopy (**Fig.3**). Pathological diagnoses of biopsies obtained by either NBI or chromoendoscopy were comparable with statistically insignificant difference (P=0.939) as shown in (**Table.2**).

Table 1. Demographic Data

Variables	Group NBI (n = 25)		Group MBCE (n = 25)		Test of Sig.	p
Age (years)						
<50	8	32.0%	9	36.0%	χ^2=0.094	0.935
≥50	17	68.0%	16	64.0%		
Min. – Max.	20.0 – 78.0		21.0 – 70.0			
Mean ± SD.	53.48 ± 14.28		54.45 ± 13.13		t=0.093	0.926
Sex						
Male	14	56.0%	15	60%	χ^2=0.088	0.840
Female	11	44.0%	10	40%		
Residence area						
Rural	9	36.0%	10	40.0%	χ^2=0.085	0.771
Urban	16	64.0%	15	60.0%		

SD: Standard deviation; t: Student's t-test; χ^2: Chi-square test; p: Probability value for comparison between the studied groups. *p ≤ 0.05 was considered statistically significant.

Table 2. Comparison of histopathological findings between Baseline conventional Endoscopy and the four-quadrant biopsy with both NBI and Chromoendoscopy techniques

Method / Histopathology in biopsies	Group NBI				Group MBCE			
	Conventional		NBI		Conventional		Chromoendoscopy	
	No.	%	No.	%	No.	%	No.	%
Normal stratified squamous epithelium	12	48.0	9	36.0	11	44.0	10	40.0
Esophagitis	6	24.0	5	20.0	9	36.0	6	24.0
Barrett's with high-grade dysplasia	1	4.0	4	16.0	1	4.0	2	8.0
Barrett's with low-grade dysplasia	1	4.0	1	4.0	0	0.0	2	8.0
Barrett's metaplasia	3	12.0	4	16.0	3	12.0	4	16.0
Adenocarcinoma	2	8.0	2	8.0	1	4.0	1	4.0

NBI: Narrow-band imaging–targeted biopsies; MBCE: Methylene blue chromoendoscopy–targeted biopsies.

(A) (B)

Fig. 2. A) Conventional endoscopic view of Barrett's esophagus and B) Narrow Band Imaging (NBI) highlighting a suspicious lesion at the gastroesophageal junction, where targeted biopsies were obtained.

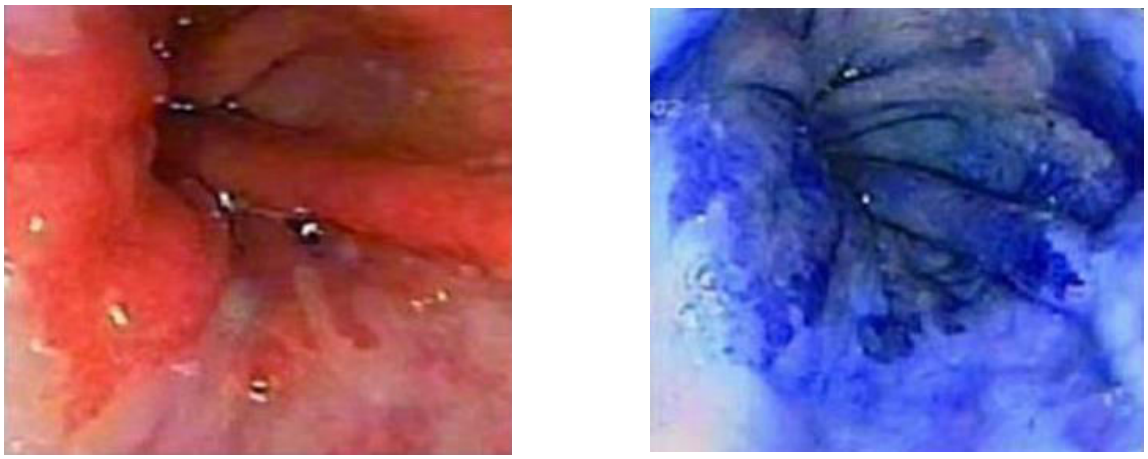

Fig. 3. A) Conventional endoscopic view of Barrett's esophagus and B) high-resolution methylene blue chromoendoscopy highlighting a suspicious lesion at the gastroesophageal junction, from which targeted biopsies were obtained.

The diagnostic performance of narrow-band imaging and methylene blue chromoendoscopy for BE and EAC was comparable and matched with result of the gold standard method (**Table.3**)

Table 3. Sensitivity, specificity, and accuracy for both NBI and Chromoendoscopy techniques in different groups compared to baseline conventional Endoscopy and the four-quadrant biopsy in detecting Barrett's esophagus and its dysplastic changes.

Histopathology		Four-quadrant biopsies (gold standard)		Sensitivity	Specificity	PPV	NPV	Accuracy
		Abnormal	Normal					
		No.	No.					
NBI	Abnormal	5	4	100.0	80.0	55.56	100.0	84.0
	Normal	0	16					
	Total (n=25)	5	20					
Chromoendoscopy	Abnormal	4	4	100.0	80.95	50.0	100.0	84.0
	Normal	0	17					
	Total (n=25)	4	21					
Test of significance				NA	0.074	0.012	NA	NA
P value				NA	0.785	0.912	NA	NA

PPV: Positive predictive value; NPV: Negative predictive value; NA: Not applicable; p: value for comparison between the studied groups. *$p \leq 0.05$ was considered statistically significant.

Discussion

Comparison between narrow band imaging targeted biopsies and chromoendoscopy targeted biopsies has been investigated in previous studies. **Bisschops et al. (2018)**, reported that NBI has the potential to replace chromoendoscopy as it is easy and convenient to apply, even though both methods don't vary too much in the detection of dysplasia. In other study, NBI-guided targeted biopsy technique was assessed and the authors found excellent repeatability and precision in detecting and describing dysplasia as well as intestinal metaplasia in BE **(Feldman and Wolf, 2014)**. **Hajelssedig et al. (2021)** Concluded in their meta-analysis and systematic review that NBI guided biopsy had high diagnostic correctness and can replace hazardous biopsies taken by other techniques. In another meta-analysis, NBI was found more effective than conventional endoscopy in determining esophageal dysplasia and adenocarcinoma **(Sharma et al., 2016)**. In a study involving 1,911 participants done by **Morita et al. (2017)** NBI was more effective than the traditional chromoendoscopy used with Lugol's iodine, in identifying advanced intraepithelial neoplasia and esophageal squamous cell carcinoma.

On the other hand, some reports have suggested that chromoendoscopy with high-resolution may clarify the mucosal architecture in Barrett's esophagus, which matches up with specialized intestinal metaplasia and high-grade dysplasia **(Qumseya et al., 2013)**.

However, **Bisschops et al. (2018)** stated that although chromoendoscopy and NBI are comparable in diagnosis of

dysplasia, the easy usefulness of NBI and the lengthy withdrawal time for chromoendoscopy make NBI efficiently replace chromoendoscopy **(Yamasaki et al., 2020).**

To determine which method is more efficient in screening of Barrett's esophagus in patients with chronic GERD, this study compared the accuracy of narrow band guided biopsy versus chromoendoscopy guided biopsy.

Fifty patients in total, 25 in each group participated in our study, the age and sex distribution was matched in the two groups. The distribution of patients between the two groups in terms of their urban and rural origins also did not significantly differ.

In this study, comparison between narrow band imaging target biopsy and methylene blue target biopsy revealed that the number of patients diagnosed as BE with different degrees of dysplasia and patients diagnosed as adenocarcinoma were almost the same in the two methods and mildly differ from each other, this difference was not statistically significant.

Comparing the two methods with the gold standard 4 quadrant biopsy method, two patients were diagnosed with adenocarcinoma by NBI-targeted biopsies and by four quadrant biopsies in group 1 and 9 patients were confirmed to have Barrett's esophagus by NBI-targeted biopsies and only 5 patients were confirmed to have Barrett's esophagus by the gold standard four- quadrant biopsy in group 1.

In the present study by using chromoendoscopy targeted biopsies, 1 patient diagnosed as adenocarcinoma and 8 patients as Barrett's esophagus but by the gold standard four-quadrant biopsy, one patient diagnosed as adenocarcinoma and 4 patients diagnosed as Barrett's esophagus. Our results suggest that both narrow-band imaging and methylene blue chromoendoscopy are comparable in screening of Barrett's esophagus.

Conclusion

Our findings suggested that both NBI and methylene blue chromoendoscopy can be effective screening methods for Barrett's esophagus in patients with chronic GERD, and they add benefit to the standard four-quadrant biopsy, and both are comparable in the screening of Barrett's esophagus.

Author contributions: Case collection and clinical assessment were performed by Abdelgawad, ZME, and supervised by Albana, AAS. Mostafa NR was responsible for the C-UDIE; Abdelaaty E underwent the NBI and MBCE. Each author was blinded to the data obtained by the others. Pathological examination was the duty of Alsedfy ASM, who was blinded to the endoscopic results. Mostafa NR was responsible for performing the statistical analyses, interpreting the results, and drawing conclusions. Abdelaaty E. handled the conceptualization and methodology. Writing of the full text, and title/abstract was the duty of Mostafa NR.

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