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Usefulness of Chromoendoscopy and Narrow Band Imaging in Barrett's Esophagus

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Abstract

Barrett's esophagus (BE) is the most important risk factor for esophageal adenocarcinoma. High resolution magnification endoscopy with Narrow band imaging (NBI) facilitates mucosal surface evaluation and may improve the endoscopic diagnosis of Barrett's esophagus. The aim of this work was to study the diagnostic value of chromo endoscopy versus NBI in detection of Barrett's esophagus. Patients and methods*:* Forty patients their conventional white light endoscopy revealed the diagnosis of GERD and showed findings suggestive of Barrett's esophagus, they were divided into 20 patients underwent chromo endoscopy and 20 patients underwent Narrow band imaging (NBI), The endoscopic results of both groups were compared with the final histo pathological diagnosis. Results: NBI showed higher accuracy than chromo endoscopy 75 % which vs. 70 % P< 0.05 in detection of BE. NBI had an accuracy of 70 and 75 % in type A pattern (round pits with regular microvasculature) to predict columnar mucosa without intestinal metaplasia and type B pattern (villous pits with regular microvasculature) to predict specialized intestinal metaplasia respectively. Conclusion: NBI is not only helpful in detecting metaplasia but also in differentiating cardiac from intestinal metaplasia, as it allows clear visualization of micro structural and micro vascular patterns.

Keywords: Barrett's esophagus; narrow band imaging; chromo endoscopy.

Introduction

Barrett's esophagus (BE) is defined histologically by the replacement of the normal squamous epithelium of the esophagus with specialized intestinal metaplasia (SIM) [1]. Special attention is being paid to BE as it has been recognized as a precursor for esophageal adenocarcinoma (EAC) [2]. Barrett's associated esophageal cancer occurs by way of the metaplasia-dysplasia-carcinoma sequence [3]. Current protocols recommend upper endoscopy surveillance with four-quadrant random biopsies at 2 cm intervals of Barrett's epithelium and targeted biopsies of abnormal mucosa to detect neoplastic changes, but it is commonly known that apart from being time consuming and uncomfortable random biopsies are associated with sizeable sampling errors [4]. It has been described as a "hit and miss" approach as areas of high-grade dysplasia or microscopic carcinoma in BE are often small and it is often difficult to detect the subtle, early dysplastic appearing lesions in BE even by the most rigorous biopsy protocols [5]. A plethora of new

techniques have been applied to overcome the limitations of surveillance by random biopsy and optically detect SIM and early neoplasia, including light scattering spectroscopy, laser-induced fluorescence spectroscopy, and optical coherence tomography. However, most of these techniques require expensive instruments and are technically demanding [3]. Chromo endoscopy has been assessed with various staining agents in BE, but there are various problems associated with it; sometimes these dyes do not spread uniformly on the surface of the mucosa; they can be messy to prepare; and there have been some concerns regarding toxicity [6]. Narrow band imaging (NBI) is a recent advance in endoscopic technology, which uses spectral narrow band filters (red, green and blue bands (RGB)) that allow for visualization of esophageal mucosal and vascular patterns, similar to chromo endoscopy without the time or expense of spraying dye. In addition, the narrow band filters can be turned on and off with the push of a button on the endoscope, enabling examination with white light endoscopy (WLE) as well [7].

Aim of the work: was to study the diagnostic value of chromo endoscopy versus NBI in detection of Barrett's esophagus.

Patients and methods

Forty patients with GERD symptoms their conventional white light endoscopy revealed the diagnosis of GERD and findings suggestive of Barrett's esophagus recruited from Ain Shams university hospital out patients clinic were enrolled in the study they were divided into: 20 patients underwent white light endoscopy with chromo endoscopy (group A) and 20 patients underwent High resolution endoscopy and Narrow band imaging (HRE-NBI)(group B). Inclusion Criteria: Patients age: ≥ 18 years, undergoing endoscopy for surveillance of BE, for female subjects of childbearing potential, a negative urine pregnancy test within 2 weeks of enrollment. Patients with one or more of the following criteria were excluded from the study: Evidence of cancer or mass lesion in the esophagus, esophageal stricture preventing passage of endoscope or catheter, esophageal varices, severely uncontrolled coagulopathy, pregnant females and prior history of esophageal or gastric surgery. All subjects were subjected to the following after giving a written consent: Full history taking and thorough clinical examination, routine lab investigations: CBC, ESR, liver profile (AST, ALT, GGT, ALP, serum albumin, PT, INR, Bilirubin (total and direct), and renal profile (serum creatinine and BUN) and abdominal ultrasound.

Conventional white light endoscopy using the gastroscope (EG 3440.pentax). The esophagus was first examined the endoscopist recorded the presence and the length of hiatus hernia, A complete evaluation of the stomach and duodenum was performed, then the cardia, SCJ and distal esophagus were reexamined. The presence of GERD, and columnar-lined esophagus were noted.

Chromo endoscopy for Group A. Methelene blue (MB) (0.2 %) was injected through the catheter; Pan staining was performed by directing the spray catheter tip toward the mucosa and spraying the dye while rotating the shaft of the endoscope in a repeated clockwise-counterclockwise fashion and simultaneously slowly withdrawing the endoscope. A water rinse was typically carried out 1 to 2 minutes after staining to remove excess dye. Positive staining for BE was suggested by the presence of dark blue–stained mucosa that persists despite vigorous irrigation [8]. Targeted biopsies were obtained. Four quadrant biopsies every 2 cm, together with targeted biopsies of visible lesions were obtained.

High resolution magnification endoscopy with Narrow band imaging for Group B. Endoscopy was performed using the high resolution zoom gastro scope (GIF-H 180Z, Olympus). The esophagus was first examined and the presence of GERD, Barrett's segment, hiatal hernia and any other obvious lesions was recorded. A complete evaluation of the stomach and duodenum was performed then the cardia, SCJ, and distal esophagus were reexamined. Subsequently, NBI was activated (The NBI filter can be deployed by a switch on the endoscope which then electronically places it between the RGB filter and the light source in 1-2 s. This enables the endoscopist to alternate between WLE and NBI views and back again at any time during the procedure), then the whole mucosa was inspected in the overview mode for detection of any macroscopically visible abnormal lesions. If focal abnormalities were seen suggesting metaplasia (brown–white hue in contrast to bluish white image of normal esophageal mucosa) these were examined under magnification. After inspection of the BE segment, any endoscopically visible subtle lesions were described, biopsied and placed in separate specimen jars. All Micro structural patterns observed by (HRE-NBI) were classified as: A) Round pits with regular microvasculature. B) Villous/ridge pits

with regular microvasculature. C) Absent pits with regular microvasculature. D) Distorted pits with irregular microvasculature [6].

All biopsy specimens were taken biopsy forceps (FB-2415K). Biopsy specimens were routinely processed and stained by (H&E). These were then reviewed by a single expert gastrointestinal pathologist who was blinded to the endoscopic findings for purposes of this study, but was aware of the clinical history of the patient.

The endoscopic results of both groups were compared with the final histo pathological diagnosis that required IM for BE diagnosis BE [9].

Statistical analysis: All collected data were expressed as mean± SD and analyzed by using SPSS version 13 using the following tests: Student t-test, Mann-Whitney test, X2 Chi-square test and diagnostic validity test. $P > 0.05$ was considered non-significant, $P < 0.05$ was considered significant and $P < 0.01$ was considered highly significant.

Results

From January 2012 to August 2013 a total of 40 patients presented by symptoms suggestive of GERD and their conventional white light endoscopy revealed the diagnosis of GERD and showed findings suggestive of BE (salmon pink areas above Z line), were prospectively enrolled in the study. 27 (67.5 %) were males and 13 (32.5 %) were females, their mean age was 37.5±8.07year (range 26–60). Heart burn was the most common presenting symptom (85 %), the mean symptom duration was (3.31±2.5 year). All patients had either GERD grade A in (11 (27.5%)) or GERD grade B (29(72.5 %). All patients showed signs suggestive of BE (multiple salmon pink areas above Z line) (figure 1). Incompetent cadia (IC) was found in 14 (35 %). Hiatus hernia was found in 16 (40 %).

Histopathological examination revealed that all of the patients had findings of reflux esophagitis, 10 % in both groups had cardiac metaplasia (figure 6) and none of them had low or high grade dysplasia (table 1). However (13 (65 %) in group A and (12 (60 %) in group B had BE (IM)(figure 7). Of the 15 patients (75 %) showed positive staining of suspected areas with MB 11 patients (73.3 %) were proved to have non-dysplastic BE (figure 3). However NBI-Z had positive finding (brownish hue in contrast to bluish white normal esophageal mucosa) in 15 (75 %) and BE was proved histopathologically in 11 patients (73.3 %) of them (figure 2). HRE-NBI showed higher sensitivity 85.71 %, specificity 50 % and accuracy 75 % in detection of BE than chromoendoscopy which results showed 84.62 for Sensitivity, 42.86 % for specificity, and 70 % for accuracy $P< 0.05$ (table 2).

Table 1: Comparison between group A and B as regard histopathology

Histopathology	**chromo endoscopy**		**NBI**		**P**
	No	**%**	**No**	**%**	
Reflux esophagitis	20	100	20	100	>0.05
Cardiac metaplasia	2	10%	2	10%	>0.05
IM	13	65%	12	60%	>0.05
Dysplasia	_		_		

Table 2: Comparison between chromo endoscopy and NBI as regard diagnostic value

	Narrow band imaging	Chromo endoscopy	P
NPV	60%	60%	>0.05
PPV	80%	73.33%	<0.05
Sensitivity	85.71%%	84.62%	>0.05
Specificity	50%	42.86%	<0.05
Accuracy	75%	70%	<0.05

Two types of mucosal patterns were detected by NBI-Z; Type A (Round pits with regular microvasculature) (figure 4) and Type B (Villous/ridge pits with regular microvasculature) (figure 5) neither type C (Absent pits with regular microvasculature) or D (Distorted pits with irregular microvasculature) were detected. The patterns were compared to the final histopathological diagnosis. The accuracy of type A pattern to detect columnar mucosa without intestinal metaplasia was 70% while the accuracy of type B to detect SIM was 75 % (table 3).

Table 3: The diagnostic value of correlation of type A pattern to cardiac metaplasia and type B pattern to IM.

NBI–Z pattern prediction of (histology)	Sensitivity	Specificity	PPV	NPV	Accuracy
A to (Cardiac metaplasia)	25%	81.25%	25%	81.25%	70%
B to (IM)	80%	70%	72.73%	77.78%	75%

Figure (1) figure (2) figure (3)

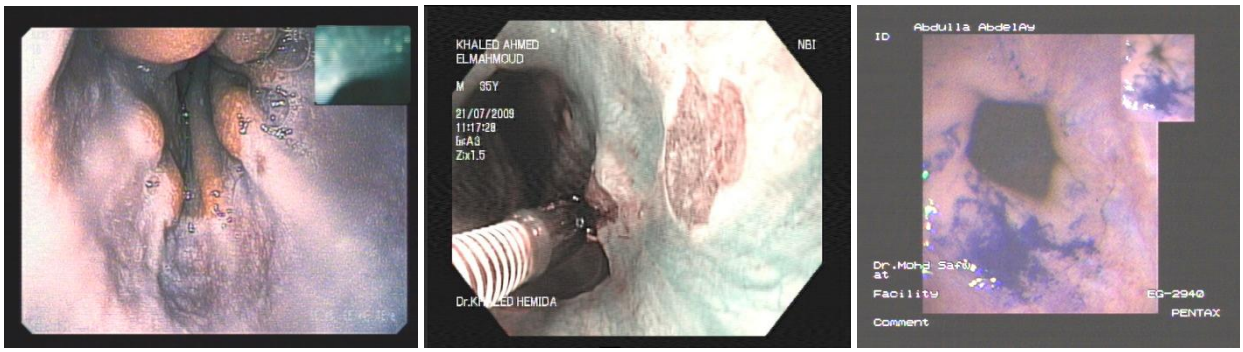

Figure (1): Areas of metaplasia as seen by WLE
Figure (2): Areas of BE visualized by NBI. NBI in this case provides sharp contrast between squamous and columnar mucosa
Figure (3): Positive staining suspected areas with MB squamous epithelium is stained only weakly, whereas Barrett's epithelium takes up more dye.

Figure (4) figure (5)

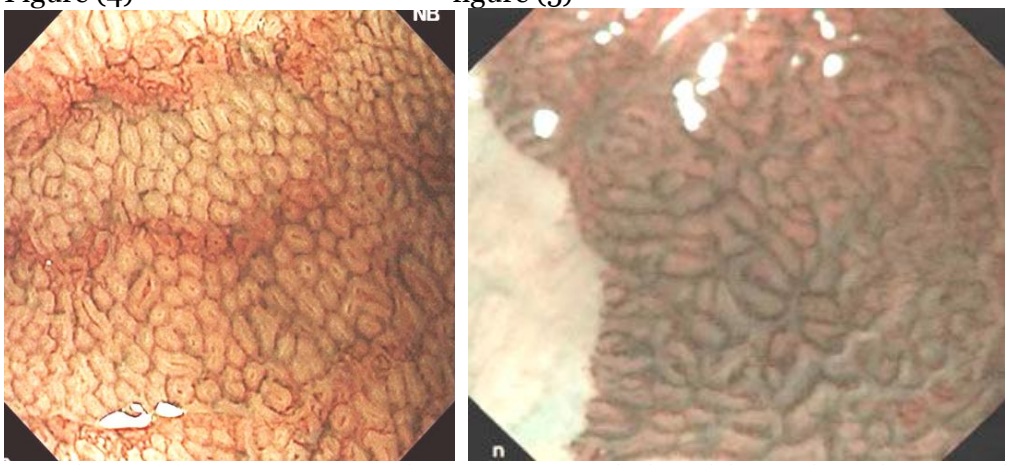

Figure (4): Type A mucosal pattern: Round pits with regular microvasculature. (The pathology in this case revealed cardiac metaplasia).

Figure (5): Type B mucosal pattern: Villous/ridge pits with regular microvasculature. (The pathology in this case revealed BE).

Figure (6)

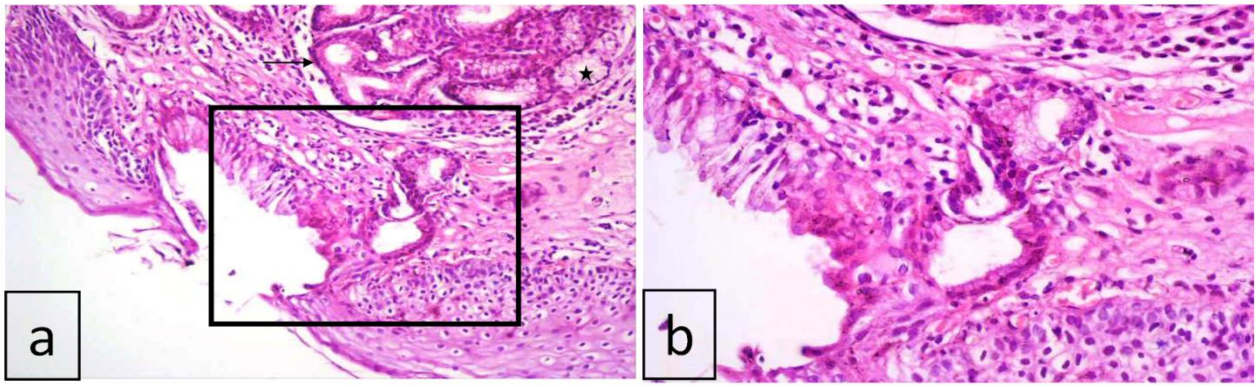

Figure (6): Histologic features of columnar metaplasia in an esophageal biopsy.
a; Low power view for the metaplastic epithelial segment in-between the stratified squamous epithelium with underlying mixed mucous (asterisk) and/or oxyntic glands (arrows) [H&E x200].
b; High power view of the boxed area in (a) show the mild lympho-plasmacytic infiltrate of the lamina propria [H&E x400].

Figure (7)

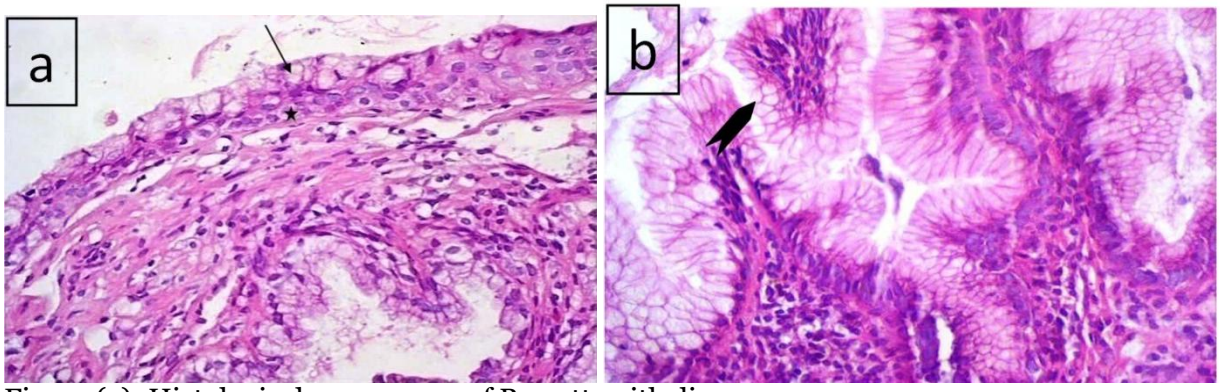

Figure (7): Histological appearance of Barrett epithelium.

a; Low power view of an area of the metaplastic epithelium composed of goblet cells (asterisk) and intervening nongoblet columnar cells (arrow) with underlying mucous glands that is interposed between normal stratified squamous epithelium. The crypts show slight architectural irregularity, budding, and distortion. The lamina propria shows a mild lymphocytic and plasma-cell infiltrate (arrowhead) [H&E ×200].

b; High power view of the boxed area in (a) showing a focus of multilayered epithelium [H&E x400].

Discussion

The Narrow Band Imaging often referred to as 'digital chromo endoscopy', was developed as an alternative method of obtaining visual enhancement of tissue similar to that seen in chromo endoscopy – a procedure that uses the absorptive properties of various dyes, such as indigo carmine, rather than optical filters [10]. A number of preliminary studies have demonstrated that new imaging techniques including electronic chromo endoscopy (NBI) disclose specific surface mucosal patterns that correlate with the histological presence/absence of IM (confirming BE during endoscopic screening) [11].

In our study chromo endoscopy had a negative predictive value (NPV) of 60 % to exclude IM with a sensitivity of 84.62 % and a positive predictive value (PPV) to confirm IM of 73.33 % with a specificity of 42.86 %, the diagnostic accuracy of chromo endoscopy in the diagnosis of IM was 70 %. Studies reported conflicting results on the PPVs and NPVs of chromo endoscopy compared with histopathology, for example Egger et al. [12] reported a sensitivity of 71 % and positive predictive values of 58 %, specificity of 50 %. Horwhat et al. [13] found the sensitivity of MB for IM was 75.2 % and the PPV was 51 %. however Ragunath et al [8] stated that MB more sensitive for IM

(91 % in 57 patients). MB chromoendoscopy has a comparable yield with random biopsy for the detection of SIM during endoscopic evaluation of patients with BE [14]. These variances of results could be attributed to variable distribution of stain or biopsy targeting problems.

Using NBI in patients with BE, different mucosal (regular, round, oval, villous, irregular or abnormal) and vascular (normal, regular, irregular or abnormal) patterns can be recognized, and these patterns have the ability to predict histology [7].

In our study, the NBI had an accuracy of 75 % for detection of BE, moreover, NBI increased the potentially detect not just Barrett's, but also cardiac metaplasia arising in the background of Barrett's, as we found that it had an accuracy of 70 % and 75 % in type A pattern to predict columnar mucosa without intestinal metaplasia and type B to predict specialized intestinal metaplasia (SIM) respectively.

Sharma et al [15] in a prospective study included 51 patients with known or suspected BE. The sensitivity, specificity, and positive predictive value of ridge/villous pattern for diagnosis of IM without HGD were 93.5 %, 86.7 %, and 94.7 %, respectively. The sensitivity, specificity, and positive predictive value of irregular/distorted pattern for HGD were 100 %, 98.7 %, and 95.3 %, respectively. In the study by *Anagnostopoulos et al.* [3] found that 50 patients who were enrolled in a regular BE surveillance program were recruited. The sensitivity, positive and negative predictive values of combination of regular tubular / villous micro structural pattern with regular micro vascular pattern (corresponding to type B in *Singh et al.* [6] classification which was used in our study) for detecting SIM were higher compared to our study 100 %, 86.6 % and 100 %, respectively, for detecting SIM were higher compared to our study 100 %, 86.6 % and 100 %, respectively, but the specificity was lower; 45.4 %. The sensitivity, specificity, positive and negative predictive values of the irregular micro structural and irregular micro vascular patterns (corresponding to type D) for the prediction of HGD in was 83.3 %, 97.7 %, 83.3 % and 97.7 % respectively. The variability in NBI diagnostic values could be due to the differences in sample size, patients selection in our study was based upon GERD symptomatology and their conventional white light endoscopy and not histopathologically confirmed BE as the case in all previous studies assessing NBI.

NBI showed higher accuracy than chromo endoscopy 75 % which vs. 70% $P< 0.05$), in detection of BE. Previous trials have compared the efficacy of NBI with either standard endoscopy or other techniques such as chromo endoscopy showed variable results. Wolfsen *et al* [16] compared NBI with standard resolution WLE in patients with BE undergoing surveillance for previously detected dysplasia and showed a significantly higher rate of dysplasia detection (57 % for NBI vs 43 % for standard) with fewer biopsies (4.7 per patient vs to 8.,5 respectively; $p < 0.001$) for NBI. Curvers et al [17] investigated chromo endoscopy, NBI and high-resolution magnification endoscopy in patients with BE, they found that high-resolution endoscopy alone had an 86 % yield of identifying high-grade dysplasia, while the combinations of white-light endoscopy with NBI, indigo carmine chromo endoscopy and acetic acid chromo endoscopy had 84 %, 70 % and 83 % yields, respectively. Kara et al [18] investigated chromo endoscopy versus NBI, both in combination with high-resolution endoscopy, in a prospective, randomized crossover study with 14 patients. The sensitivity of chromo endoscopy and NBI was 93 % and 86 %, respectively, compared with 79 % for four-quadrant biopsies with conventional endoscopy in the diagnosis of high-grade dysplasia or early cancer in patients with BE. However, *Huang et al* [19] found that the lesion detection rate of NBI was significantly lower than that of chromo endoscopy, but this study Lugoul′s iodine solution was used instead of MB. Although much research concerning the use of chromo endoscopy has been conducted, its widespread use has not been adopted for various reasons including the increased time involved with the procedure and the lack of training as many training centres do not use it regularly.

Sharma et al [7] found that advancements in chromoendoscopy, endoscope digital enhancements and enhanced-magnification have not been shown to be significantly superior to the currently accepted practice of random four-quadrant biopsies at 2cm intervals. However, Yamashina et al [20] concluded that Chromoendoscopy and magnifying NBI are complementary methods, with both being required for the accurate diagnosis of tumor extent in patients with superficial Barrett's esophageal adenocarcinoma. As they found that Chromoendoscopy enhances the characteristics of the mucosa and improves detection and delineation of small or flat lesions

difficult to identify by conventional endoscopy. NBI can view only a narrow area of the mucosa, this method cannot determine the circumference of the lesion and evaluate its complete extent

Conclusion

NBI is not only helpful in detecting metaplasia but also in differentiating cardiac from intestinal metaplasia. Thereby NBI may improve the efficiency and costs of BE screening and surveillance. NBI is recommended as a primary method of screening for Barrett's esophagus in routine practice. NBI or chromo endoscopy could be used as an adjunct to conventional white-light endoscopy to investigate areas appearing suspicious after initial screening.

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