Gastric Cancer (2012) 15:414–418
DOI 10.1007/s10120-011-0133-2

ORIGINAL ARTICLE

Magnifying endoscopy with narrow-band imaging helps determine the management of gastric adenomas

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Received: 13 August 2011 / Accepted: 9 December 2011 / Published online: 18 January 2012

Abstract
Background There are no clear clinical criteria for the management of gastric lesions diagnosed as adenomas (Vienna classification category 3) by pre-treatment biopsy. In the present study, we examined the feasibility of magnifying endoscopy with narrow-band imaging (ME–NBI) in discriminating early gastric cancers (Vienna classification category 4 or 5) from adenomas in lesions diagnosed as adenomas by pre-treatment biopsy.
Methods This was a single-center cross-sectional retrospective study at a tertiary referral center. One hundred thirty-seven consecutive cases of gastric lesions diagnosed as adenomas in pre-treatment forceps biopsy were examined with conventional non-magnifying endoscopy under white light, non-magnifying chromoendoscopy, and ME–NBI. We investigated the association between the final pathological diagnoses (carcinoma or adenoma) and the following factors: lesion size (mm), color (red or white), macroscopic type (depressed or others), presence of ulceration, and positive ME–NBI finding. The presence of an irregular microvascular pattern or an irregular microsurface pattern with a demarcation line between the lesion and the surrounding area was regarded as a positive ME–NBI finding.
Results Lesion size was significantly larger in carcinomas than adenomas ($P = 0.005$). Depressed lesion ($P = 0.011$), red color ($P < 0.001$), and positive ME–NBI finding ($P < 0.001$) were significant predictive factors for carcinoma. Multivariate logistic regression confirmed that red color (odds ratio [OR] 3.04, 95% confidence interval [CI] 1.26–7.34, $P = 0.14$) and a positive ME–NBI finding (OR 13.68, 95% CI 5.69–32.88, $P < 0.001$) were independent predictive factors for carcinomas. A positive ME–NBI finding was the strongest predictive factor.
Conclusions ME–NBI is useful in planning the management of lesions diagnosed as adenomas by pre-treatment forceps biopsy.

Keywords Magnifying endoscopy · Narrow-band imaging · Gastric adenoma

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Introduction

There is debate regarding the best clinical practice for treating gastric lesions diagnosed as adenomas (Vienna classification category 3) by pre-treatment biopsy. Some gastroenterologists prefer to perform endoscopic resection (ER) of the above lesions, while others elect to observe

without treatment [1–4]. The malignant potential of gastric adenoma is thought to be relatively low [4]. However, we often find that the pre-treatment biopsy of gastric lesions supports a diagnosis of non-invasive low-grade neoplasia, but after ER histology is upgraded to high-grade neoplasia or invasive neoplasia [5–7]. One reason for this diagnostic imprecision is that small biopsy samples often do not contain enough tissue for an accurate judgment of structural atypia [8]. Thus, there is no consensus on the management of gastric lesions diagnosed as adenomas by pre-treatment biopsy. The Japanese Gastric Cancer Association *Gastric cancer treatment guidelines* 2010 recommend that the indication for ER should be determined by carefully assessing endoscopic findings, including lesion size [1].

Recent improvements in the technique of magnifying endoscopy with narrow-band imaging (ME–NBI) have increased the accuracy of discrimination between cancers and non-cancerous lesions [9–18]. If clinicians can more accurately detect gastric cancers by ME–NBI, it will help to determine the management of the lesions with a non-committal strategy, endoscopic treatment or follow-up. More accurate discrimination between adenomas and cancerous lesions can minimize the chances that the latter will be misdiagnosed as the former, thus minimizing the chances that the latter will go untreated. Some studies have tried to differentiate between these lesions with ME–NBI, but the findings are not sufficient to propose a new criterion [9, 16, 17]. In the present study, we examined the feasibility of using ME–NBI to discriminate early gastric cancers (Vienna classification category 4 or 5) from adenomas in lesions diagnosed as adenomas (Vienna classification category 3) by pre-treatment biopsy.

Methods

Patients

The Institutional Review Board of the NTT Medical Center Tokyo approved this study. We retrospectively evaluated our endoscopic submucosal dissection (ESD) database for patients treated between July 2007 and December 2010. In our hospital all cases of low-grade neoplasia or adenoma (Vienna classification category 3) were resected endoscopically. We extracted 137 consecutive lesions diagnosed as low-grade neoplasia by preoperative biopsy and investigated them with ME–NBI. All of the 137 lesions were later resected endoscopically and examined pathologically.

Endoscopic procedures and diagnosis

All patients submitted their written informed consent before examination and treatment. We used a high-resolution magnifying upper gastrointestinal endoscope (GIF-Q240Z, GIF-H260Z; Olympus, Tokyo, Japan) and an electronic endoscopy system (EVIS LUCERA SPECTRUM; Olympus) in preoperative endoscopic examinations. Preoperative endoscopy procedures were as follows: (1) examination of a target lesion with conventional non-magnifying endoscopy under white light, (2) examination with non-magnifying chromoendoscopy using indigo carmine dye solution, and (3) examination with ME–NBI. In this system we can easily change the light from white light to NBI only by pushing a button on the handle of the endoscope. These endoscopic examinations were performed by four experienced endoscopists, who had each performed more than 2000 upper gastrointestinal endoscopies. Video images of all procedures were recorded on DVDs. ESD was later performed on the target lesion using a Flex Knife and IT-Knife 2 (Olympus). Resected specimens were fixed in 10% buffered formalin and segmented at 2-mm intervals. Each section was stained with hematoxylin and eosin and examined pathologically. A single pathologist who was blinded to the endoscopic findings confirmed the histological diagnosis. The pathological diagnostic criteria were based on the revised Vienna classification [19]: category 4 (non-invasive high-grade neoplasia) or category 5 (invasive neoplasia) lesions were regarded as carcinoma, while category 3 (non-invasive low-grade neoplasia) lesions were regarded as adenoma.

In non-magnifying endoscopy, lesion size, color (red or white), macroscopic type of the lesion (depressed or others), and the presence of ulceration were examined, based on the past reports about the association between endoscopic findings and histological malignancy [6, 17, 20, 21]. Lesion size was determined using a measuring forceps. In ME–NBI, our diagnostic criteria were based on the classification proposed by Yao et al. [13] (VS classification): (1) irregular microvascular (MV) pattern with a demarcation line between the lesion and the surrounding area, and (2) irregular microsurface (MS) pattern with a demarcation line between the lesion and the surrounding area. If a target lesion had finding of (1) or (2), it was judged to be positive (Figs. 1, 2, 3). In the present study, all endoscopic images were retrospectively reviewed by two authors (Y.T, K.O), who were blinded to the pathology results.

Data analysis

We examined the relationship between the final pathological diagnosis (carcinoma or adenoma) of ESD and the following factors: lesion size (mm), color (red or white), macroscopic type of the lesion (depressed or not), presence of ulceration, and a positive ME–NBI finding.

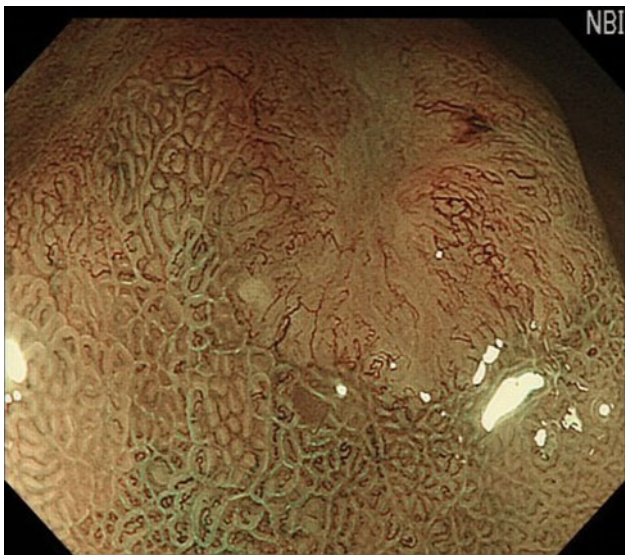

Fig. 1 Magnifying endoscopy with narrow-band imaging (NBI), showing a typical finding of irregular microvascular pattern

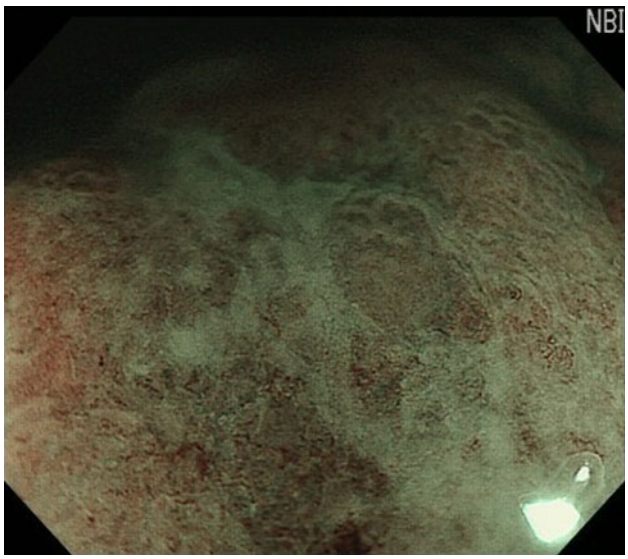

Fig. 2 Magnifying endoscopy with NBI, showing a typical finding of irregular microsurface pattern (irregular white opaque substance)

Statistical analysis

We used the χ^2 test (without the Yates correction) and Fisher's exact test for categorical comparison of the data. Differences in the means of continuous data were compared using Student's *t*-test. To identify important factors for carcinoma, predictors showing a *P* value of less than 0.2 in a univariate analysis were then included in a backward, stepwise multiple logistic-regression model. A *P* value of less than 0.05 was considered statistically significant. All tests were two-sided. All statistical analyses were performed on a personal computer with PASW Statistics 18 for Windows (SPSS, Tokyo, Japan).

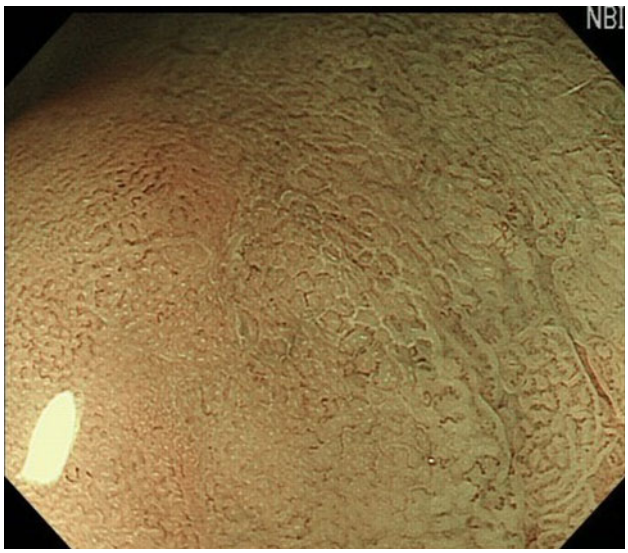

Fig. 3 Magnifying endoscopy with NBI, showing a typical finding of regular microvascular and microsurface pattern

Results

Baseline characteristics and endoscopic features of the 137 lesions are listed in Table 1. The results of univariate analysis were as follows. Lesion size was significantly larger in carcinomas than adenomas ($P = 0.005$). Depressed lesion ($P = 0.011$), red color ($P < 0.001$), and a positive ME–NBI finding ($P < 0.001$) were significant predictive factors for carcinoma. The details of the ME–NBI findings are shown in Table 2. Multivariate logistic regression analysis confirmed that red color (odds ratio [OR] 3.04, 95% confidence interval [CI] 1.26–7.34, $P = 0.014$) and a positive ME–NBI finding (OR 13.68, 95% CI 5.69–32.88, $P < 0.001$) were independent predictive factors for carcinomas. A positive ME–NBI finding was the strongest predictive factor. The diagnostic sensitivity and specificity of ME–NBI for carcinoma were 75.0 and 84.9%, respectively. The positive predictive value was 81.4%.

Discussion

Accurate diagnosis of gastric lesions is essential for the optimal treatment of these potentially deadly tumors. The histology of pre-treatment forceps biopsy samples does not always accurately identify malignancies, while tissue from endoscopic resection (ER) tends to yield a more accurate histological diagnosis. The discrepancy rate between

Table 1 Univariate analysis of baseline characteristics and endoscopic features in adenomas and carcinomas

	Adenoma ($N = 73$)	Carcinoma ($N = 64$)	P value
Sex: men/women (% men)	53/20 (72.6%)	48/16 (75.0%)	0.750
Age (years)	67.7 ± 10.3	67.6 ± 10.4	0.957
Diameter of lesion (mm)	13.8 ± 7.1	18.5 ± 11.4	0.005
Lesion type			
Ulcer: with/without (% with)	3/70 (4.1%)	3/61 (4.7%)	1.000
Lesion type: depressed/not depressed (% depressed)	5/68 (6.8%)	14/50 (21.9%)	0.011
Color: red/white (% red)	17/56 (23.3%)	38/26 (59.4%)	<0.001
ME–NBI finding: positive/negative (% positive)	11/62 (15.1%)	48/16 (75.0%)	<0.001

Quantitative data are presented as means ± standard deviation

ME–NBI magnifying endoscopy with narrow-band imaging

Table 2 ME–NBI findings of all 137 lesions

Cancerous lesions ($n = 64$)			Adenomatous lesions ($n = 73$)		
V pattern	S pattern	n	V pattern	S pattern	n
Regular	Regular	12	Regular	Regular	51
Regular	Irregular	6	Regular	Irregular	2
Regular	Absent	0	Regular	Absent	0
Irregular	Regular	11	Irregular	Regular	5
Irregular	Irregular	14	Irregular	Irregular	0
Irregular	Absent	14	Irregular	Absent	4
Absent	Regular	4	Absent	Regular	11
Absent	Irregular	3	Absent	Irregular	0
Absent	Absent	0	Absent	Absent	0

ME–NBI magnifying endoscopy with narrow-band imaging, *V* vascular *S* surface

forceps biopsy and ER has ranged from about 20 to 45% [5–7]. This discrepancy calls into question the accuracy of forceps biopsy in differentiating adenomas from cancerous lesions. Lee et al. [5] suggested that ER should be routine practice, to obtain an accurate histological diagnosis, but ER is an invasive technique that can lead to complications, including perforation or postoperative bleeding [22]. Therefore, it is desirable to predict malignancy more accurately for adenomas diagnosed by pre-treatment forceps biopsy.

Conventional non-magnifying endoscopy under white light helps discriminate carcinomas from adenomas to some extent [20, 21]. In the univariate analysis in the present study, lesion size was significantly larger in carcinomas than in adenomas. Similarly, depressed lesions were more likely to be carcinomas. However, these two factors were not statistically significantly predictive in the multivariate analysis, with similar results having been obtained by other investigators [20, 21]. The strongest predictive factor for carcinoma in the multivariate logistic regression analysis in the present study was a positive ME–NBI finding, although red color also remained a significant factor, with a much smaller OR (13.7 vs. 3.0).

ME–NBI enables us to clearly visualize the MV and MS architecture [13]. Tamai et al. [17] reported that depressed adenomas showed a regular ultrafine network pattern of mucosal microvasculature in ME–NBI, but none of the protruding adenomas possessed these MV patterns. Yao et al. also reported some difficulties in discriminating carcinomas from adenomas only by visualizing MV patterns, due to the obscurity of MV patterns in superficial elevated (0-IIa) lesions. However, they proposed the idea of a white opaque substance, and they argued that the presence of an irregular white opaque substance could be a sign of carcinoma [16].

Nakamura et al. [9] reported that ME–NBI could help discriminate carcinomas from adenomas in adenomas diagnosed by biopsy. They analyzed only 14 biopsy-diagnosed adenomas by their unique ME–NBI classification. In the present study, we examined 137 biopsy-diagnosed adenomas, based on the VS classification by Yao et al. [13], which was a widely utilized classification. Although,

as a possible limitation, this study was a single-center retrospective study, we believe that the large sample size confers significant power.

The diagnostic accuracy of ME–NBI has been debated. For example, Ezoe et al. [12] reported that the sensitivity, specificity, and positive predictive values of ME–NBI for carcinoma were 70, 89, and 79%, respectively. A similar report by Kato et al. [10] showed sensitivity, specificity, and positive predictive values of ME–NBI of 92.9, 94.7, and 56.5%, respectively. One key difference between these previous reports and our present study is a difference in target lesions. While the previous studies examined depressed lesions exclusively, we analyzed both depressed and non-depressed lesions. Future studies should consider a variety of lesion presentations and should also assess inter- and intra-observer diagnostic concordance rates. Further advances in the diagnostic process for gastric lesions will improve diagnostic efficiency.

In summary, we demonstrated that ME–NBI helps in planning the management of gastric neoplasms diagnosed as adenoma by pre-treatment biopsy. If an adenomatous lesion diagnosed by forceps biopsy shows a positive ME–NBI finding, it should be resected endoscopically.

Conflict of interest We have no conflict of interest.

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