Narrow band imaging (NBI) magnification predicts the histology and invasion depth of colorectal tumors

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Backgrounds: There are several reports concerning the differential diagnosis of non-neoplastic and neoplastic colorectal lesions by narrow band imaging (NBI). However, there are only a few NBI reports assessing invasion depth.

Objective: To determine the clinical usefulness of NBI magnification for evaluating microvessel architecture in relation to pit appearances and in the qualitative diagnosis of colorectal tumors.

Design: Retrospective study.

Setting: Department of Endoscopy, Hiroshima University, Hiroshima, Japan.

Patients and Main Outcome Measurements: A total of 289 colorectal lesions were analyzed: 12 hyperplasias (HPs), 165 tubular adenomas (TAs), 65 carcinomas with intramucosal to scanty submucosal invasion (M~SM-s), and 47 carcinomas with massive submucosal invasion (SM-m). Lesions were observed by NBI magnifying endoscopy and classified according to microvessel features and pit appearances, type A, type B, or type C. Type C was divided into three subtypes (C1, C2, and C3) according to the detailed NBI magnifying findings of pits visibility, vessel diameter, irregularity and distribution. These were compared to histologic findings.

Results: Histologic findings of HP and TA were found in 80.0% and 20.0% in type A lesions, respectively. TA and M~SM-s were found in 79.7% and 20.3% in type B lesions, respectively. TA, M~SM-s and SM-m were found in 21.6%, 29.9% and 48.5 in type C lesions, respectively. HPs were observed significantly more often than TAs in Type A lesions, TAs were observed significantly more often than carcinomas in Type B lesions, carcinomas were observed significantly more often than TAs in Type C ($P < 0.01$). TA, M~SM-s, and SM-m were found in 46.7%, 42.2%, and 11.1% in type C1 lesions, respectively. M~SM-s and SM-m were found in 45.5% and 54.5% in type C2 lesions, respectively. SM-m was found in 100% in type C3 lesions. TAs and M~SM-s were observed significantly more often than SM-m in Type C1 lesions, and SM-m were observed significantly more often than TAs and M~SM-s in Type C3 lesions ($P < 0.01$).

Conclusions: NBI magnification findings of colorectal lesions are associated with histologic grade and invasion depth.

Key words: narrow band imaging (NBI); magnification; colorectal tumors

Narrow band imaging (NBI) is a new technology that involves the use of 3 optical filters for sequential red-blue-green illumination of the videoendoscopic target and narrows the bandwidth of the spectral transmittance. The central wavelengths of the 3 optical filters are 500 nm, 445 nm, and 415 nm, and each has a bandwidth of 30 nm. Such properties provide limited penetration of light into the mucosal surface and enhanced visualization of capillary vessels and their fine structure in the surface layer.[1-4]

Reports on the use of NBI for colorectal tumors include those assessing its ability to differentiate neoplastic from non-neoplastic lesions.[3-7] With regard to adenomas, there are several reports that the detectability of adenoma by NBI is not significantly different from that by white light,[8,9] although in heredity nonpolyposis colorectal cancer, NBI is able to detect twice as many adenomas as white light,[10] and Rastogi reported that NBI detected an additional colon polyps.[11] Thus, the use of NBI in lesion detection remains controversial. With regard to the detection of dysplasia in ulcerative colitis in cases with prolonged courses, Dekker, et al reported that NBI is equal to conventional endoscopy.[12] East, et al[13] reported that pit patterns observed by chromoendoscopy can differ from those observed by NBI. We have reported that types I~IV of Kudo and Tsuruta pit-pattern Classification can be identified by NBI magnification of vascular pattern, but it is difficult to identify a type V pit pattern by NBI

magnification.[5] Thus whereas the use of NBI for colorectal tumors has been studied, there are few reports on the use of NBI for the qualitative diagnosis of colorectal tumors.[14]

In this study, we classified the NBI magnification findings in relation to pit appearances.[5] We studied the association between this classification and histologic atypia or invasion depth of carcinoma in colorectal tumors.

PATENTS AND SETTING

Lesions and colonoscopic observation

We analyzed 289 colorectal lesions from 223 patients, 124 were men and 99 were women, who underwent endoscopic resection or surgery at Hiroshima University Hospital during the period January 2004 through July 2007. The colorectal lesions comprised 12 hyperplasias (HPs), 165 tubular adenomas (TAs), 65 carcinomas with intramucosal to scanty submucosal invasion (M~SM-s), and 47 carcinomas with massive submucosal invasion (SM-m). Mean lseion sizes were as follows: HPs, 4.6±2.5mm (range: 2-10 mm); TAs, 15.6±13.4mm (range: 2-80 mm); M~SM-s, 24.2±13.3mm (range: 6-70 mm); SM-m, 20.1±8.3mm (range: 8-50 mm). All patients provided informed consent before participating in the study. The lesions were detected first by conventional colonoscopy, and then observed by NBI magnification.

The instruments used in this study were a magnifying videoendoscope system (CF-H260AZI; Olympus Corp., Tokyo, Japan) and a standard optical videoendoscopic system, 2 light sources, and a digital image filing system. One light source was for the standard optical filter (broadband), and the other was for the NBI system. After detailed observation by NBI magnification, all lesions were resected endoscopically or surgically.

The resected specimens were pinned to a board and fixed in 10% buffered formalin for 12~48 hours. The specimens were then cut into 2-3 mm blocks. Pathologic examinations were performed on hematoxylin and eosin stained sections by a single pathologist unaware of the features of each case. Histologic diagnosis was based on the World Health Organization criteria.[15] In this study, massive submucosal invasion was defined as an invasion depth of 1,000 μm, or more, as described previously.[16,17,18] Measurement of the depth of submucosal invasion was performed according to General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus of the Japanese Society for Cancer of the Colon and Rectum.[19]

NBI magnification findings

NBI magnification findings were classified according to microvessel architecture and pit appearance identified by NBI magnification, type A, type B, or type C (Fig. 1). NBI maginification findings were considered type A when microvessels were not observed or were extremely opaque; type B when fine microvessels were observed around the pits, and clear pits could be observed via the nest of microvessels; and type C when the microvessels were irregular, and the vessel diameter or distribution was heterogeneous. Type C was divided into 3 subtypes (C1, C2, or C3) according to the detailed NBI magnification findings of pits visibility, vessel diameter, irregularity and distribution (Fig. 2). Lesions were considered type C1 when microvessels comprised an irregular network, pits observed via the microvessels were slightly nondistinct, and vessel diameter or distribution was homogeneous; type C2 when microvessels comprised an irregular network, pits observed via the microvessels were irregular, and vessel diameter or distribution was heterogeneous; type C3 when pits via the microvessels were invisible, irregular vessel diameter was thick or the vessel distribution was heterogeneous, and avascular areas were observed. In addition, the NBI magnification findings employed the most significant type (C3 > C2 > C1 > B > A) when there were a variety of types within a single finding.

We then examined the relationship between the NBI magnification findings and histologic findings. Three endoscopists who had at least 10 years of experience determined the NBI classification using only the NBI magnification findings under conditions where the histological findings were blinded. All data were analyzed by the chi-square test, and statistical significance was accepted at $P < 0.05$.

RESULTS

Relation between NBI magnification findings and histologic findings in colorectal lesions are listed in Table 1. Histologic findings of HP and TA were found in 80.0% (12/15) and 20.0% (3/15) in type A lesions, respectively. TA and M~SM-s were found in 79.7% (141/177) and 20.3% (36/177) in type B lesions, respectively. TA, M~SM-s and SM-m were found in 21.6% (21/97), 29.9% (29/97) and 48.5 (47/97) in type C lesions, respectively. HPs were observed significantly more often than TAs in type A lesions, TAs were observed significantly more often than carcinomas in type B lesions, carcinomas were observed significantly more often than TAs in type C lesions ($P < 0.01$). The sensitivity and specificity of type A lesions for the diagnosis of HP lesions were 100% and 98.9%, those of type B lesions for the diagnosis of TA were

85.5% and 71.0%, and those of type C lesions for the diagnosis of carcinoma were 67.9% and 88.1%, respectively.

Relation between detailed NBI magnification findings of type C colorectal lesions and histologic findings are listed in Table 2. TA, M~SM-s, and SM-m were found in 46.7% (21/45), 42.2% (19/45), and 11.1% (5/45) in type C1 lesions, respectively. M~SM-s and SM-m were found in 45.5% (10/22) and 54.5% (12/22) in type C2 lesions, respectively. SM-m was found in 100% (30/30) in type C3 lesions. TAs and M~SM-s were observed significantly more often than SM-m in Type C1 lesions, and SM-m were observed significantly more often than TAs and M~SM-s in Type C3 lesions ($P < 0.01$). The sensitivity and specificity of type C1 lesions for diagnosis of TAs or M~SM-s were 80.0% and 89.4%, and those of type C3 lesions for the diagnosis of SM-m were 63.8% and 100%, respectively. The positive predictive value and negative predictive value of type C1 lesions for diagnosis of SM-m were 11.1% and 19.2%, and those of type C3 lesions for diagnosis of Sm-m were 100% and 74.6%, respectively.

DISCUSSION

Little risk of lymph node metastasis has been reported in cases of early colorectal carcinoma involving the shallow layer of the submucosa (less than 1,000 μm from the muscularis mucosae).[16-19,] It is therefore important to distinguish lesions involving submucosal invasion depth equal to or deeper than 1,000 μm from those involving submucosal invasion depth less than 1,000 μm to minimize the performance of unnecessary surgical resections.

The pit pattern classification of colorectal lesions initially proposed by Kudo[20] and modified by Kudo and Tsuruta,[21] is related to the histologic characteristics of the lesions.[22-27] As reported previously, magnifying colonoscopy is useful for the differential diagnosis of neoplastic from non-neoplastic lesions[22, 24, 28-34] and for assessing the depth of invasion of early colorectal carcinoma.[22, 35-39] Many studies have shown type V_N pit pattern to be an indicator of massive submucosal invasion.[22, 36, 38, 39] However, colorectal neoplasms of type V_I pit pattern include various histologic features such as TA, SM-s, and SM-m.[22, 40] It is therefore difficult to determine optimal therapeutic strategies for colorectal neoplasms based on pit pattern classification alone.

Sano et al[4] proposed the term ‘meshed capillary’ to distinguish neoplastic from non-neoplastic lesions and the capillary classification ‘capillary pattern’ for the differential diagnosis of colorectal lesions by NBI observation. However, it is difficult to distinguish

between endoscopically treatable early invasive carcinoma and untreatable carcinoma based on 'capillary pattern' alone. It is therefore desired to determine in some ways whether SM infiltration is equal to or deeper than 1,000 μm before surgery to help in determining therapeutic strategy. According to the NBI classification of the present study, all type B and most type C1 lesions showed TA or M~SM-s (89%), and all type C3 lesions showed SM-m. Endoscopic resection should be selected for type B and C1 lesions, and surgical resection should be selected for type C3 lesions. The detailed analysis of NBI magnification is very useful for the selection of optimal therapeutic strategy. In addition, it is advantageous that chromo-agents are not required for the assessment of NBI magnification. However, because type C2 lesions include various histologic features such as M~SM-s to SM-m, it is difficult determine therapeutic strategy with this classification. In patients for whom it is not easy to determine whether SM infiltration is equal to or deeper than 1,000 μm, it is important to combine conventional endoscopic findings, conventional pit pattern findings,[22] and ultrasound endoscopic diagnoses.[41-43] It will be necessary to elucidate associations between NBI magnification findings and conventional pit pattern findings based on histology, and to study associations between NBI magnification findings and vascular proliferation factors / molecular pathologic markers as well as to clarify pathophysiology.

In conclusion, the NBI magnification findings of colorectal lesions are associated with histologic grade and submucosal invasion depth of carcinoma deeper than 1,000 μm. These results indicate that NBI magnification classification in this study is useful for predicting histology and for selecting optimal therapeutic strategies for colorectal tumors.

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FIGURE LEGENDS

Figure 1. Narrow band imaging magnification findings of colorectal lesion. **Type A,** microvessels are not observed or are extremely opaque. **Type B,** fine microvessels are observed around the pits, and clear pits can be observed via the nest of microvessels. **Type C,** microvessels are irregular, and the vessel diameter or distribution is heterogeneous.

Figure 2. Narrow band imaging magnification subclassification of type C. **C1,** microvessels comprise an irregular network, pits observed via the microvessels are slightly nondistinct, and vessel diameter or distribution is homogeneous. **C2,** microvessels comprise an irregular network, pits observed via the microvessels are irregular, and vessel diameter or distribution is heterogeneous (between type C1 and C3). **C3,** pits via the microvessels are invisible, irregular vessel diameter is thick or the vessel distribution is heterogeneous, and avascular areas are observed.

Table1. Relation between NBI magnification findings of colorectal lesions and histologic findings

NBI magnification findings	No. of Lesions (%)	HP (%)	TA (%)	Carcinoma	
				M~SM-s (%)	SM-m (%)
type A	15 (100)	12 (80.0)	3 (20.0)		
		*			
type B	177 (100)		141 (79.7)	36 (20.3)	
			*		
type C	97 (100)		21 (21.6)	29 (29.9)	47 (48.5)
			*		
Total	289	12	165	65	47

Sensitivity and specificity of type A for diagnosis of HP were 100% and 98.9%, those of type B for diagnosis of TA were 85.5% and 71.0%, and those of type C for diagnosis of Carcinoma were 67.9% and 88.1%.

* $p < 0.01$

Table2. Relation between detailed NBI magnification findings of type C colorectal lesions and histologic findings

NBI magnification findings		No. of Lesions (%)	TA (%)	Carcinoma	
				M~SM-s (%)	SM-m (%)
type C	1	45 (100)	21 (46.7)	19 (42.2)	5 (11.1)
	2	22 (100)		10 (45.5) *	12 (54.5)
	3	30 (100)			30 (100) *
Total		97	21	29	47

Sensitivity and specificity of type C1 for diagnosis of TA or M~SM-s were 80.0% and 89.4%, and those of type C3 for diagnosis of SM-m were 63.8% and 100%. The positive predictive value and negative predictive value of type C1 lesions for diagnosis of SM-m were 11.1% and 19.2%, and those of type C3 lesions for diagnosis of Sm-m were 100% and 74.6%, respectively.

* $p < 0.01$

Figure. 1

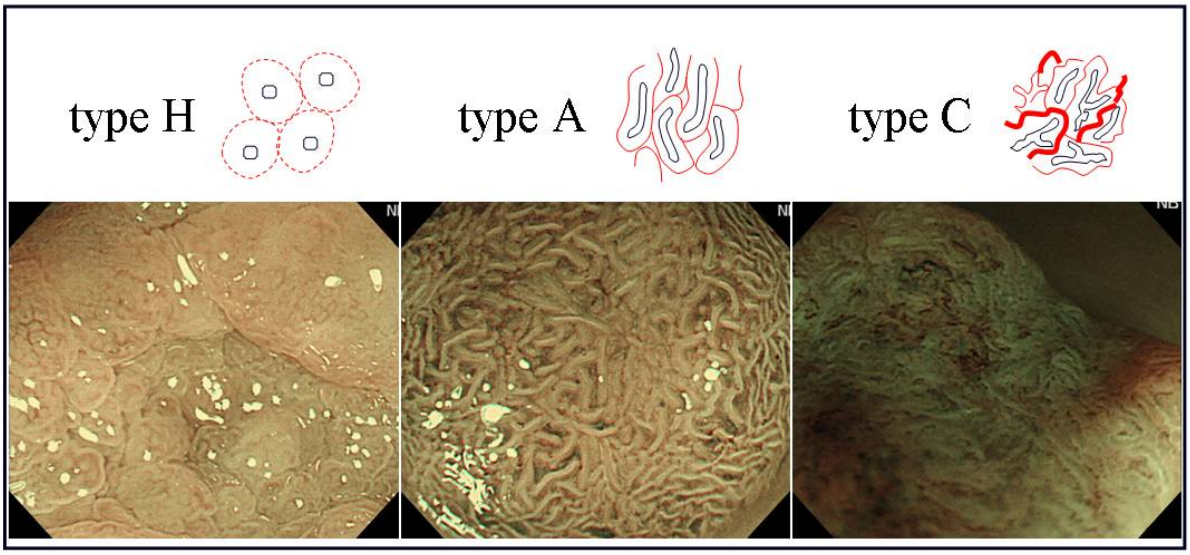

Figure. 2