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Correlation of Narrow Band Imaging with Magnifying Colonoscopy and Histology in Colorectal Tumors

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Background/Aims: Narrow band imaging (NBI) is a new technique that uses optical filters for imaging of mucosal morphology. The aim of this study was to correlate findings of NBI with magnifying colonoscopy and histology for prediction of neoplastic colorectal lesion.

Methods: Between September 2005 and December 2007, 107 colon polyps from 68 patients were detected by conventional colonoscopy and subsequently evaluated by NBI with magnifying colonoscopy and analyzed for a pit pattern and a capillary pattern. More analysis was done regarding thickness and irregularity of capillary features.

Results: Pit pattern with NBI magnification to discriminate between neoplastic and non-neoplastic lesions had a sensitivity of 88.9% and a specificity of 87.5%; capillary pattern yielded test performance characteristics of 91.9% and 87.5%. In respect of capillary thickness, invisible capillaries were found significantly more often in hyperplastic lesions. All thick capillaries were found in neoplastic polyps, and found significantly more often in carcinomas with submucosal massive invasion (sm-m) (p<0.01). In respect of capillary irregularity, invisible capillaries were found significantly more often in hyperplasic lesions, and severely irregular capillaries were found significantly more often in sm-m lesions (p<0.01).

Conclusions: Observation of capillary thickness and irregularity by NBI magnification is useful for correlating histological grade with carcinoma, especially with depth of submucosal invasion.

Key Words: Narrow band imaging; Magnifying colonoscopy; Histology; Colorectal tumor

INTRODUCTION

Narrow band imaging (NBI) endoscopy is a newly developed technique that uses 2 optical filters to pass only the short (blue/green) wavelengths enhancing the visualization of microvessels and their fine structures on the mucosal surface, based on the fact that the depth of light infiltration depends on its wavelength. The contrast on the vessel areas could be increased by artificially narrowing the wavelength area using filters because the sharpness may be improved by eliminating the wavelength areas with dispersed lights. NBI uses 415 nm and 540 nm of wavelength; the former enhances microvessels in the mucosal surface layer with brown image, whereas the latter enhances the submucosal layer or microvessels in the submucosal layer with green image, both enabling detailed observation of mucosal structure and capillary pattern.[1-3] NBI is not only useful for the detection of tumors but also for the differential diagnosis between tubular adenoma and hyperplastic polyp.[4,5]

NBI with magnifying endoscopy is reported to be useful for patients with Barrett's esophagus or gastric tumors[6,7] but was not sufficiently investigated for colorectal disease in South Korea.

There are also very few reports on correlation between NBI and histologic findings. This study observed the structure of mucosal surface and blood vessel and correlated with histologic diagnosis of colorectal tumors.

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MATERIALS AND METHODS

Patients and colonoscopic observations

This study was performed in 107 colorectal lesions of 68 patients who received endoscopic resection of colorectal tumors at Soonchunhyang University Hospital in Bucheon, South Korea, between September 2005 and December 2007. These lesions were first detected by conventional view, and then observed by NBI system. Every lesion was detected using white-light colonoscopy (CF-Q240ZI, CF-H260AZI; Olympus, Tokyo, Japan), and EVIS LUCERA system (Olympus Optical, Tokyo, Japan) was used for videoendoscope system. Endoscopic specialists with more than 5 years of experience in the field of colonscopy performed the endoscopic observations in this study. After detailed observation by NBI magnification, all lesions were resected endoscopically. Specimens were pinned to a board and fixed in 10% buffered formalin for 24 hours. Then these specimens were cut into 2 to 3-mm blocks and performed on hematoxylin and eosin-stained sections. Pathologic examination was performed based on the World Health Organization criteria by a single pathologist unaware of the features of each case. Following histologic diagnosis, a total of 107 lesions were categorized into 8 groups based on their histologic grade and depth of submucosal invasion: hyperplastic polyp, inflammatory polyp, low grade tubular adenoma, high grade tubular adenoma, tubulovillous adenoma, villous adenoma, carcinoma with intramucosal-scant submucosal invasion (m-sm1), and carcinoma with submucosal massive invasion (sm-m). Submucosal massive invasion was defined as the invasion of more than 1,000 μm for this study.[8]

Capillary patterns and features according to NBI magnification (Table 1)

Pit patterns and capillary patterns were categorized using NBI magnification system (Fig. 1), the former following the Kudo's classification and the latter Sano's classification. Pit pattern types III, IV, and V based on Kudo's classification and capillary pattern types II and III based on Sano's classification were determined as neoplastic lesions.[9,10]

NBI magnification enables the observation of capillary patterns on the surface layer of tumors. Each lesion was further categorized according to thickness and irregularity of their capillary by close observation with NBI magnification. Capillaries were divided into invisible, thin, or thick capillary based on their thickness. Based on NBI findings, lesions without microvessel or of extreme opacity were determined as invisible capillary; lesions with thin pits and even blood vessel diameters throughout the lesion were determined as thin capillary; and mixture of blood vessels small but larger than 'thin' capillaries are determined as thick capillary (Fig. 2). Capillaries were also divided into invisible, regular, or irregular type based on their irregularity. Invisible capillary type was determined by absence of or extremely opaque capillary; regular capillary type by smooth capillary running with apparent regular meshwork of capillaries across the pits and lesion; and irregular capillary type by irregular running of capillaries with apparent irregular meshwork of capillaries across the pits and lesion (Fig. 3). Lesions with thin and thick, or regular and irregular capillaries were determined as neoplastic. These capillary types by NBI and histologic findings were correlated afterwards.

SPSS for windows version 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis with χ^2 test for data analysis. *p*-values of less than 0.05 were determined statistically significant.

RESULTS

Patients characteristics

A total of 68 patients (49 male, 19 female) were enrolled in the study, and their mean age was 59 years old (range, 42 to 84) (Table 2). White-light colonoscopy and NBI with magnifying colonoscopy were performed in every patient, with successful intubation of cecum. Bowel preparation was well conducted in every test, and lesions in every patient were

Table 1. Capillary Patterns and Capillary Features Identified by NBI Magnification

Capillary pattern[10]	I	Absent meshed brown capillary vessel
	II	Present meshed brown capillary vessel, slightly thicker and loose capillary density
	III	Present meshed brown capillary vessel, thicker, branching, irregularity capillary and dense capillary density
Capillary thickness	Invisible	
	Thin	Thin and even thickness
	Thick	Uneven thickness
Capillary irregularity	Invisible	
	Regular	Capillaries running smoothly between pits and an apparent regular meshwork of capillaries throughout
	Irregular	Capillaries running irregularly between pits and an apparent irregular meshwork of capillaries throughout

NBI, narrow band imaging.

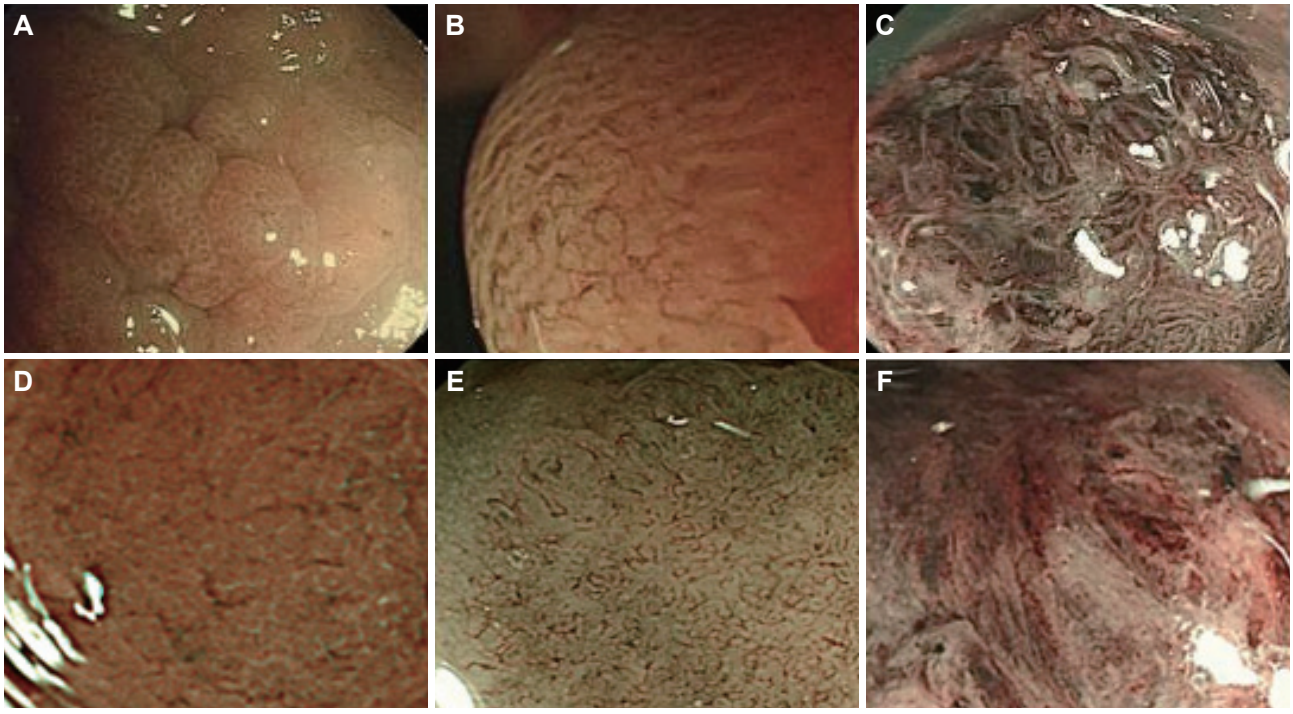

Fig. 1. Classification of capillary pattern. (A, B) Capillary pattern type I shows absence of meshed brown capillary vessel. (C, D) Capillary pattern type II shows presence of meshed brown capillary vessel, slightly thicker and loose capillary density. (E, F) Capillary pattern type III shows presence of meshed brown capillary vessel, thicker, branching, irregularity of capillary and dense capillary density.

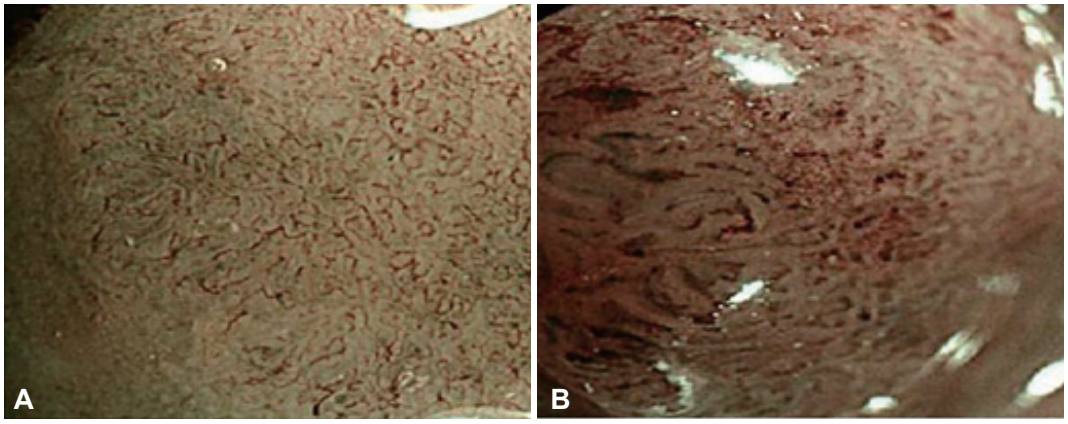

Fig. 2. Classification of microvessel thickness as determined by narrow band imaging. (A) Microvessels were classified as thin when they were thin and even thickness. (B) Microvessels were classified as thick when they were uneven thickness.

categorized proficiently following the observation of colorectal mucosa by NBI.

Lesions and colonoscopic observations

A total of 107 colon tumors detected by white-light colonoscopy were distributed as follows: ascending colon 18 cases, transverse colon 26 cases, descending colon 14 cases, sigmoid colon 26 cases, and rectum 23 cases. The types of resected tumors were sessile polyp 32 cases (29.9%), subpedunculated polyp 35 cases (32.7%), flat-elevated polyp 18 cases (16.8%), laterally spreading tumor 13 cases (12.1%), and pedunculated polyp 9 cases (8.4%). The mean tumor size was 11.25 mm ranging from 2 mm to 40 mm (Table 2).

Histologic findings of lesions

Histologic findings of total 107 lesions were non-neoplastic in 8 cases, which were further divided again as 7 cases of hyperplastic polyp and 1 case of inflammatory polyp; the remaining 99 cases were neoplastic, which were divided again as low grade tubular adenoma in 55 cases, high grade tubular adenoma in 16 cases, tubulovillous adenoma in 10 cases, villous adenoma in 2 cases, carcinoma with intramucosal to scant submucosal invasion in 10 cases, and carcinoma with submucosal massive invasion in 6 cases (Table 2).

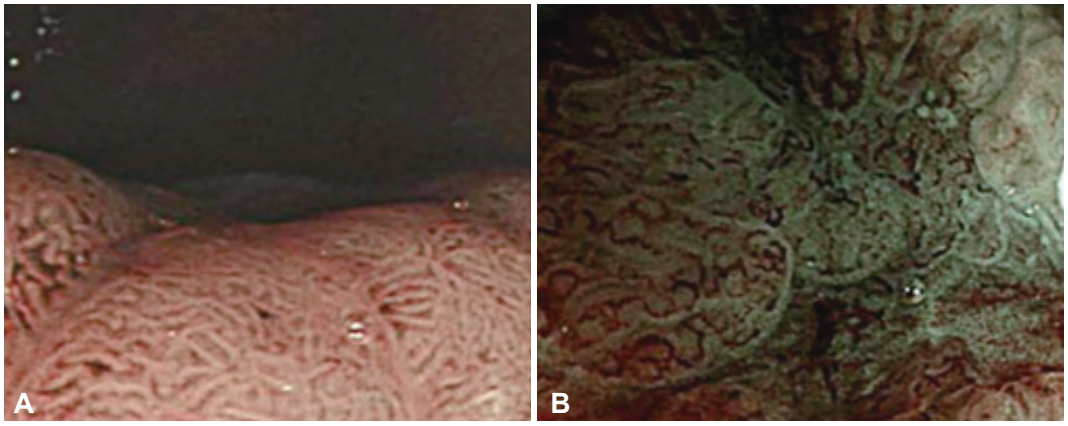

Fig. 3. Classification of microvascular features as determined by narrow band imaging. (A) Microvessels were classified regular when lesions had microvessels running smoothly between pits and an apparent regular meshwork of microvessels throughout. (B) Microvessels were classified irregular when lesions had microvessels running irregularly between pits and an apparent irregular meshwork of microvessels throughout.

Table 2. Demographics of Study Participants and Clinicopathological Characteristics of Study Lesions

Variable	Value
Patients	68
Sex, M:F	49:19
Mean age (minimum, maximum)	59 (42, 84)
Lesion	107
Location	
Ascending colon	18
Transverse colon	26
Descending colon	14
Sigmoid colon	26
Rectum	23
Morphology	
Sessile polyp (Is), No. (%)	32 (29.9)
Subpedunculated polyp (Isp), No. (%)	35 (32.7)
Flat-elevated polyp (IIa), No. (%)	18 (16.8)
Pedunculated polyp (Ip), No. (%)	9 (8.4)
Laterally spreading tumor (LST)	13 (12.1)
Mean size in mm (range)	11.25 (2-40)
Histolopathology	
Non-neoplastic	8
Hyperplastic polyp	7
Inflammatory polyp	1
Neoplastic	99
Tubular adenoma-low grade	55
Tubular adenoma-high grade	16
Tubulovillous adenoma	10
Villous adenoma	2
Adenocarcinoma-m-sm1	10
Adenocarcinoma-sm-m	6

m-sm1, intramucosal-scant submucosal invasion; sm-m, submucosal massive invasion.

NBI magnification and histological finding

Differential diagnosis of neoplastic lesions by Kudo's pit patterns classification on NBI with magnifying colonoscopy showed sensitivity and specificity of 88.9% and 87.5%, respectively; the positive predictive value and negative predictive value were 98.9% and 38.9%, respectively. The capillary patterns by Sano's classification also showed high sensitivity and specificity of 91.9% and 87.5%, respectively; the positive predictive value and negative predictive value were estimated as 98.9% and 46.7%, respectively. The classification by capillary thickness showed sensitivity and specificity of 99.0% and 62.5%, respectively; the positive predictive value and negative predictive value were estimated as 97.0% and 83.3%. The classification by capillary irregularity revealed sensitivity and specificity of 100% and 62.5%, respectively; the positive predictive value and negative predictive value were estimated as 97.1% and 100% (Table 3).

Table 4 shows the relationship between capillary pattern as determined by NBI magnification and histologic findings. Hyperplastic polyp was most common among cases of capillary pattern type I (6/15), while carcinoma accounted 50% of capillary pattern type III cases (12/24) including submucosal massive invasion of 6 cases, suggesting the increasing trend of carcinoma and submucosal massive invasion toward the capillary pattern type III (p<0.01).

Table 5 shows relationship between capillary thickness as determined by NBI magnification and histologic findings. Invisible capillary was more common among hyperplastic polyp (5/6), while thin capillary was more common among low grade tubular adenoma (35/58). All cases with thick capillary were diagnosed as neoplastic lesions (43/43); 13 cases of them were carcinoma (13/43). Six cases with submucosal massive invasion were all determined as thick capillary (p<0.01).

Table 3. Diagnostic Accuracy of NBI Colonoscopy

	Pit pattern		Capillary pattern		Capillary thickness		Capillary irregularity	
	Neoplastic	Non-neoplastic	Neoplastic	Non-neoplastic	Neoplastic	Non-neoplastic	Neoplastic	Non-neoplastic
Histologic diagnosis								
Neoplastic	88	11	91	8	98	1	99	0
Non-neoplastic	1	7	1	7	3	5	3	5
Sensitivity, %	88.9		91.9		99.0		100	
Specificity, %	87.5		87.5		62.5		62.5	
PPV, %	98.9		98.9		97.0		97.1	
NPV, %	38.9		46.7		83.3		100	

NBI, narrow band imaging; PPV, positive predictive value; NPV, negative predictive value.

Table 4. Relationship between Capillary Pattern[10] as Determined by NBI Findings and Histologic Findings

	HP	IP	Tubular adenoma		TVA	VA	Carcinoma		No.
			Low	High			m-sm1	sm-m	
CP I	6[a)]	1	8						15
(%)	(40)	(6.7)	(53.3)						
CP II	1		43	12	7	1	4		68
(%)	(1.5)		(63.2)	(17.6)	(10.3)	(1.5)	(5.9)		
CP III			4	4	3	1	6[a)]	6[a)]	24
(%)			(16.7)	(16.7)	(12.5)	(4.2)	(25)	(25)	
Total	7	1	55	16	10	2	10	6	107

NBI, narrow band imaging; CP, capillary pattern; HP, hyperplastic polyp; IP, inflammatory polyp; TVA, tubulovillous adenoma; VA, villous adenoma; m-sm1, intramucosal-scant submucosal invasion; sm-m, submucosal massive invasion.
[a)] $p<0.01$.

Table 5. Relationship between Capillary Thickness as Determined by NBI Findings and Histologic Findings

	HP	IP	Tubular adenoma		TVA	VA	Carcinoma		No.
			Low	High			m-sm1	sm-m	
Invisible	5[a,b)]		1[b)]						6
(%)	(83.3)		(16.7)						
Thin	2[b)]	1[b)]	35[b)]	11[b)]	5[b)]	1[b)]	3		58
(%)	(3.4)	(1.7)	(60.3)	(19)	(8.6)	(1.7)	(5.2)		
Thick			19	5	5	1	7[c)]	6[a,c)]	43
(%)			(44.2)	(11.6)	(11.6)	(2.3)	(16.3)	(14)	
Total	7	1	55	16	10	2	10	6	107

NBI, narrow band imaging; HP, hyperplastic polyp; IP, inflammatory polyp; TVA, tubulovillous adenoma; VA, villous adenoma; m-sm1, intramucosal-scant submucosal invasion; sm-m, submucosal massive invasion.
[a)] $p<0.01$; [b)]vs. [c)] $p<0.01$.

Table 6 shows relationship between capillary irregularity as determined by NBI magnification and histologic findings. All hyperplastic polyp cases were determined as invisible capillary (5/5). Regular capillary was more common among low grade tubular adenoma cases (51/78); while irregular capillary was more common among carcinoma cases (12/24) and accounted the whole cases of neoplastic lesions (24/24) and submucosal massive invasion (6/6) ($p<0.01$).

DISCUSSION

Magnifying endoscopy provides details of the surface of the gastrointestinal tract, and enables pit pattern examination of colorectal tumors by using indigo carmine or cresyl violet.[9,11-14] The pit pattern of colorectal tumors (type I-V pit pattern) was suggested by Kudo et al.[9,13] using stereomicroscopy, and is useful for histologic evaluation of tumors. The pit pattern was developed for differential diagnosis between

Table 6. Relationship between Capillary Irregularity as Determined by NBI Findings and Histologic Findings

	HP	IP	Tubular adenoma		TVA	VA	Carcinoma		No.
			Low	High			m-sm1	sm-m	
Invisible	5[a,b)]								5
(%)	(100)								
Regular	2[b)]	1[b)]	51[b)]	11[b)]	8[b)]	1[b)]	4		78
(%)	(2.6)	(1.3)	(65.4)	(14.1)	(10.3)	(1.3)	(5.1)		
Irregular			4	5	2	1	6[c)]	6[a,c)]	24
(%)			(16.7)	(20.8)	(8.3)	(4.2)	(25)	(25)	
Total	7	1	55	16	10	2	10	6	107

NBI, narrow band imaging; HP, hyperplastic polyp; IP, inflammatory polyp; TVA, tubulovillous adenoma; VA, villous adenoma; m-sm1, intramucosal-scant submucosal invasion; sm-m, submucosal massive invasion.
[a)]$p<0.01$; [b)]vs. [c)]$p<0.01$.

neoplasia and non-neoplasia, and is used for determining the degree of histologic atypia and depth of early carcinoma, presence of minute residual tumor after endoscopic resection,[11-15] the degree of histologic inflammation when ulcerative colitis is present, and diagnosis of dysplasia and colitis-associated carcinoma.[16-18]

NBI with magnifying endoscopy is capable of observing both the mucosal pit pattern and surface layer capillary pattern without dye spray but only with mode conversion.[3] This is why the NBI endoscopy is also called as an 'electronic chromoendoscopy.' NBI with magnifying endoscopy can indirectly measure capillary pit patterns similar to the regular pit pattern type II, III, and IV, although the capillary pit pattern type V, a marker of carcinoma, is not measured sufficiently yet.[5,19-21] Capillary evaluation is a useful alternative to the pit patterns for the diagnosis of a colorectal tumor appearing as a type V pit pattern. Recently, a number of studies are attempting to evaluate capillary features (vessel diameter, irregularity and capillary structure) for the diagnosis of colorectal tumors using NBI magnification.[5,19,21-25]

This study classified lesions firstly by the capillary patterns by Sano's classification, and additionally classified by capillary features; that is, thin or thick according to the capillary thickness and regular or irregular according to the capillary irregularity. Thin and regular capillary could be included in the capillary pattern type II, while thick and irregular capillary could be included in the capillary pattern type III, with similar features on tumor observation. Capillary pattern type I was quite common including invisible or faintly visible mucosal capillary meshwork. The capillary meshwork in this type was invisible in general or regional in some cases, and previous biopsy site performed in some cases at other hospitals revealed regional capillary meshwork (Fig. 1B).

The sensitivity and specificity of differential diagnosis between neoplasia or non-neoplasia based on the capillary meshwork of Sano's classification were 96.4% and 92.3%, respectively in a previous study,[26] and were slightly lower in this study with 91.9% and 87.5%, respectively. Classification by capillary thickness or irregularity showed higher sensitivity but slightly lower specificity compared to the classification by capillary pattern (Table 3).

Among capillary patterns based on the NBI with magnifying endoscopy, neoplastic lesion was slightly more common among capillary pattern type I, carcinoma was more apparent in type III, and all 6 cases of submucosal massive invasion were type III. Among capillary thickness based on the NBI with magnifying endoscopy, invisible capillary was more common among hyperplastic lesions but only 1 case of neoplastic lesions belonged to it. Most carcinoma and all 6 cases of submucosal massive invasion showed thick pattern. Among capillary irregularity, irregular capillary was histologically worse than regular pattern and most common among carcinoma lesions included all 6 cases of submucosal massive invasion. Since capillary pattern by Sano's classification could be interpreted differently between observer, we simplified to capillary thickness or irregularity for this study. The results showed that capillary thickness or irregularity by NBI endoscopy was useful enough to correlate between submucosal massive invasion and histologic finding of colorectal tumor.

This study confirmed that NBI with magnifying endoscopy enables the differential diagnosis between neoplastic and non-neoplastic lesion.[1] NBI with magnifying endoscopy was also found useful when determining whether the depth of submucosal invasion is more than 1,000 μm or not, a key factor in deciding an endoscopic therapy of early colorectal carcinoma. NBI endoscopy is simple to perform for both endoscopists and patients, and does not require special instrument or dye. The capillary features such as capillary thickness or irregularity by NBI magnification is simpler and easier for clinical use than classifications by pit patterns or capillary patterns.

NBI with magnifying endoscopy is expected to be widely used clinically for capillary evaluation and proper diagnosis of colorectal tumor. This was a small retrospective study, and the classifications presented in the study require further investigation in multicenter, randomized, controlled trials, regarding the degree of conformity with endoscopic findings and the superiority of NBI colonoscopy compared to conventional colonoscopy in detection and prediction of histologic diagnosis of the tumor.

Conflicts of Interest

The authors have no financial conflicts of interest.

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