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ORIGINAL ARTICLE

Evaluation of Microvessels in Colorectal Tumors by Narrow Band Imaging Magnification: Including Comparison with Magnifying Chromoendoscopy

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Abstracts

Background/Aims Narrow band imaging (NBI) magnification analysis has entered use in clinical settings to diagnose colorectal tumors. Pit pattern analysis with magnifying endoscopy is already widely used to assess colorectal lesions and invasion depth. Our study compared diagnoses by vascular pattern analysis and pit pattern analysis with NBI magnification.

Methods We examined 296 colorectal lesions—15 hyperplastic polyps (HP), 213 low-grade adenomas (L-Ad), 26 high-grade adenomas (H-Ad), 31 with intramucosal to scanty submucosal invasion (M-Sm-s), and 11 with massive submucosal invasion (Sm-m)—applying the system of Kudo et al. to analyze pit patterns, and the system of Tanaka et al. to analyze and classify vascular patterns by NBI into three categories: type A (hyperplasia pattern), type B (adenomatous pattern), and type C (carcinomatous pattern). Type C cases were subdivided into subtypes C1, C2, and C3. We used this system to examine histology type and invasion depth.

Results Diagnostic sensitivity, specificity, and accuracy were 100% for both type II pit pattern HP and type A HP. Diagnostic sensitivity, specificity, and accuracy were 85.4, 94.5, and 93.2% for Vi and Vn pit pattern cancer and 95.2, 91.7, and 92.2% for type C cancer (no significant differences in sensitivity, specificity, or accuracy). Diagnostic sensitivity, specificity, and accuracy were comparable for Vi high-grade irregularity and Vn pit pattern Sm-m (90.9, 96.8, and 96.7%) and type C2/C3 Sm-m (90.1, 98.2, and 98.0%), with no significant differences in sensitivity, specificity, or accuracy.

Conclusions Vascular pattern analysis by NBI magnification proved comparable to pit pattern analysis.

Keywords Narrow band imaging magnification · Colorectal tumor · Pit pattern analysis

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Introduction

Pit pattern analysis using Kudo's classification system based on magnifying chromoendoscopy is an effective technique for making qualitative diagnoses of colorectal lesions [1].

With advances in endoscopy technologies in recent years, endoscopy using a narrow band imaging (NBI) system [2] has been developed for applications in image-enhanced endoscopy and has gradually entered wider use.

Short-wavelength light generally does not penetrate deep into the body and is observed as reflected light due to scattering and absorption at the surface of the skin. In contrast, long-wavelength light will penetrate deep into the body and in some cases pass entirely through the body. The narrow band imaging (NBI) system applies this principal to shift spectral properties to the short wavelength side using

a narrow band RGB filter of a frame-sequential electron endoscope. This reduces the depth to which light penetrates into the body and enables a new diagnostic imaging technique capable of delineating the alignment of capillaries in the superficial layer of the mucous membrane [3, 4].

The processor for the electron endoscope system incorporates the NBI system. No special device is needed, resulting in a highly convenient diagnostic technique capable of switching instantly between normal imaging and NBI imaging at the simple press of a button located in the same area as the scope controls.

Here, we assessed the effectiveness of pit pattern analysis and narrow band imaging (NBI) magnification analysis in qualitative diagnoses of colorectal lesions and evaluated the invasion depth of these lesions.

Methods

The subject group consisted of 173 patients (125 men and 48 women) with a mean age of 63.5 years, presenting with a total of 296 colorectal lesions. This group had undergone endoscopic or surgical resection at our department in the period from August 2007 to March 2009 (Table 1). We obtained informed consent from all patients before admittance to the study. All lesions were detected by conventional colonoscopy, and the detected lesions were each observed twice: by magnifying colonoscopy with a light source with the NBI systems, then by magnifying chromoendoscopy with 0.2% indigo carmine dye spraying and a light source with standard optical filters. We assessed pit patterns under each modality and recorded the findings. In addition, we subjected lesions with suspected type V pit patterns to magnified observations with crystal violet staining, as previously reported [5, 6]. The instruments used in this study consisted of a magnifying videoendoscope system (CF-PCF Q240ZI, Olympus Tokyo Japan) and a standard optical videoendoscopic system with two light sources and a digital image filing system. One light source was used for the standard optical filter (broadband), while the other was used for the NBI system. In practice, the light sources could be easily and manually exchanged with the endoscope remaining in place. Following detailed observations, all lesions were resected endoscopically or surgically.

Each resected specimen was fixed in 10% buffered formalin for 12–48 h after extension with pinning on a board, then embedded in paraffin. The entire tumor was then cut into serial 2-mm-thick slices. A histological section was made from each block and stained with hematoxylin eosin.

We performed detailed microscopic histologic assessments according to the procedure described in General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus [7].

Table 1 Patient characteristics

Size of respected polyp	<10 mm	≥10 mm	Total
No. of patients/lesions*	84/153	117/143	173/296
Sex (male/female)*	63/21	83/34	125/48
Mean age (range)	63.6 (38–87)	63.3 (37–86)	63.5 (37–87)
Macro scope[a]			
Is	62	41	103
Isp	44	75	119
IIa	45	9	54
IIc	2	5	7
LST	0	13	13
Mean size of resected polyp (mm)	6.1	15.1	10.3
Localization[b]			
Right	85	51	136
Left	54	70	124
Rectum	14	22	36
Histology[c]			
HP	13	2	15
L-Ad	130	83	213
H-Ad	5	21	26
m-SM-s	4	27	31
SM-m	1	10	11

* Contains duplicate records

[a] According to the General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus [7]

[b] *Right*: cecum, ascending colon and transverse colon; *left*: descending colon and sigmoid colon

[c] *HP* hyperplastic polyp, *L-Ad* low-grade adenoma, *H-Ad* high-grade adenoma, *m-SM-s* intramucosal to scanty submucosal invasion, *SM-m* massive submucosal invasion

Based on past studies [8, 9], the depth of submucosal penetration was classified into the following two groups: Sm-s (≤1,000 μm penetration into submucosa) and Sm-m (>1,000 μm).

Pit patterns were assessed according to the classification system of Kudo and Tsuruta [1, 10].

Using the classification system of Hirata and Tanaka et al. developed in 2008 [11], we classified the NBI magnification findings as follows (Fig. 1a, b):

Type A: Microvessels are invisible.

Type B: Microvessels form regular mesh structures. Regular glandular structures are observed indirectly.

Type C-1: Microvessels form irregular mesh structures. Irregular glandular structures are observed indirectly. Vessel thickness and distribution are constant.

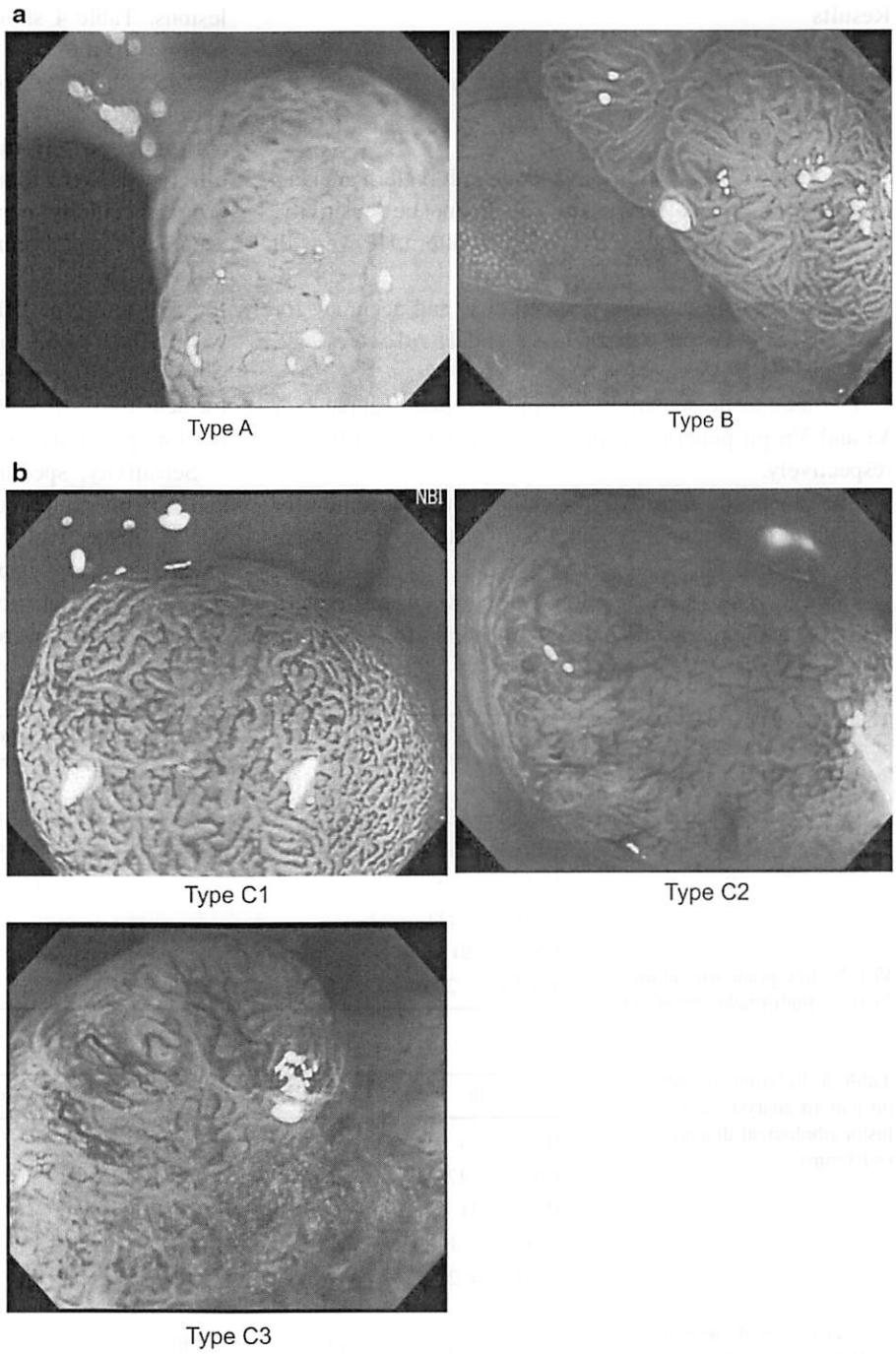

Fig. 1 **a** NBI magnification findings of colorectal lesion. *Type A*: microvessels are invisible. *Type B*: microvessels form regular mesh structures. Regular glandular structures are observed indirectly. **b** *Type C-1*: microvessels form irregular mesh structures. Irregular glandular structures are observed indirectly. Vessel thickness and distribution are constant. *Type C-2*: microvessels form irregular mesh structures. Irregular glandular structures are observed indirectly. Vessel thickness and distribution are uneven. *Type C-3*: mesh structures are destroyed. Glandular structures cannot be observed indirectly. Vessel thickness and distribution are uneven. Avascular areas are apparent. Irregular vessels are sporadically ruptured and fragmented

Type C-2: Microvessels form irregular mesh structures. Irregular glandular structures are observed indirectly. Vessel thickness and distribution are uneven.

Type C-3: Mesh structures are destroyed. Glandular structures cannot be observed indirectly. Vessel thickness and distribution are uneven. Avascular areas are apparent. Irregular vessels are sporadically ruptured and fragmented.

We compared qualitative diagnoses and invasion depths and compared vascular pattern and pit pattern analyses based on NBI imaging.

Colorectal lesions in the preceding studies were divided into those measuring 10 mm or greater in diameter or those less than 10 mm in diameter.

In the present study, as part of the testing, one endoscopist performed vascular pattern diagnoses and pit pattern analyses by NBI. Each case was then reviewed by multiple physicians by NBI to reach a consensus on vascular pattern and pit pattern analyses. Values were expressed as mean ± SD. Data were evaluated by the Chi-square test. A p value of less than 0.05 was considered to be significant.

Results

Relationship Between Pit Pattern Analysis and Histopathological Diagnosis

Table 2 shows the relationship between pit pattern analysis and histopathological diagnosis. The diagnostic sensitivity, specificity, and accuracy for type II pit pattern HP were all 100%.

The diagnostic sensitivity, specificity, and accuracy for type IIIL and IV pit pattern L-Ad and H-Ad were 94.2, 89.3, and 93.2%, respectively.

The diagnostic sensitivity, specificity, and accuracy for Vi and Vn pit pattern cancer were 85.4, 94.5, and 93.2%, respectively.

The diagnostic sensitivity, specificity, and accuracy for Vi high-grade irregularity and Vn pit pattern Sm-m were 90.9, 96.8, and 96.7%, respectively.

Table 3 shows the relationship between pit pattern analysis and histopathological diagnosis for <10-mm lesions. Table 4 shows the relationship for lesions measuring ≥10-mm.

The sensitivity, specificity, and accuracy of diagnostic performance for type-II pit-pattern HP were 100% for both <10-mm and ≥10-mm lesions. No statistically significant differences were found between the two groups in sensitivity, specificity, or accuracy. Sensitivity, specificity, and accuracy for <10-mm type IIIL and IV pit pattern L-Ad and H-Ad were 97.8, 94.4, and 97.4%, respectively; those for ≥10-mm type IIIL and IV pit pattern L-Ad and H-Ad were 90.4, 84.6, and 88.8%, respectively. Statistically significant differences between the two groups were found for sensitivity ($p = 0.013$) and accuracy ($p = 0.003$), but not for specificity ($p = 0.280$).

Sensitivity, specificity, and accuracy for <10-mm Vi and Vn pit pattern cancer lesions were 80.0, 98.0, and 97.4%, respectively; those for ≥10-mm Vi and Vn pit pattern cancer lesions were 83.4, 90.6, and 88.9%, respectively. Statistically significant differences between the two groups were found for specificity ($p = 0.009$)

Table 2 Relationship between pit pattern analysis and histopathological diagnosis (total)

Pit pattern	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
II ($n = 15$)	15 (100)				
IIIL ($n = 206$)		194 (91.1)	9 (34.6)	3 (9.6)	
IV ($n = 27$)		19 (8.9)	4 (15.4)	3 (9.6)	1 (9.0)
Vi-L ($n = 29$)			13 (50.0)	16 (51.7)	
Vi-H ($n = 11$)				8 (25.9)	3 (27.3)
VN ($n = 8$)				1 (3.2)	7 (63.6)
Total ($n = 296$)	15	213	26	31	11

Vi-L Vi low-grade irregularity, *Vi-H* Vi high-grade irregularity

Table 3 Relationship between pit pattern analysis and histopathological diagnosis (<10 mm)

Pit pattern	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
II ($n = 13$)	13 (100)				
IIIL ($n = 128$)		125 (96.2)	2 (40.0)	1 (25.0)	
IV ($n = 5$)		5 (3.8)			
Vi-L ($n = 4$)			3 (60.0)	1 (25.0)	
Vi-H ($n = 2$)				1 (25.0)	1 (100)
VN ($n = 1$)				1 (25.0)	
Total ($n = 153$)	13	130	5	4	1

Vi-L Vi low-grade irregularity, *Vi-H* Vi high-grade irregularity

Table 4 Relationship between pit pattern analysis and histopathological diagnosis (≥10 mm)

Pit pattern	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
II ($n = 2$)	2 (100)				
IIIL ($n = 78$)		69 (83.1)	7 (33.3)	2 (7.4)	
IV ($n = 22$)		14 (16.9)	4 (19.0)	3 (11.1)	1 (10.0)
Vi-L ($n = 25$)			10 (47.6)	15 (55.6)	
Vi-H ($n = 9$)				7 (25.9)	2 (20.0)
VN ($n = 7$)					7 (70.0)
Total ($n = 143$)	2	83	21	27	10

Vi-L Vi low-grade irregularity, *Vi-H* Vi high-grade irregularity

and accuracy ($p = 0.003$), but not for sensitivity ($p = 0.812$).

Sensitivity, specificity, and accuracy for <10-mm Vi high-grade irregularities and Vn pit pattern Sm-m were 100, 98.7, and 98.7%, respectively; those for ≥10-mm Vi high-grade irregularities and Vn pit pattern Sm-m were 90.0, 94.8, and 99.4%, respectively. Statistically significant differences between the two groups were found for accuracy ($p = 0.041$) but not for sensitivity ($p = 0.9$) or specificity ($p = 0.058$).

Relationship Between Microvascular Pattern Classification and Histopathological Diagnosis Based on NBI Magnification

Table 5 shows the relationship between microvascular pattern classification and histopathological diagnosis based on NBI magnification analysis

The diagnostic sensitivity, specificity, and accuracy for type A HP were all 100%.

The diagnostic sensitivity, specificity, and accuracy for type B L-Ad and H-Ad were 91.2, 96.5, and 92.2%, respectively.

The diagnostic sensitivity, specificity, and accuracy for type C cancer were 95.2, 91.7, and 92.2%, respectively.

The diagnostic sensitivity, specificity, and accuracy for type C2/C3 Sm-m were 90.1, 98.2, and 98.0%, respectively.

Table 6 shows the relationship between microvascular pattern classifications and histopathological diagnoses for colorectal lesions measuring <10 mm. Table 7 shows the relationship for colorectal lesions measuring ≥10 mm.

Sensitivity, specificity, and accuracy for <10-mm and ≥10-mm type A HP were 100% No statistically significant differences were found between the two groups for sensitivity, specificity, or accuracy.

Sensitivity, specificity, and accuracy for <10-mm type B L-Ad and H-Ad were 97.0, 100, and 97.4%, respectively; those for ≥10-mm type B L-Ad and H-Ad were 83.7, 94.9, and 86.7%, respectively. Statistically significant differences between the two groups were found for sensitivity ($p = 0.0003$) and accuracy ($p = 0.0005$), but not for specificity ($p = 0.46$).

Sensitivity, specificity, and accuracy for type C cancer lesions measuring <10 mm were 100, 97.3, and 97.4%, respectively, while type C cancer lesions measuring

Table 5 Relationship between microvascular pattern classification histopathological diagnosis based on NBI magnification (total)

NBI magnification findings	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
Type A ($n = 15$)	15 (100)				
Type B ($n = 220$)		210 (98.6)	8 (30.8)	2 (6.5)	
Type C1 ($n = 46$)		3 (1.4)	18 (69.2)	24 (77.4)	1 (9.1)
Type C2 ($n = 6$)				4 (12.9)	2 (18.2)
Type C3 ($n = 9$)				1 (3.2)	8 (72.7)
Total ($n = 296$)	15	213	26	31	11

Table 6 Relationship between microvascular pattern classification histopathological diagnosis based on NBI magnification (<10 mm)

NBI magnification findings	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
Type A ($n = 13$)	13 (100)				
Type B ($n = 131$)		130 (100)	1 (25.0)		
Type C1 ($n = 7$)			4 (80.0)	3 (75.0)	
Type C2 ($n = 1$)					1 (100)
Type C3 ($n = 1$)				1 (25.0)	
Total ($n = 153$)	13	130	5	4	1

Table 7 Relationship between microvascular pattern classification histopathological diagnosis based on NBI magnification (≥10 mm)

NBI magnification findings	HP (%)	L-Ad (%)	H-Ad (%)	M-SM-s (%)	SM-m (%)
Type A ($n = 2$)	2 (100)				
Type B ($n = 89$)		80 (96.4)	7 (33.3)	2 (7.4)	
Type C1 ($n = 39$)		3 (3.6)	14 (66.7)	21 (77.8)	1 (10.0)
Type C2 ($n = 5$)				4 (14.8)	1 (10.0)
Type C3 ($n = 8$)					8 (80.0)
Total ($n = 143$)	2	83	21	27	10

≥10 mm were 94.6, 84.0, and 86.7%, respectively. Statistically significant differences between the two groups were found for specificity ($p = 0.0002$) and accuracy ($p = 0.0005$), but not for sensitivity ($p = 0.773$).

Sensitivity, specificity, and accuracy for <10-mm type C2/C3 Sm-m were 100, 99.3, and 99.3%, respectively, while those for ≥10-mm type C2/C3 Sm-m were 90.0, 96.3, and 96.5%, respectively. No statistically significant differences between the two groups were found for sensitivity ($p = 0.90$), specificity ($p = 0.146$), or accuracy ($p = 0.09$).

(1) No statistically significant differences were confirmed in diagnostic sensitivity, specificity, or accuracy between type II pit pattern HP and type A HP.
(2) No statistically significant differences were found in diagnostic sensitivity, specificity, or accuracy between type IIIL and IV pit pattern L-Ad and H-Ad and type B L-Ad and H-Ad.
(3) No statistically significant differences were observed in diagnostic sensitivity, specificity, or accuracy between Vi and Vn pit pattern cancer and type C cancer.
(4) No statistically significant differences were found in diagnostic sensitivity, specificity, or accuracy between Vi high-grade irregularity and Vn pit pattern Sm-m and type C2/C3 Sm-m.

In the above studies, colorectal lesions measuring <10 mm (1)–(4) showed no statistically significant differences in sensitivity, specificity, or accuracy.

In the same way, in the above studies, colorectal lesions measuring ≥10 mm (1)–(4) showed no statistically significant differences for sensitivity, specificity, and accuracy.

Discussion

Magnifying endoscopy provides detailed images of the surface of the GI tract, making it possible to examine pit patterns of colorectal tumors, even during routine colonoscopic examination, using dye spraying (e.g., indigo carmine) [1, 5, 10].

Reports indicate that the pit pattern classification of colorectal tumors (type I–V pit patterns), based on stereomicroscopy proposed by Kudo et al. [1, 10] is useful in evaluating the histologic features of tumors.

Assessments of pit pattern are clinically significant in making differential diagnoses of neoplasia versus non-neoplasia, in determining the degree of histologic atypia, and in determining the depth of early carcinoma [5, 6, 12].

In recent years, narrow band imaging (NBI) magnification has been developed for endoscopic diagnoses of colorectal tumors and used in practical applications. NBI diagnosis is useful for differentiating colorectal tumors from non-tumors [2, 13].

However, to the best of our knowledge, no study published in English has attempted a detailed classification of colorectal lesions into HP, adenoma, M (carcinoma in situ), Sm-s (≤1,000 μm penetration into submucosa), and Sm-m (>1,000 μm) and compared and investigated pit pattern and NBI magnification analysis (qualitative diagnosis and invasion depth).

In the present study, we performed NBI-based vascular pattern analysis and pit pattern analysis to diagnose colorectal tumors qualitatively and to evaluate their invasion depth. We then compared and analyzed the results.

With pit pattern analysis, the diagnostic sensitivity, specificity, and accuracy for type II pit pattern HP were all 100%.

With NBI magnification analysis, the diagnostic sensitivity, specificity, and accuracy for type A HP were 100%.

In a study similar to ours, Kanao et al. [14] obtained sensitivity and specificity for type A HP of 100 and 98.8%, respectively, results comparable to our own.

Sano et al. [15] used NBI magnification analysis to differentiate HP from adenoma, reporting favorable diagnostic performance: 95.3% accuracy, 96.4% sensitivity, and 92.3% specificity.

Machida et al. [2] also performed pit pattern and NBI magnification analysis to diagnose HP and adenoma, reporting accuracy, sensitivity, and specificity of 93.4, 100, and 75.0%, respectively.

High diagnostic performance has been reported for HP using NBI magnification at our facility and at other facilities [2, 14, 15].

The diagnostic sensitivity, specificity, and accuracy for Vi and Vn pit pattern cancer observed in the present study were 85.4, 94.5, and 93.2%, respectively.

The diagnostic sensitivity, specificity, and accuracy for type C cancer were 95.2, 91.7, and 92.2%, respectively.

For the cancer diagnostic performance of NBI magnification, Kanao [14] reports 67.9% sensitivity and 88.1% specificity. Although the sensitivity observed in our report was slightly lower (67.9%), this study involved a total of 112 cancer cases, with a relatively high number of type B M-Sm-s cancer cases (36; 32.1%). This may have worked against the achievement of more favorable diagnostic results.

The diagnostic sensitivity, specificity, and accuracy for Vi high-grade irregularity and Vn pit pattern Sm-m were 90.9, 96.8, and 96.7%, respectively.

The diagnostic sensitivity, specificity, and accuracy for type C2/C3 Sm-m were 90.1, 98.2, and 98.0%, respectively.

Wada et al. [16] observed diagnostic sensitivity, specificity, and accuracy for Vi high-grade irregularity and Vn