Clinical Significance of Diminutive Colonic Polyps in Elderly Patients

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ABSTRACT

Background and Objectives: Colorectal cancer is the third leading cause of cancer-related death. Excision of premalignant polyps has a *significant* impact on reducing colorectal cancer mortality and morbidity. Colonoscopy is considered to be the gold standard for the diagnosis and affords an opportunity for treatment of colonic polyps. In recent years, serious debates have taken place because of the biological characteristics of diminutive polyps (DPs), polypectomy complications, and serious costs. There has not yet been a consensus on the management of DPs. The objectives of this study were to demonstrate the real clinical importance of DPs smaller than 5 mm in diameter, which are frequently seen in geriatric patients by new endoscopic techniques, and to help in determining screening and surveillance programs.

Methods: The patients who underwent colonoscopy and were found to have a diminutive colorectal polyp (<5 mm from September 1, 2016 through September 1, 2017), were classified into 3 groups according to the imaging method used: flexible spectral imaging color enhancement (FICE), narrow band imaging (NBI), or I-SCAN. In all groups, demographic data were compared according to Paris classification (morphologic) and Kudo classification (correlation between the prediction of endoscopic diagnosis and final pathological examination) in terms of sensitivity, specificity, and negative and positive predictive values.

Results: Two hundred sixty-seven patients were included in the study: 97 in the NBI group, 83 in the FICE group, and 87 in the I-SCAN group. There were no statistically significant differences between NBI, FICE, and I-SCAN in differentiating neoplastic and nonneoplastic polyps, according to the Kruskal-Wallis test ($P = .809$).

Conclusions: The estimated progression rates of DPs to advanced adenomas or colorectal cancer (CRC) are very low. Missing these polyps or not excising them may lead to failure to diagnose some cancers. There is a need for further comprehensive studies of removing all polyps to determine whether non–high-risk lesions require further pathologic examination and to re-examine routine surveillance programs.

Key Words: colonoscopy, dimunitive polyps, I-SCAN, FICE, NBI.

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INTRODUCTION

Development of colorectal cancer is dependent on a stepwise progression from polyp to carcinoma, according to the theory of the adenoma–carcinoma sequence.[1] Therefore, excision of precancerous polyps which is detected in colonoscopy has been reported to prevent cancer development. The image quality of colonoscopy has improved because of the latest developments in technology. Also, screening programs have become widespread. As a result, polyp detection has increased. The excision of all polyps, polypectomy complications, and taking these polyps to the surveillance program bring a significant cost.

The most important factors reported in the development into carcinoma of polyps are size and surface features. Polyps are considered to be advanced adenomas when they are ≥1 cm or exhibit a villous component or high-grade dysplasia. Advanced adenomas have an increased risk of malignancy.[1,2] Most of the polyps detected in screening colonoscopy are small and benign. Smaller than 5-mm polyps are called diminutive polyps (DPs). Although DPs are accepted as premalignant according to the adenocarcinoma sequence, invasive carcinoma occurs in a small proportion of them.[2] Some studies have shown that DPs tend to grow.[3]

DPs are a matter for debate because of their low malignancy potential and high screening costs. Chaput et al[2] and Gschwantler et al[4] reported that the rate of advanced adenomas in polyps smaller than 10 mm was between 6.6 and 12.5% , and resections of these polyps may be beneficial.[2,4] On the other hand, some radiologists have deemed the DPs detected in computed tomographic colonography as insignificant because of their small size.[5] Premalignant DPs may be missed because they are not resected (because of the cost).

They also may not be diagnosed and undergo follow-up because of the lack of advanced pathologic examination. Surface features and vascular pattern can be better identified by the new endoscopic techniques. Examination of DPs with advanced endoscopic methods such as flexible spectral imaging color enhancement (FICE; Fujinon Corp. Saitama, Japan), narrow band imaging (NBI; Olympus, Center Valley, Pennsylvania, USA), and I-SCAN (Pentax, Tokyo, Japan) can reduce the cost and complications related to the unnecessary resection of polyps, the advanced pathologic examination, and the enhanced screening programs by ensuring the identification of the histologic characteristics of these polyps.

In geriatric patients, multiple overlapping comorbidities increase the risk rates of surgical procedures. Early diagnosis of precancerous polyps and early-stage cancers is a primary clinical goal, and if possible, treatment of these lesions by minimally invasive endoscopic methods is very important.

Because data on DPs are sparse, the actual clinical importance of these polyps is uncertain. It also appears that there is no consensus on the removal of DPs or on the surveillance programs. To demonstrate the real histologic importance of DPs and to help determine the clinical approach to them were among the objectives of this study.

MATERIALS AND METHODS

This prospective study was conducted at the University of Health Sciences (Istanbul, Turkey). The patients who were older than 65 years, underwent colonoscopy, and were found to have a colorectal DP (diameter, <5 mm) from September 1, 2016 through September 1, 2017, were classified into 3 groups, according to the imaging method that was used: FICE, NBI or I-SCAN. In all 3 groups, DPs were morphologically classified according to the Paris classification.[6] After histologic diagnosis, predictions are made according to Kudo's pit pattern classification,[7] and all excised polyps were sent for pathologic examination.

In all groups, the demographic data were compared according to the Paris (morphologic) and Kudo (correlation between the prediction of endoscopic diagnosis and final pathological examination) classifications, in terms of sensitivity, specificity, and negative and positive predictive values. In addition, the polyps were separated into 2 groups according to the locations: the polyps in the proximal part of the splenic flexure were classified as right localization, and the polyps in the distal part of it were classified as left localization.

Kudo Classification

Characteristic pit patterns of mucosa distinguish nonneoplastic from neoplastic colonic mucosal lesions (**Table 1**).

Paris Classification

Type 0 lesions are classified in 3 distinct groups (**Table 2**) : type 0-I, polypoid; type 0-II, nonpolypoid and nonexcavated; and type 0-III, nonpolypoid with a frank ulcer.

NBI Technique

The prototype of NBI technology was developed by Olympus in the United States. It is performed by using a filter in the light source unit and a function on the video processor. This method can provide up to 1000-fold magnification. The white light is filtered, resulting in narrowband light, which consists of 2 wavelengths: 415-nm blue light and 540-nm green light. This wavelength is strongly absorbed by the hemoglobin, and thus the NBI increases the contrast between the blood vessels (**Figure 1**).

Gastrointestinal cancers can expand from the mucosa into the deeper layers. Therefore, the details of the submucosal area facilitate the histologic diagnosis of the lesion. Although the deep mucosal structures are visualized by conventional colonoscopy, particularly superficial lesions are better demonstrated by the NBI technique.

FICE Technique

The prototype of this method was developed by Fujinon. The FICE technique changes the color of endoscopic images in real time (**Figure 2**). FICE has 10 preset wavelength settings that can be manually converted to achieve the best enhancement of the image.[8]

The real image replaces the light's properties with different wavelengths with virtual electronic filters and converts it to 10 new images, thus revealing the fine mucosal details to obtain a clearer image.

Table 1.
Pit Pattern Classification According to Kudo et al.

Pit Pattern Type	Characteristic Features	Figure
I	Roundish pits	
II	Stellar or papillary pits	
IIIS	Small, roundish, or tubular pits (smaller than type I pits)	
IIIL	Large roundish or tubular pits (larger than type I pits)	
IV	Branch-like or gyrus-like pits	
V	Nonstructured pits	

I-SCAN Technique

The prototype of I-SCAN technology was developed by Pentax. The I-SCAN is a digital image processing technology used with Pentax endoscopy systems.[9] It includes the modification of each image obtained with white light. The images obtained by conventional endoscopy are processed in software and converted to new images at the same time.[9–11] Thus, the superficial details of the mucosa and capillary architecture are visualized and allow the identification of previously nonvisualized lesions.[10]

White light illuminates the area of interest, and there are 3 algorithms for real-time image processing: *surface enhancement*, which is useful for visualizing the edges of anatomic structures by improving the light–dark contrast (this mode has 3 levels of image enhancement: low, medium, and high); *contrast enhancement*, which is used to visualize depressed areas by digitally adding blue to relatively dark areas. The resulting images are in the foreground and show superficial and vascular patterns similar to NBI (**Figure 3**); and *tone enhancement*, which changes the color contrast of the normal view to improve the

Table 2.
Paris Classification of Colonic Polyps

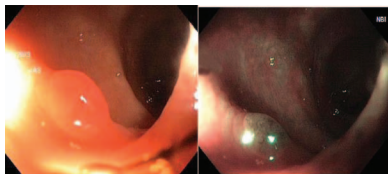| Paris Class	Characteristic Features	Figure
Ip	Pedunculated polyp	
Is	Sessile polyp	
IIa	Flat elevation of mucosa	
IIb	Flat mucosal change	
IIc	Mucosal depression	
III	Mucosal depression with raised edge	

Figure 1. The image on the left was obtained by conventional white light colonoscopy and the image on the right by NBI. With NBI, polyp surface and tissue vascularity were better visualized.
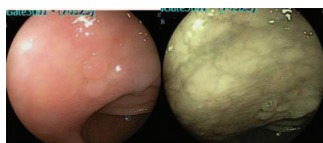

Figure 2. The image on the left was obtained by conventional white light colonoscopy and the image on the right was obtained by the FICE method. The details of the mucosal surface are more apparent with FICE.

visibility of minute mucosal structures and create a more advanced image with color changes.[8]

The superficial and vascular model can be evaluated according to the pit pattern classification (**Table 1**) recom-
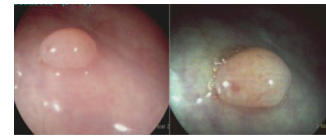

Figure 3. The image on the left was obtained by conventional white light colonoscopy and the image on the right by i-scan. The image on the right shows better vascularity with changes in the polyp and mucosal surface.

mended by Kudo using I-SCAN for polyps and precancerous lesions.[7] In addition to the pit pattern, information about the extent of the lesion, early mucosal changes, and angiogenesis can be demonstrated by image enhancement techniques.[10,11]

Statistical Analysis

The means and standard deviations of experimental data were calculated and analyzed with the Kruskal-Wallis test, Mann-Whitney U test, and χ^2 test. A 2 × 2 table was tabulated to determine the sensitivity, specificity, and positive and negative predictive values. The χ^2 test involved 2 × 2 tables, as well. The nonparametric Kruskal-Wallis Test was used in the evaluation of 3 categorical variables. The Mann-Whitney U test was used for the binary comparison between the 3 endoscopic techniques.

All P-values reported are 2-tailed and $P < .05$ was set as the level of significance. Statistical analyses were performed with SPSS Ver. 22.0 software (IBM Japan, Ltd., Tokyo, Japan).

RESULTS

Two hundred sixty-seven patients were included in the study. There were 97 patients in the NBI group, 83 in the FICE group, and 87 in the I-SCAN group. Age, gender, and polyp size and localization in all 3 groups are shown in **Table 3**.

The sensitivity, specificity, negative and positive predictive values, and P-values of the new endoscopic techniques for identifying DPs are shown in **Table 4**. When the prediction of endoscopic diagnosis of DPs and final pathologic examination results were compared in the NBI, FICE, and I-SCAN groups, the P-values for each group were found to be statistically significant in differentiating the polyps as neoplastic and nonneoplastic (**Table 4**).

There was no statistically significant difference between NBI, FICE, and I-SCAN in differentiating neoplastic and nonneoplastic polyps according to the Kruskal-Wallis test ($P = .809$).

Table 3.
Demographic Data of the Patients

	NBI (n)	FICE (n)	I-SCAN (n)	Total
Sex				
Male	43	40	44	127
Female	54	43	43	140
Polyp size (mm)				
1	1	2	1	4
2	20	12	13	45
3	36	31	35	102
4	24	19	20	63
5	16	19	18	53
Polyp localization				
Right	46	33	38	117
Left	51	50	49	150
Kudo classification				
2	17	19	21	57
3	72	55	57	184
4	7	9	9	25
5	1	0	0	1
Paris classification				
2a	94	80	83	257
2b	2	2	3	7
2c	1	1	3	3

All data are the number of each category.

Table 4.
Sensitivity, Specificity, Positive and Negative Predictive Values

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	P
NBI	82	80	97	67	.00019
FICE	84,6	80	98,5	75	.000038
I-SCAN	85	84	98	88	.000044

All data are percentages. Differences are statistically significant.

Table 5.
The Binary Comparison of NBI, FICE, and I-SCAN, According to the Kudo and Paris Classifications

	Kudo Classification P	Paris Classification P
NBI and FICE	.676	.846
NBI and I-SCAN	.518	.598
FICE and I-SCAN	.841	.751

The binary comparisons of NBI, FICE, and I-SCAN, according to the Kudo and Paris classifications, are shown in **Table 5**.

DISCUSSION

Barrett's esophagus, inflammatory bowel disease, colonic polyps, and gastrointestinal (GI) cancers can be detected in vivo by NBI, a simple technique that can be performed

with a single keystroke and a standard colonoscope and thus does not require a long procedure time. In contrast to confocal laser endomicroscopy and chromoendoscopy, lesions can be detected by NBI without the need for dyes.

Machida and colleagues[12] reported that chromoendoscopy and NBI are equally effective for differentiating neoplasia from non-neoplasia, with 100% sensitivity and 75% specificity. Fukuzawa et al[13] showed that NBI is superior to conventional endoscopy for the diagnosis of early-stage colorectal cancer. Differentiating of neoplastic from non-neoplastic DPs with to NBI yielded the statistically significant results shown in **Table 4**.

Mouri et al[14] reported that the green light (wavelength, 500–530-nm) produces the greatest contrast between normal mucosa and neoplastic tissue. Because white light has a broad wavelength range of 400–700 nm, it cannot produce a high contrast between the normal mucosa and early-stage cancer tissue, and carries the risk of overlooking early-stage neoplasms. The contrast difference so created enables detection of early stage cancer.[15,16] FICE does not increase the frequency of detection of colorectal polyps,[17,18] but can determine whether an adenoma is neoplastic.[19] The capillary patterns of adenomas are better demonstrated by FICE than by conventional endoscopy.[20,21] The differentiation of neoplastic from non-neoplastic DPs with FICE was statistically significant (**Table 4**).

I-SCAN technology increases diagnostic accuracy by revealing fine details of the gastrointestinal mucosa. Unlike chromoendoscopy, no dye or contrast material is used with I-SCAN. Moreover, I-SCAN does not make use of the contrast created by light of different wavelengths, such as NBI. I-SCAN is a software-based imaging method. In a study by Hoffman and colleagues[22] involving 200 patients that compared I-SCAN with conventional colonoscopy, the rate of detection of neoplastic lesions by conventional colonoscopy was 13%, compared with 38% by ISCAN. In the same study, I-SCAN was used to differentiate neoplastic from non-neoplastic lesions with a sensitivity of 98.6%. In our study, in the differentiation of neoplasia–non-neoplasia for DPs with I-SCAN, was statistically significant (**Table 4**).

Anandasabapathy et al[11] found that inflammatory bowel disease lesions with a risk of malignancy are flat rather than morphologically polypoid. Mucosal surface changes can be visualized using I-SCAN-1 and the vascular pattern using I-SCAN-2, enabling prediction of the lesion malignant potential. I-SCAN-3 provides detailed information regarding the borders of lesions.

The new endoscopic technologies described herein improve the prognosis of GI cancers by enabling their diagnosis and treatment at an early stage. However, these new techniques require experience if they are to be used effectively. The manufacturers are improving the ease of use of their products and increasing their adoption by continual innovation. Although these novel techniques are more costly than conventional colonoscopy, this disadvantage is outweighed by their diagnostic advantages, which improve the prognosis of patients with GI cancers.

In our study, we found that each of the NBI, FICE, and I-SCAN methods are successful in differentiating neoplastic and non-neoplastic DPs. However we could not demonstrate the superiority of one method over another (**Table 5**). The digital chromoendoscopy techniques have been widely used in clinics because they require no dye, are easy to use, do not extend the processing time, and differentiate neoplastic from non-neoplastic lesions successfully. If all endoscopists become familiar with these methods and increase their experience, unnecessary polypectomies and pathologic examination costs will be reduced in the future.

According to our clinical experience, chromoendoscopy and endomicroscopy remain limited because, besides a need for use of stain with potential hazards of allergic complications, they have a long learning curve, a long procedure time, and high cost. FICE, NBI, and I-SCAN have widespread use because there is no need for stain, they are convenient, and times of the procedures are shorter. Our work involves only patients of geriatric age. There is a need for further studies in this area that involve a more comprehensive group of patients.

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