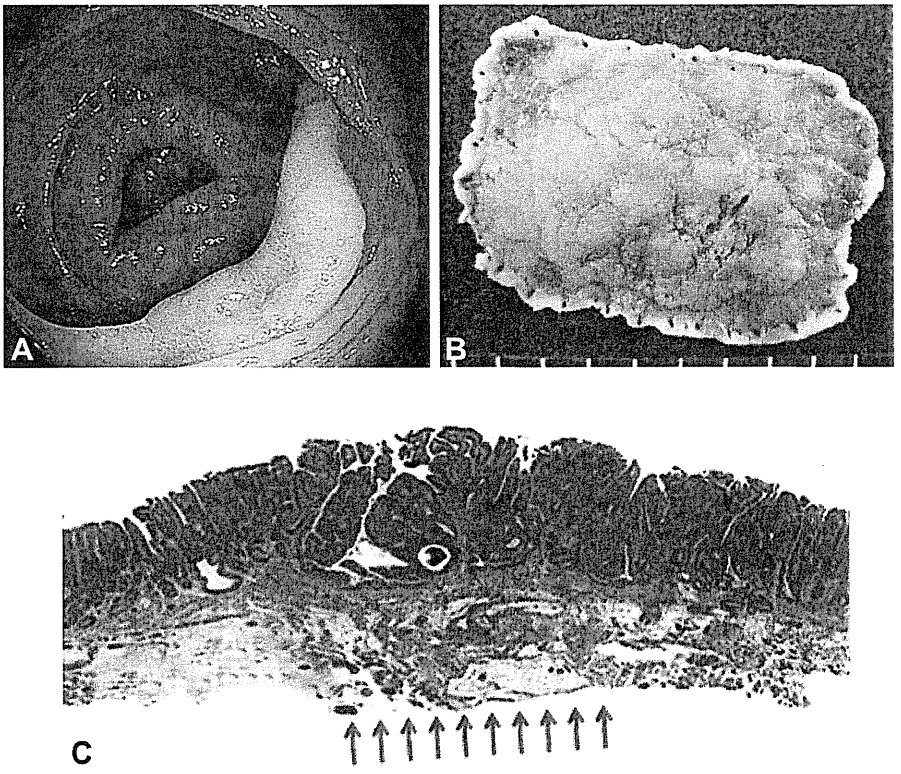

Figure 3. A positive vertical tumor margin after endoscopic mucosal dissection for submucosal colorectal carcinoma, Paris classification 0–IIa, ascending colon, 25 mm in diameter. **A,** Standard colonoscopic view. **B,** ESD specimen. **C,** Pathological examination revealed tubular adenocarcinoma with mucinous component. Submucosal invasion depth was 3500 μm, and vertically cut end of the tumor (mucinous component: *arrows*) was positive.

factors (including operator skill) do play a role during ESDs performed by beginners and less-experienced endoscopists. On the other hand, the highest standards of excellence and expertise should be established. Thus, the study is strong for having analyzed only 1 endoscopist. Nevertheless, other studies involving trainees at ESD centers should be performed in the near future. Because the main focus of this research is exploratory in nature, meant to highlight any potential relationships, there was no adjustment of nominal *P* values to correct for multiple testing of outcome data arising from individual patients. Thus, there may be instances of overstating significance, which necessarily leaves open the possibility of overfitting in the main results. Hence, these results should be taken as descriptive only, suggesting potential relationships to future researchers.

In conclusion, poor endoscopic operability was a significant independent predictor of incomplete resection and perforation during colorectal ESD, and location in the colon and the presence of a lesion on a flexure were significant predictors of poor endoscopic operability. SM deep invasion and severe fibrosis were significant independent predictors of perforation. These results will be helpful when considering appropriate approaches before performing colorectal ESD.

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Detection of Nonpolypoid Colorectal Neoplasia Using Magnifying Endoscopy in Colonic Inflammatory Bowel Disease

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KEYWORDS

- Colitis-associated dysplasia/cancer • Inflammatory bowel disease
- Ulcerative colitis • Image-enhanced endoscopy • Narrow band imaging
- Autofluorescence imaging • Magnifying endoscopy

KEY POINTS

- Most nonpolypoid colorectal neoplasms (NP-CRNs) are visible, and their detection can be facilitated by the use of chromoendoscopy.
- Chromoendoscopy using indigo carmine, in turn, also augments our further evaluation of the border and pit pattern of the lesion.
- Magnifying endoscopy can assist us to further visualize the surface pattern, although chronic inflammation and its sequela in patients with inflammatory bowel disease (IBD) make the use of the pit pattern analysis less useful.
- In Japan, at present, efforts are given to clarify the merit for random biopsy.
- A nationwide randomized controlled trial is ongoing to clarify whether target biopsy or random step biopsy is effective for the detection of NP-CRN.

INTRODUCTION

Patients with inflammatory bowel disease (IBD) have a high risk of colitis-associated dysplasia and cancer.[1,2] These types of dysplasia and cancer, as compared with sporadic adenoma/carcinoma, seem to have a distinct growth pattern, which can be flat,

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multifocal, or anaplastic.[3–7] Therefore, it is important that careful surveillance with colonoscopy is performed for all patients with IBD and, more frequently, for those considered to be at high risk.[8–12] Traditionally, flat dysplasia in ulcerative colitis (UC) has been considered to be detectable only by using random biopsy specimens of mucosa that appeared unremarkable during endoscopy.[13–15] However, recent studies have shown that most of them are visible; thus, their detection as nonpolypoid colorectal neoplasms (NP-CRNs) is an integral component in the prevention of colitic cancer.[9,16–18]

Unlike dysplasia-associated lesions or masses, which are readily visible using conventional endoscopy,[19] the detection of NP-CRN can be more difficult. NP-CRN in colitic IBD (cIBD) is often present simply as redness or a granular patch of mucosa that may not be readily distinguishable from the surrounding inflamed mucosa. Because it is often difficult to identify NP-CRN in cIBD using white light endoscopy, random blind biopsies are still commonly practiced, especially in Western countries, to potentially help detect these lesions. An alternative to random biopsy is to enhance the appearance of NP-CRN by using image-enhanced endoscopy and, in turn, to target the biopsy on areas that appear abnormal.

Several recent trials have evaluated dye-based image enhanced endoscopy (chromoendoscopy),[20–28] magnifying endoscopy,[16,29–33] and equipment-based image-enhanced endoscopy (IEE)[34–45] to detect NP-CRN in cIBD. Of these techniques, the indigo carmine dye spray IEE has been shown to effectively increase the detection of areas suspected to contain NP-CRN and to delineate the border and surface of suspected and obvious lesions.[46] Equipment-based IEE is a promising, but unproven, method that is designed to visualize small vessels and minute mucosal patterns. Of the currently available equipment-based IEE: narrow band imaging [NBI; Olympus, Tokyo, Japan], flexible spectral imaging color enhancement [Fujifilm, Tokyo, Japan], blue laser image [Fujifilm, Tokyo, Japan], autofluorescence imaging [AFI; Olympus, Tokyo, Japan], and i-scan [Pentax, Tokyo, Japan], clinical trials on the diagnosis of NP-CRN in cIBD have been published only for NBI and AFI.[34–45]

In this article, the authors describe the present status of the use of IEE to diagnose NP-CRN using magnifying colonoscope and illustrate their practice at the Hiroshima University Hospital. The authors have collated a few cases to provide examples of their practice. The authors do not reiterate data reporting on the utility of chromoendoscopy as Subramanian and Bisschops have summarized them.

THE PREVALENCE OF NP-CRN IN PATIENTS WITH IBD

Data show that nonpolypoid colorectal lesions are common in patients with IBD. The true prevalence of NP-CRN in UC is difficult to estimate with the present endoscopic modality. Several studies provide a general estimate. Sada and colleagues[16] reported that with surveillance colonoscopy in 1115 patients with UC, 39 colitic dysplasias or cancers in 31 patients were detected; 30% of dysplasias (6 of 20) were flat, and 16% of cancers (3 of 19) were depressed lesions. Toruner and colleagues[17] reported that among 635 patients with IBD, 36 dysplasias were detected; 24 (67%) were nonpolypoid and 12 (33%) were polypoid. Rutter and colleagues[18] reported that 77% of 110 colitic dysplasias or cancers in 525 patients with UC were detected endoscopically, with 23% being flat. In an investigation by the Japanese Ministry of Health, Labor, and Welfare, 42 lesions (79%) were polypoid and 11 lesions (21%) were nonpolypoid. Other reports have shown that more NP-CRN were detected and diagnosed using magnifying endoscopy as compared with chromoendoscopy.[16,28–33]

DETECTION OF NP-CRN WITH CHROMOENDOSCOPY

The recent use of high-definition endoscopy with chromoendoscopy has enabled endoscopists to directly visualize, localize, and diagnose NP-CRN in patients with UC (see Table 1). Indigo carmine solution enhances the visualization of the border and surface topography of the lesion to improve contrast compared with the surrounding mucosa in patients with UC.[46] A meta-analysis has demonstrated that chromoendoscopy has medium to high sensitivity (83.3%, 95% confidence interval [CI]: 35.9–99.6), specificity (91.3%, 95% CI: 43.8–100), and high diagnostic accuracy (odds ratio 17.544, 95% CI: 1.245–247.14) for dysplastic lesions[47] and is superior to white light colonoscopy for the proportion of lesions detected by biopsies (44%, 95% CI: 28.6–59.1) as well as for flat dysplasia (27%, 95% CI: 11.2–41.9) in patients with UC.[26]

Kiesslich and colleagues[20] reported 165 patients with long-standing UC who were randomized to conventional colonoscopy or colonoscopy with chromoendoscopy using 0.1% methylene blue. More targeted biopsies were possible, and significant intraepithelial neoplasia was detected in the chromoendoscopy group (32 vs 10; $P = .003$). Rutter and colleagues[23] reported the importance of indigo carmine dye spraying for the detection of dysplasia in UC. They emphasized that no dysplasia was detected in 2904 nontargeted biopsies. In comparison, chromoendoscopy with targeted biopsy led to fewer biopsies and detected 9 dysplastic lesions, 7 of which were only visible after indigo carmine application. They concluded that the indigo carmine dye spraying of the whole colon is feasible, and dysplasia detection may be more effective than taking large numbers of random biopsies. Hurlstone and colleagues[31] also emphasized that indigo carmine–assisted high-magnification chromoendoscopy and improved the detection of intraepithelial neoplasia in the endoscopic screening of patients with UC.

However, pancolonic chromoendoscopy has potential limitations: dye on the mucosa is not always equally spread; dye pooling can lead to difficult observation; more time is needed; and some biopsies may be false negative.

In the authors' institution, they routinely perform high-magnification colonoscopy with indigo carmine chromoendoscopy after they suspect the presence of NP-CRN in patients with cIBD. Morphologically, NP-CRN in IBD appear to be slightly elevated, completely flat, or slightly depressed as compared with the surrounding mucosa. In order to detect them, the authors look for the presence of a slightly elevated lesion, focal friability, obscure vascular pattern, discoloration (uneven redness or a patch or redness), villous mucosa (velvety appearance), and irregular nodularity. The finding of any of these signs typically alerts the authors to become suspicious of the possible presence of NP-CRN and leads them to wash out the mucus or debris from the surface on the target lesion and apply the dye for magnifying colonoscopy.[15]

MAGNIFYING COLONOSCOPY USING DYE SPRAYING FOR NP-CRN

After dye spraying but before the authors perform a biopsy or resection, they will typically evaluate the border of the lesion. The authors look for the presence of dye pooling within the lesion, which would suggest the diagnosis of a depressed lesions. The authors study the pit pattern of the mucosal surface.[15] The authors' experience and others', however, suggest that the current pit pattern classification may not be completely applicable in UC, because the pit pattern of the regenerative hyperplastic villous mucosa in UC (with the pits becoming elongated and irregular, depending on the degree of inflammation) is difficult to distinguish from neoplastic pit patterns. Instead of using the current pit pattern classification,[48] the authors have previously reported that high residual density of pits and irregular pit margins with magnification

Table 1
Studies on the use of chromoendoscopy in IBD

Author, Published Year	No. of Patients	Study Design	Setting	Dye (%)	Endoscopy Compared	Indication	Main Outcomes	Statistics: *P* Value for Comparison
Kiesslich et al,[20] 2003	165	Parallel randomized trial	UC surveillance	MB 0.1	WLE	Dysplasia detection	True-positive lesions, CE 32 vs WLE 10	.00315
Matsumoto et al,[21] 2003	57	Prospective study	UC surveillance	IC 0.2	WLE	Dysplasia detection	Sensitivity, CE 86% vs WLE 38%	NS
Rutter et al,[23] 2004	100	Prospective study	UC surveillance	IC 0.1	WLE	Dysplasia detection	True-positive lesions, CE 9 vs WLE 2	.06
Hurlstone et al,[31] 2005	81	Prospective study	UC surveillance	IC 0.5	WLE	Dysplasia detection	True-positive lesions, CE 69 vs WLE 24	<.0001
Kiesslich et al,[9] 2007	153	Parallel randomized trial	UC surveillance	MB 0.1	WLE	Dysplasia detection	True-positive lesions, CE 19 vs WLE 4	.005
Marion et al,[25] 2008	102	Cross-sectional study	IBD surveillance	MB 0.1	WLE	Dysplasia detection	True-positive patients, CE 17 vs WLE 3	.001
Günther et al,[27] 2011	150	Parallel randomized trial	IBD surveillance	IC 0.1	WLE	Dysplasia detection	True-positive patients, CE 6 vs WLE 0	<.05

Abbreviations: CE, chromoendoscopy; IC, indigo carmine; MB, methylene blue; NS, not significant; WLE, white light endoscopy.

after indigo carmine dye spraying were useful to differentiate between colitis-associated neoplastic and non-neoplastic lesions.[33] Therefore, in the authors' practice, they focus on the high residual density of pits and irregular pit margins observed under magnifying chromocolonoscopy.[33]

The main pit patterns of neoplasia in cIBD have been reported as type IV and type III_S with a III_L pit pattern. Sada and colleagues[16] described that magnifying colonoscopy of 15 neoplasias and showed that the patterns being type III_S- to III_L or type IV pit. Hata and colleagues[30] reported that they found no neoplastic lesions in regions characterized by type II or I pit patterns. However, they also noted that some non-neoplastic flat lesions also have type III and IV pit patterns, which are neoplastic patterns. After completion of the characterization of the lesion, the authors perform the biopsy or remove the lesion.

DETECTION OF NP-CRN USING EQUIPMENT-BASED IEE

NBI

NBI is commonly used for the management of colorectal lesions in Japan. A large body of the literature has reported on the utility of NBI for the detection of colorectal polyps[49–54] and for differentiating the diagnosis between neoplastic and non-neoplastic lesions.[49,55–61] Conversely, some studies have suggested that NBI magnification is not effective for the detection of colorectal neoplasia.[62–66] An advantage of NBI magnification is that it can be achieved without spraying dye, thus potentially reducing the cost. Because NBI involves a simple one-touch operation, NBI magnification may shorten the procedure time required for diagnosing NP-CRN in IBD and make the surveillance colonoscopy efficient. The major limitation of NBI, however, is that the visual field becomes too dark during its application. A newer generation of NBI has, therefore, been developed with improved brightness, although prospective trials have not been performed.

In the previous clinical research on the significance of NBI endoscopy in detecting NP-CRN in patients with UC, surveillance colonoscopy using NBI was associated with negative results[34–37]; no significant difference in the ability to detect NP-CRN was found between NBI and white light endoscopy (Table 2). Dekker and colleagues[35] reported that 52 visible lesions were identified in 17 patients during NBI endoscopy compared with 28 visible lesions identified in patients using white light endoscopy. A pathologic evaluation of target biopsies showed 11 patients with neoplasia, which was detected by both techniques in 4 patients, whereas only 4 cases were detected using NBI endoscopy alone and 3 cases using white light endoscopy. Van den Broek and colleagues[38] also reported that 11 of 16 (69%) neoplastic lesions were detected by white light, whereas NBI endoscopy detected 13 of 16 (81%) cases (nonsignificant differences). Efthymiou and colleagues[42] reported that when using chromoendoscopy, 131 lesions (92%) were detected as compared with 102 lesions (70%) with NBI ($P<.001$); the median number of lesions detected per patient was 3 with chromoendoscopy and 1.5 with NBI ($P = .002$).

NBI magnification, however, was not used in these clinical studies. The authors, thus, have continued to study the use of magnifying endoscopy with NBI in their unit in Hiroshima (Figs. 1–3). The authors think that it is possible that the reported results in the literature were negative because of the difficulty to accurately discriminate between active inflammation and neoplasia. The authors also studied other potential advantages of the use of NBI magnification. Bisschops and colleagues[40] reported that the withdrawal time for NBI was significantly shorter than that of CE, although NBI endoscopy and CE showed equivalent dysplasia detection rates. Pellisé and

Table 2
Studies on the use of image-enhanced endoscopy in IBD

Author, Published Year	No. of Patients	Study Design	Setting	IEE	Endoscopy Compared	Indication	Main Outcomes	Statistics: *P* Value for Comparison
Dekker et al,[35] 2007	42	Randomized crossover trial	UC surveillance	NBI	WLE	Dysplasia detection	Suspicious lesions, NBI 52 vs WLE 28 True-positive lesions, NBI 9 vs WLE 12 False-positive lesions, NBI 43 vs WLE 16	.026 .672 .015
Matsumoto et al,[36] 2007	46	Cross-sectional study	UC surveillance	NBI	WLE	Dysplasia differentiation	Positive rate of dysplasia, tortuous pattern (4/50 sites, 8%) vs honeycomblike or villous patterns (1/246 sites, 0.4%)	.003
Van den Broek et al,[44] 2008	50	Randomized crossover trial	UC surveillance	AFI	WLE	Dysplasia detection	Neoplasia miss rates, AFI 0% vs and WLE 50%	.036
				NBI	AFI	Dysplasia differentiation	AFI (sensitivity 100%) vs NBI (sensitivity 75%, specificity 81%)	
Matsumoto et al,[43] 2010	48	Prospective study	UC surveillance	AFI	WLE	Dysplasia detection	Positive rate of dysplasia, protrusions (30%) vs flat mucosa (3.3%) Positive rate of dysplasia in flat lesions, low AF (8.2%) vs high AFI (0%)	<.0001 .3
Pellise et al,[37] 2011	60	Randomized crossover trial	UC surveillance	NBI	WLE with indigo carmine	Dysplasia detection	Suspicious lesions, NBI 136 vs WLE 208 True-positive lesions, NBI 10 vs WLE 12 False-positive lesions, NBI 126 vs WLI 196	.001 .644 .001
van den Broek et al,[38] 2011	48	Randomized crossover trial	IBD surveillance	NBI	WLE	Dysplasia detection	True-positive lesions, NBI 13 vs WLE 11	.727
Ignjatovic et al,[41] 2012	112	Parallel randomized trial	UC surveillance	NBI	WLE	Dysplasia detection	True-positive lesions, NBI 5 vs WLE 7 False-positive lesions, NBI 12 vs WLI 4	.57 .06
Efthymiou et al,[42] 2013	144	Randomized crossover trial	UC surveillance	NBI	WLE	Dysplasia detection	Suspicious lesions, NBI 102 vs WLE 131 True-positive lesions, NBI 20 vs WLE 23	<.001 .18

Abbreviation: WLE, white light endoscopy.

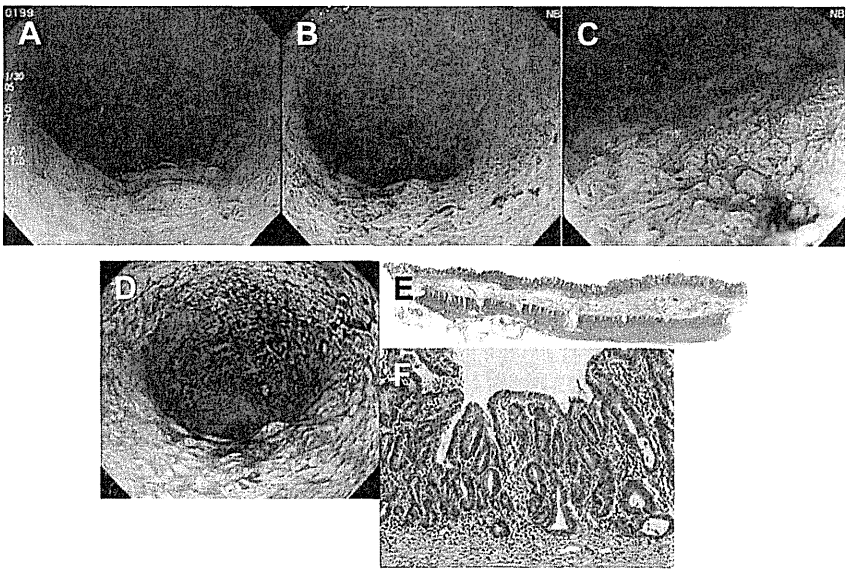

Fig. 1. A 53-year-old woman, 10 years after the onset of UC. (*A*) Ordinary colonoscopic view. A flat elevated lesion was noted in the rectum. (*B*) NBI showed the slightly elevated lesion with mucus present. (*C*) High-magnification imaging with NBI revealed the irregular surface pattern. (*D*) View with indigo carmine dye spraying. The focal lesion that is not covered with the indigo carmine solution is unclear. Proctocolectomy was performed. (*E*) Cross section of the specimen (hematoxylin-eosin). (*F*) The lesion was diagnosed histologically as intramucosal well-differentiated adenocarcinoma.

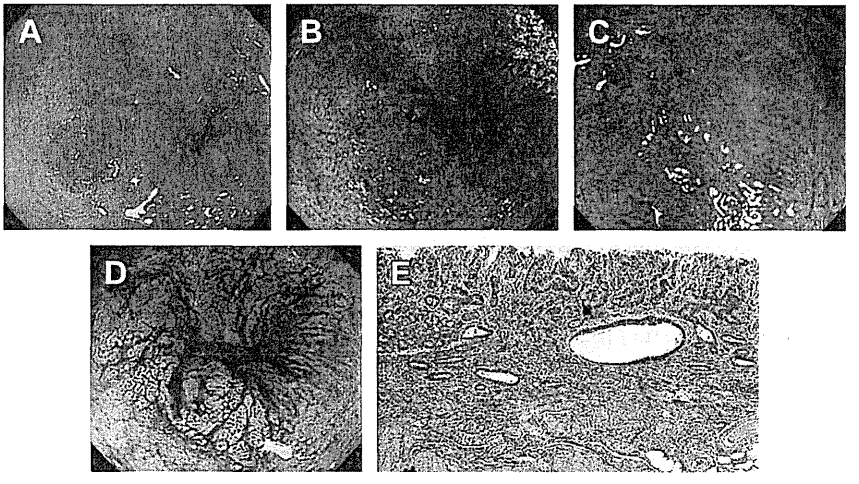

Fig. 2. A 35-year-old man, 21 years after the onset of UC. (*A*) Ordinary colonoscopic view. The reddened flat lesion was identified. (*B*) NBI showed the flat lesion as a brownish area. (*C*) High-magnification imaging with NBI revealed the irregular surface pattern and microvessels. (*D*) View with indigo carmine dye spraying. A 0-IIa+IIc lesion was clearly delineated. Proctocolectomy was performed. (*E*) The lesion was diagnosed histologically as submucosal invasive well-differentiated adenocarcinoma.

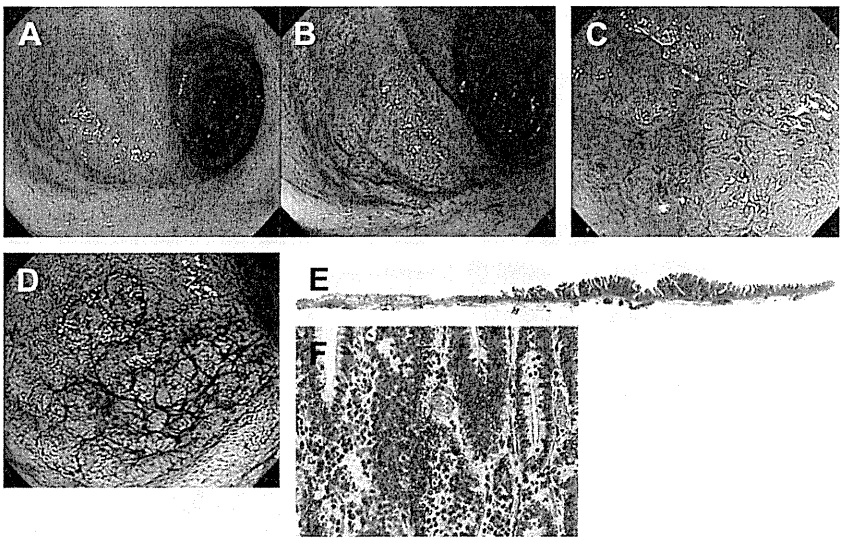

Fig. 3. A 47-year-old woman, 5 years after the onset of UC. (*A*) Ordinary colonoscopic view. A whitish flat elevated lesion was noted in the rectum. (*B*) NBI showed the slightly elevated lesion. (*C*) High-magnification imaging with NBI revealed the mild irregular surface pattern. (*D*) View with indigo carmine dye spraying. The focal lesion was relatively clear. Endoscopic submucosal dissection was performed on the lesion. (*E*) Cross section of the specimen (hematoxylin-eosin). (*F*) The lesion was diagnosed histologically as low-grade dysplasia.

colleagues[37] reported that NBI endoscopy had a significantly inferior false-positive biopsy rate and a similar true-positive rate compared with CE. It has been reported that the magnified observation of UC using NBI is useful to discriminate between dysplastic/neoplastic and non-neoplastic lesions and to guide for the necessity of performing a target biopsy. East and colleagues found that dysplasias were seen as darker capillary vascular patterns. Matsumoto and colleagues[36] reported that the tortuous pattern of capillaries determined by NBI endoscopy might be a clue for the identification of dysplasia during surveillance colonoscopy for patients with UC. The authors have previously reported the clinical usefulness of NBI magnification for the qualitative diagnosis of sporadic colorectal lesions by the combined evaluation of both surface pattern and microvessel features.[55] The surface pattern is thought to be more useful for endoscopic findings because inflammation causes the structure of microvessel features to become disordered.

AFI

AFI is a novel technique that uses a short-wavelength light to excite endogenous tissue fluorophores that emit fluorescent light of longer wavelength. AFI highlights neoplastic tissue without the administration of exogenous fluorophores as described earlier in UC.[43–45] AFI images of UC lesions can be classified into 4 categories: green, green with purple spots, purple with green spots, and purple. The strength of the purple staining in AFI images of UC lesions is related to the histologic severity. Using AFI, colitis-associated neoplasias are observed as a purple area, regardless of their macroscopic types.[43–45]

AFI endoscopy has been reported to be promising for the detection of dysplasia in UC,[43–45] although the clinical potential of AFI in routine colonoscopy has been complicated by high false-positive detection rates, particularly in cases of NP-CRN (see

Table 2). Van den Broek and colleagues[44] reported that AFI endoscopy improves the diagnosis of dysplasia in patients with UC. However, the interpretation of the results should be done with caution because the study initially excluded patients with active inflammation. Because AFI is attenuated in colonic inflammation as well as in neoplasm, such exclusion seems to have contributed positively to the assessment of AFI endoscopy by decreasing the number of false-positive areas. Matsumoto and colleagues[45] reported that AFI endoscopy identified 14 dysplasias in 4 patients during surveillance colonoscopy of 48 patients with UC. Eleven lesions were polypoid lesions, and the other 3 lesions were flat lesions. Autofluorescence as determined by AFI was regarded to be low in 12 lesions and to be normal in 2 lesions. Thus, the specificity of AFI endoscopy for the detection of flat dysplasia was, in fact, less than those of the prior investigations by NBI endoscopy or chromoendoscopy.[44,45] This finding seems to be a consequence of patchy inflammation in the observed area because autofluorescence under AFI endoscopy was altered according to the grade of inflammation in patients with UC. In order to use AFI for surveillance colonoscopy in patients with UC, it is necessary to express autofluorescence numerically and objectively and to clarify the discrimination between the inflammation and neoplastic lesions. There have not been any large trials on the usefulness of AFI for the detection of colitis-associated dysplasia and cancer. AFI may have great potential for the detection of non–polypoid colitis–associated dysplasia and cancer without magnification.

SUMMARY

Most NP-CRNs are visible, and their detection can be facilitated by the use of chromoendoscopy. Chromoendoscopy using indigo carmine, in turn, also augments the further evaluation of the border and surface pattern of the lesion. Magnifying endoscopy can assist in further visualizing the surface pattern, although chronic inflammation and its sequela in patients with IBD make the use of the pit pattern analysis less useful. In Japan, at present, efforts are given to clarify the merit for random biopsy. A nationwide randomized controlled trial is ongoing to clarify whether target biopsy or random step biopsy is effective for the detection of NP-CRN.[67]

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Treatment strategy of diminutive colorectal polyp <5 mm in size – Should it be removed and discarded without pathologic assessment?

Current status and future perspectives of endoscopic diagnosis and treatment of diminutive colorectal polyps

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During colonoscopy, small and diminutive colorectal polyps are commonly encountered. It is estimated that at least one adenomatous polyp is detected in almost half of all patients undergoing screening colonoscopy. In contrast, the 'predict, resect, and discard' strategy for diminutive and small colorectal polyps is a current topic especially in Western countries. 'Is this an acceptable policy in Japan?' Herein, we report the results of a questionnaire survey with regard to the management of diminutive colorectal polyps, including the thoughts of Japanese endoscopists regarding the 'predict, resect, and discard' strategy. At the moment, we propose that this strategy should be used by skilled endoscopists only.

Key words: colonoscopy, colorectal polyp, diminutive polyp, endoscopic management, resect and discard strategy

INTRODUCTION

COLORECTAL CANCER IS the third most important cause of cancer mortality in Japan.[1] In terms of secondary prevention, early detection and endoscopic removal of adenomatous polyps reduce the incidence and mortality of colorectal cancer.[2–4] Therefore, colonic polyps with malignant potential are routinely removed using endoscopic procedures. During colonoscopy, small (6–9 mm) and diminutive (≤5 mm) colorectal polyps are commonly encountered. It is estimated that at least one adenomatous polyp is detected in almost half of all patients undergoing screening colonoscopy.

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In contrast, the 'predict, resect, and discard' strategy for diminutive and small colorectal polyps is a current strategy especially in Western countries.[5–7] Pathological assessment is still considered essential to determine the interval of a patient's next surveillance colonoscopy. This process enables the differentiation of neoplastic from non-neoplastic lesions and the identification of advanced histology (high-grade dysplasia or villous components), which require more intensive surveillance. However, even histopathological assessment, which is considered the gold standard for polyp characterization, may have some limitations. Indeed, some authors have reported that the median kappa value for interobserver agreement for the diagnosis of adenomas versus hyperplastic polyps is not perfect (0.89; range 0.79–1.0).[8]

Recently, magnifying chromoendoscopy has become available as well as other newly developed modalities in daily practice (e.g. narrow-band imaging [NBI], flexible

spectral imaging color enhancement [FICE], and autofluorescence imaging [AFI] etc.). These new techniques are more than 90% accurate in the differentiation of adenomas and hyperplastic polyps.[9–15] However, such useful modalities have not yet become standardized worldwide. We report keynote lecture presentations from the Endoscopic Forum Japan (EFJ) 2013 in Otaru, Hokkaido, given on 3–4 August 2013. In this part of the program, discussion was held with regard to the treatment strategy of diminutive colorectal polyps <5 mm in size and the 'predict, resect, and discard' strategy based on a questionnaire that was completed by all Japanese discussers involved in this conference.

PREVALENCE OF CARCINOMA IN DIMINUTIVE AND SMALL POLYPS: DATA FROM FIVE INSTITUTIONS

A TOTAL OF 18 705 colorectal lesions treated endoscopically or surgically were collected from five Japanese institutions (National Cancer Center Hospital, Tokyo; National Cancer Center Hospital East, Kashiwa; Tochigi Cancer Center, Tochigi; Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka; Hiroshima University, Hiroshima). To clarify the prevalence of carcinoma in diminutive and small lesions, we classified all lesions into three groups based on lesion size (diminutive: ≤5 mm, small: 6–9 mm and large: ≥10 mm) as shown in Figure 1.

There were 8663 diminutive (46.3%), 5210 small (27.9%) and 4832 large polyps (25.8%). Among all diminutive polyps, there were 35 (0.4%) carcinomas of which four (0.04%) were diagnosed as submucosal (SM) invasive cancers. In contrast, the incidence of intramucosal: (M/SM) carcinoma was 3.0% (2.5%/0.5%) and 25.2% (17.5%/7.7%) in small and large polyps, respectively (Table 1).

In general, the prevalence of carcinoma in colorectal polyps ≤5 mm is low; however, the proportion of depressed lesions is significantly higher in carcinomas than in adenomas.[16] These data have important implications for the potential use of the 'predict, resect, and discard strategy' for diminutive colorectal polyps.

Table 1 Pathological diagnosis of all polyps using data from five institutions

Size	Pathological diagnosis		
	Carcinoma (pM/pSM)	Adenoma	Others†
≤5 mm	35 (31/4)	7486	1142
	0.4% (0.36%/0.04%)	(86.4%)	(13.2%)
6–9 mm	156 (131/25)	4534	520
	3.0% (2.5%/0.5%)	(87.0%)	(10.0%)
≥10 mm	1216 (846/370)	3137	479
	25.2% (17.5%/7.7%)	(64.9%)	(9.9%)

Total: n = 18 705.
†Hyperplastic polyp, inflammatory polyp, hamartoma etc.

SURVEY ON THE CURRENT STATUS OF ENDOSCOPIC MANAGEMENT FOR COLORECTAL POLYPS

THIS SURVEY WAS carried out prior to the meeting. The aim of the present survey was to assess the current status of endoscopic management for diminutive/small colorectal polyps in Japan.

Question 1: Do you routinely remove all adenomatous polyps?

Colonoscopy with adenoma resection has demonstrated that it reduces the risk of subsequent colorectal cancer by as much as 80%[2] and is one of the primary screening methods in the USA and in some European countries. However, some Japanese endoscopists leave diminutive adenomatous polyps unresected after detailed observation and close follow up because they consider that many polypectomies are unnecessary and expose patients to added risks during colonoscopy. Fifty-six percent of the Japanese participants responded 'Yes; remove all adenomatous polyps during screening colonoscopy except in elderly and/or patients with

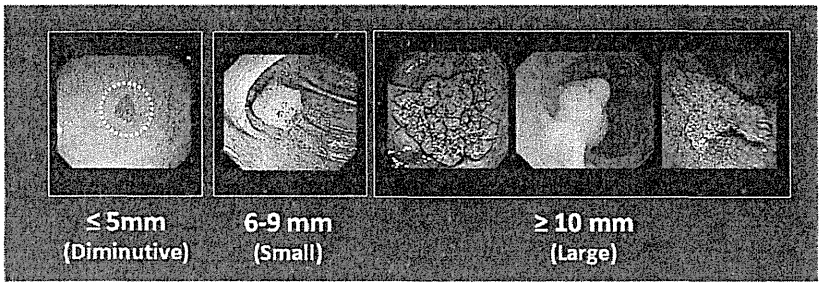

Figure 1 Pathological diagnosis of all polyps. Data are from five institutions with 18 705 lesions treated by endoscopic resection or surgery.

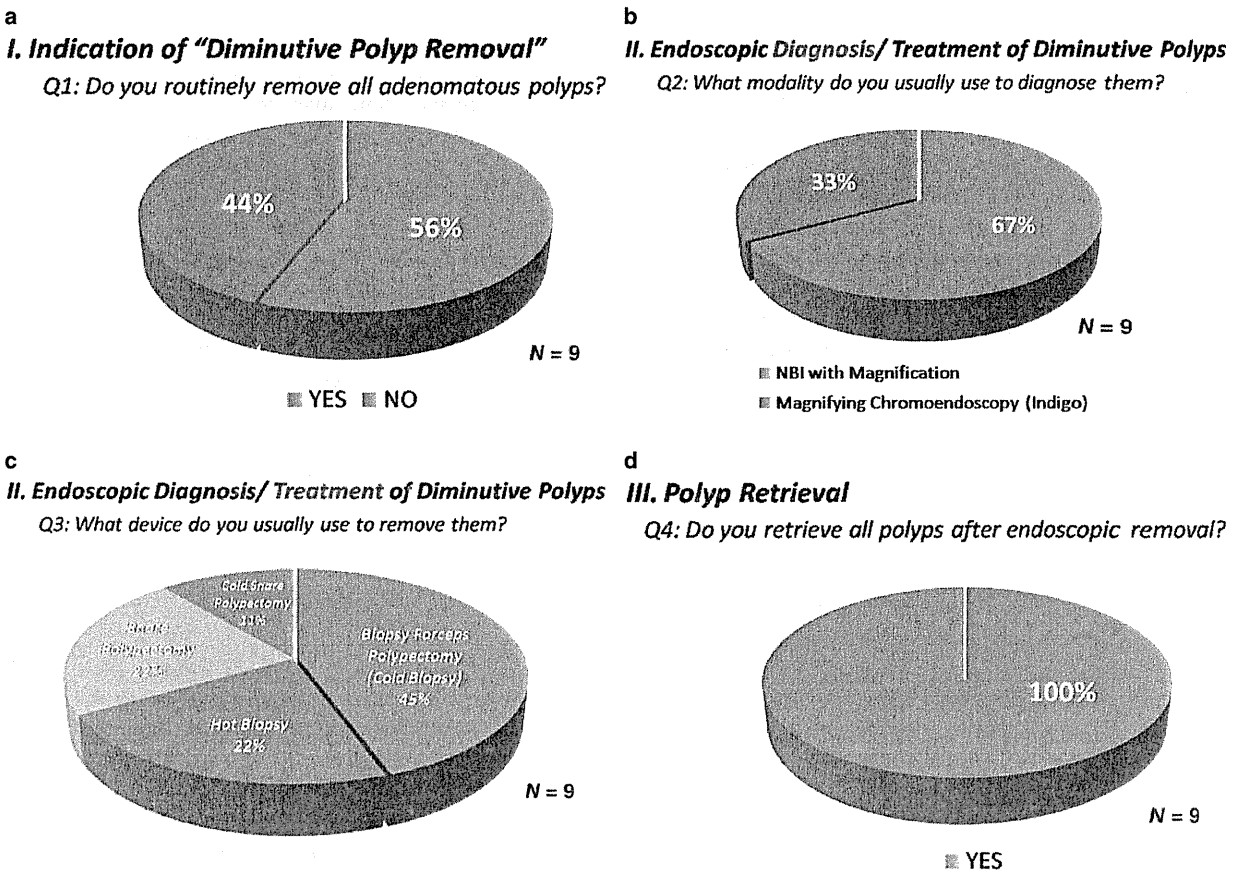

Figure 2 (a) Questionnaire survey report on the indications for diminutive polyp removal. Question 1: Do you routinely remove all adenomatous polyps? (b) Endoscopic diagnosis of diminutive polyps. Question 2: What modality do you usually use to diagnose them? (c) Endoscopic treatment of diminutive polyps. Question 3: What device do you usually use to remove them? (d) Polyp retrieval. Question 4: Do you retrieve all polyps after endoscopic removal? NBI, narrow band imaging.

severe comorbidity' (Fig. 2a). It is considered that the number of colonoscopic examinations in Japan is approximately three million per year. The capacity of endoscopy units is limited; therefore, it is crucial to distribute screening colonoscopies broadly to the unscreened population.

Question 2: What modality do you use to diagnose diminutive polyps?

Conventional colonoscopy (white-light) has limited accuracy in differentiating neoplastic and non-neoplastic lesions. For expert endoscopists, the application of indigocarmine dyes with optical magnification and pit pattern diagnosis enables a very accurate optical diagnosis (85–96%).[9–11,17,18] In contrast, narrow band imaging (NBI) is a newly developed image-enhanced modality. In previous studies, NBI with magnification has shown a diagnostic accuracy similar to magnifying chromoendoscopy.[13,19,20] Sixty-seven percent of the participants answered 'NBI with magnification' to diagnose diminutive colorectal polyps (Fig. 2b). The major advantages of using NBI are 'time saving' and 'easy to use'.

Question 3: What device do you use to remove diminutive polyps?

Recently, some authors have reported the safety and efficacy of cold polypectomy for removing diminutive/small colorectal polyps.[21–23] However, according to a survey of US gastroenterologists, various techniques were chosen to remove small (size: 4–6 mm) colorectal polyps (i.e. 59% of gastroenterologists responded using 'hot snare', 21% 'hot biopsy forceps', 19% 'cold biopsy forceps', and 15% 'cold snare'.).[24] In contrast, 45% (4 out of 9) of the Japanese participants responded using 'cold biopsy forceps', 22% 'hot

biopsy forceps', 'hot snare', and 11% 'cold snare' (Fig. 2c). In the EFJ 2013 colorectal session, Dr Uraoka introduced jumbo biopsy forceps that have been designed to remove larger tissue samples, as they have a greater capacity for this purpose (Radial Jaw 4 jumbo forceps; Boston Scientific, Natick, MA, USA). Some advantages of the jumbo biopsy forceps were reported as having a higher en-bloc resection rate and a lower delayed bleeding rate for diminutive polyps.[25]

Question 4: Do you retrieve and submit for pathology all resected polyps?

The current practice of removing all diminutive colorectal polyps and submitting them for histopathological assessment has several drawbacks. According to the data of five Japanese institutions ($n = 8663$, diminutive polyps), the likelihood of having non-neoplastic histology (hyperplastic polyp, inflammatory polyp, hamartoma etc.) was 13.2%, as shown in Table 1. In general, it is considered that approximately 40% of diminutive lesions (≤5 mm) and approximately 25% of small lesions (6–9 mm) are non-neoplastic, mainly hyperplastic, polyps, which is much higher than that seen in the Japanese data. Japanese endoscopists probably diagnose such diminutive/small lesions more accurately using magnifying chromoendoscopy or image-enhanced endoscopy. However, all Japanese participants responded 'Yes; basically, retrieve all resected polyps and submit them for pathology' (Fig. 2d). Further analyses on the cost-effectiveness and learning curve of endoscopic diagnosis using newly developed modalities are strongly required. For the moment, the 'predict, resect, and discard' strategy should be applied selectively with an accurate inform for further endoscopic evaluations.

DISCUSSION AND CONCLUSION

RECENTLY, THE AMERICAN Society for Gastrointestinal Endoscopy (ASGE) has developed a Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) program.[26] Specific clinical issues addressed by the PIVI are: (i) What accuracy in prediction of histology to determine post-polypectomy surveillance intervals is required for an endoscopic imaging technology to allow colorectal polyps <5 mm in size to be 'resected and discarded'?; and (ii) What accuracy is required in endoscopic diagnosis to leave rectosigmoid hyperplastic polyps <5 mm in size unresected?. Thresholds to satisfy specific clinical issues were the following: (i) the technology should provide >90% agreement in determining post-polypectomy surveillance intervals when compared to pathological assessment of all identified polyps; and (ii) an endoscopic technology should provide >90% negative predictive value for adenomatous histology to leave suspected rectosigmoid hyperplastic polyps unremoved. The main barrier to applying these results in our clinical practice is the difference between the health-care financial policies in Japan and that in Western countries. As the cost of colonoscopy or pathological assessment is cheaper in Japan, there would be no substantial cost-effectiveness improvement compared to Western countries. Considering the development and widespread use of available new technology, real-time endoscopic diagnosis could be a good alternative for pathological assessment in the near future.

According to the survey at the EFJ 2013 colorectal session, most of the Japanese participants routinely used 'NBI with magnification' to diagnose diminutive colorectal polyps and removed them using 'cold biopsy' or the 'cold snare' technique. Recently, the number of patients who receive oral anticoagulants is increasing. Therefore, we should shift from 'hot snare/biopsy' to 'cold snare/biopsy' to prevent delayed bleeding. Moreover, the 'predict, resect, and discard' strategy is spreading globally; however, all Japanese participants responded that they 'retrieve all resected polyps and submit them to the pathology department'. In conclusion, we propose that the 'predict, resect, and discard' strategy should be used only by endoscopists trained with an appropriate diagnostic method in Japan.

CONFLICT OF INTERESTS

AUTHORS DECLARE NO conflict of interests for this article.

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