Pit Pattern Analysis by Magnifying Chromoendoscopy for the Diagnosis of Colorectal Polyps

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Background and Purpose: The development of magnifying chromoendoscopy has facilitated the observation of mucosal pit patterns. This study investigated the value of this technology in predicting the histologic findings of colorectal lesions.
Methods: A total of 954 colorectal polyps were included. After identifying the lesions at colonoscopy, 0.2% indigo-carmine solution was sprayed and then the zoom apparatus was switched to make a magnified view of the stained crypt orifice at a maximum 100 times magnification. The observed pit patterns were classified into 6 categories (I, II, III_L, III_S, IV, and V) according to Kudo's classification. Type I and II were designated as non-neoplastic patterns whereas other types were neoplastic. Correlation of the pit pattern with the findings of histologic examinations of resected or biopsied polyps was performed.
Results: There were 678 diminutive (≤ 5mm) polyps (71.1%) and 705 neoplastic polyps (73.9%), including 695 adenomas and 10 carcinomas. When comparing histologically confirmed neoplastic lesions to non-neoplastic lesions, prediction of neoplastic lesions by endoscopists based on magnifying chromoendoscopy had a sensitivity of 90.8%, a specificity of 72.7%, a positive predictive value of 90.4%, a negative predictive value of 73.6%, and an overall accuracy of 86.1%. The diagnostic accuracy for neoplastic lesions was not associated with polyp size and location but was related to the operator's experience.
Conclusions: Characteristic pit patterns obtained by magnifying chromoendoscopy provide useful clues for differentiation of adenomatous from non-adenomatous polyps. Used appropriately in experienced hands, this technique offers a valuable adjunct to standard colonoscopy in predicting the histologic characteristics of colorectal polyps.

Key words: Colonoscopy; Colonic polyps; Ademona/diagnosis; Dyes, diagnostic use

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Colorectal cancer (CRC) is a major worldwide disease responsible for numerous deaths.[1,2] The majority of CRCs arise from adenomatous polyps (APs).[3,4] Endoscopic polypectomy or mucosal resection of adenomatous precursor lesions has significantly reduced the incidence and mortality of CRC.[5] However, not all colorectal polyps found at colonoscopy are neoplastic ones that warrant polypectomy. Hyperplastic polyps (HPs) are considered to be non-neoplastic. Resection of HPs is not only unnecessary and time-consuming but also poses a risk of bleeding and perforation after such treatment.[6,7]

Although accurate differentiation between APs and HPs at colonoscopy is critical, there are no reliable endoscopic criteria that can discriminate HPs from APs.[8–12] Early data suggested that 80 to 90% of diminutive polyps (≤ 5 mm) were histologically hyperplastic.[8,9] However, recent data has shown that 40 to 60% of diminutive colorectal polyps are neoplastic.[10–12] The issue is further complicated by recent reports showing that some small flat adenomas have a relatively high incidence of dysplasia or even invasive carcinomas.[13–16] Thus, the value of standard colonoscopy for differentiating polyps remains unclear.

Recently, the observation of pit pattern by magnifying chromoendoscopy has been shown to reflect the histology of colorectal lesions quite well by several researchers.[17–24] Due to these encouraging reports and the limited data from Taiwan,[25] this study evaluated whether pit pattern analysis by magnifying chromoendoscopy could assist in the differential diagnosis of neoplastic and non-neoplastic lesions during routine colonoscopy in a large series of patients with colorectal polyps.

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Methods

Patients

This prospective, uncontrolled, non-randomized study assessed the diagnostic accuracy of magnifying chromoendoscopy in colorectal polyps. Those patients who had completed total colonoscopy with standard histopathology for polypoid lesions between November 1997 and June 2002 in our clinic were selected for the study. The same operator performed the colonoscopic examinations including magnifying chromoendoscopy, biopsy, and polypectomy in all cases. Patients with insufficient colon preparation, total or subtotal stenosis of colon, or incomplete colonoscopic or histologic data were excluded. Carcinoid tumors and submucosal tumors were also not included because they do not always come out to the surface and the histology of such tumors do not constantly reflect a pit pattern.[21]

Magnifying chromoendoscopy

After being prepared by polyethylene glycol solution lavage method, each patient underwent colonoscopy with a magnifying colonoscopy type CF 200Z (November 1997 to June 2001) or CF240 Z (July 2001 to June 2002) [Olympus Corp., Tokyo, Japan]. These instruments are similar in size and flexibility to a standard endoscope and can be inserted into the cecum for normal observation, as with an ordinary colonoscope. Moreover, the instrument allows adjustable image magnification up to 100 times by simple rotation of a knob on the scope (CF 200Z) or stepping on the footpad (CF 240Z). When a macroscopically visible lesion was suspected by routine videocolonoscopy, the mucus on the surface of the lesion was washed away with tap water and 0.2% indigocarmine dye was sprayed through a catheter or injected directly into the forceps channel with a 20 mL syringe. This technique, referred to as the contrast method, enhances the view of mucosal lesions because the dye is retained within the pits and grooves that characterize the mucosal surface. The zoom apparatus of the colonoscope was then used to make a magnified observation at a high-power view from 40 to 100 times. By making such magnified observations, all stained lesions were categorized in real time according to the pit pattern classification proposed by Kudo,[19] who classified 6 categories labeled from I to V as follows: type I, round pit; type II, stellar or papillary pit; type III_L, large tubular or roundish pit; type III_S, small tubular or roundish pit; type IV, branch-like or gyrus-like pit; type V, non-structured pit. Representative examples of different pit patterns are illustrated (Fig.). The size and location of the lesions and the duration of the colonoscopic examinations were also recorded. The

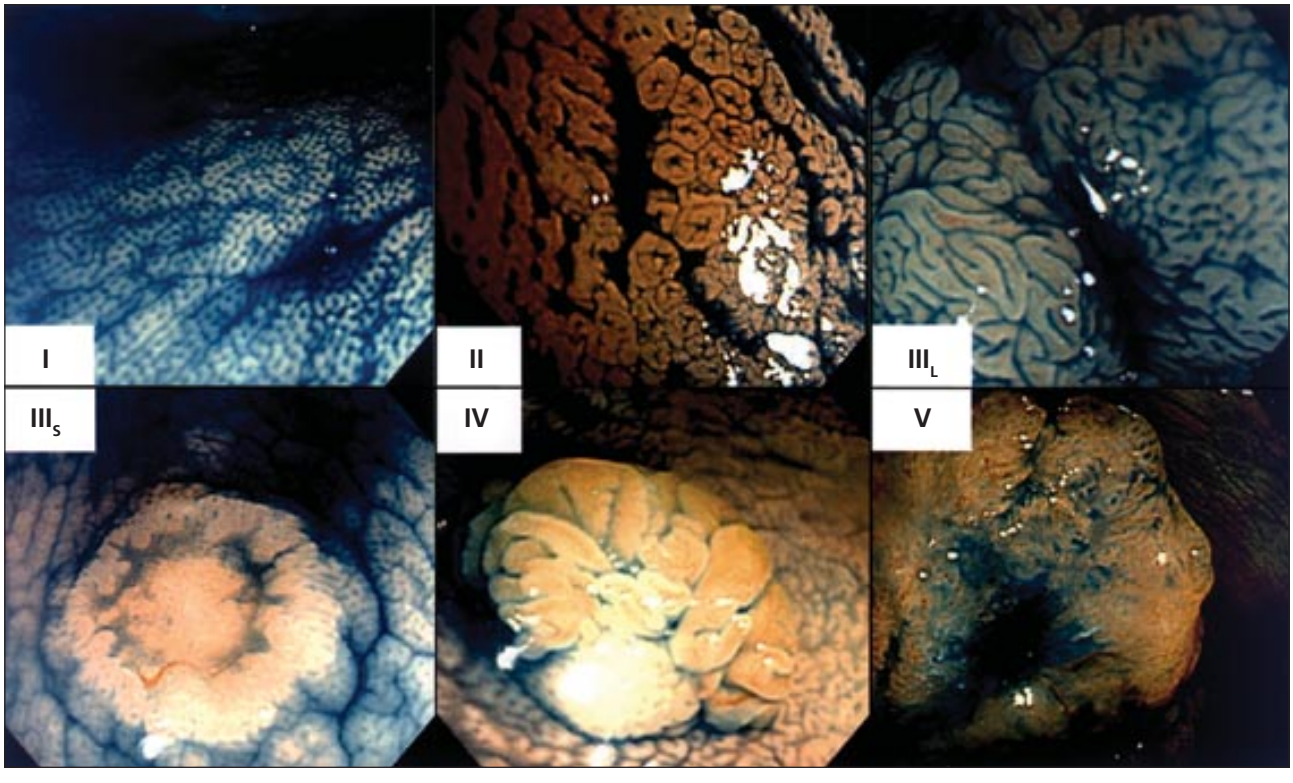

Fig. Representative examples of different pit patterns: type I, round pits; type II, stellar or papillary pits; type III_L, large tubular or roundish pits; type III_S, small tubular or roundish pits; type IV, branch-like or gyrus-like pits; and type V, non-structural pits.

polyps were included in 1 of 2 groups according to their pit pattern: non-neoplastic for type I and II; and neoplastic for type III, IV and V.

Correlation of magnifying chromoendoscopy and histological findings

All lesions identified were removed for histologic examinations by either biopsy, polypectomy, or conventional surgery. The resected or biopsied specimens were formalin fixed and stained with hematoxylin and eosin. The pathologist, who was not aware of the pit pattern of polyps, made a final histological verification. Adenomas and carcinomas were defined as neoplastic lesions, while hyperplastic polyps, inflammatory polyps, Peutz-Jeghers polyps, juvenile polyps, and lymphoid polyps were defined as non-neoplastic lesions.[21] Correlation of histologic findings with pit patterns and calculation of sensitivity, specificity and accuracy for magnifying chromoendoscopy was performed.

Results

A total of 1021 colorectal polyps from 948 patients were included. Among the 1021 polyps, 67 were excluded because of inadequate staining or inability to see the pits or grooves on chromoendoscopy. Finally, a total of 954 polyps were subjected to analyses. Location, size, and histology of all polyps are summarized in Table 1. There were 678 diminutive (≤ 5 mm) polyps (71.1%) and 705 neoplastic polyps (73.9%), including 695 adenomas and 10 carcinomas. The relationship between pit patterns and histology of the lesions is shown in Table 2. All carcinomas showed either a III, IV, or V pit pattern. When comparing histologically confirmed neoplastic lesions to non-neoplastic lesions, prediction of neoplastic lesion by the endoscopist based on magnifying chromoendoscopy had a sensitivity of 90.8%, a specificity of 72.7%, a positive predictive value of 90.4%, a negative predictive value of 73.6%, and an overall accuracy of 86.1% (Table 3). The accuracy of differentiation for the first 100 lesions was only 75%, in contrast to an average of 86% after the first 100 lesions in the series.

Table 1. Characteristics of 954 colorectal polyps.

Characteristic	Number (%)
Location	
Distal to splenic flexure	801 (84.0)
Proximal to splenic flexure	153 (16.0)
Size	
≤ 5 mm	678 (71.1)
6–10 mm	190 (19.9)
≥ 11 mm	86 (9.0)
Histology	
Carcinoma	10 (1.0)
Adenoma	695 (72.9)
Hyperplastic polyp	192 (20.1)
Others*	57 (6.0)

* Including normal colonic mucosa, lymphoid aggregates, and inflammatory polyps.

Table 2. Relationship between pit patterns and histologic findings (n).

Histologic finding	Pit pattern					
	I	II	III_L	III_S	IV	V
Non-neoplastic						
Hyperplastic (n = 192)	7	128	43	5	9	0
Others (n = 57)*	10	36	7	0	2	2
Neoplastic						
Adenoma (n = 695)	5	60	530	20	70	10
Carcinoma (n = 10)	0	0	2	1	2	5

* Including normal mucosa, lymphoid aggregates, and inflammatory polyps.

Discussion

Magnifying chromoendoscopy can amplify what is seen by standard endoscopic observation and facilitate clear visualization of the mucosal surface. Knowledge of different pit patterns seen with this novel technique provides additional valuable information for endoscopic diagnosis that is virtually consistent with the histologic diagnosis.[26,27] In Kudo's classifications of pit patterns, it has been suggested that types I and II are characteristic of non-neoplastic lesions, while types III, IV, and V represent neoplastic lesions.[19] By adopting or modifying these criteria, several studies as well as the present study have found a good correlation between mucosal pit patterns found on magnifying chromoendoscopy and the histologic findings.[19–25] Taken together, combined magnification and chromoendoscopy enables endoscopists to observe very small colonic lesions and assists the determination of appropriate endoscopic interventions.

However, the reported sensitivity, specificity, and accuracy of pit patterns in differential diagnosis of adenomatous and non-adenomatous polyps varied greatly in previous studies.[19–25] The reported results ranged widely for sensitivity (82 to 94%), specificity (65 to 93%), and accuracy (80 to 93%).[19–24] In Japan, Kudo et al evaluated pit patterns in patients with adenomas, villous adenomas and cancers and noted neoplastic pit patterns in 96.7% (1335/1381) of adenomas, 100% of villous adenomas (64/64) and 100% of cancers (168/168).[19] In Taiwan, Tung et al analyzed 175 colorectal polyps and achieved 93.8% sensitivity, 64.6% specificity, and 80.1% accuracy.[25] Our results of 90.8% sensitivity, 72.7% specificity, and 86.1% accuracy fell in previously reported ranges. The size and morphology of polyps, poor bowel

Table 3. Relationship between endoscopic prediction and actual histology.

Actual histology (n)	Endoscopic prediction (n)			Accuracy (%)
	Neoplastic	Non-neoplastic	Total	
Neoplastic	640	65	705	90.8*
Non-neoplastic	68	181	249	72.7†
Total	708	246	954	86.1

* sensitivity; † specificity.

preparation, and inadequate cleaning of mucus have been assumed to be responsible for the variable results.[26,27] In addition to these factors, our study indicated that a learning curve might be important in the identification of pit patterns for endoscopic diagnosis. After the operator had evaluated 100 lesions, the accuracy of immediate endoscopic diagnosis significantly increased. A similar phenomenon was observed by Togashi et al, who pointed out that evaluation of approximately 200 lesions was needed to overcome the learning curve.[21] This may also explain why a multicenter trial by Eisen et al[24] had a relatively lower accuracy compared with other studies.[19–23]

Besides providing morphological detail of diminutive colorectal polyps that allows discrimination between hyperplastic and adenomatous lesions, magnifying chromoendoscopy has another distinct advantage. After polypectomy, remnants of polyp tissue can be demarcated from surrounding normal mucosa according to the pit pattern, thus enabling targeted removal of remaining polyp tissues. Such clues are particularly important in endoscopic mucosal resection of so-called early colon cancers.[15,16] In this series of 10 colon carcinomas, 3 cases were flat adenomas with malignant changes. Resection with the aid of chromoendoscopy was successful in all 3 of these patients. No recurrence was noted in these cases during a follow-up of 2 to 3 years.

Kiesslich et al recently reported that magnifying chromoendoscopy might unmask multiple mucosal lesions, including early carcinomas, which are not identified by routine videocolonoscopy.[23] Since small flat adenomas or de novo colon carcinomas with highly invasive potential are difficult to detect endoscopically even for experienced observers,[15,16] pit pattern analysis by magnifying chromoendoscopy in small suspicious lesions or macroscopically nomal mucosa could promote the identification of more cases of early colon cancer.[26,27]

Although magnifying chromoendoscopy is by no means a highly specialized technique, use of this method requires training. In this study, the staining procedure took very little time and it was possible in most cases to evaluate the pit pattern immediately after indigocarmine staining. A prerequisite for good results is excellent bowel preparation and mucus washing and the availability of high magnification endoscopes. A previous study demonstrated that the magnification endoscope appears to be superior to high-resolution videocolonoscope in the differentiation of pit patterns.[28] However, pit pattern analysis is not a substitute for histology, despite the fact that the former can predict histology of polyps. Mucosal biopsy remains the gold standard for the diagnosis of colorectal polyps. Data from previous reports[19–25] and this study suggest that magnifying chromoendoscopy, if used appropriately and by an adequately trained operator, could serve as part of the routine diagnostic armamentarium for endoscopists.

This study has several limitations. All cases were performed by a single colonoscopist, a potential source of bias. Moreover, the selection of polyps for inclusion in the study may also have been biased, due to a single source of enrolling patients. Additional investigations of this promising technique are warranted.

In summary, this study of a large series of 954 colorectal polyps revealed that magnifying chromoendoscopy is a promising technique for differentiating colorectal lesions, and for visualizing their extent and margins. Pit pattern analysis by this technology is a valuable adjunct to standard endoscopy for discrimination between hyperplastic and adenomatous lesions. Used appropriately in experienced hands, such examination might help in choosing further endoscopic interventions.

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