

THE ROLE OF STANDARD VIDEOCHROMOCOLONOSCOPY IN DISTINGUISHING ADENOMATOUS FROM NONADENOMATOUS DIMINUTIVE COLORECTAL POLYPS

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SUMMARY - To date, there are no reliable endoscopic criteria to discriminate a diminutive (<5 mm) colorectal adenomatous from nonadenomatous polyps. Studies have demonstrated the usefulness of high-resolution chromoendoscopy (high-resolution colonoscopy with topically applied indigo carmine dye) in discrimination of adenomatous from nonadenomatous colorectal polyps. However, the clinical utility of standard videocolonoscopy and chromoscopy with indigo carmine dye in differentiating diminutive colorectal polyps has not yet been completely defined. The aim of this study was to determine whether a combination of standard videocolonoscopy and staining with indigo carmine dye could differentiate between adenomatous and nonadenomatous colorectal polyps smaller than 5 mm. Colonoscopy by use of an Olympus EVIS 140 video system was performed in 42 patients in whom colorectal polyps smaller than 5 mm were found. Polyps were sprayed with up to 40 ml of 0.5% indigo carmine dye, and polypectomy was performed, and the material was referred for histology. In 42 patients included in the study, 48 polyps sized <5 mm were detected. Histologic analysis showed 14 of them to be adenomatous and 34 nonadenomatous polyps. Endoscopist's diagnosis was confirmed by histology in 12 of 14 (85.7%) adenomatous and 31 of 34 (91.2%) nonadenomatous colorectal diminutive polyps. The sensitivity, specificity, positive predictive value and negative predictive value of standard videochromocolonoscopy in distinguishing between adenomatous and nonadenomatous polyps sized <5 mm were 85.7%, 91.2%, 80% and 93.9%, respectively. The likelihood ratios (LR) were 0.157 (LR-) and 9.74 (LR+). In conclusion, standard videocolonoscopy combined with indigo carmine dye is a reliable method to differentiate adenomatous from nonadenomatous colorectal polyps sized <5 mm. Such a technique could limit the requests for unnecessary biopsies and repeat colonoscopy, thus significantly reducing the cost of colorectal cancer screening.

Key words: *Colonic neoplasms, diagnosis; Colonic polyps, diagnosis; Adenoma, diagnosis; Colonoscopy, methods*

Introduction

To date, there are no reliable endoscopic criteria to discriminate between diminutive (usually less than 5 mm) colorectal adenomatous polyps and nonadenomatous polyps. Studies have pointed to the clinical usefulness of

high-resolution chromoendoscopy, i.e. colonoscopy with topically applied agents, in an attempt to discriminate neoplastic from non-neoplastic colorectal polyps¹⁻³. Using both specially designed videocoloscopes that produce high-resolution images at great magnification and indigo carmine dye, a contrast stain which accentuates epithelial topography, thus allowing recognition of otherwise unnoticeable epithelial changes, it seems possible to distinguish adenomatous from nonadenomatous colorectal polyps measuring <10 mm³. The clinical utility of standard videocolonoscopy and staining with indigo

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Received July 10, 2001, accepted August 16, 2001

carminic dye, especially in the diagnosis of very small colorectal polyps sized <5 mm, has not yet been fully defined. According to the experience of George *et al.*⁴, published in an abstract form, standard videocolonoscopy combined with 0.2% indigo carmine dye predicted polyp histology in a small number of cases with only 45% accuracy. On the other hand, results of two studies conducted in the USA^{5,6}, also recently published in the form of abstracts, showed standard videocolonoscopy and chromoscopy with indigo carmine dye to have acceptable sensitivity and specificity in differentiation between adenomatous and nonadenomatous polyps. To our knowledge, there are no European experiences related to chromoendoscopy and diminutive colorectal polyps that have been published in the form of *in extenso* articles. Therefore, the aim of this study was to determine whether a combination of standard videocolonoscopy and chromoscopy with indigo carmine dye could differentiate adenomatous from nonadenomatous diminutive colorectal polyps.

Patients and Methods

Between October 1998 and October 1999, colonoscopy was performed in 42 patients in whom diminutive (<5 mm) colorectal polyps were detected. Polyps measuring >5 mm were excluded from analysis. An informed consent in writing was obtained from all patients before entering the study. All colonoscopies were performed with an Olympus EVIS 140 videocolonoscope system. Cecum was reached in all patients. None of the study patients had a personal history of colorectal malignancy or obvious signs of cancer on colonoscopic examination. The indications for colonoscopy included polyp(s) follow-up (n=14), family history of colon cancer (n=19), and anemia (n=9).

The size of diminutive polyps was measured by the open forceps technique. Once the polyp was within sight, a 'spraying' catheter (PW-5L-1, Olympus Corp., Japan) was used, which considerably facilitated the application of indigo carmine dye⁷. A 5% solution of indigo carmine dye was sprayed directly onto the colonic mucosa in a volume of up to 60 ml. A mean indigo carmine dye staining of 36 ml (range 20-60 ml) was used. The endoscopy procedure was prolonged by 7 (3-11) minutes on an average with indigo carmine dye staining. Each polyp was recorded on a videotape and removed by snare polypectomy. All diminutive polyps were referred for histologic analysis, and the pathologist was blinded for endoscopic finding.

Results

In 42 patients included in the study, 48 diminutive (<5 mm) colorectal polyps were found. There were 19 men and 23 women, median age 59.8 (range 38-81) years. In all patients, indigo carmine dye spraying allowed for successful polyp assessment, followed by snare polypectomy.

Table 1 shows distribution and histology of all 48 diminutive colorectal polyps detected. Histology findings revealed 14 adenomatous and 34 nonadenomatous polyps; in 11 cases, neither adenomatous nor hyperplastic histologic features were seen on histology. These included 7 inflammatory polyps, one lymphoid aggregate, and 3 specimens with normal mucosa. Hyperplastic polyps were most often seen in the rectum and sigmoid, whereas adenomatous polyps were more commonly observed in the right colon. Mild dysplasia was found in two (14.3%) diminutive adenomatous polyps.

Table 1. Histology and distribution of diminutive (<5 mm) colorectal polyps (N=48)

Localization	Adenomatous n	Hyperplastic n	Other n
Rectum	3	11	2 ^{a,b}
Sigmoid	2	7	2 ^{a,c}
Descending colon	1	4	
Transverse colon			1 ^c
Ascending colon	3	1	1 ^a
Cecum	5		5 ^{a,b,c}

^ainflammatory colorectal polyp; ^blymphoid aggregate; ^cnormal mucosa

The application of an indigo carmine dye forms a 'coating' over the surface of the colonic mucosa, thereby highlighting mucosal topography. Therefore, detailed morphological characteristics of the polyps were only seen upon the application of indigo carmine dye. In contrast to nonadenomatous polyps, where indigo carmine staining revealed a typical pitted appearance morphologically similar to the surrounding mucosa (Fig. 1), adenomatous polyps had a characteristic folded appearance (Fig. 2).

The histology was correctly predicted by the endoscopist in 12 of 14 (85.7%) adenomatous, and 31 of 34 (91.2%) nonadenomatous diminutive colorectal polyps (Table 2). Two adenomatous polyps were predicted to be nonadenomatous, and 3 were predicted to be adenomatous (2 inflammatory polyps and one lymphoid aggregate).



Fig. 1. Upon indigo carmine dye application, an orderly arrangement of surface pits (so-called dots) was observed, suggesting the presence of nonadenomatous polyp. Histology revealed a hyperplastic polyp.



Fig. 2. Upon indigo carmine dye application, the presence of sulcus-like grooves and absence of surface pits were observed, suggesting the presence of adenomatous polyp. Histology revealed an adenomatous polyp.

gate). The sensitivity, specificity, positive predictive value and negative predictive value of standard videochromocolonoscopy in distinguishing adenomatous from nonadenomatous polyps were 85.7%, 91.2%, 80% and 93.9%, respectively. The likelihood ratios (LR) were 0.157 (LR-) and 9.74 (LR+).

Table 2. Actual and predicted histology of diminutive (<5 mm) colorectal polyps (N=48)

Actual histology	Endoscopist's prediction	
	Adenomatous	Nonadenomatous
Adenomatous (n=14)	12	2
Nonadenomatous (n=34)	3	31

Specificity 91.2%; sensitivity 85.7%; positive predictive value 80%; negative predictive value 93.9%; likelihood ratio (LR): LR+ 9.74; LR- 0.157

Discussion

Despite the fact that histology remains the gold standard in the diagnosis of colorectal polyps, recent investigations have shown that high-magnification chromocolonoscopy with indigo carmine dye could be a reliable method in discrimination of adenomatous from nonadenomatous polyps^{2,3}. However, there is a great amount of

conflicting data concerning the usefulness of standard videocolonoscopy and chromoscopy with indigo carmine dye. Recent, predominantly U.S. trials published in the form of abstracts report on conflicting results⁴⁻⁶. In a study from Cleveland, in which 0.2% indigo carmine dye was sprayed onto the surface of polyps, it was not possible to reliably differentiate adenomatous from nonadenomatous polyps⁴. Encouraging results have come from two recent trials. Investigators from Georgetown University used 0.4% indigo carmine dye and achieved 96% sensitivity and 81% specificity for adenomatous polyps⁵. This study led to a multicenter U.S. study, in which investigators evaluated 513 polyps with a mean diameter of 4 to 7 mm⁶. In attempts to distinguish adenomatous from nonadenomatous polyps, the use of videocolonoscopy with indigo carmine dye has yielded a sensitivity of 81% and specificity of 82%, with a negative predictive value of 88%. The results of this study and our data appear to be quite close to those obtained in the studies in which high-resolution videoendoscopes were used³. It seems, therefore, that in case of diminutive colorectal polyps there is no need to use sophisticated equipment for chromoendoscopy with indigo carmine dye. It has been proposed that, like most endoscopic procedures, there must be a 'learning curve' involved⁸. Namely, despite the fact that technical difficulties of tissue staining are minimal and usually prolong the length of endoscopic procedure by 7 minutes at the most, the interpretation of findings is a matter of due experience in the field. Also, it is very important that all colorectal mucosa surrounding the polyp as well as the entire polyp are completely 'covered' with a sufficient amount of indigo

carmine dye applied as a solution at appropriate concentration, preferably 0.4% or even more.

A large volume of recent data show that 40% to 60% of diminutive colorectal polyps are neoplastic⁹⁻¹¹. Even more disconcerting are reports on small, flat or nonpolypoid adenomas that have a relatively high incidence of moderate to severe dysplasia¹²⁻¹⁴. However, there is a debate about whether these small flat lesions have global implications. Large studies in the U.S. failed to reveal high-grade dysplastic lesions anywhere at a frequency close to that in Japanese studies¹⁵. On the other hand, a study performed in Sweden by Jaramillo *et al.*¹⁴ demonstrated a similar prevalence of flat adenomas to that described in the Japanese literature. Thus, the issue is unsolved. In spite of the fact that this study was limited to a small number of patients, it is very interesting that approximately 30% of diminutive polyps sized less than 5 mm were found to be adenomatous, and that mild dysplasia was observed in 14% of cases. Therefore, when even a small mucosal abnormality is suspected on routine colonoscopy, indigo carmine dye should be sprayed onto the surface to help detect such lesions. Many endoscopists would argue that the technique is of limited utility unless having a 100% accuracy, as otherwise some diminutive adenomas may be missed. A counterargument would be that follow-up strategies could be developed to observe the patients suspect to have hyperplastic polyps less frequently than those with no polyps at all, but less extensively than those with adenomatous polyps. Such a strategy would be more cost-effective and important reduction could be anticipated in the cost of colon cancer screening.

In conclusion, the present study confirmed that standard videochromocolonoscopy with indigo carmine dye is a reliable method in differentiating adenomatous from nonadenomatous diminutive colorectal polyps. Particularly if the feasibility and effectiveness of 'once-in-a-lifetime' screening to reduce the mortality from colorectal cancer be accepted, chromocolonoscopy would be a valuable tool for screening examinations and would lead to substantial cost savings by avoiding the need for unnecessary biopsies and/or unnecessary repeat colonoscopies.

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Sažetak

ULOGA STANDARDNE VIDEO-KROMOKOLONOSKOPIJE U RAZLIKOVANJU ADENOMATOZNIH OD NEADENOMATOZNIH SITNIH KOLOREKTALNIH POLIPA

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Danas ne postoje pouzdani endoskopski kriteriji koji bi razlikovali sitne (<5 mm) kolorektalne adenomatozne od neadenomatoznih polipa. Ranije su studije pokazale korisnu uporabu visoko-rezolucijske kromoendoskopije (visoko-rezolucijska kolonoskopija s topičkom primjenom indigo crvene boje) u razlikovanju adenomatoznih od neadenomatoznih kolorektalnih polipa. Ipak, klinička upotreba standardne video-kolonoskopije i kromoskopije s indigo crvenom bojom u razlikovanju sitnih kolorektalnih polipa nije još potpuno utvrđena. Namjera ovoga ispitivanja bila je utvrditi može li se kombinacijom standardne video-kolonoskopije i bojanja indigo crvenom bojom razlikovati adenomatozne od neadenomatoznih kolorektalnih polipa manjih od 5 mm. Kolonoskopija uz primjenu video sustava Olympus EVIS 140 izvedena je u 42 bolesnika u kojih su nađeni kolorektalni polipi manji od 5 mm. Polipi su poprskani 0,5%-tnom indigo crvenom bojom u količini do 40 mL, izvedena je polipektomija i provedena histološka analiza. U 42 bolesnika uključenih u ispitivanje nađeno je 48 polipa manjih od 5 mm. Histološka analiza pokazala je postojanje 14 adenomatoznih i 34 neadenomatoznih polipa. Endoskopist je ispravno predvidio histološki nalaz u 12 od 14 (85,7%) adenomatoznih, te u 31 od 34 (91,2%) neadenomatoznih kolorektalnih sitnih polipa. Osjetljivost, specifičnost, pozitivna prediktivna vrijednost i negativna prediktivna vrijednost standardne video-kromokolonoskopije u razlikovanju adenomatoznih od neadenomatoznih polipa manjih od 5 mm bile su 85,7%, 91,2%, 80%, odnosno 93,9%. Omjer vjerojatnosti (LR) iznosio je 0,157 (LR-) i 9,74 (LR+). Standardna video-kolonoskopija u kombinaciji s indigo crvenom bojom pouzdana je metoda za razlikovanje adenomatoznih od neadenomatoznih kolorektalnih polipa manjih od 5 mm. Ovakvom bi se tehnikom mogli smanjiti zahtjevi za nepotrebnim biopsijama i opetovanim kolonoskopijama, te tako značajno sniziti troškovi probiranja na kolorektalni karcinom.

Ključne riječi: Neoplazme kolona, dijagnostika; Polipi kolona, dijagnostika; Adenom, dijagnostika; Kolonoskopija, metode