Original Article

A Study of Colorectal Polyp Miss Rate as Determined by Same-Day Back-to-Back Colonoscopies in Asymptomatic Colorectal Cancer Screening Subjects

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ABSTRACT

Background: High definition (HD) colonoscopy may better detect colorectal polyps. However, polyps can be easily missed, and this may account for an interval cancer. There are other reasons also for missed polyps, including endoscopist's factors, technical factors, and polyps characters, etc.

Objective: To evaluate colorectal polyp miss rates by using HD colonoscope (Olympus CF-HQ190) for same-day back-to-back colonoscopies and to identify other independent factors for missed polyps.

Method: Between January 2014 and November 2014, back-to-back colonoscopies in asymptomatic subjects aged 50-75 years were performed in a randomized order by four different experienced endoscopists with more than 1,000 colonoscopies and with previous record of adenoma detection rate (ADR)>25%. During each round of colonoscopy, detected polyps were removed either by means of a biopsy forceps or a snare. The results of the first-round colonoscopy were blinded to the following endoscopists. All polyps detected and removed by the first or the second endoscopists were recorded. The quality of bowel preparation, withdrawal time, location, size and histology of polyps were recorded. Advanced adenoma (AA) was defined as an adenoma with size ≥10 mm or an adenoma with high-grade dysplasia or villous histology. The polyp miss rate was calculated as the total number of polyps missed from the first colonoscopy/the total number of polyps detected by both the first and the second colonoscopists.

Results: One-hundred-and-nine subjects were enrolled, and 218 complete colonoscopies were performed. One-hundred-and-six (97%) of subjects had good to excellent bowel preparation. The mean withdrawal times of the first and the second colonoscopies were 12.5 ± 10 and 9.1±2.9 min, respectively. The overall detection rate of adenoma, advanced adenoma and cancer were 48%, 13% and 1%, respectively. Of all 109 subjects, 306 polyps were found in 84 subjects. Among 306 polyps, there were 140 (45.8%) non-adenoma, 166 (54.2%) adenoma. There were 32 (10.4%) AA and 1 (0.3%) cancer. The miss rates for non-adenoma, adenoma and AA were 26.8%, 28.3% and 21.9%, respectively. No carcinoma was missed. In the univariate analysis, non-pedunculated lesion and the withdrawal time < 9 min were the significant factors for polyps miss rate. There was a trend of higher miss rate for proximal polyp location and for polyp size ≤5 mm, but not statistically significant. In the multivariate analysis, the independent significant associated factors for polyps miss rate were non-pedunculated lesion [Odd ratio 11.49 (95% CI: 1.44-91.59); p= 0.02] and duration of withdrawal time less than 9 min. [Odd ratio 3.02 (95% CI: 1.67-5.45); p<0.001].

Conclusion: Under HD colonoscopy, polyp miss rate still occurs. Non-pedunculated lesions and the withdrawal time less than 9 minutes were the significant factors for this phenomenon.

Key words : Back to back colonoscopy, colorectal cancer screening, missed polyps

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Introduction

Colorectal cancer is one of the most common cancers and a leading cause of cancer deaths worldwide. In Thailand, colorectal cancer is the third most common cancer in men, and the fifth most common cancer in female women. The highest incidence rate for both sexes is documented in Bangkok, and the lowest incidence rate is in NakhonPhanom province. The number of colorectal cancers has shown a rising trend. Most cases of colorectal cancer were diagnosed at an advanced stage with a poor prognosis[1].

Colorectal cancer screening to detect and remove precancerous lesions or early colorectal cancers has been recognized as very important in preventing and reducing the occurrence of colorectal cancer and death[2]. Although colonoscopy is the gold standard and is highly effective for screening colorectal cancers, some persons are still diagnosed with colorectal cancer at a relatively short interval after a screening colonoscopy. Such interval cancers account for 0.6-9% of all colorectal cancers[3-6] and are inversely associated with the adenoma detection rate (ADR)[7]. Interval colorectal cancers are related to missed lesions, incompletely resected lesions, or rapidly progressive new lesions. Missed lesions are the major factor and appear to account for 52% of all interval cancers[3].

Previous studies reported that the polyp miss rates varied between 14% and 30%[8] while the adenoma miss rate was 15%-32%[8]. Moreover, the miss rate of advanced adenoma was 0-11%[8,9]. Previous analyses demonstrated that the factors associated with miss polyps included polyp factors, endoscopist factors and procedure factors. However, there were limitations of these studies, such as differences in the enrolled subjects, in the indications for colonoscopy, and in a controlled quality of colonoscopy[8-11].

The aims of this study were 1) to determine the polyp miss rate using HD colonoscopy 2) to identify independent factors that could influence the miss rate as determined by same-day back-to-back colonoscopies in asymptomatic colorectal cancer screening subject.

Materials and Methods

Study population

We conducted a study between January 2014 and November 2014. Asymptomatic subjects who participated in a health promotion program at the King Chulalongkorn Memorial Hospital were recruited. Asymptomatic subjects aged 50 to 75 were enrolled. Exclusion criteria were family history of hereditary colorectal cancer (≥ 2 first degree relatives with CRC or at least 1 first degree relative with CRC before 60 years)[12], inflammatory bowel disease, prior history of colorectal cancer,previous colorectal surgery, severe coexisting illness (American Society of Anesthesiologists grade 3 or 4)[13], previous colon examination (endoscopy and radiological imaging) within the previous 5 years, and symptoms of lower GI tract (a lower gastrointestinal bleeding, bowel habit changes, unexplained weight loss, and anemia). All subjects provided a written informed consent. The study was approved by the Chulalongkorn Medical Institutional Review Board.

Back-to-back colonoscopy

All subjects underwent standard bowel preparation as described previously[14]. Sedation with intravenous midazolam and/or meperidine was prescribed. Olympus CF-HQ190 colonoscope (Olympus Optical, Tokyo, Japan) was used. Back-to-back colonoscopy was performed by two experienced endoscopists from among 4 staff gastroenterologists who had performed >1,000 colonoscopies with adenoma detection rate>25% (S.A., P.A., R.P. and V.V.).

During the first colonoscopy, the colonoscope was inserted as for as the cecum and all detected polyps were removed either by biopsy forceps or snare. Tiny diminutive polyps (less than 5 mm in diameter) with hyperplastic appearance under magnification and narrow band imaging in the rectosigmoid area were unremoved. After the first endoscopist completed withdrawing the colonoscope from the anus, the second endoscopist reintubated. The result of the first colonoscopy was blinded to the second endoscopist. All remaining polyps were defined as a miss polyp, except for tiny polyps in the rectosigmoid area which were left as with the first colonoscopy. All polyps detected and removed by the first and the second endoscopists were recorded. Aronchick bowel preparation scales were used for the rating of colon cleansing[15]. The cecal intubation rate, the withdrawal time, and the location of polyps were recorded. Polyp size was measured with an opened biopsy forceps, which is 7 mm in diameter. All removed polyps were examined by a special gastrointestinal pathologist (N.K.).

DEFINITION

Polyps were pathologically classified as non-neoplastic and neoplastic. Neoplastic polyps were categorized to adenoma, advanced adenoma (AA) and colorectal carcinoma. AA was defined as an adenoma larger than 10 mm or an adenoma with high-grade dysplasia, or villous adenoma (at least 25%) or carcinoma[16]. The polyp morphology was classified as per Paris classification[17]. The proximal colon was defined as the splenic flexure and the more proximal part of the colon. The distal colon was defined as the colon distal to the splenic flexure[18].

The polyp miss rate was calculated as the total number of polyps missed from the first colonoscopy/ the total number of polyps detected at both the first and the second colonoscopies. Polyps miss rates were calculated for all polyps (non-neoplastic and neoplastic polyp), adenomas, and advanced adenomas.

Statistical analysis

Statistical analysis was performed with SPSS version 17.0. All baseline characteristics such as age, gender, body mass index, alcohol, smoking, other comorbidity as well as polyp size, shape, location and the number of polyps were included in the univariate and the multivariate analyse to find out the independent factors associated with missed polyps.

RESULTS

Subject characteristics

A total of 109 asymptomatic subjects were screened and enrolled. The mean age was 60±7 yrs. Sixty-seven (61.5%) subjects were female. All subjects completed the back-to-back colonoscopies. One-hundred-and-six (97%) of subjects were good to excellent bowel preparation. The mean withdrawal time for the first and the second colonoscopies were 12.5 ± 10 and 9.1 ± 2.9 minutes, respectively. The cecal intubation rate was 100%. There were no serious adverse events from the colonoscopy procedures. The prevalences of adenoma, advanced adenoma and cancer were 52 (48 %), 14 (13%) and 1 (1%), respectively.

Polyp characteristics

Overall, 306 polyps were detected in 84 subjects. Of the 306 polyps, 140 (46%) were non-neoplastic polyps and 166 (54%) were neoplastic polyps. There were 134 (80.7%) adenomas, 31 (18.7%) advanced adenoma and 1 (0.6%) carcinoma.

The mean diameter of polyps was 4.9±2.9 mm. The sessile, pedunculated, flat and depress shapes were demonstrated in 270 (88%), 23 (7.5%), 12 (4%) and 1 (0.5%), respectively. One-hundred-and-thirty-one (42.8%) polyps and 175 (57.2%) polyps were located in the proximal colon and in the distal colon respec-

Table 1. Characteristics of all 306 polyps detected in 218 back-to-back colonoscopies.

Characteristics of polyps	N (%)	
	Overall polyps (n=306)	Neoplastic polyps (n=166)
Histopathology		
• Non-neoplastic polyp	140 (45.8)	-
• Adenomas	134 (43.8)	134 (80.7)
• Advanced adenomas	32 (10.5)	32 (19.3)
Size of polyp (mm) (mean±S.D)	4.98 ± 2.95	5.70 ± 3.40
• Size ≤ 5 mm	230 (75.2)	110 (66.3)
• Size > 5 mm	76 (24.8)	56 (33.7)
Morphology of polyp		
• Sessile	270 (88.2)	139 (83.8)
• Pedunculated	23 (7.5)	17 (10.2)
• Flat	12 (3.9)	9 (5.4)
• Depressed	1 (0.3)	1 (0.6)
Location		
• Proximal colon	131 (42.8)	86 (51.8)
• Distal colon	175 (57.2)	80 (48.2)

tively (Table1).

Characteristics of the miss polyps

Eighty-two polyps were found at the second colonoscopy, apparently missed during the first colonoscopy. The miss rates for polyp, adenoma and advanced adenoma were 26.8%, 28.3% and 21.9% respectively. No carcinoma was missed. The miss polyps are shown in Table 2.

Of the 82 missed polyp, the sessile, flat, pedunculated and depressed shapes were recorded in 73 (89%), 7 (8.6%), 1 (1.2%) and 1 (1.2%) polyps, respectively. The missed polyps were found in the proximal colon (51.2%) as much as in the distal colon

Table 2. The number and miss rate of each type of polyps.

Total	Number of miss polyps at 1st colonoscopy	Miss rate (%)
All polyps (n=306)	82	26.8
Polyp with size < 5 mm (n=230)	61	26.5
Polyp with size > 5 mm (n=76)	21	27.6
Adenoma (n=166)	47	28.3
Adenoma with size < 5 mm (n=110)	32	29.1
Adenoma with size > 5 mm (n=56)	15	26.8
Advanced adenoma (n=32)	7	21.9
Serrated adenoma (n=3)	2	66.7
Carcinoma (n=1)	0	0

Table 3. Characteristics and percentages of miss polyps and adenomas.

Lesion (n)		Location, n (%)		Morphology, n (%)				No. of lesions, n (%)			Diameter (mm)		
Type	Total	Proximal	Distal	Pedunculate	Sessile	Flat	Depressed	1	2	≥3	Mean	Median	Range
Polyps (n=306)													
Not missed	224	89 (67.9)	135 (77.1)	22 (95.7)	197 (73)	5 (41.7)	0 (0)	14 (73.7)	32 (69.6)	178 (73.9)	5.1±2.9	5	2-20
Missed	82	42 (32.1)	40 (22.9)	1 (4.3)	73 (27)	7 (58.3)	1 (100)	5 (26.3)	14 (30.4)	63 (26.1)	4.8±2.9	5	1-15
Adenoma (n=166)													
Not missed	119	58 (67.4)	61 (76.3)	16 (94.1)	99 (71.2)	4 (44.4)	0 (0)	15 (68.2)	27 (79.4)	77 (70)	5.9±3.5	5	2-20
Missed	47	28 (32.6)	19 (23.7)	1 (5.9)	40 (28.8)	5 (55.6)	1 (100)	7 (31.8)	7 (20.6)	33 (30)	5.2±3.0	5	2-15
Advanced adenoma (n=32)													
Not missed	25	8 (61.5)	17 (89.5)	12 (100)	11 (68.8)	2 (50)	0 (0)	3 (100)	3 (75)	19 (76)	11.7±2.8	10	10-20
Missed	7	5 (38.5)	2 (10.5)	0 (0)	5 (31.2)	2 (502)	0 (0)	0 (0)	1 (25)	6 (24)	10.7±1.9	10	10-15
Serrated adenoma (n=3)													
Not missed	1	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	5	5	5
Missed	2	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	10	10	10

Table 4. Univariate and multivariate analysis of the 82 miss polyps and the 47 miss adenomas out of 306 polyps and 166 adenomas.

Variable	Miss rate (%)	Univariate analysis		Multivariate analysis	
		Odd ratio (95% CI)	*p*-value	Odd ratio (95% CI)	*p*-value
Overall polyps (n=306)	82 (26.8%)				
Polyp size					
• Size < 5 mm (n=230)	61 (26.5%)	1		1	
• Size >5 mm (n=76)	21 (27.6%)	1.06 (0.59-1.89)	*p* =0.85	1.41 (0.74-2.69)	*p* =0.3
Polyp shape					
• Pedunculated (n=23)	1 (4.3%)	1		1	
• Sessile/ flat/depressed (n=283)	81 (28.6%)	8.82 (1.17-66.54)	*p* =0.03	11.49 (1.44-91.59)	*p* =0.02*
Location of polyp					
• Distal colon (n=175)	40 (22.9%)	1		1	
• Proximal colon (n=131)	42 (32.1%)	1.59 (0.95-2.65)	*p* =0.07	1.51 (0.87-2.59)	*p* =0.14
Histology					
• Non-neoplastic polyp (n=140)	35 (25.0%)	1		1	
• Neoplastic polyp (n=166)	47 (28.3%)	1.18 (0.71-1.97)	*p* =0.51	1.27 (0.72-2.24)	*p* =0.4
Total number of polyp					
• 1-2 (n=65)	19 (29.2%)	1		1	
• > 3 (n=241)	63 (26.1%)	0.86 (0.46-1.57)	*p* =0.62	1.04 (0.55-1.96)	*p* =0.9
Duration of withdrawal time					
• > 9 minutes (n=235)	51 (21.7%)	1		1	
• < 9 minutes (n=71)	31 (43.7%)	2.79 (1.59-4.91)	*p* <0.001	3.02 (1.67-5.45)	*p* <0.001*
Adenoma (n=166)	47 (28.3%)				
Adenoma size					
• Size < 5 mm (n=110)	32 (29.1%)	1		1	
• Size > 5 mm (n=56)	15 (26.8%)	0.89 (0.43-1.83)	*p* =0.75	0.77 (0.35-1.69)	*p* =0.51
Adenoma shape					
• Pedunculated (n=17)	1 (5.9%)	1		1	
• Sessile/ flat/depressed (n=149)	46 (30.9%)	7.96 (1.02-61.95)	*p* =0.04	10.26 (1.16-90.61)	*p* =0.04*
Adenoma location					
• Distal colon (n=80)	19 (23.8%)	1		1	
• Proximal colon (n=86)	28 (32.6%)	1.55 (0.78-3.07)	*p* =0.21	1.49 (0.71-3.14)	*p* =0.29
Total number of adenoma					
• 1-2 (n=56)	14 (25.0%)	1		1	
• > 3 (n=110)	33 (30.0%)	0.87 (0.44-1.73)	*p* =0.69	1.18 (0.56-2.49)	*p* =0.66
Duration of withdrawal time					
• > 9 minutes (n=135)	31 (23.0%)	1		1	
• < 9 minutes (n=31)	16 (51.6%)	3.96 (1.76-8.89)	*p* =0.001	4.72 (1.95-11.46)	*p* =0.001*

(48.8%). Among the 47 missed adenomas, there were pedunculated (2.1%), sessile (85.1%), flat (10.7%) and depressed (2.1%) polyps. There were higher adenoma miss rate in the proximal colon (59.6%) than in the distal colon (40.4%) [Odd ratio 2.09 (95% CI: 1.07-4.11); p= 0.03].

Of the 7 miss advanced adenomas, 5 (71.4%) were located in the proximal colon. All miss serrated adenomas were in the proximal colon. The characteristics of missed polyps and adenomas are shown in Table 3.

From univariate analysis, there were two significant factors for polyp miss rate and adenomas. The first factor was the non-pedunculated shape, the miss rates for non-pedunculated polyps and adenomas being 28.6% [Odd ratio 8.82 (95% CI: 1.17-66.54); p= 0.03] and 30.9% [Odd ratio 7.96 (95% CI: 1.02-61.95); p=0.04], respectively. The second factor was the withdrawal time less than 9 minutes, the miss rates for polyps and adenomas when withdrawal time for less than 9 minutes being 43.7% [Odd ratio 2.79 (95% CI: 1.59-4.91); p<0.001] and 51.6% [Odd ratio 3.96 (95% CI: 1.76-8.89); p=0.001], respectively. There was a trend for higher adenoma miss rate in the proximal colon and for adenoma size less than 5 mm, but there was no statistical significance.

From multivariate analysis, the independent significant associated factors for polyp miss rate were the non-pedunculated shape [Odd ratio 11.49 (95% CI: 1.44-91.59); p=0.02] and the duration of withdrawal time less than 9 minutes. [Odd ratio 3.02 (95% CI: 1.67-5.45); p<0.001] (Table 4).

Discussion

While screening colonoscopy has contributed to a notable reduction in colorectal cancer incidence and mortality[2], its sensitivity and accuracy remains questionable due to rather high incidence of post-colonoscopy interval cancer[14]. The crucial factor for interval cancer is missed lesions[13]. There are many reasons for missed lesions that can be classified into three categories. First, patients and polyps factors; there are data showing that female gender, increasing age, co-morbidities and diverticulosis are risk factors for interval colorectal cancer[19]. Poor-quality bowel preparation obscures visualization of the colon and is associated with high miss rate[20,21]. The polyp features including smaller size[8], flat lesions[21], location polyps behind mucosal folds[22] or in the right side of the colon[19] may influence the miss rate. Second, endoscopist's factor; many studies showed that endoscopists with less skill or experience were associated with development of post-colonoscopy colorectal cancer[4,19,23]. Colonoscopy quality indicators including adenoma detection rate more than 25% in male/female population, average withdrawal time in negative-result screening colonoscopies at least 6 minutes, and cecal intubation rate in asymptomatic screening more than 95%, are the standard requirements for all endoscopists[14]. Third, technology; there are many recent technological innovations aimed at enhancing mucosal imaging, but almost all still require further assessment before recommendation for routine practice. A meta-analysis showed only high definition colonoscopy having marginal benefit over standard colonoscopy for the polyps and adenoma detection[24]. Dye chromoendoscopy could also enhance pre-malignant polyps detection but was too time-consuming for routine colonoscopy[25,26]. On the contrary, neither virtual endoscopy (FICE, i-scan, NBI), autofluorescence nor cap-assisted colonoscopy could improve adenoma detection rate over standard high-definition white light endoscopy[26]. There are few studies showing an advantage of third-eye retroscopy[27] and full-spectrum endoscopy[28] in polyp and adenoma detection.

According to back-to-back colonoscopies, which is by for the most reliable approach for assessing miss rates[8], the adenoma miss rate and the advanced adenoma (AA) miss rate were reported at 15-32% and 0-11%, respectively[8-11].

The present study demonstrated a significant adenoma miss rate of 28.3%, and an advanced adenoma miss rate of 21.9%, even by using high definition colonoscopy with a precise methodology to limit confounding factors related to screening indication, good bowel preparation, withdrawal time at least 6 minutes, cecal intubation rate more than 95%, qualified endoscopists with baseline ADR more than 25%, as well as other technological factors.

Several previous studies showed that the higher adenoma miss rate was closely related to the smaller polyp size[8-11] and the higher number of adenomas detected at the first colonoscopy[10,11]. In our study, there was a trend of a high miss rate for adenoma size less than 5 mm, but without statistical significance. Whereas the location and the number of polyps were not associated with miss polyps. The explanation for such dif-

ferences may be due to the special attention of the endoscopist in screening subjects with small polyps and multiple adenomas.

The overall adenoma miss rate in the proximal colon was higher than that in the distal colon (32.6% vs. 23.8%). The difference, however, was not statistically significant. There was a trend for a higher miss rate in the right-sided polyps, because the proximal polyps especially those with advanced histology were usually flat and smaller than the distal polyps[29,30]. Regarding the shape of adenoma, this study showed that non-pedunculated lesions, including sessile, flat, and depressed lesions, are a significant risk factor associated with a high miss rate. This observation is similar to results from the previous study[9].

Moreover, non-pedunculated lesions are a significant risk factor resulting in a high miss rate. Our study suggested that colonoscopy withdrawal time less than 9 minutes was another independent factor for the adenoma miss rate. This result highlights the recommendation that endoscopists should spend sufficient colonoscopic withdrawal time to completely examine the colonic mucosa in order to lower the polyp miss rate.

Interestingly, our study revealed a high miss rate of 66.7% for sessile serrated adenoma. The explanation is that sessile serrated adenomas typically are of the same color shade as that of the surrounding mucosa, with a translucent appearance, in addition to being rather flat with faint borders. There are data showing that the sessile serrated adenomas acquire a rapid growth at later stage and have similar genetic changes to those of interval cancer[31]. Thus, it is a possible cause of post-colonoscopy interval cancer.

There are some limitations in this study. First, we could not absolutely blind the endoscopists about his order in back-to-back colonoscopies due to postpolypectomy lesions. Second, although ADR is a good quality indicator for colonoscopy, it does not reflect full colonoscopic examination. Thus, the endoscopist with ADR more than 25% did not get the same quality for colonoscopy. The sequence of different quality endoscopists should result in the different miss rate. Finally, a larger study with more subjects is needed to confirm the results of this study.

Conclusion

Colon polyp miss rate remained considerable in spite of high definition colonoscopy technology and attempted to limit confounding factors such as high-quality bowel preparation, adequate withdrawal time, cecal intubation and experienced endoscopists. Non-pedunculated lesions and withdrawal time less than 9 minutes were significant risk factors. Regarding sessile serrated adenoma, there was the high miss rate. Therefore adequate withdrawal time for complete mucosal examination is important to minimize missed polyps.

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