ORIGINAL ARTICLE

The Miss Rate for Colorectal Adenoma Determined by Quality-Adjusted, Back-to-Back Colonoscopies

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Background/Aims: Colonoscopy is considered to be the gold standard for detecting adenomatous polyps. Polyps are missed during colonoscopic examination at a rate that varies from 6% to 27%. The adenoma miss rate affects colonoscopic surveillance intervals and procedural quality. We aimed to assess the adenoma miss rate and the variables affecting the rate using same-day, quality-adjusted, back-to-back colonoscopies. **Methods:** This prospective study was performed at a single institution and included 149 patients. Two consecutive same-day colonoscopies were performed by two experienced endoscopists. The adenoma miss rates and variables affecting the missed adenomas, including polyp characteristics and procedure times, were evaluated. **Results:** The miss rates of polyps, adenomas, and advanced adenomas were 16.8%, 17%, and 5.4%, respectively. The smaller polyps and increased number of polyps detected during the first colonoscopy were more likely to be missed. A longer insertion time during the colonoscopy was correlated with an increased adenoma detection rate. **Conclusions:** There was a significant miss rate in the detection of colonic adenomas even in quality-adjusted, back-to-back colonoscopies. The adenoma miss rate can be reduced with a sufficient observation time during colonoscopic insertion. The development of specific technological methods to reduce the adenoma miss rate is necessary. **(Gut Liver 2012;6:64-70)**

Key Words: Colonoscopy; Adenoma; Miss rate; Quality

INTRODUCTION

Colonoscopy is the only procedure that allows removal of adenomatous polyps through the colon, substantially reducing colon cancer incidence.[1,2] The sensitivity of colonoscopy for the detection of polyps is of clinical importance, as the risk of colorectal cancer has been shown to be reduced by the detection and removal of adenomatous polyps. Missing adenomas during colonoscopy might reduce preventive efficacy against colon cancer.[3,4] The adenoma miss rate varies from 6% to 27% because of study heterogeneity.[3,5-7]

Recently, several studies involving special colonoscopic techniques including narrow band imaging (NBI), autofluorescence, and chromoendoscopy have been conducted to improve detection of polyps and flat lesions. So far, there were no impressive promising benefits of NBI, autofluorescence, and third-eye retroscope in improving polyp detection, as well as being relatively expensive.[8-10] In addition, even though pan-chromoendoscopy increased the detection rate of small flat adenomas, it is considered too laborious and time-consuming to be used for routine colonoscopy.[11]

Quality indicators for colonoscopy include the adenoma detection rate, adenoma miss rate, cecal intubation rate, bowel preparation, and withdrawal time. Cecal intubation and good bowel preparation are minimal requirements for qualified colonoscopic examination.[12] The reasons why polyps are missed are not clear, but it may be related to the size, shape, and number of polyps of an individual. The colonoscopic withdrawal time, quality of bowel preparation, and optimal observation techniques of colonoscopist are also important in reducing the adenoma miss rate.[13] The most reliable method for assessing the adenoma miss rate is "tandem" or "back-to-back" colonoscopy, a method in which two same-day colonoscopies are performed on each patient.[7]

We investigated the polyp and adenoma miss rate with same day back-to-back colonoscopy under the circumstances of adequate withdrawal time, bowel preparation, and cecal intubation rate. We also analyzed the variables affecting the miss rate for

colorectal adenomas.

MATERIALS AND METHODS

1. Study population

Patients were selected by endoscopists and randomized using the last numeric digit of the patient registration number on the procedure day. Patients were not consecutively enrolled but included between May 2007 and December 2008. We enrolled the patients between the ages of 18 and 80 years who were scheduled for elective colonoscopy. Patients were excluded if they had undergone a previous surgical resection, had inflammatory bowel diseases, familial polyposis coli, or poor bowel preparation, were under anticoagulation therapy, or were in a poor general condition (American Society of Anesthesiologists grade 3 or 4) for two colonoscopies in the same day.

The study was approved by the Institutional Review Board of Hanyang University Guri Hospital, and informed consent was obtained from all patients.

2. Colonoscopic procedure

Before colonoscopy, all patients completed the demographic and medical history questionnaires. Subjects took a standardized preparation on the day prior to colonoscopy with a large volume (4 L) of polyethylene glycol. The examinations were performed by two experienced endoscopists who had each performed at least 3,000 colonoscopies and related procedures.

All endoscopic examinations were performed under conscious sedation in the left lateral decubitus position. Changing position and abdominal compression were performed if necessary. During each procedure, the quality of bowel preparation was rated by the endoscopists as excellent (colon empty and clean), good (minor amount of fluid in the gut, but easily removed by suction), moderate (fluid or semisolid residual stool, fully removable by suction or displaceable), bad (fluid or semisolid residual stool, only partially removable with risk of incomplete mucosal visualization) or very bad (colon full of semisolid or solid stool) according to the scale of Ell et al.[14] Patients with bad or very bad preparation were excluded from the analysis. After endoscopists reached the ileocecal area, they took photos and recorded the insertion time. Withdrawal time excluding time needed for polyp removal was also measured. All endoscopists spent at least 6 minutes for observation during withdrawal.

The colonoscopes used were forward viewing colonoscope, CF-H260AI (Olympus Optical Co., Ltd., Tokyo, Japan) and an identical type of colonoscope was used during the second colonoscopic examination. We did not use chromoendoscopy or a NBI system.

3. Back-to-back colonoscopy

All patients underwent back-to-back colonoscopy examination, with a conventional colonoscopy followed immediately by the second endoscopy. In all patients, both the first and second colonoscopies were performed by the same examiner. In the first examination, colonoscope was inserted into the cecum, and polyps identified during insertion and withdrawal were counted and removed. Numerous tiny hyperplastic polyps in the rectum and sigmoid colon were not subjected to removal.

In the second examination, we recorded any remaining polyps not found on the initial examination and defined these as 'missed polyp'. Again, all remaining polyps, except tiny hyperplastic polyps of the rectum and sigmoid colon, were removed.

All polyps detected by the first and second examination, along with the size, shape, location, and polypectomy[15] method were noted. A pair of colonoscopy was included for analysis if both procedures were completed to the ileocecal area and the observation time during withdrawal was at least 6 minutes. The polyp shape was determined according to the Paris classification. We classified type Ip polyp as pedunculated polyp, and both type Is and Isp as sessile polyp, and both type IIa and IIb as flat polyp. Polyp size was determined by comparing with opened biopsy forceps pushed up against the polyp or, in some cases of pedunculated polyps by direct measurement after retrieval.

All the endoscopic lesions removed were reviewed by a gastrointestinal specialized pathologist. Those adenomas larger than 1 cm at endoscopy and/or with high grade dysplasia or a villous component >25% at histology were defined as an advanced adenoma.

4. Calculation of adenoma miss rate and statistical analysis

Miss rates were calculated for adenomas, adenomas ≥6 mm, advanced adenomas, and all polyps. A pooled miss rate for polyps was calculated as: total number of missed polyps/(total number of missed polyps+total number of polyps on initial examination). Miss rates were calculated overall and within strata of polyp size, location, and shape.

Statistical analysis was performed with SPSS for Windows software version 13.0 (SPSS Inc., Chicago, IL, USA). Demographic findings such as age, gender, body mass index, alcohol, smoking, chronic diseases as well as adequacy of colonic preparation were included for analysis. Polyp size, shape, location, and the number of polyps were included in a logistic regression analysis to identify the variables associated with missed polyps.

RESULTS

1. Clinical characteristics

A total of 165 patients was enrolled in the study, and 149 completed both colonoscopies. 16 patients were excluded. The reasons for exclusion were poor bowel preparation (n=15) and failure to complete a second examination to the cecum due to pain after a successful initial examination (n=1). The 149 pa-

tients included 106 men, and the mean age was 53.3 years. The indications of colonoscopy were screening (n=48), abdominal pain (n=31), bowel habit change (n=19), previous history of colon adenoma (n=13), positive stool occult blood (n=11), family history of colon cancer (n=4), and others (n=23). The quality of bowel preparation was described as excellent in 38%, good in 31%, and moderate in 31%. The median durations of the first and second examination were 14.1±3.6 (range, 8.8 to 46.6) and 12.3±3.4 (range, 8.2 to 29.8) minutes, respectively. The median durations of withdrawal for the first and second examination were 10.0±3.4 (range, 6 to 30) and 9.0±1.9 (range, 6 to 20) minutes, respectively. There were no differences of polyp miss rates (24.7% vs 35.9%, p=0.15), insertion time (3.9 minutes vs 4.3 minutes), and withdrawal time (7.1 minutes vs 6.8 minutes) between the two endoscopists.

2. Polyp characteristics

A total of 344 polyps were found in 114 patients. Thirty-five patients had no colon polyp. The mean diameter of the polyps was 5.3±3.4 mm and 27.0% of all polyps were larger than 5 mm (n=93). The histologic findings of polyps were tubular adenoma (n=232), high grade dysplasia (n=9), serrated adenoma (n=4), adenocarcinoma (n=1), hyperplastic and inflammatory polyps (n=98). A total of 37 advanced adenomas were observed

in 29 patients. The mean diameter of the advanced adenomas was 13.1±4.4 mm. Twelve advanced adenomas were found in the right colon and twenty-five were found in the left colon.

3. Polyp miss rate and associated variables

From the 149 colonoscopy pairs, a total of 344 polyps (neoplastic and non-neoplastic polyps) were found, while 58 polyps (adenomatous and non-adenomatous) and 42 adenomatous polyps were missed. The miss rates for polyps, adenomas, adenomas 6 to 9 mm, and advanced adenomas were 16.8%, 17%, 7.2%, and 5.4%, respectively (Table 1).

The location of polyps did not affect the miss rate (Table 2). The overall miss rate for adenomas in the right colon (proximal to the splenic flexure) was 19.1% compared with 14.5% in the left colon (p=0.11). The smaller the polyp size, the higher was the miss rate. The miss rate for adenomas smaller than 5 mm was 22.9%. The miss rates for adenomas 6 to 9 mm and more than 10 mm were 7.2% and 5.8%, respectively.

The shape of polyps did not affect the miss rate. Among 42 missed adenomas, 3 (12%) were pedunculated, 34 (18%) were sessile, 5 (15%) were flat lesions. We missed 3 out of 26 (12%) pedunculated adenomas, 34 out of 185 (18%) sessile adenomas, and 5 out of 33 (15%) flat adenomas. The miss rates were higher for sessile and flat polyps (19% and 13%, respectively), but the shape of the polyps did not show a significant relation with the miss rates. Two advanced adenomas were missed; one was a pedunculated polyp (10 mm) in the ascending colon, the other was a sessile polyp (10 mm) in the sigmoid colon.

Adenoma miss rate increased with the number of adenomas detected during the first examination. The adenoma miss rate according to the number of adenomas detected during the initial examination was as follows: 14% for patients with one adenoma on the first examination, 28% for two adenomas, 44% for three adenomas, and 66% for more than three adenomas, respectively (Table 3).

Logistic regression analysis was performed to identify independent variables associated with missed polyps. The number

Table 1. Number of Polyps and Adenomas Detected During the First and Second Colonoscopic Examinations

Type of lesion	First examination	Second examination	Miss rate, %
Total polyps	286	58	16.8
Polyps <6 mm	195	51	20.7
Total adenomas	204	42	17.0
Adenomas <6 mm	121	36	22.9
Adenomas 6-9 mm	51	5	7.2
Adenomas ≥10 mm	32	2	5.8
Advanced adenomas	35	2	5.4

Table 2. The Number and Percentage of Missed Polyps and Adenomas Based on Location

Type of lesion	Colonic location					
	Total	AC	TC	DC	Sigmoid	Rectum
Total polyps (missed/total)	58/344 (17)	18/100 (18)	16/68 (23)	5/50 (10)	14/88 (16)	5/38 (13)
Polyps <6 mm (missed/total)	51/246 (21)	14/69 (20)	15/50 (30)	4/31 (13)	13/68 (19)	5/28 (18)
Total adenomas (missed/total)	42/246 (17)	15/81 (19)	11/55 (20)	5/39 (13)	10/56 (18)	1/15 (7)
Adenomas <6 mm (missed/total)	36/157 (23)	11/51 (22)	11/41 (27)	4/21 (19)	9/38 (24)	1/6 (17)
Adenomas 6-9 mm (missed/total)	4/55 (7)	3/22 (14)	0/11 (0)	1/13 (7)	0/6 (0)	0/3 (0)
Adenomas ≥10 mm (missed/total)	2/34 (6)	1/8 (13)	0/3 (0)	0/5 (0)	1/12 (8)	0/6 (0)
Advanced adenomas (missed/total)	2/37 (5)	1/8 (13)	0/4 (0)	0/6 (0)	1/13 (7)	0/6 (0)

Data are presented as number (%).
AC, ascending colon; TC, transverse colon; DC, descending colon.

Table 3. The Miss Rates for Adenomas Based on the Number of Adenomas Detected During the First Examination

Findings at first examination				Findings at second examination		
No. of adenoma	No. of patients	Total/ withdrawal time, min	Bowel cleansing (E/G/M), No.	No. of patients with adenoma, No. (%)	Total/ withdrawal time, min	Bowel cleansing (E/G/M), No.
0	42	12.4/8.4	24/29/14	7 (17)	11.1/7.4	24/29/14
1	44	13.6/9.3	15/8/13	6 (14)	11.5/9.5	15/8/13
2	18	14.9/10.2	10/3/4	5 (28)	13.3/11.7	10/3/4
3	16	13.1/10.1	3/1/6	7 (44)	12.4/10.9	3/1/6
≥4	29	17.8/13.3	5/5/9	19 (66)	11.0/9.3	5/5/9

E/G/M, excellent/good/moderate in quality of bowel preparation.

Table 4. The Univariate Logistic Regression Analysis of the Independent Variables Associated with Missed Polyps

Variable	OR (95% CI)	p-value
Preparation		
Moderate	1	
Good	0.80 (0.34–1.87)	0.61
Excellent	0.81 (0.33–1.98)	0.65
Sex	1.03 (0.47–2.24)	0.93
Age	1.02 (0.99–1.06)	0.09
BMI	1.04 (0.90–1.20)	0.56
Insertion time (1 min increments)	0.99 (0.98–0.99)	0.02
No. of polyp		
0	1	
1	0.81 (0.24–2.65)	0.72
2	1.92 (0.51–7.14)	0.32
≥3	6.84 (2.5–18.67)	<0.01
Polyp size (1 mm increments)	0.83 (0.73–0.96)	0.11
Polyp location		
Right colon	1	
Left colon	0.62 (0.34–1.12)	0.11
Polyp shape		
Sessile	1	
Pedunculated	1.45 (0.35–6.03)	0.60
Flat	0.63 (0.28–1.39)	0.25

OR, odds ratio; CI, confidence interval; BMI, body mass index.

Table 5. The Multiple Logistic Regression Analysis of the Independent Variables Associated with Missed Polyps

Variable	OR (95% CI)	p-value
Insertion time (1 min increments)	0.99 (0.98–0.99)	0.01
Sex	0.54 (0.20–1.45)	0.22
Age	0.99 (0.95–1.04)	0.89
Colonoscopists	0.64 (0.28–1.50)	0.30
No. of polyp		
0	1	
1	0.91 (0.26–3.08)	0.88
2	2.82 (0.69–11.52)	0.14
≥3	7.93 (2.57–24.48)	<0.01
Polyp size (1 mm increments)	0.80 (0.68–0.94)	0.01

OR, odds ratio; CI, confidence interval.

of polyps, size of polyps, and colonoscopic insertion time were independent variables in univariate and multiple logistic regression analysis (Tables 4 and 5).

DISCUSSION

In the present study, we observed a significant miss rate for adenomas of about 17% even in quality-adjusted back-to-back colonoscopies. The number of adenomas, size of adenoma, and colonoscopic insertion time were independent variables for the adenoma miss rate. We found that longer insertion time corre-

lated with increased adenoma detection rate.

Colonoscopy is widely considered the gold standard for detection of colonic neoplasia. In the National Polyp Study, the estimated reduction in the incidence of colorectal cancer ranged from 76% to 90% over a prolonged period of surveillance after colonoscopic polypectomy.[15] However, colonoscopy is not perfect because a considerable number of adenomas can be missed during colonoscopy, and the occasional interval cancer is detected in patients with a history of recent normal colonoscopy.[16,17]

The colonoscopic miss rate of adenoma might affect screening and surveillance interval for colon cancer prevention, and is an important factor for cost-effective analysis. The most reliable method to estimate adenoma miss rate is by 'back-to-back colonoscopy,' a method in which two consecutive same-day colonoscopies are performed in a single patient.[7] Several studies have evaluated the adenoma miss rates of colonoscopy by performing 'back-to-back colonoscopy'. The overall miss rates for adenomas ranged from 15% to 24%, and the miss rate for advanced adenomas was 11% in previous back-to-back colonoscopy studies.[3,4,6,18] Our study estimated the adenoma miss rate utilizing the most reliable method known, the back-to-back colonoscopy method, and demonstrated miss rates of 17% and

5.4% for adenoma and advanced adenoma, respectively, which were similar to previous studies. However, in this study, quality-adjusted colonoscopy with adequate bowel preparation, withdrawal time, quality of endoscopic image, and the experience of endoscopist, was performed.

The reasons why polyps are missed are not clear, but it may be related to the size, shape, and number of polyps of an individual. The colonoscopic withdrawal time, quality of bowel preparation, and optimal observation techniques of the colonoscopist are also important in reducing the miss rate.[13]

In the present study, we have compared the adenoma miss rate of a quality-adjusted colonoscopic examination with those of previous studies. If the miss rate of a quality-adjusted colonoscopy is significantly lower, efforts to improve the quality of conventional colonoscopy should be the ultimate goal, rather than focusing on specific technological methods. On the other hand, if the miss rate of quality-adjusted colonoscopy is still high, efforts to develop or improve specific technological methods to reduce the adenoma miss rate should be performed in future studies.

In this study, patients with poor bowel preparation or whose colonoscopic cecal intubation was not performed were excluded, while examinations were performed by two experienced endoscopists who had each performed at least 3,000 colonoscopies and related procedures, using the high definition colonoscope and spending at least 6 minutes for observation during withdrawal. However, miss rates of 17% and 5.4% for adenoma and advanced adenoma, respectively, were noted even in quality-adjusted colonoscopy, demonstrating the fact that quite a significant number of adenomas are being missed during colonoscopy. This indicates that although the improvement of quality of conventional colonoscopic examination may be important in reducing the adenoma miss rate, the development of various new endoscopic techniques to overcome the technical limitations of the present colonoscopic examination is also important.

The miss rate of colon adenomas are closely related to the characteristics of adenomas such as size and number of adenomas. In the present study, the miss rate for adenomas smaller than 5 mm, 6 to 9 mm, and larger than 10 mm were 22.9%, 7.2%, and 5.8%, respectively. This showed that the smaller the adenoma size, the higher was the adenoma miss rate, which is similar to the results of previous studies.[3,4,7,18]

It has been known that flat lesions are significantly associated with higher miss rates. However, our study did not show a similar result. In the present study, the miss rates for sessile adenoma, flat adenoma and pedunculated adenoma were 18%, 15%, and 12%, respectively. This difference might be related to clinical experiences because most East Asian colonoscopists are more familiar with flat lesions than Western colonoscopists.

In the present study, overall adenoma miss rate in the right colon was higher than that in the left colon (19.1% vs 14.5%), although this difference did not reach statistical significance.

This result may partly explain the observation in the postpolypectomy surveillance studies that metachronous adenomas are more detected in the right colon.[19,20]

The number of adenomas detected at the initial examination has been known to be a significant predictor of adenoma miss rates.[3,4,6] However, in a recent study by Heresbach et al.,[18] the more polyps that were found in a patient, the fewer polyps that were found to have been missed. In contrast, our study showed adenoma miss rates increased with the number of adenomas detected during the first examination; 14% for one adenoma, 28% for two adenomas, 44% for three adenomas, and 66% for more than three adenomas. Although the explanation of these differences is uncertain, we should pay special attention to patients with multiple adenomas and even adenomas of relatively small size to decrease the adenoma miss rate.

Although slightly different according to the follow-up interval after colon polypectomy, the rate of adenoma recurrence is known to be around 30% to 50%.[21] Postpolypectomy surveillance colonoscopy studies[22,23] have shown that size and number of adenomas detected on the initial colonoscopy were important predictors of adenoma recurrence in the subsequent surveillance colonoscopy. Like the results of previous studies, the present study demonstrated that the smaller the adenoma size or higher the number of adenomas detected on the first colonoscopy, the more likely there were to be missed adenomas. Therefore, significant number of recurrent adenomas detected during postpolypectomy surveillance colonoscopy may be missed adenomas in the initial colonoscopy.

Interestingly, in our study, colonoscopic insertion time affected the adenoma miss rate. The longer insertion time took, the lower the adenoma miss rate (p=0.01). It is well known that longer withdrawal time is associated with higher adenoma detection rate.[24-26] Since we spent at least 6 minutes during colonoscopic withdrawal, there was no correlation between withdrawal time and miss rate. Also, a recent study reported that most advanced neoplasia are detected during the insertion period although withdrawal time has been shown to be important.[27] Slow and careful observation during the withdrawal period after a rapid insertion is common during colonoscopic procedures. It seems to be reasonable that observation during the insertion period is also important because the colon is not shortened and folded, and we can watch larger surface by inflation during insertion. Our result emphasizes that colonoscopists should spend sufficient time during both insertion and withdrawal. However, intentional observation for adenoma is not wise during the stage of insertion. It may induce various discomforts to the patient and even act as a potential risk for complication.

This study has several limitations. First, we can not know the true adenoma miss rate because we used a second colonoscopy as a gold standard. Second, we enrolled the patients who presented to a single center, and only two endoscopists participated in the study. In addition, the first and second colonoscopy

were performed by the same endoscopist. However, it has been known that there was no significant difference in adenoma miss rates between the results performed by the same and different endoscopists.[4] A large scaled, prospective, multicenter study is needed to validate the factors affecting the adenoma miss rate.

In summary, a significant miss rate for colon adenomas is observed even during quality-adjusted colonoscopy with controlled bowel preparation, withdrawal time, and cecal intubation. The smaller the adenoma size or higher the number of adenomas detected on the first colonoscopy, the more likely there are to be missed adenomas. Adenoma miss rate can be reduced by performing vigilant and meticulous examination and allowing sufficient observation time including a longer insertion time. In the future, efforts to develop special technological methods to reduce the adenoma miss rate are warranted.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

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