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ORIGINAL ARTICLE

Risk Factors Related to Polyp Miss Rate of Short-Term Repeated Colonoscopy

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Abstract

Background Colonoscopy is regarded as the gold standard for colorectal cancer screening and surveillance. However, previous studies have reported large numbers of polyps were missed during routine colonoscopy.

Aims To evaluate polyp miss rate in short-term repeated colonoscopy and explore the related risk factors.

Methods A total of 3695 patients and 12,412 polyps were included in our studies. We calculated the miss rate for polyps of different sizes, pathologies, morphologies and locations, and patients of different characteristics. Univariate and multivariate logistic regression analyses were performed to evaluate risk factors related to miss rate.

Results The polyp miss rate was 26.3% and the adenoma miss rate was 22.4% in our study. The advanced adenoma miss rate was 11.0% and the proportion of missed advanced adenomas in missed adenomas sized > 5 mm was up to 22.8%. Polyps sized < 5 mm had a significantly higher miss rate. The miss rate of pedunculated polyps was lower than that of flat or sessile polyps. Polyps in the right colon were prone to be missed than that in the left colon. For older men, current smokers, individuals with multiple polyps detected in the first colonoscopy, the risk of missing polyps was significantly higher.

Conclusion Nearly a quarter of polyps were missed during routine colonoscopy. Diminutive, flat, sessile, and right-side colon polyps were at higher risk of missing. The risk of missing polyps was higher in older men, current smokers, and individuals with multiple polyps detected in the first colonoscopy than their counterparts.

Keywords Polyp miss rate · Adenoma miss rate · Advanced adenoma · Colonoscopy

Abbreviations

CRC	Colorectal cancer
SSL	Sessile serrated lesion
PCCRC	Post-colonoscopy colorectal cancer
PMR	Polyp miss rate
AMR	Adenoma miss rate
BMI	Body mass index
OR	Odds ratio
CI	Confidence interval
SMR	Serrated polyp miss rate
AAMR	Advanced adenoma miss rate
TEC	Third-eye colonoscopy
WLI	White-light imaging
BLI	Blue-light laser imaging
FUSE	Full spectrum endoscopy
CADe	Computer-aided detection
ADR	Adenoma detection rate
APC	Adenomas per colonoscopy
APPC	Adenomas per positive participant

Introduction

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer death [1]. Adenomatous polyps and sessile serrated lesions (SSLs) are precursors to the majority of CRC [2]. Colonoscopy is regarded as the gold standard for CRC screening and surveillance by detecting and removing polyps [3]. A meta-analysis reported that colonoscopy combined with polypectomy resulted in a reduction of 69% in CRC incidence and 68% in CRC mortality [4]. However, colonoscopy cannot discover all colonic lesions, and CRC can be diagnosed within a short

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interval following a negative colonoscopy, which called post-colonoscopy CRC (PCCRC) [5]. Common origins for PCCRC include missed lesions, new lesions, and incompletely resected lesions, of which missed lesions account for the majority. A study reported a PCCRC-3y rate of 4.7% and indicated that even with adequate preparation, 27% of PCCRCs were attributed to probable missed lesions [6]. Therefore, reducing missed polyps is of great significance in clinical practice.

Previous studies have included tandem endoscopy or back-to-back endoscopy as an indicator to evaluate the polyp miss rate (PMR) and adenoma miss rate (AMR), which means two same-day colonoscopies perform on one patient both with polypectomy [7]. A meta-analysis included that 15,152 tandem colonoscopies found a miss rate of 28% for polyps and 26% for adenomas [8]. Although tandem colonoscopy accurately estimate the miss rate for colonic lesions, it is rarely performed in routine practice in China due to its heavy burden on medical resources. In China, when polyps needed treatment are found in screening colonoscopy, patients are hospitalized for a second colonoscopy with polypectomy. Recently, Sekiguchi et al. [9] appointed that observational colonoscopy followed by deferred polypectomy could be a safe and feasible option in terms of lesion detectability compared with colonoscopy with simultaneous polypectomy.

Therefore, we investigated the miss rate of polyps and adenomas during short-term repeated colonoscopy. And the aims of the current study were to evaluate the PMR and AMR in daily clinical practice, and explore polyp- and patient-related risk factors that affect the miss rate during colonoscopy, in order to improve the quality of colonoscopy and reduce the incidence of PCCRC.

Methods

Study Design and Participants

We performed a cross-sectional, retrospective study of patients who underwent two colonoscopies: the first colonoscopy detected polyps and the second one removed polyps.

Patients underwent colonoscopy with polypectomy were enrolled at the First Affiliated Hospital, School of Medicine, Zhejiang University, from January 1, 2021 to December 31, 2021. Inclusion criteria included patients aged 18 years or older, received two total colonoscopies (cecum insertion) and had adequate bowel preparation (Boston Bowel Preparation Score ≥ 5). Exclusion criteria were as follows: no previous non-therapeutic colonoscopy in our hospital or interval between the first and second colonoscopy longer than 6 months; history of polyposis, inflammatory bowel disease, colorectal cancer, or colectomy; incomplete information of patient characteristics; and two colonoscopies.

The study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (No. 2022-547) and conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from all patients at the time of endoscopy.

Data Collection

The data of patient characteristics and two colonoscopies were collected by reviewing the medical records. Patients information included age (≤ 60 years old or > 60 years old), gender (male or female), body mass index (BMI) (< 18.5 kg/m^2, 18.5–25 kg/m^2, or ≥ 25 kg/m^2), smoking (current smoker, past smoker, or non-smoker), alcohol drinking (current drinker, past drinker, or non-drinker), diabetes mellitus, hypertension, history of tumor and abdominal surgery, interval between two colonoscopies (< 3 months or 3–6 months), and the number of polyps during the first colonoscopy (1 or ≥ 2).

We documented polyps in two colonoscopies. Polyps removed by biopsy forceps during the first colonoscopy were included, and polyps found during the first colonoscopy but missed during the second colonoscopy were excluded. When the term "multiple polyps" appeared in the colonoscopy report, the number of polyps was assumed to be 3. Polyps were grouped into non-adenomatous and adenomatous polyps. Adenomas were further subdivided depending on their histology (tubular, villous, tubulovillous, or serrated). Advanced adenomas were defined as adenomas larger than 10 mm, with villous component, high-grade dysplasia, or carcinoma in situ [10]. Polyp size was determined as diminutive (≤ 5 mm), medium (6–9 mm), and large (≥ 10 mm) by comparison with open biopsy forceps. Polyps were also divided by morphology (flat, sessile, or pedunculated), and location in the colon (cecum, ascending colon, transverse colon, descending colon, sigmoid colon, or rectum). To further investigate the relationship between missed polyps and location, two adjusted models were conducted into analysis: location 1 (right colon: cecum, ascending colon, and transverse colon; or left colon: descending colon, sigmoid colon, and rectum) and location 2 (right colon: cecum, ascending colon, and transverse colon; or left colon: descending colon, and sigmoid colon; or rectum).

Outcome Measures

PMR and AMR were defined as the number of polyps (adenomas) detected only during the second colonoscopy

divided by the total number of polyps (adenomas) detected during two colonoscopy [8]. The primary outcomes were PMR and AMR, and the secondary outcomes were miss rate for polyps of different sizes, pathologies, morphologies and locations, and patients of different characteristics.

Statistical Analysis

Continuous variables were presented as mean with standard deviations or medians with first quartile and third quartile. Categorical variables were expressed as frequencies with percentages. Comparison of two groups were conducted by Student-*T* test or Mann–Whitney *U* test for continuous, and chi-square test for categorical variables. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression models. Univariate and multivariate analyses were performed to evaluate risk factors related to missed polyps. A two-tailed *P* value < 0.05 was considered to be statistically significant. Statistical analyses were conducted using SPSS 26.0 software (SPSS Inc, Chicago, IL, USA).

Results

Baseline Characteristics of Patients

A total of 3695 patients were included in our study. The flowchart of inclusion and exclusion criteria is shown in Fig. 1. The median age of these patients was 58 (51–65) years, and 62.5% were males. The median BMI was 23.6 (21.6, 25.8) kg/m^2. 61.8% of patients had at least 2 polyps during the first colonoscopy, and median interval between two colonoscopies was 23 (11, 46) days. The baseline characteristics of included patients were summarized in Table 1.

Table 1 Baseline characteristics of patients who underwent two colonoscopies

Characteristics	Patients, $n = 3695$
Gender, *n* (%)	
Male	2311 (62.5%)
Female	1384 (37.5%)
Age, years, median (Q1,Q3)[a]	58 (51, 65)
Body mass index, kg/m^2,median (Q1,Q3)[b]	23.6 (21.6, 25.8)
Smoking, *n* (%)	
Current smoker	652 (17.7%)
Past smoker	226 (6.1%)
Non-smoker	2817 (76.2%)
Alcohol drinking, *n* (%)	
Current drinker	557 (15.1%)
Past drinker	147 (4.0%)
Non-drinker	2991 (81.0%)
Diabetes mellitus, *n* (%)	297 (8.0%)
Hypertension, *n* (%)	1146 (31.0%)
History of tumor, *n* (%)	138 (3.7%)
History of abdominal surgery, *n* (%)	621 (16.8%)
Surveillance interval, days, median (Q1,Q3)	23 (11, 46)
Number of polyps during the first colonoscopy, *n* (%)	
1	1413 (38.2%)
≥2	2282 (61.8%)

[a]Q1, first quartile; Q3, third quartile

[b]Body mass index information was not available for all patients

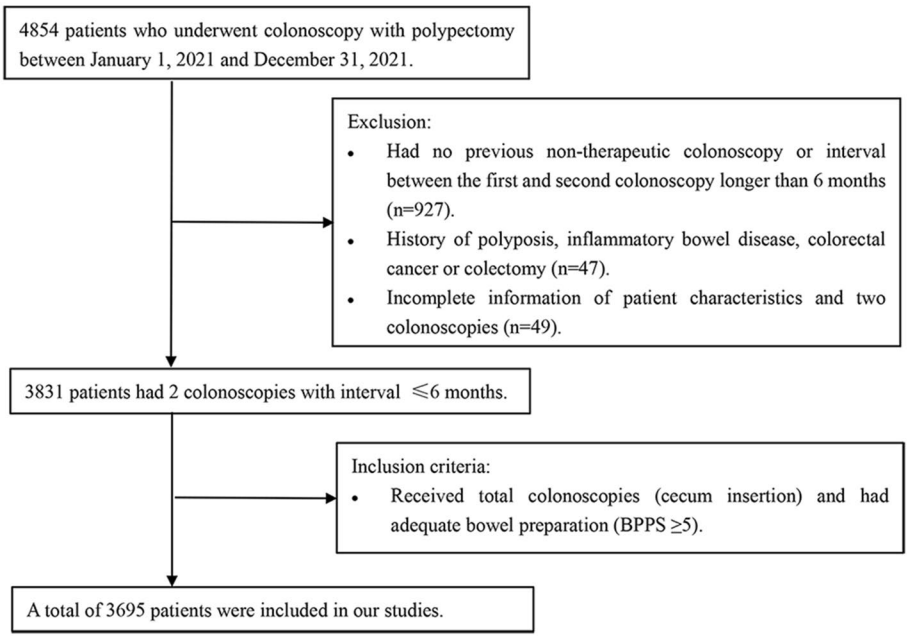

Fig. 1 Flowchart of patients' selection

Polyp Miss Rate and Risk Factors Related to Missed Polyps

Overall, 12,412 adenomatous or non-adenomatous polyps were detected, with 9146 polyps detected during the first colonoscopy and 3266 newly detected during the second one. And the PMR was 26.3%. Discounting diminutive polyps, the PMR was 16.0%. Risk factors associated with missed polyps are shown in Table 2. In univariate analysis, adenomatous or non-adenomatous polyps, size, morphology, and location were associated with missed polyps. In multivariate analysis, diminutive in size (OR 3.66, 95% CI 3.05–4.39) and sessile (OR 1.99, 95% CI 1.63–2.42) or flat shape (OR 2.10, 95% CI 1.70–2.59) were significantly associated with a higher PMR. The risk of missing adenomatous or non-adenomatous polyps was not different ($P = 0.097$). The miss rate was significantly lower in the rectum and higher in other colons. Further analysis found that PMR in the left colon was significantly lower than that in the right colon ($P < 0.001$ in location 1 and $P < 0.001$ in location 2, respectively) (Fig. 2A).

Adenoma Miss Rate and Risk Factors Related to Missed Adenomas

6563 adenomas were detected in two colonoscopies, of which 1469 adenomas were newly detected in the second colonoscopy. The AMR was 22.4%. If discounting diminutive adenomas, the AMR was15.9%. Besides, serrated polyp miss rate (SMR) was 15.0%, and the advanced adenoma miss rate (AAMR) was 11.0%. Risk factors associated with missed adenomas are shown in Table 3. In univariate analysis, histology, size, morphology, and location were associated with missed adenomas. Advanced adenomas were less likely to be missed than non-advanced adenomas (OR 0.36, 95% CI 0.30–0.42). The detailed composition of advanced adenomas is seen in Supplementary Table 1. Considering the overlap of advanced adenomas and adenoma size or histology, advanced adenomas were no longer included in the multivariate analysis. In multivariate analysis, diminutive in size (OR 3.42, 95% CI 2.76–4.23) and sessile (OR 1.76, 95% CI 1.41–2.20) or flat shape (OR 1.90, 95% CI 1.48–2.45) were independently associated with an increase in the AMR. Histology of adenomas had no effect on the risk of miss rate. Adenomas located in the sigmoid colon and rectum had a reduced miss rate compared with other colons. In addition, the risk of missed adenomas in the left colon was also significantly decreased compared with that

Table 2 Risk factors related to missed polyps

	No missed lesions	Missed lesions	Miss rate (%)	Univariate		Multivariate[a]	
				Odds ratio (95% confidence interval)	*P* value	Odds ratio (95% confidence interval)	*P* value
Polyps	9146	3266	26.3				
Non-adenomatous	4052	1797	30.7	1		1	
Adenomatous	5094	1469	22.4	0.65 (0.60–0.74)	***P* < 0.001**	0.93 (0.84–1.01)	*P* = 0.097
Size							
Diminutive	4260	2332	35.4	4.61 (3.90–5.44)	***P* < 0.001**	3.66 (3.05–4.39)	***P* < 0.001**
Medium	3447	763	18.1	1.86 (1.56–2.22)	***P* < 0.001**	1.47 (1.23–1.77)	***P* < 0.001**
Large	1439	171	10.6	1		1	
Morphology							
Pedunculated	1227	135	9.9	1		1	
Sessile	6254	2464	28.3	3.58 (2.98–4.30)	***P* < 0.001**	1.99 (1.63–2.42)	***P* < 0.001**
Flat	1665	667	28.6	3.64 (2.98–4.44)	***P* < 0.001**	2.10 (1.70–2.59)	***P* < 0.001**
Location							
Cecum	383	159	29.3	1.38 (1.12–1.70)	***P* = 0.003**	1.52 (1.23–1.89)	***P* < 0.001**
Ascending colon	1322	519	28.2	1.31 (1.13–1.50)	***P* < 0.001**	1.74 (1.49–2.01)	***P* < 0.001**
Transverse colon	1756	730	29.4	1.38 (1.21–1.58)	***P* < 0.001**	1.82 (1.58–2.09)	***P* < 0.001**
Descending colon	1064	435	29.0	1.36 (1.17–1.58)	***P* < 0.001**	1.82 (1.56–2.13)	***P* < 0.001**
Sigmoid colon	2882	900	23.8	1.04 (0.92–1.12)	*P* = 0.549	1.29 (1.14–1.47)	***P* < 0.001**
Rectum	1739	523	23.1	1		1	

Bold indicates values with statistical significance

[a]Adjusted for polyps, size, morphology, location

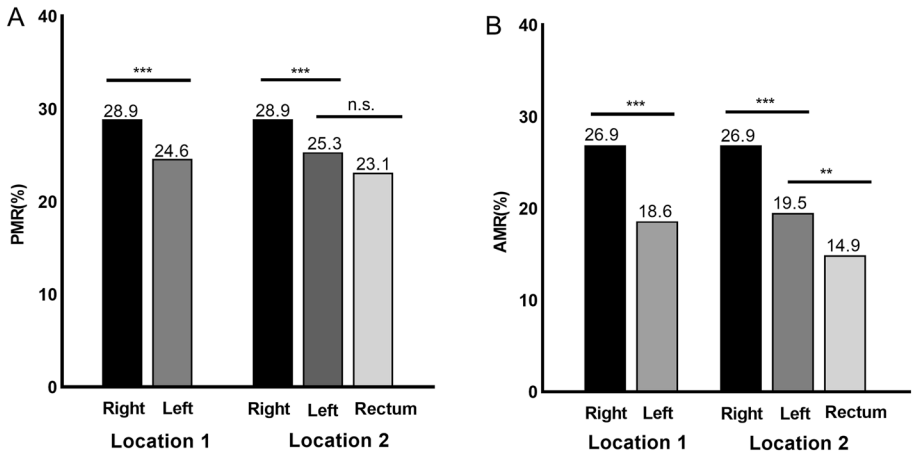

Fig. 2 **A** Differences in polyp miss rate between the right colon and the left colon. **B** Differences in adenoma miss rate between the right colon and the left colon. *PMR* polyp miss rate, *AMR* adenoma miss rate. Location 1, right colon: cecum, ascending colon, and transverse colon; or left colon: descending colon, sigmoid colon, and rectum. Location 2, right colon: cecum, ascending colon, and transverse colon; or left colon: descending colon, and sigmoid colon; or rectum. $*P<0.05$, $**P<0.01$, $***P<0.001$. *n.s.* nonsignificant

Table 3 Risk factors related to missed adenomas

	No missed lesions	Missed lesions	Miss rate (%)	Univariate		Multivariate[a]	
				Odds ratio (95% confidence interval)	*P* value	Odds ratio (95% confidence interval)	*P* value
Adenomas	5094	1469	22.4				
Histology[b]							
Tubular	4583	1402	23.4	1		1	
Tubulovillous	383	46	10.7	0.40 (0.29–0.54)	**P < 0.001**	0.84 (0.60–1.17)	P = 0.297
Villous	4	1	20.0	0.82 (0.09–7.32)	P = 0.857	1.47 (1.16–13.55)	P = 0.735
Serrated	113	20	15.0	0.58 (0.36–0.93)	**P = 0.025**	0.82 (0.50–1.35)	P = 0.441
Type							
Non-advanced adenoma	3743	1302	25.8	1			
Advanced adenoma	1351	167	11.0	0.36 (0.30–0.42)	**P < 0.001**		
Size							
Diminutive	1421	776	35.3	4.76 (3.91–5.78)	**P < 0.001**	3.42 (2.76–4.23)	**P < 0.001**
Medium	2445	552	18.4	1.97 (1.61–2.40)	**P < 0.001**	1.49 (1.20–1.84)	**P < 0.001**
Large	1228	141	10.3	1		1	
Morphology							
Pedunculated	1010	112	10.0	1		1	
Sessile	3268	1074	24.7	2.96 (2.41–3.65)	**P < 0.001**	1.76 (1.41–2.20)	**P < 0.001**
Flat	816	283	25.8	3.13 (2.47–3.97)	**P < 0.001**	1.90 (1.48–2.45)	**P < 0.001**
Location							
Cecum	183	64	25.9	2.00 (1.40–2.85)	**P < 0.001**	1.64 (1.14–2.36)	**P = 0.008**
Ascending colon	873	303	25.8	1.99 (1.55–2.55)	**P < 0.001**	1.79 (1.39–2.31)	**P < 0.001**
Transverse colon	1114	432	27.9	2.22 (1.75–2.82)	**P < 0.001**	1.99 (1.55–2.54)	**P < 0.001**
Descending colon	690	248	26.4	2.06 (1.60–2.66)	**P < 0.001**	1.89 (1.45–2.47)	**P < 0.001**
Sigmoid colon	1662	322	16.2	1.11 (0.87–1.41)	P = 0.409	1.13 (0.88–1.45)	P = 0.350
Rectum	572	100	14.9	1		1	

Bold indicates values with statistical significance

[a]Adjusted for histology, size, morphology, location

[b]Histology-information was not available for all adenomas

in the right colon ($P < 0.001$ in location 1 and $P < 0.001$ in location 2, respectively) (Fig. 2B).

Per-Polyp and Per-Patient Analyses on Missed Advanced Adenomas

The per-polyp and per-patient analyses on missed advanced adenomas were conducted. There were totally 1518 advanced adenomas, of which 167 were missed in the first colonoscopy (158 were sized > 5 mm). The proportions of missed advanced adenomas in missed polyps, missed adenomas, missed polyps sized > 5 mm, missed adenomas sized > 5 mm were respectively, 5.1% (167/3266), 11.4% (167/1469), 16.9% (158/934), and 22.8% (158/693).

There were 1153 patients with at least one of advanced adenomas, of which 143 patients had at least one of advanced adenomas missed in the first colonoscopy. In the general population, the risk of missing advanced adenomas was 3.9% (143/3695). In patients with advanced adenomas, the risk of missing advanced adenomas was 12.4% (143/1153). The proportions of patients with missed advanced adenomas among those with missed polyps and adenomas were 8.5% (143/1678) and 15.7% (143/908).

Risk Factors Related to Patients with Missed Polyps

We further explored patient factors associated with missed polyps, as shown in Table 4. Totally, 1678 individuals were detected to have missed polyps in the first colonoscopy (45.4% of all patients). In univariate analysis, gender, age, BMI, smoking, alcohol drinking, diabetes mellitus, hypertension, and number of polyps at the first colonoscopy were associated with missed polyps. In multivariate analysis, patients with missed polyps were more likely to be male (OR 1.31; 95%CI 1.12–1.53), older (OR 1.52; 95% CI 1.32–1.75), and current smoker (OR 1.24; 95% CI 1.01–1.53). Besides, in patients with 2 or more polyps detected during the first endoscopy, the risk of missing polyps was significantly increased (OR 1.74; 95% CI 1.51–2.00). There was no statistically significant difference in miss rate between surveillance interval < 3 months and 3–6 months ($P = 0.251$).

Discussion

This retrospective study investigated the miss rate of colonic lesions during short-term repeated colonoscopy, and found that the PMR was 26.3% and the AMR was 22.4%, which was in line with previous tandem colonoscopy studies [11, 12]. Our study also indicated that deferred polypectomy ≤ 6 months did not increase the PMR. There were limited studies on the PMR in short-term repeated colonoscopy. Wang CL et al. [13] reported overall PMR of 26.5% and AMR of 24.7% during two colonoscopies with interval less than half a year in China. While a Japanese study demonstrated a higher colorectal neoplastic lesions proper detection rate of 86.5% (1151/1331) and a lower miss rate of 13.2% (175/1326) at the secondary colonoscopy in deferred polypectomy patients whose surveillance interval < 1 year [9]. The reasons for the difference were not only different medical conditions and study designs, but also varied polyp sizes. Most polyps in the Japanese study were > 5 mm, so they were less likely to be missed. While in our study, diminutive polyps made up the majority. After discounting the diminutive polyps, results were similar. These studies suggested that short-term repeated colonoscopy with deferred polypectomy did not affect polyps detection and increase CRC incidence compared with simultaneous endoscopy. Therefore, it is a feasible and cost-effective option for real-world clinical practice.

To further explore why polyps are missed in the colonoscopy and improve the colonoscopy quality, we analyzed the risk factors related to missed polyps and patients with missed polyps. In our study, we found adenomas were less frequently missed than other polyps (22.4% vs 30.7%). However, consistent with previous findings [11, 12], no significant differences were observed between these two groups in further analysis. And no matter adenomatous and non-adenomatous polyps, size, and morphology were important factors affecting the miss rate. Polyps sized < 5 mm had a significantly higher miss rate than polyps > 10 mm (35.4% vs 10.6%). However, small polyps (< 10 mm) rarely developed into high-grade dysplasia and carcinoma with a risk lower than 1.0% [14, 15]. Diminutive polyps (including adenomas) sized ≤ 5 mm without advanced histology, can be followed up without resection [10]. Besides, we reported a miss rate of 28.6% for flat polyps, which was similar to sessile polyps (28.3%) but significantly higher than pedunculated polyps (9.9%). Xiang et al. [16] revealed that AMR for flat adenomas was 44.3%, significantly higher than that of protruding adenomas (15.1%). A meta-analysis similarly indicated a difference between flat adenoma and (semi) pedunculated (34.0% vs 12.0%) [8]. Although it was still controversial whether flat polyps were more likely to malignant transformation [15, 17], they were easier to be missed for their flat shape and usually smaller size, which required the attention of endoscopists.

The location of missed polyps was mostly on the backside of folds, the inner aspect of hepatic and splenic flexures, and the distal rectum [18]. Our studies indicated polyps in the right colon were prone to be missed than that in the left colon. The PMR in the right colon were 28.9% and AMR were 26.9%. Pickhardt et al. and Wang et al. [13, 18] came to the same conclusion. The reasons were as follows. First,

Table 4 Risk factors related to patients with missed polyps

	Patients without missed lesions	Patients with missed lesions	Miss rate (%)	Univariate		Multivariate[a]	
				Odds ratio (95% confidence interval)	*P* value	Odds ratio (95% confidence interval)	*P* value
Gender, *n*							
Male	1167	1144	49.5	1.56 (1.36–1.79)	***P* < 0.001**	1.31 (1.12–1.53)	***P* = 0.001**
Female	850	534	38.6	1		1	
Age, years							
≤ 60	1248	832	40.0	1		1	
> 60	769	846	52.4	1.65(1.45–1.88)	***P* < 0.001**	1.52 (1.32–1.75)	***P* < 0.001**
Body mass index, kg/m^2[b]							
< 18.5	87	57	39.6	1		1	
18.5–25	1300	981	43.0	1.15 (0.82–1.62)	*P* = 0.421	1.02 (0.71–1.45)	*P* = 0.926
≥ 25	606	614	50.3	1.55 (1.09–2.20)	***P* = 0.015**	1.26 (0.87–1.81)	*P* = 0.225
Smoking, *n*							
Current smoker	303	349	53.5	1.51 (1.28–1.80)	***P* < 0.001**	1.24 (1.01–1.53)	***P* = 0.039**
Past smoker	114	112	49.6	1.29 (0.99–1.69)	*P* = 0.064	0.94 (0.68–1.30)	*P* = 0.709
Non-smoker	1600	1217	43.2	1		1	
Alcohol drinking, *n*							
Current drinker	272	285	51.2	1.34 (1.12–1.61)	***P* = 0.002**	0.98 (0.79–1.21)	*P* = 0.836
Past drinker	66	81	55.1	1.57 (1.13–2.19)	***P* = 0.008**	1.25 (0.85–1.85)	*P* = 0.255
Non-drinker	1679	1312	43.9	1		1	
Diabetes mellitus, *n*							
Present	144	153	51.5	1.31 (1.03–1.66)	***P* = 0.028**	1.01 (0.79–1.30)	*P* = 0.940
Absent	1873	1525	44.9	1		1	
Hypertension, *n*							
Present	560	586	51.1	1.40 (1.21–1.61)	***P* < 0.001**	1.11 (0.95–1.30)	*P* = 0.180
Absent	1457	1092	42.8	1		1	
History of tumor, *n*							
Present	74	64	46.4	1.04 (0.74–1.46)	*P* = 0.817		
Absent	1943	1614	45.4	1			
History of abdominal surgery, *n*							
Present	343	278	44.8	0.97 (0.82–1.15)	*P* = 0.723		
Absent	1674	1400	45.5	1			
Surveillance interval, *n*							
< 3 months	1834	1507	45.1	1			
3-6 months	183	171	48.3	1.14 (0.91–1.42)	*P* = 0.251		
Number of polyps during the first colonoscopy, n							
1	915	498	35.2	1		1	
≥ 2	1102	1180	51.7	1.97 (1.72–2.26)	***P* < 0.001**	1.74 (1.51–2.00)	***P* < 0.001**

[a]Adjusted for gender, age, body mass index, smoking, alcohol drinking, diabetes mellitus, hypertension, and number of polyps during the first colonoscopy

[b]Body mass index information was not available for all patients

Bold indicates values with statistical significance

polyps in the right colon were more often flat or depressed. Second, polyps in the right colon had increased rate of growth compared with that in the left. Thirdly, it was difficult for colonoscope to adequately visualize the right colon. Studies also showed that colonoscopy significantly decreased the incidence and mortality from distal CRC but not proximal CRC [19]. Therefore, reducing the miss rate of polyps on the right colon was of great significance for cancer prevention [20]. On the contrary, Heresbach et al. and Leufkens et al. [11, 12] proposed that polyps on the left colon were more frequently missed because splenic flexure and the sigmoid were challenging to fully inspect. The miss rate of colonic lesions in sigmoid colon ranged from 31.3 to 33.0% in former studies [12, 13], while in our study, it was 23.8% for polyps and 16.2% for adenomas, quite lower than other part of colons except rectum. This may be explained by the increased attention of endoscopists.

Our study reported a higher AAMR (11.0% vs 9.0%) than a previous meta-analysis [8]. Although advanced adenomas accounted for only 1.3% of the total number of polyps, the proportion of missed advanced adenomas in missed adenomas sized > 5 mm was up to 22.8%. Advanced adenomas are at greatly increased risk for CRC. A study reported that CRC incidence rates were 20, 9.1, and 7.5 per 10,000 person-years for the advanced, non-advanced, and no adenoma groups [21]. Notwithstanding the relatively lower miss rate for advanced adenomas than non-advanced adenomas, endoscopists should be aware to the risk of missing advanced adenomas and intensive surveillance colonoscopy within 3 years was strongly recommended [22].

Older male and current smokers were risk factors for missed polyps. These factors were also important risk factors for polyps and CRC [23]. One study appointed that patients with more than 2 polyps detected during the first colonoscopy had a significantly higher risk of missing other polyps [12], while another study revealed that polyps ≥ 3 were independently associated with a lower miss rate. We reported a miss rate of 51.7% for patients with multiple polyps, higher than patients with 1 polyps (35.2%), which resulted from "one-and-done" phenomenon. The detection of the first polyps may reduce the attention of the endoscopist, and multiple polyps may increase the time pressure of the endoscopist. Years after the training of endoscopists were negatively correlated with the detection of polyps, so strengthening training was also a good way to reduce the miss rate [24].

A decade or so, numerous enhanced technologies for preventing missed polyps have emerged. Retroflexion and second forward view in the right colon can yield more polyp detections [25]. Third-eye colonoscopy (TEC) largely reduced the miss rate of polyps behind the folds by enlarging the visualization area [26]. Compared with traditional white-light imaging (WLI), blue-light laser imaging (BLI) obtained a lower miss rate of colon lesions (1.6% vs 10.0%) with its advantages of magnifying observation and obtaining histopathological information [27]. Full spectrum endoscopy (FUSE) allowed viewing with a 330-degree field of view, which was superior to conventional colonoscopy [28]. The EndoCuff [29] and the G-EYE [30] were new devices to flattern the folds of the colorectal mucosa for improved vision during withdrawal and reduce the miss rate. Nowadays artificial intelligence was introduced to assist colonoscopy. Kamba et al. explored the role of computer-aided detection (CADe) device in colonoscopy and found promising results in reducing miss rate of all kinds of polyps [31]. Although a significant reduction in missed polyps during colonoscopy was observed with newer endoscopic techniques, it also increased healthcare costs [32]. More researches are needed to investigate the economic benefits of different endoscopic devices.

The strengths of our study include a large sample size, a strict selection, a detailed classification, and the adjustment of many confounding factors, which accurately reflect PMR and related risk factors in real-world practice. The present study also has several limitations. First, it was a single-center retrospective study, and selection bias cannot be avoided. Second, the seniority of endoscopists, withdrawal time, and whether patients were anesthetized during colonoscopy differed in our study. We cannot further analyze the confounding effect of the above factors. Third, due to the experimental design, we were unable to perform other colonoscopy quality indicators, such as adenoma detection rate (ADR), the total number of adenomas per colonoscopy (APC), and the total number of adenomas per positive participant (APPC) [33].

In conclusion, our study indicated that short-term repeated colonoscopy did not affect PMR and was feasible in daily clinical practice. Diminutive, flat, sessile, and right-side colon polyps were more likely to be missed. Although the risk of missing advanced adenomas was relatively low, they accounted for a large proportion in missed larger lesions and carried a higher risk of carcinogenesis. And older men, current smokers, individuals with multiple polyps were at higher risk for missed polyps. Endoscopists should pay more attention to the risk factors of PMR to reduce the incidence of CRC.

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Author's contribution Guarantor of the article: ZS. Author contributions: FJ, CY, and ZS conceived and designed the study. WJ, LX, SZ, ZL, and JW collected the data. WJ and LX analyzed and interpreted

the data. WJ, LX, and ZS drafted and revised the paper. All authors approved the final version of the manuscript.

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Declarations

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