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ORIGINAL ARTICLE

Quality of Preoperative Colonoscopy Affects Missed Postoperative Adenoma Detection in Colorectal Cancer Patients

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Abstract

Background Despite thorough preoperative screening, 19–30% of synchronous polyps or adenomas are detected after colon cancer surgery. Remnant synchronous lesions require additional colonoscopy procedures or surgery.

Aim To investigate factors of preoperative colonoscopy potentially affecting the detection of missed lesions in patients subjected to colorectal cancer surgery.

Methods Of 1147 colorectal cancer patients subjected to curative open or laparoscopic colectomy and colonoscopy at the Chungnam National University Hospital from January 2012 to December 2016, 518 patients underwent pre- and postoperative colonoscopy. The index colonoscopy was defined as the last preoperative endoscopy performed. We analyzed pre- and postoperative medical charts for colonoscopy and pathological data. The effects of patient, procedure, and tumor factors on the postoperative adenoma detection rate, advanced adenoma detection rate, and adenoma miss rate (AMR) were analyzed.

Results The overall AMR was 25.7% (95% confidence interval, 22.2–29.8%). Comparing optimal and non-optimal bowel preparation groups, the latter had greater postoperative polyp missed rate (PMR), AMR ($p < 0.01$), and AAMR ($p = 0.272$). The optimal preparation group allowed identification of more synchronous adenomas than in the fair (OR 5.72) and poor (OR 11.39) preparation groups. On univariate analysis, patient age and left-sided colectomy ($p < 0.01$) influenced AMR. Multivariate analysis showed that age, preoperative bowel preparation, and left colon resection influenced postoperative AMR.

Conclusion A better quality of index colonoscopy had a positive effect on lowering the detection rate of postoperative adenoma. Older age and suboptimal bowel preparation at the index colonoscopy and left-sided colectomy had negative effects on lowering the postoperative AMR.

Keywords Synchronous · Adenoma · Preoperative · Colonoscopy

Introduction

Identifying all lesions before colon cancer surgery is essential for proper treatment planning. Despite thorough preoperative screening, approximately 19–30% of synchronous polyps or adenomas are detected after colon cancer surgery. According to data from the UK and the USA, the proportion of advanced neoplasia in surveillance endoscopy is approximately 10–11%, and of these, 3.5% are carcinomas [1]. In a population-based study from France, 21% of cases involved synchronous adenoma with colorectal cancer (CRC) [2], and in a Dutch study, 3.9% synchronous CRCs were detected in primary CRC [3].

Despite successful procedures for primary CRC, any residual missed adenoma requires additional colonoscopic procedures or surgery [4]. Postic et al. reported a study of 156 patients who underwent surgery for colon cancer. Despite thorough preoperative colonoscopy, missed synchronous adenomas were found in 23% of resected colons, with two cases diagnosed as cancer [5]. In a study of 5157 patients by le Clercq et al., 93 metastatic CRCs were identified and approximately 43% metachronous CRCs (mCRCs) (diagnosed > 6 months after the primary CRC) were due

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to missed lesions. Of these mCRCs, 14 cases (15%) were identified within 1 year after surgery and 40.8% were found within 3 years [6]. Considering the possibility that missed adenoma in the index colonoscopy may develop into a metachronous tumor [6–9] leading to a poor prognosis in the patient, it is important to determine what factors in the preoperative index colonoscopy may affect detection of postoperative adenoma.

Approximately 40% of postoperative adenomas occur within the first two to three years [10]; thus, it is important to study factors that may influence missed adenoma detection. The aim of the present study was to investigate how the quality of preoperative colonoscopy could affect the detection of missed lesions in the remnant colon in patients subjected to CRC surgical procedures.

Methods

Patients

Of the 49,256 patients who underwent colonoscopy at the Chungnam National University Hospital (CNUH) from January 1, 2012, to December 31, 2016, we retrospectively analyzed 1147 CRC patients indicated for curative open or laparoscopic colectomy and colonoscopy. A total of 518 patients underwent colonoscopy before and after surgery (Fig. 1). We analyzed the medical records of patients who received colonoscopy including operative records, pre- and postoperative colonoscopy records, and pathology records. The exclusion criteria were as follows: (1) inappropriate bowel preparation that required additional bowel preparation, (2) incomplete examination due to stenosis, (3) sigmoidoscopy procedures only, (4) patients with concurrent chemoradiation therapy (CCRT), (5) patients subjected to total colectomy, (6) patients with > 10 polyps present in the index colonoscopy, (7) insufficient preoperative data or no preoperative colonoscopy, (8) recurrence at the anastomosis site, and (9) evidence of genetic disease. We analyzed pre- and postoperative colonoscopy, pathology data, and medical charts. The effects of bowel preparation, index colonoscopy, polyps or adenoma, physician and patient factors on postoperative adenoma detection rate (ADR), adenoma miss rate (AMR), the advanced adenoma detection rate (AADR) were analyzed. The Aronchick Bowel Preparation Scale grade of "excellent" or "good" and a Boston Bowel Preparation Scale ≥ 5 were defined as optimal bowel preparation. This study was reviewed and approved by the Chungnam National University Hospital Institutional Review Board (IRB file No. CNUH 2019-02-017) and was performed in accordance with the ethical standards set by the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Procedure

Colonoscopy was performed by four gastroenterologists with a total experience of over 10 years with an ADR of > 25%. All colonoscopy procedures were performed using the CF-H260AI colonoscope (Olympus, Tokyo, Japan). The withdrawal time was based on the time difference recorded in the endoscopy image taken from the ileocecal (IC) valve to the anus. Sufficient withdrawal time

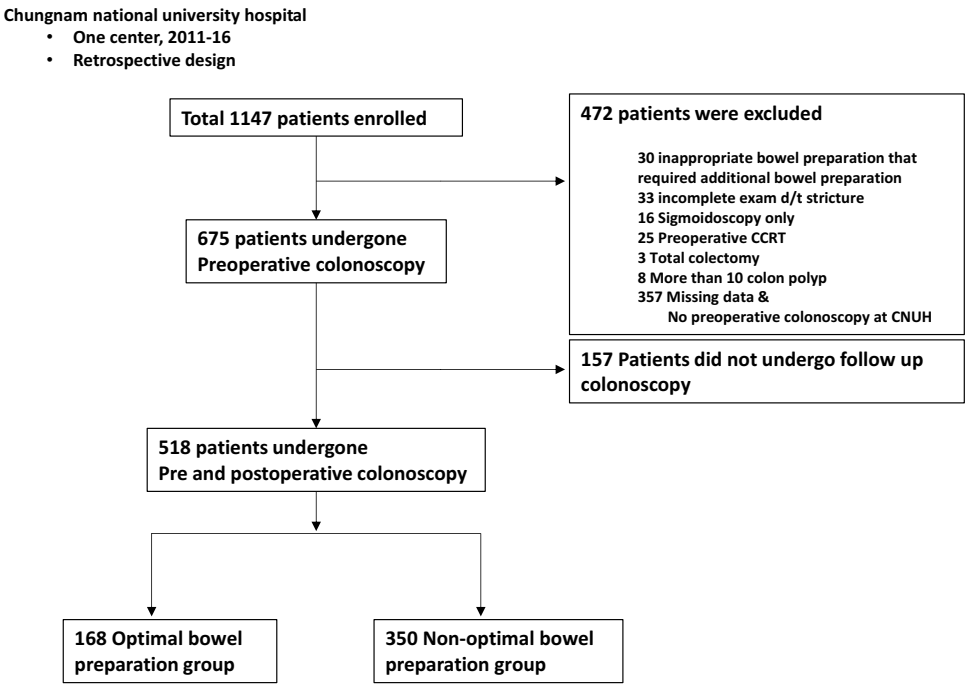

Fig. 1 Study flowchart

according to established guidelines was observed. Polyethylene glycol (PEG) 4L or PEG 2L+ascorbic acid (AA) was used for bowel preparation. The split dose regimen with oral and written educational instructions was distributed to patients as recommended by the US Multi-Society Task Force on CRC [11]. The index colonoscopy was defined as the last endoscopy performed before surgery. The quality of bowel preparation was determined during the index colonoscopy according to the Aronchick scale by two doctors, the endoscopist performing the examination and the attending fellow. During the study, bowel preparation scores were recorded using the Boston Bowel Preparation Scale and were verified by two gastroenterologists. In case of disagreement, a consensus was reached after sufficient discussion. Surveillance endoscopy was performed 1 year after surgery as recommended by the US Multi-Society Task Force on Colorectal Cancer guideline for colonoscopy surveillance [12]. All polyps were recorded by endoscopists for location, size, shape, and color in the order in which they were found. Thereafter, all polyps were removed using biopsy forceps or snares based on their size, shape, and other characteristics. After removal of the polyps, we assessed whether the area of resection was wide or the risk of bleeding was high. If necessary, hemostasis was performed using hemostatic clips or by argon plasma coagulation (APC). The ADR was defined as cases in which one or more adenomas were found in a patient receiving a first colonoscopy. Advanced adenomas were defined as adenomas characterized by size ≥ 1 cm and with tubulo-villous, villous adenoma, or high-grade dysplasia. Missed polyps were polyps that were not mentioned on colonoscopy result records but were detected on the follow-up colonoscopy. A synchronous adenoma was defined as an adenoma other than the main tumor at the index colonoscopy or an adenoma found in the first surveillance colonoscopy within 1 year after the procedure.

Statistical Analysis

The primary outcome measure was the occurrence of synchronous adenoma in the large intestine. For this analysis, we excluded cases of recurrence at the anastomotic site due to incomplete resection of the tumor during surgery. The clinical and perioperative results of the study patients were compared between the optimal and non-optimal bowel preparation group using the χ^2 test. Univariate analysis and multivariate analysis were performed with binominal logistic regression on variables identified to be significant on univariate analysis. p values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS software version 22 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Patient Characteristics

Of the 1147 CRC patients identified, we excluded 472 (41%) patients because 357 were without pre- or postoperative colonoscopy at the CNUH or had missing data, 33 had incomplete examination data due to stricture, 30 had unsatisfactory bowel preparation, 25 received preoperative concurrent chemoradiotherapy, 16 received preoperative sigmoidoscopy only, eight had > 10 colon polyps, and three received total colectomy (Fig. 1).

The median age of patients was 72 ± 10.16 years; 385 patients (74.3%) were > 60 years of age, and 343 (66.2%) were males. With regard to the American Society of Anesthesiologists (ASA) score, 347 (67%) patients scored < 2 points. Colonoscopy-related factors were assessed as the mean time interval between colectomy and time to first surveillance colonoscopy of 373.3 days (95% confidence interval [CI], 361.8–384.3) and as the withdrawal time for index colonoscopy of 13.68 min (95% CI, 13.1–14.27). Overall, 248 (47.9%) patients used PEG 4L as the bowel preparation method and 270 (52.1%) patients used PEG 2L+AA. The Aronchick score was used as the evaluation scale for bowel preparation of the preoperative colonoscopy. Excellent and good scores were 168 (32.4%), fair 189 (36.5%), and poor 161 (31.1%) (Table 1). Overall, 204 patients (39.1%) received proximal colectomy and 314 patients (60.9%) received distal colectomy. Preoperative colonoscopy revealed differentiation of the primary cancers with 16 well-differentiated lesions, 432 moderately differentiated, 45 poorly differentiated, and 25 other forms. This distribution was similar to the prevalence described in previous studies. Of the 675 patients, 518 patients received follow-up visits, while 157 patients did not.

Pre- and Postoperative Colonoscopy Results

As shown in Table 2, the per-patient analysis indicated that in the initial colonoscopy, the PDR was 48.2 (42.9–53.3) versus 37.5% (30.3–45.2, $p < 0.01$) and ADR was 38.0 (32.7–43.3) versus 31.5% (24.4–39.1, $p = 0.03$) in the optimal group and non-optimal group, respectively, and both the PDR and ADR were higher in the optimal group than in the non-optimal group. The AADR did not differ between the two groups. At the first follow-up colonoscopy, the PMR was 11.0 (6.0–16.0) versus 49.0% (43.0–53.0, $p < 0.01$) and AMR was 5.9 (2.5–10.0) versus 35.2% (30.5–40.4, $p < 0.01$) in the optimal and non-optimal groups, respectively, and both PMR and AMR were

Table 1 Baseline characteristics

	$n=518$	%
Patient-related characteristics		
Age		
< 60	133	25.7
≥ 60	385	74.3
Sex		
Male	343	66.2
Female	175	33.8
BMI (kg/m^2)		
< 23.0	146	41.2
23.0–25.0	99	28.0
> 25.0	109	30.8
Underlying disease		
DM	100	19.3
HTN	151	29.1
Smoking habits		
Present	77	14.8
Never	307	59.3
Past	134	25.9
Alcohol consumption		
Present	62	12.0
Never	290	55.9
Past	166	32.1
ASA score		
1, 2	347	67.0
3 ≤	171	33.0
Procedure-related characteristics		
Bowel preparation regimen		
PEG 4L	248	47.9%
PEG2L+AA	270	52.1%
Aronchick score		
Excellent	51	9.8
Good	117	22.6
Fair	189	36.5
Poor	161	31.1
Average withdrawal time	13.68 min	13.1–14.3 min
Average days to follow-up colonoscopy	373 days	361.9–384.7 days
Tumor-related characteristics		
Type of colectomy		
Right-sided colectomy	188	36.3
Left-sided colectomy	330	63.7
Biopsy		
Well differentiated	25	4.8
Moderately differentiated	439	84.7
Poorly differentiated	15	2.9
Mucinous	12	2.3
Others	27	5.3
Synchronous adenoma	133	25.6
Synchronous advanced adenoma	22	4.2
Synchronous cancer	1	0.2

BMI (Body mass index), American Society of Anesthesiologist (ASA) score

higher in the non-optimal group. There was no difference between the two groups in terms of the AAMR.

There was no difference in the follow-up period between the optimal bowel preparation group and the non-optimal bowel preparation group.

The number of total polyps found was 359, of which 96 (26.7%) were diminutive polyps < 5 mm in length, 66 (18.4%) were polyps ≥ 5 mm and < 1 cm, and 15 (4.1%) polyps were ≥ 1 cm.

The interval between the index colonoscopy and the follow-up endoscopy was 374.95 days (95% CI, 358.96–387.89) in the group in which the polyps were found. The number of days between the index colonoscopy and the endoscopic interval was 374.95 (95% CI, 352.24–402.03) in the group in which polyps were not identified, and there was no difference in the number of follow-up days between the two groups ($p=0.884$). The total number of missed adenomas was 240 (46.3%): 18 adenomas in the adequate bowel preparation group and 222 adenomas in the inadequate bowel preparation group. Among patients with adequate bowel preparation, the number of cases with at least one adenoma on repeat colonoscopy was 10, 5.9% (95% CI 2.5–10.0), and five patients (4.3%) had no polyps at the index colonoscopy; the mean time between colonoscopies was 376.2 (95% CI 358.14–397.17) days. Among patients with inadequate bowel preparation, 68 patients (31.3%) had no polyps detected on initial colonoscopy and the mean time between colonoscopies was 372.0 (95% CI 358.6–386.6) days.

Factors that Affected the Detection of Missed Adenoma

Table 3 lists the analysis of patients, colonoscopy, and tumor factors that affected missed adenoma detection. Factors independently affecting missed adenoma detection included older age of the patient at the time of colorectal surgery, non-optimal bowel preparation, left-sided colectomy (LCR), withdrawal time, and a larger polyps size found at the index colonoscopy. The incidence of missed adenomas was found to be higher in males, obese patients, and smokers with high body mass index, but differences were not statistically significant. There were no statistically significant differences in terms of flat and elevated polyps among those detected during colonoscopy following surgical procedures. In the multivariate analysis of these factors, the incidence of postoperative adenomas was higher in patients with older age, and in patients with non-optimal bowel preparations, and LCR.

Discussion

Our study showed that preoperative ADR could be improved, and the postoperative AMR could be reduced by a high-quality index colonoscopy. When the practitioner's

Table 2 Initial and surveillance colonoscopic result according to bowel preparation group

	Optimal group ($n=168$)	Non-optimal group ($n=350$)	p value*
Initial colonoscopy			
Per-patient analysis			
PDR (%)	48.2 (42.9–53.3)	37.5 (30.3–45.2)	0.013
ADR (%)	38.0 (32.7–43.3)	31.5 (24.4–39.1)	0.03
AADR (%)	9.5 (5.2–14.0)	13.1 (9.6–17.1)	0.25
Per-polyp analysis			
Polyps per patient	1.252 (1.054–1.473)	0.823 (0.589–1.073)	0.01
Adenomas per patient	0.795 (0.650–0.959)	0.548 (0.387–0.726)	0.04
Advanced adenomas per patient	0.129 (0.057–0.210)	0.183 (0.129–0.246)	0.46
Surveillance colonoscopy			
Per-patient analysis			
PDR (%)	11.0 (6.0–16.0)	49.0 (43.0–53.0)	< 0.01
ADR (%)	5.9 (2.5–10.0)	35.2 (30.5–40.4)	< 0.01
AADR (%)	3.0 (0.6–5.8)	4.6 (2.6–6.9)	0.272
Per-polyp analysis (95% CI)			
Polyps per patient	0.266 (0.113–0.435)	1.009 (0.858–1.174)	0.028
Adenomas per patient	0.145 (0.048–0.258)	0.700 (0.574–0.839)	0.003
Advanced adenomas per patient	0.040 (0.008–0.081)	0.050 (0.028–0.079)	0.709

PDR polyp detection rate, *ADR* adenoma detection rate, *AADR* advanced adenoma detection rate

*Chi-square test

Table 3 Univariate and multivariate analysis for the adenoma detection at first surveillance colonoscopy

	Univariate (95% CI)	p value*	Multivariate (95% CI)	p value*
Age	1.031 (1.010–1.053)	0.004	1.021 (1.001–1.043)	0.044
Sex	0.654 (0.423–1.011)	0.056	0.820 (0.535–1.258)	0.364
BMI (kg/m^2)	1.083 (0.860–1.363)	0.499		
DM	1.347 (0.849–2.139)	0.206		
HTN	0.736 (0.495–1.095)	0.130		
Smoking	0.939 (0.482–1.830)	0.854		
Alcohol	1.075 (0.575–2.011)	0.820		
ASA score	1.026 (0.624–1.687)	0.920		
Aspirin prescribed Hx.	0.712 (0.198–2.561)	0.603		
Procedure factor				
Bowel preparation				
Boston score	0.657 (0.558–0.774)	< 0.001		
Aronchick score	2.530 (1.940–3.301)	< 0.001	2.614 (2.039–3.352)	< 0.01
Optimal group	Reference (1.0)			
Non-optimal group	7.870 (4.624–13.397)	< 0.001		
Fair	5.729 (3.245–10.116)	< 0.001		
Poor	11.397 (6.379–20.363)	< 0.001		
Average withdrawal time	1.036(1.007–1.065)	0.013	1.015(0.985–1.045)	0.329
Tumor factor				
Polyp size	2.127 (1.864–2.427)	< 0.001		
Polyp color	4.156 (0.584–29.594)	0.155		
Polyp shape	–	1.000		
RCR	1.0			
LCR	1.800 (1.089–2.974)	0.22	1.742 (1.023–2.965)	0.041

*Binominal logistic regression test

high ADR and adequate withdrawal time were objectively controlled, an inadequate bowel preparation, older age, and cancer location side at index colonoscopy affected the high AMR in the multivariate analysis (Table 3). To improve the quality of index colonoscopy, a comprehensive evaluation of patient, tumor, and procedural factors should be performed. In many previous studies, a variety of patient and tumor factors have been considered to affect the discovery rate of synchronous or missed polyps. In terms of patient factors, older age [13, 14], male sex [15], obesity, and history of smoking have been implicated [16]. Tumor factors such as location of tumor [17], diminutive and sessile synchronous polyps, and mucinous histology [7] were considered independent risk factors for higher adenoma detection. Procedural factors such as the ADR and cecal intubation rate were representative of quality indicators of colonoscopy. In addition, the experience of the colonoscopist [14] as indicated by a recent review article, whereby introducing quality indicators [18], sufficient withdrawal time [19, 20], adequate bowel preparation quality [21, 22], and adherence rate to surveillance guidelines have also been impacted as relevant factors [18].

According to the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Digestive Oncology (ESDO) guidelines for endoscopic surveillance following resection for CRC published in 2019 [10], the incidence of synchronous CRC is reported to be about 4.5% and synchronous adenoma is 21% in CRC patients. According to these guidelines, an incomplete colonoscopy, rapid withdrawal time, and suboptimal ADR result in higher risk of post-colonoscopy CRCs. In another guideline [23], adequate bowel preparation, cecal intubation rate (> 90%), ADR (≥ 25%), withdrawal time, and PDR are presented as indicators of quality.

With regard to bowel preparation, Chokshi et al. [24] reported 133 colonoscopy cases that had to be repeated due to inadequate bowel preparation at the screening colonoscopy (33.8% of ADR, 18% of AADR, per-adenoma miss rate was 47.9%). In this study, in which surveillance colonoscopy was performed within 1 year after CRC surgery, the postoperative AMR was 25.6% and the postoperative missed cancers amounted to 0.2%. The AMR was 5.9% in the optimal bowel preparation group and 35.2% in the non-optimal bowel preparation group. Overall, 4.2% of patients had an advanced adenoma and there was no difference between the two groups. Considering that the gastroenterologists of this study had a high ADR with sufficient withdrawal time, the impact of the bowel preparation in the index colonoscopy on AMR is clearly shown. Patients who had undergone non-optimal colonoscopy had much lower preoperative ADR and higher postoperative AMR (Table 2).

With regard to the size of polyps, a meta-analysis including 15,000 colonoscopies showed that the AMR decreased with increasing size of the adenoma [8]. In a study evaluating synchronous lesions found in pathologic tissues after CRC surgery, small (< 1 cm) significant polyps including adenoma and advanced adenoma was missed at a clinically significant level [5]. In this study, the percentage of missed adenomas < 5 mm in size was 54.5%.

For the ADR, the importance of surveillance colonoscopy has been demonstrated previously. In a cohort study of adenoma surveillance [25], the incidence of CRC was significantly reduced in the group undergoing endoscopy compared to the group without endoscopy, particularly when the first surveillance endoscopy was performed. In other studies published to date, the ADR of the first surveillance colonoscopy was reported to be 19–30% [26–28], and the AMR was reported to be 15–24% in tandem colonoscopies performed by others on the same day, which demonstrates the importance of ADR [29–31]. It is well known that the ADR of the colonoscopist and the age of the patient are important factors in the detection of interval cancer [13]. In a recent study, a colonoscopist with a high ADR in index colonoscopy showed a strong association with high ADR on the follow-up surveillance colonoscopy [28], which suggests that the colonoscopist plays a major role in postoperative ADR. In the present study, factors such as bowel preparation and age at the time of preoperative colonoscopy had a significant effect on postoperative AMR when a colonoscopist with an ADR > 25% performed the colonoscopy. The strength of this study was that the effects of index colonoscopy factors on the postoperative AMR of surveillance colonoscopies were analyzed in situations where the colonoscopist's high ADR and adequate withdrawal time were objectively controlled. Considering that the ADR of the screening colonoscopy is associated with the ADR in CRC surveillance colonoscopy [28], colonoscopists should strive to maintain high ADR during all endoscopic procedures.

With regard to the primary colon cancer location side, the right colon is derived from within the embryonic midgut, while the left colon is derived from the embryonic hindgut. The genetic [32] and molecular characteristics of the large intestine differ [33, 34]. A previous study has shown that synchronous [33–35] and metachronous [36] adenomas are found more frequently in LCR-receiving groups. Particularly in the case of synchronous adenoma, the risk is increased when it is serrated, sessile, or has multiple characteristics. We analyzed the frequency of synchronous adenoma in the right and left colon: Patients receiving LCR had a risk of missed adenoma of approximately 1.74-fold (95% CI, 1.02–2.97) compared to patients receiving right-sided colectomy (RCR).

Among these factors, high-quality colonoscopy should be achieved by maintaining a high level of modifiable factors such as constant efforts to maintain the high ADR by the colonoscopist, adequate bowel preparation, and adequate withdrawal time. In addition, the endoscopic procedure

should be performed considering non-modifiable risk factors such as the age of the patient and the operation approach for the patient (LCR vs RCR).

According to the colonoscopy surveillance after CRC resection guidelines published by the US Multi-Society Task Force, two-thirds of metachronous cancers are asymptomatic, with an incidence rate of 0.3–0.35% per year. Metachronous cancer may develop at any time, even decades after the operation of the index colon cancer, and the risk of the all of the remaining colon is increased; thus, precise and high-quality preoperative colonoscopy is necessary for prevention. Therefore, we should pay close attention to these factors when performing preoperative colonoscopy because it may negatively affect the detection of synchronous lesions if the factors affecting the quality of colonoscopy are not met.

This study has some limitations. First, because of the retrospective nature of the study, the possibility of selection bias should be considered. Approximately 25% of patients did not receive the surveillance colonoscopy due to follow-up loss. Second, although our hospital is the only tertiary hospital in the metropolitan city, it cannot be representative of all Asian individuals.

In conclusion, high quality in index colonoscopy has a positive effect on lowering the postoperative adenoma. Older patients, poor bowel preparation at the index colonoscopy, and LCR were associated with higher rates of missed adenomas after colon cancer surgery.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study was reviewed and approved by the Chungnam National University Hospital Institutional Review Board (IRB file No. CNUH 2019-02-017).

Informed consent This was a retrospective study using medical records, and personal information protection measures were appropriately applied so that the informed consent of the participant could be exempted.

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