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Journal

Gut and Liver, 16(5)

Authors

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Publication Date

2022-09-15

DOI

10.5009/gnl210287

Peer reviewed

*Gut and Liver*
https://doi.org/10.5009/gnl210287
pISSN 1976-2283 eISSN 2005-1212

Original Article

# Correlation between Surrogate Quality Indicators for Adenoma Detection Rate and Adenoma Miss Rate in Qualified Colonoscopy, CORE Study: KASID Multicenter Study

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**Article Info**
**Received** June 29, 2021
**Revised** September 16, 2021
**Accepted** October 1, 2021
**Published online** December 21, 2021

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**Background/Aims:** The adenoma detection rate (ADR) does not reflect the complete detection of every adenoma during colonoscopy; thus, many surrogate indicators have been suggested. This study investigated whether the ADR and surrogate quality indicators reflect the adenoma miss rate (AMR) when performing qualified colonoscopy.

**Methods:** We performed a prospective, multicenter, cross-sectional study of asymptomatic examinees aged 50 to 75 years who underwent back-to-back screening colonoscopies by eight endoscopists. The ADR and surrogate quality indicators, including polyp detection rate, total number of adenomas per colonoscopy, additional adenomas found after the first adenoma per colonoscopy (ADR-Plus), and total number of adenomas per positive participant, were calculated for the prediction of AMR.

**Results:** A total of 371 back-to-back colonoscopies were performed. There was a significant difference in ADRs (range, 44% to 75.4%; p=0.024), polyp detection rates (range, 56% to 86.9%; p=0.008) and adenomas per positive participants (range, 1.19 to 2.30; p=0.038), and a tendency of a difference in adenomas per colonoscopy (range, 0.62 to 1.31; p=0.051) and ADR-Plus (range, 0.13 to 0.70; p=0.054) among the endoscopists. The overall AMR was 20.1%, and AMRs were not different (range, 13.9 to 28.6; p>0.05) among the endoscopists. No quality indicators were significantly correlated with AMR. The number of adenomas found during the first colonoscopy was an independent factor for increased AMR (odds ratio, 1.79; p<0.001).

**Conclusions:** The colonoscopy quality indicators were significantly different among high-ADR endoscopists, and none of the quality indicators reflected the AMR of good quality colonoscopy performances. The only factor influencing AMR was the number of adenomas detected during colonoscopy. **(Gut Liver 2022;16:716-725)**

**Key Words:** Colonoscopy; Adenoma; Miss rate; Quality indicator

## INTRODUCTION

As the current standard for endoscopic performance, the adenoma detection rate (ADR) is an independent quality indicator for colonoscopy.[1,2] According to a study based on the Polish colorectal cancer screening program in 2010, patients who underwent colonoscopy by endoscopists with <20% ADRs had a 10-fold higher risk for interval colorectal cancer (CRC) than those who underwent colonoscopy by endoscopists with >20% ADRs.[3] Recently, the American Society for Gastrointestinal Endoscopy has recommended an ADR target of at least >25% (30% for males and 20% for females) for average-risk populations.[2]

Although ADR is a robust quality indicator, some stud-

ies show the limitation of ADR. Wang *et al.*[4] revealed that ADR alone is not sufficient to fully measure screening colonoscopy quality. According to another research, ADR was inversely associated with interval CRC.[5] In several recent studies, adenoma miss rate (AMR) is >20% in endoscopists who have >40% ADR.[6-8] This can be explained by the result of ADR's unique "one and done" strategy which can reduce the attention of endoscopists after discovering one adenoma during colonoscopy when calculating ADR.

Regarding the evidences that ADR does not properly reflect AMR, various surrogate quality indicators have been suggested such as polyp detection rate (PDR),[9,10] the total number of adenomas per colonoscopy (APC),[2,8] recently reported total number of adenomas per positive participant (APP)[4,8] and additional adenomas found after the first adenoma per colonoscopy (ADR-Plus)[4] for reflecting undetected adenoma during colonoscopy.

A recent study by Aniwan *et al.*[8] conducted with a cross-sectional design for the direct comparison of surrogate quality indicators versus ADR in the prediction of AMR showed that only APP exhibited a strong inverse correlation with AMR. They suggested that a surrogate quality indicator could be useful for predicting AMR only when a high ADR (>40%) is achieved. Unlike this study, a recent systematic review and meta-analysis based on studies showing various ADR reported that ADR and APC were independently associated with AMR in qualified colonoscopy.[11]

Quality indicators that affect AMR have been derived differently for each study, and still, we are not certain which quality indicators best reflect AMR or whether there is a quality indicator that can accurately reflect AMR. In the present study, we conducted a reconstruction study of the research by Aniwan *et al.*,[8] using a multicenter, back-to-back colonoscopy model to evaluate the correlation of surrogate quality indicators (PDR, ADR-Plus, APP, and APC) for ADR and AMR, and also investigate factors affecting AMR.

## MATERIALS AND METHODS

### 1. Study population

We conducted a multicenter, cross-sectional study during the period of July 2018 to June 2020. This study was approved by each review board of the participating institutions, including Soonchunhyang University (IRB number: SCHUH 2016-08-032) and was registered on an open clinical trial registry (www.clinicaltrials.gov, NCT03919487). Institutional review board approved this study in September 2016, but patient enrollment was possible from July 2018 due to the delay in participation in the study by five participating institutions. All asymptomatic participants aged 50 to 75 years undergoing screening colonoscopy

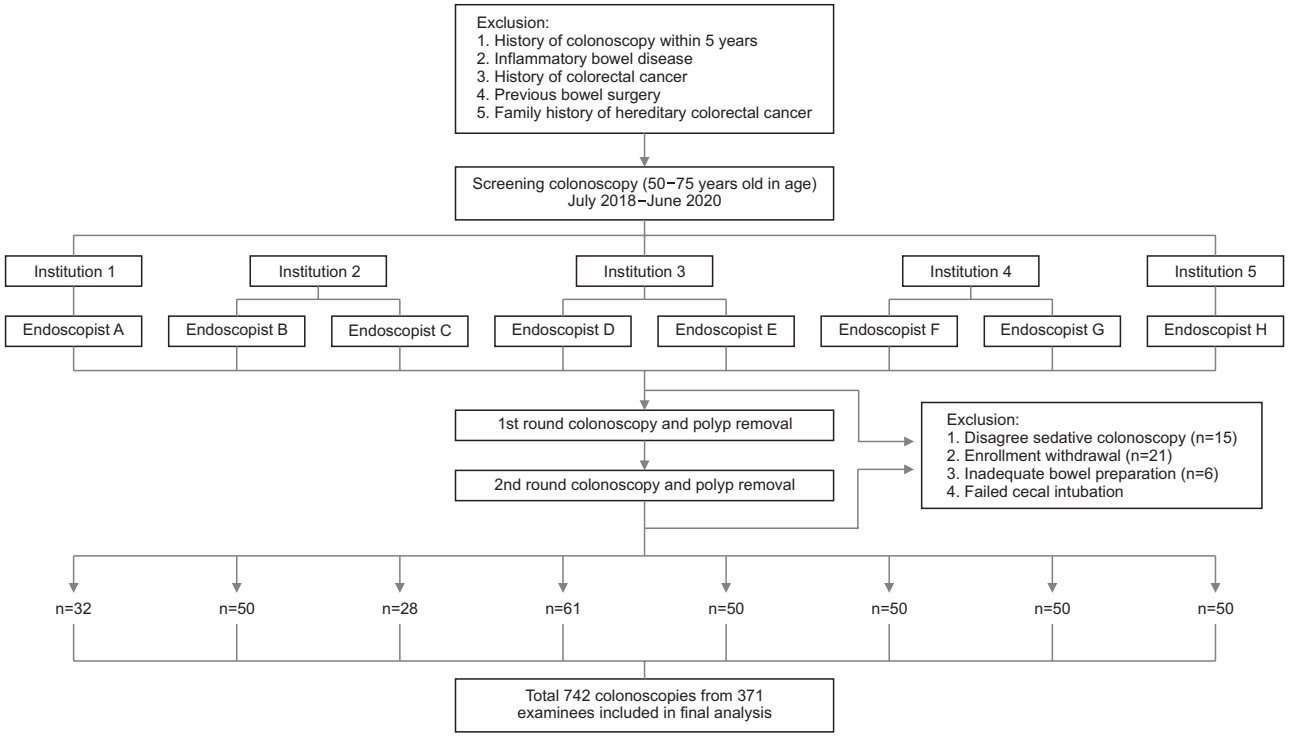


**Fig. 1.** Study flow diagram. Eight endoscopists from five institutions performed screening colonoscopies from July 2018 to June 2020. A total of 742 back-to-back colonoscopies were performed in 371 examinees.

with no previous colonoscopy experience or no history of colonoscopy within the last 5 years were recruited through outpatient clinics of referred hospitals. Participants were excluded if they had inflammatory bowel disease, a family history of hereditary CRC (≥2 first degree relatives with CRC or at least one first degree relative with CRC before the age of 60), a history of CRC, previous colorectal surgery, bowel preparation status of Boston Bowel Preparation Scale (BBPS) ≤3, inadequate bowel preparation, failed cecal intubation or refused sedative colonoscopy (Fig. 1). All subjects provided written informed consent.

### 2. Back-to-back colonoscopic procedure

According to statistical sample calculation, eight endoscopists from five university hospitals performed back-to-back colonoscopies. All endoscopists were faculty members with over 5 years of professional experience performing colonoscopy. All participants complied to the split bowel preparation method which is a bowel cleansing regimen divided between the night prior and the morning of the colonoscopy. Oral and written education for bowel preparation was delivered by an educated nurse in each institution. Bowel preparation was performed with different agents using 4 L polyethylene glycol, 2 L polyethylene glycol with ascorbic acid, and sodium picosulfate with magnesium citrate for each institution. All colonoscopies were performed within 3 to 4 hours after finishing bowel preparation.

Every examinee underwent colonoscopies under conscious sedation in the left lateral decubitus position. $CO_2$ gas was used for insufflation. Back-to-back colonoscopies were performed by the same endoscopist. After the endoscopists reached the ileocecal area, they took photos and started recording the withdrawal time using a stopwatch. The withdrawal time should be at least 6 minutes, excluding the time necessary for any polyp removal. The quality of bowel preparation was rated by the endoscopists based on the BBPS during withdrawal time. Although the examinees with BBPS ≤3 were excluded from the study, inadequate bowel preparation was defined as BBPS <6 or any region scores <2.[12] Forward viewing colonoscopes were used for the colonoscopies, CF-HQ290 (Olympus Optical Co., Ltd., Tokyo, Japan) and an identical type of colonoscope was used during the second colonoscopy. All participants underwent back-to-back colonoscopy examination, with a conventional colonoscopy followed immediately by a second endoscopy. Both the first and second colonoscopies were performed with the same settings by the same examiner. In the first examination, the colonoscope was inserted into the cecum, and polyps identified during insertion and withdrawal were counted and removed. Numerous tiny (<5 mm in size) hyperplastic polyps (based on narrow band imaging with near focus view) in the rectum and sigmoid colon were documented by photography and were not removed.

During the second examination, any remaining polyps that were not found in the first examination were recorded according to colonic location and endoscopic appearance, and were defined as "missed polyp." Endoscopic appearance was determined according to the Japanese classification and was categorized into four types: pedunculated, sessile, flat or depressed, and laterally spreading tumors.[13] Colonic location was divided into two groups; proximal colon (cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure) and distal colon.

Again, all remaining polyps, except tiny hyperplastic polyps of the rectum and sigmoid colon, were removed. All resected polyps were reviewed by a gastrointestinal pathologist. The pathological diagnosis of polyps was classified as non-neoplastic and neoplastic polyps. The neoplastic polyps were categorized as adenomas, advanced adenomas, and colorectal carcinomas as described elsewhere. Advanced adenoma was defined as an adenoma with villous features (>25%), size of 1.0 cm or more, or high-grade dysplasia.[14] Sessile serrated lesions were excluded from the analysis of missing adenoma.

### 3. Quality indicators of colonoscopy

ADR was calculated as the number of participants with ≥1 adenoma detected during the first colonoscopy divided by the number of first colonoscopies. PDR was calculated as the number of participants with ≥1 polyp including adenoma detected during the first colonoscopy divided by the number of first colonoscopies. APC rate was calculated as the number of adenomas detected during the first colonoscopy divided by the number of first colonoscopies. ADR-Plus was calculated as the number of additional adenomas detected after the first adenoma during the first colonoscopy divided by the number of first colonoscopies. APP was calculated as the number of total adenomas detected during the first colonoscopy divided by the number of adenoma-positive participants during the first colonoscopy. AMR was calculated as the number of adenomas missed in the first colonoscopy divided by the total number of adenomas detected during both the first and second colonoscopies.

### 4. Statistical analysis

We calculated the sample size based on each correlation coefficient "r" between AMR and each quality indicator. Based on the reference study, r was –0.99 to –0.25 and mean r was 0.75 with 0.05 of the significance probability and 80% of power.[8] It was found that at least eight endos-

copists, and 50 participants per each endoscopist were required. We calculated descriptive statistics for the demographic characteristics of age, gender, smoking history, body mass index, and colon cancer family history, and the colonoscopic variables of withdrawal time, cecal intubation rate, and the quality of bowel preparation. In terms of the quality of the colonoscopies, the indicators were calculated as averages per endoscopist. We used one-way analysis of variances and chi-square tests for the continuous and categorical variables, respectively. To assess the qualities of the colonoscopies as determined by the AMR, we calculated the PDR, ADR, APC, ADR-Plus and APP for each endoscopist and compared the measures with the AMR using the Spearman correlation coefficients. A two-sided p-value <0.05 was considered significant. Demographic findings such as age, gender, body mass index, smoking history, colon cancer family history, bowel preparation, withdrawal time, and the number of adenomas found during the first colonoscopy were included in a logistic regression analysis to identify the variables associated with missed lesions. In variable selection, a stepwise selection method was performed. Finally, we used power calculations to identify the results ("pwr" and "powerMediation" packages in R version 3.6.3). Statistical analyses were performed by Rex version 3.0.3 (RexSoft Inc., Seoul, Korea) and SPSS statistics software version 22.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

### 1. General characteristics

Initially, each of the eight endoscopists attempted to perform back-to-back colonoscopy of 50 patients, but two endoscopists (A and C in Tables) failed to enroll 50 back-to back colonoscopies during the study period. However, we did not exclude the data of these two endoscopists, but included them in the calculation for colonoscopy quality. Table 1 displays the characteristics of the participants categorized according to the eight endoscopists. A total of 742 colonoscopies were performed in 371 back-to-back colonoscopy procedures during the study period. The mean age of the participants was 58.5±7.4 years, 181 (48.8%) were male. Each endoscopist reported a 100% cecal intubation rate in both of the first and second colonoscopies performed.

Two of the endoscopists were female doctors (B and E in Tables) and there was a significant difference in the sex ratio of the examinees according to the endoscopist; 28.6% of the examinees of endoscopist B were male participants and 34% of those of endoscopist E were male (p<0.001). Thus, the proportion of smokers was significantly lower in

**Table 1.** Characteristics of the Participants Categorized by Endoscopist

| Characteristics | Endoscopist (number of back-to-back colonoscopies) | | | | | | | | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | A (n=32) | B (n=50) | C (n=28) | D (n=61) | E (n=50) | F (n=50) | G (n=50) | H (n=50) | |
| Male sex | 13 (40.6) | 14 (28.6) | 17 (60.7) | 35 (57.4) | 17 (34.0) | 35 (70.0) | 25 (50.0) | 25 (50.0) | <0.001 |
| Age, yr | 58.5±7.7 | 59.5±6.9 | 61.6±7.1 | 58.1±9.8 | 57.1±5.7 | 58.1±7.4 | 58.7±6.9 | 58.6±7.5 | 0.316 |
| Smoker | 7 (21.9) | 4 (8.0) | 10 (35.7) | 12 (19.7) | 5 (10.0) | 20 (40.0) | 11 (22.0) | 9 (18.0) | 0.001 |
| Colon cancer family history | 1 (3.1) | 3 (6.0) | 0 | 0 | 0 | 0 | 1 (2.0) | 1 (2.0) | 0.191 |
| Body mass index, kg/m$^2$ | 24.5±3.6 | 23.3±3.3 | 23.2±2.9 | 24.5±2.8 | 24.2±2.9 | 25.0±2.8 | 23.6±2.9 | 23.8±2.9 | 0.051 |
| Adequate bowel preparation | 29 (90.6) | 49 (98.0) | 28 (100) | 60 (98.4) | 49 (98.0) | 50 (100) | 48 (96.0) | 50 (100) | 0.114 |
| Withdrawal time, min | 8.4±2.5 | 9.5±1.6 | 14.2±4.2 | 11.8±5.7 | 8.8±3.3 | 7.4±1.3 | 8.8±2.6 | 9.9±4.4 | <0.001 |
| Patients with multiple polyps | 9 (28.1) | 7 (14.0) | 8 (28.6) | 26 (42.6) | 16 (32.0) | 15 (30.0) | 13 (26.0) | 15 (30.0) | 0.124 |

Data are presented as number (%) or mean±SD.

**Table 2.** Numbers of Adenomas Detected by Each Endoscopist

| Parameter | Endoscopist (number of back-to-back colonoscopies) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | A (n=32) | B (n=50) | C (n=28) | D (n=61) | E (n=50) | F (n=50) | G (n=50) | H (n=50) |
| First colonoscopy finding | | | | | | | | |
| No. of adenoma | 25 | 31 | 33 | 80 | 62 | 49 | 36 | 46 |
| Participants with adenoma | 21 | 22 | 18 | 46 | 27 | 24 | 26 | 30 |
| Additional number of adenoma after 1st detection of adenoma | 4 | 9 | 15 | 34 | 35 | 25 | 10 | 16 |
| Missed finding from the 1st colonoscopy | | | | | | | | |
| No. of missed adenoma | 10 | 3 | 7 | 21 | 18 | 6 | 12 | 14 |
| Participants with missed adenoma | 9 | 3 | 4 | 15 | 14 | 5 | 9 | 10 |

**Table 3.** Quality Indicators of Each Endoscopist

| Total | Endoscopist (number of back-to-back colonoscopies) | | | | | | | | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | A (n=32) | B (n=50) | C (n=28) | D (n=61) | E (n=50) | F (n=50) | G (n=50) | H (n=50) | |
| ADR, No. (%) | 21 (65.6) | 22 (44.0) | 18 (64.3) | 46 (75.4) | 27 (54.0) | 24 (48.0) | 26 (52.0) | 30 (60.0) | 0.024* |
| PDR, No. (%) | 21 (65.6) | 28 (56.0) | 22 (78.6) | 53 (86.9) | 35 (70.0) | 28 (56.0) | 31 (62.0) | 33 (66.0) | 0.008* |
| APC | 0.78 | 0.62 | 1.18 | 1.31 | 1.24 | 0.98 | 0.72 | 0.92 | 0.051† |
| ADR-P | 0.13 | 0.18 | 0.54 | 0.56 | 0.70 | 0.50 | 0.20 | 0.32 | 0.054† |
| APP | 1.19 | 1.41 | 1.83 | 1.74 | 2.30 | 2.04 | 1.38 | 1.55 | 0.038† |
| AMR, % | 28.6 | 8.8 | 17.5 | 20.8 | 22.5 | 10.9 | 25.0 | 23.3 | 0.271* |

ADR, adenoma detection rate; PDR, polyp detection rate; APC, total number of adenomas per colonoscopy; ADR-P, additional adenomas found after the first adenoma per colonoscopy; APP, a total number of adenomas per positive participant; AMR, adenoma miss rate.

*The chi-square test was conducted; †One-way analysis of variance test was conducted.

the examinee groups of endoscopists B and E (p=0.001).

Adequate bowel preparation rate was more than 90% in all groups. The mean withdrawal time was 9.7±4.0 minutes. All of the endoscopists satisfied the colonoscopy withdrawal time of more than 6 minutes. However, there was a significant difference between the endoscopists regarding withdrawal time (p<0.001).

### 2. Adenoma detection and surrogate quality indicators

The number of adenomas detected during the colonoscopies are shown in Table 2. The total number of adenomas found during the first colonoscopy was 362 including one adenocarcinoma, from 371 patients and the prevalence of adenomas was 57.7% (214/371) of participants.

There were significant differences in the ADRs, PDRs, APPs between each endoscopist (Table 3). The ADRs of endoscopists A, B, C, D, E, F, G, and H were 65.6%, 44%, 64.3%, 75.4%, 54%, 48%, 52%, and 60%, respectively (p=0.024). The PDRs of endoscopists A, B, C, D, E, F, G, and H were 65.6%, 56%, 78.6%, 86.9%, 70%, 56%, 62%, and 66%, respectively (p=0.008). The APPs of endoscopists A, B, C, D, E, F, G, and H were 1.19, 1.41, 1.83, 1.74, 2.30, 2.04, 1.38, and 1.55, respectively (p=0.038). Both APCs (p=0.051) and ADR-Ps (p=0.054) tended to be different among the endoscopists.

### 3. AMR results

The number of missed adenoma found during the second colonoscopy was 91 and the overall AMR was 20.1%. There was no significant difference in the AMR of each endoscopist and the AMRs of each endoscopist were 28.6%, 8.8%, 17.5%, 20.8%, 22.5%, 10.9%, 25%, and 23.3% (p=0.271) (Table 3). Forty-eight (52.7%) missed adenomas

**Table 4.** Correlation between Quality Indicators with AMR and ADR

| Quality indicators | Correlation with AMR | | | Correlation with ADR | | |
|---|---|---|---|---|---|---|
| | Endoscopist (n) | r | p-value* | Endoscopist (n) | r | p-value* |
| ADR | 8 | 0.476 | 0.243 | | | |
| AMR | | | | 8 | 0.476 | 0.243 |
| PDR | 8 | 0.204 | 0.629 | 8 | 0.826 | 0.011 |
| APC | 8 | −0.095 | 0.840 | 8 | 0.571 | 0.151 |
| APP | 8 | −0.357 | 0.389 | 8 | −0.048 | 0.935 |
| ADR-P | 8 | −0.262 | 0.536 | 8 | 0.238 | 0.582 |
| Withdrawal time | 8 | −0.167 | 0.693 | 8 | 0.667 | 0.071 |

AMR, adenoma miss rate; ADR, adenoma detection rate; PDR, polyp detection rate; APC, adenomas per colonoscopy including adenoma; APP, total number of adenomas per positive participant; ADR-P, additional adenomas found after the first adenoma per colonoscopy.
*p-value by the Spearman r (rho) correlation analysis.

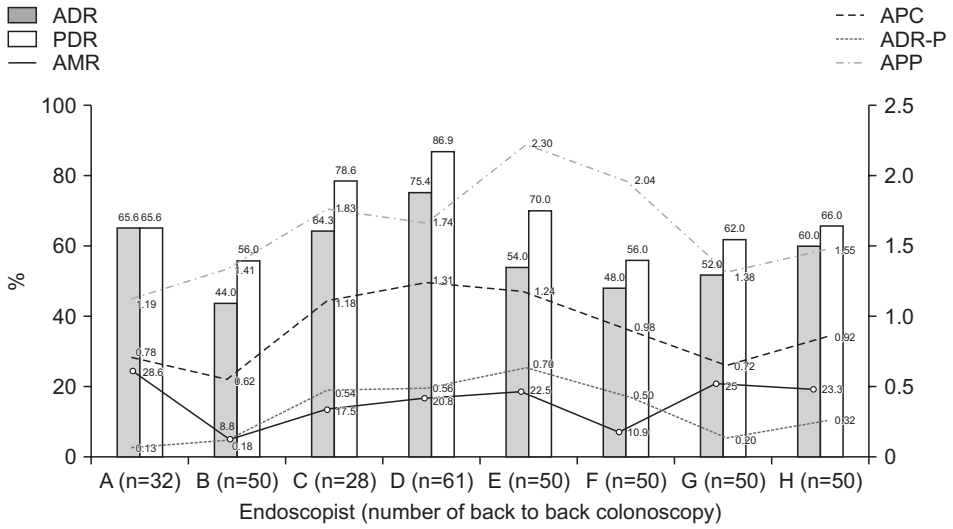


**Fig. 2.** Numerical distribution of colonoscopy quality indicators of eight endoscopists. There was a significant correlation between ADR and PDR (r=0.826, p=0.011), but there was no significant correlation between quality indicators and AMR (AMR and ADR: r=0.476, p=0.243; AMR and APC: r=−0.095, p=0.840; AMR and PDR: r=0.204, p=0.629; AMR and APP: r=−0.375, p=0.389; AMR and ADR-P: r=−0.262, p=0.536).
ADR, adenoma detection rate; PDR, polyp detection rate; APC, adenomas per colonoscopy; ADR-P, additional adenomas found after the first adenoma per colonoscopy; APP, total number of adenomas per positive participant; AMR, adenoma miss rate; r, rho.

were located in the proximal colon and 43 were in the distal colon (47.3%). Regarding endoscopic appearance, 70 adenomas (77%) were sessile morphology and 11 adenomas (11%) were flat. There was no cancer missed and the advanced AMR including six (7.2%) missed adenomas ≥1 cm in size was 10.9% (10/91).

### 4. Correlations between the quality indicators

There was no significant correlation between the ADR and AMR (rho=0.476, p=0.243) and the PDR and AMR (rho=0.204, p=0.629) (Table 4, Fig. 2). Although APC, APP and ADR-Plus appeared to be inversely correlated with AMR, these relationships were not significant (rho=–0.095, p=0.840; rho=–0.357, p=0.389; rho=–0.262, p=0.536, respectively) (Table 4).

Regarding the analysis of correlation between ADR and other quality indicators, PDR was significantly correlated with ADR (rho=0.826, p=0.011). However, APC, ADR-Plus and APP had no significant correlation with ADR.

### 5. Risk factor of missed lesions

Logistic regression analysis was performed to identify independent variables, including patient characteristics and colonoscopy quality factors, associated with missed polyps. The number of adenomas found during the first colonoscopy were independent factors for missed polyps (odds ratio, 1.79; 95% confidence interval, 1.45 to 2.22; p<0.001) in a multivariate logistic regression analysis (Table 5).

## DISCUSSION

The best method to estimate AMR is through back-to-back colonoscopy, a method of two consecutive same-day colonoscopies performed in a single patient. In a meta-analysis of 43 publications, more than 15,000 tandem colonoscopies revealed a 26% AMR.[11] In our study, the mean AMR estimated by back-to-back colonoscopy was 20.1%, similar to previous studies. Back-to-back colonoscopy is not an easy method regarding the practical aspects of being more time-consuming, and also patients experience discomfort by undergoing double exams. A quality indicator that could adequately reflect AMR would enable a relatively easy estimation method for AMR and thus increase colonoscopy quality and also reduce interval cancer. Although ADR is recommended as the primary indicator of good colonoscopy, it is still unknown whether AMR can be adequately reflected. A large retrospective study from the Minnesota group showed that endoscopists with ADR <25% and those with ADR ≥25% had no significant difference regarding incidence of interval CRC of their patients.[15] According to Aniwan *et al.*,[8] high ADR (>40%) endoscopists missed 13% to 36% of adenomas. In our study, while all eight endoscopists obtained high ADRs (>40%), they showed a variety of AMRs (8.8 to 28.6), indicating that a high ADR does not guarantee a low AMR. Wang *et al.*[4] has proven that ADR is necessary but insufficient for distinguishing high versus low endoscopist performance, and an endoscopist with a high ADR can still miss many adenomas in patients who already have adenomas detected. In our study, endoscopist A had a higher ADR (65.6%) than endoscopist E (54%) and F (48%), however the AMR of endoscopist A (28.6%) was higher than that of endoscopist E (22.5%) and F (10.9%).

PDR has the advantage of not requiring pathology results and it correlates well with ADR.[16,17] Also in our study, PDR showed significant correlation with ADR (rho=0.826, p=0.011). However, both ADR and PDR could be calculated as the "one and done" phenomenon, and do not seem to

**Table 5.** Logistic Regression Analysis of Independent Variables Associated with Missed Polyps

| Variable | | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|---|
| | | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Sex | Male | Reference | | | |
| | Female | 0.66 (0.39–1.12) | 0.661 | | |
| Age | | 1.02 (0.98–1.05) | 0.399 | | |
| Smoking | None | Reference | | | |
| | Presence | 0.93 (0.49–1.77) | 0.815 | | |
| Family History | None | Reference | | | |
| | Presence | 0.86 (0.09–7.46) | 0.858 | | |
| BMI | | 1.02 (0.93–1.11) | 0.741 | | |
| Bowel preparation | Adequate | Reference | | | |
| | Inadequate | 1.45 (0.29–7.32) | 0.656 | | |
| Withdrawal time | | 1.01 (0.94–1.07) | 0.851 | | |
| Numbers of adenoma during 1st colonoscopy | | 1.79 (1.44–2.21) | <0.001 | 1.79 (1.45–2.22) | <0.001 |

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

reflect the procedural technique of meticulous observation without missing the lesion.

In our study, ADR and PDR had positive correlations with AMR. APC, APP and ADR-Plus had negative correlations with AMR similar to the study by Aniwan *et al.*[8] APP showed a significant inverse correlation with AMR in Aniwan's study, whereas in our study, none of the surrogate quality indicators showed a significant inverse correlation with AMR. We believe that the main reason which this study did not show any significant correlation was due to the participants' heterogeneity. Unlike Aniwan's study, the eight endoscopists who performed colonoscopy in our study were not from the same institution, but were from five different institutions. In particular, two (endoscopist B and E) of the eight endoscopists were female and the female examinee percentage was significantly higher than that of other endoscopists. Interestingly, endoscopist B with the most female examinees showed the lowest ADR, APC, and ADR-P levels among endoscopists, however, the AMR was also the lowest.

In the present study, all endoscopists were highly experienced colonoscopy experts and achieved the indicators of high-quality recommended by the American Society for Gastrointestinal Endoscopy.[2] They had a high ADR (>40%) with a 100% cecal intubation success rate, adequate bowel preparation (BBPS ≥6) and adequate withdrawal time (>6 minutes). Despite these efforts, we found AMRs were measured as high as 28.6%, similar to previous studies. The meaningful outcome of the present study was that high ADR endoscopists showed varied AMR on quality adjusted colonoscopy, and the number of adenomas during first colonoscopy was an independent factor associated with missed lesions.

APC and ADR-Plus are similar with ADR in that they use the total number of performed colonoscopies for calculation. However, they are different with ADR in that APC uses the numbers of total adenoma while ADR-Plus uses the numbers of adenoma after first adenoma for calculation. In the majority of cases, APP correlates well with ADR, however, APP is not completely influenced by ADR. This is because ADR uses all participants as the divisor whereas APP uses only the number of adenoma-positive participants as the divisor.[4,18-20] Therefore, APC, APP, and ADR-Plus are indicators that could result in higher levels with an increased number of detected adenomas during colonoscopy, and are considered to well reflect AMR than ADR. The study by Aniwan *et al.*[8] suggested that APP is a better representative of metric addressing participants with adenoma. According to the recent meta-analysis, ADR, APC and APP showed independent association with AMR.[11] However, there are some theoretical points to consider. The most significant difference between APC, ADR-Plus, and APP from ADR is that it can vary according to the examinee's number of adenomas. In the case of ADR, the ratio depends on the presence or absence of adenoma regardless of the adenoma number. However, for APC, ADR-Plus, and APP, the number may increase if many adenomas are detected. In this regard, it can be considered that APC, ADR-Plus, and APP can reflect AMR better than ADR, but not in a consistent manner.

The number of adenomas during the first colonoscopy is a well-known risk factor for polyp missing, along with factors such as small size, flat or sessile shape, and proximal colon.[6,21,22] If a large number of adenomas is detected while performing colonoscopy, the probability of missing the lesion may increase. Therefore, colonoscopists in referred hospitals performing colonoscopy of examinees with a relatively large number of adenomas may consistently show a similar AMR to that of the previous studies, even while adhering to the current guidelines for intra-procedural quality indicators. In other words, quality indicators such as APC, ADR-Plus, and APP can show high values without significantly decreasing AMR for examinees with a relatively large number of adenomas. Therefore, additional research on examinees with a large number of adenomas may be needed to determine whether these surrogate quality indicators are useful in actual clinical practice.

Our study has several limitations. First, we conducted a multicenter study and recruited participants from outpatient clinics of each hospital. Thus, the distribution of participants was not well-controlled. There was an uneven gender distribution in participants, and male and female numbers showed a statistically significant difference. The prevalence of colon adenoma also might have affected the results of this study. However, this epidemiological result may be a characteristic of multicenter research with different clinical environments. Also, it was difficult to arbitrarily control the distribution of examinees, so in a way, this study may have been a natural composition of examinees. Second, eight endoscopists participated in the present study, targeting 50 examinees according to statistical calculation. However, two endoscopists failed to perform colonoscopies on a total of 50 examinees. Although this study performed more back-to-back colonoscopy than Aniwan's study, the number of registrations is smaller than the target number. Therefore, questions may arise as to whether this affected the statistical interpretation of the results of this study. Results showed "rho" was 0.826 for a significant outcome, and the power was not as low as 78.6%. In addition, the power of a significant result (odds ratio, 1.79; 95% confidence interval, 1.45 to 2.22) in the final analysis was very high at 99.4%, with fewer subjects than the initial study

protocol, thus the results may be considered to be reliable.

Third, we did not recruit endoscopists with low ADRs. In this study all endoscopists showed high ADRs (>40%) with qualified colonoscopy performances. Therefore, we could not analyze the PDR, APP, APC and ADR-Plus as surrogate quality indicators which reflect AMR for endoscopists with conventional ADRs. Although the reference study suggested that surrogate quality indicators would be more useful for reflecting colonoscopy quality with endoscopists showing high ADR, the calculation of quality indicators is different between ADR and surrogate indicators, as ADR is calculated with the "one and done" strategy. In terms of simplicity in calculating actual quality indicators, quality parameters other than ADR may not be easy to use in general in actual clinical practice as surrogate indicators are more complicated than ADR. Considering such practical aspects and the results of this study, surrogate indicators may not superior to ADR in reflecting AMR. Further research is needed on whether the surrogate quality indicators could reflect AMR according to ADR level.

Lastly, back-to-back colonoscopy was performed by the same endoscopist in our study. In the case of back-to-back colonoscopy performed by the same endoscopist, there may be concerns that lesions may be continuously missed. However, according to previous studies, the AMR was not affected by identical or different endoscopists performing in back-to-back colonoscopies.[21,23]

In conclusion, our study showed that a high ADR alone is not sufficient to guarantee a low AMR. In addition, surrogate quality indicators including APC, ADR-Plus, and APP did not reflect AMR for endoscopists with high ADRs performing qualified colonoscopies. These surrogate quality indicators may appear at a high level in examinees with many colon adenomas, known to have a high risk of adenoma missing, and thus may not properly reflect the AMR of examinees with such a large number of colon adenomas. Additional large-scale studies on optimal quality indicators that can reflect AMR for various examinees in various clinical environments are necessary.

## CONFLICTS OF INTEREST

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

## ACKNOWLEDGEMENTS

This work was supported by the Soonchunhyang University Research Fund and the Korean Association for the Study of Intestinal Diseases Research Fund.

## AUTHOR CONTRIBUTIONS

Study concept and design: H.G.K. Data acquisition: E.M.A., S.R.J., J.M.C., M.S.K., Y.J., J.E.S., H.D.S., Y.S.C. Data analysis and interpretation: H.G.K., S.P., J.H.H. Drafting of manuscript: J.H.H., H.G.K. Critical revision of manuscript for important intellectual content: H.G.K., S.P., J.M.C., M.S.K., Y.J., J.E.S., H.D.S., Y.S.C. Statistical analysis: S.P. Approval of final manuscript: all authors.

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