JGH Open An open access journal of gastroenterology and hepatology Open Access

JGHF Journal of Gastroenterology and Hepatology Foundation

doi:10.1002/jgh3.12084

ORIGINAL ARTICLE

Impact of retroflexion in the right colon after repeated forward-view examinations

Hideaki Miyamoto,* Hideaki Naoe,* Yasushi Oda,† Takashi Shono,* Rei Narita,*,†,‡ Shinichiro Oyama,* Syunpei Hashigo,*,† Ayako Okuda,§ Kiwamu Hasuda,§ Motohiko Tanaka,* Kouichi Sakurai,§ Yoshitaka Murakami¶ and Yutaka Sasaki*

*Department of Gastroenterology and Hepatology, Graduate School of Medical Sciences, Kumamoto University, †Oda GI Endoscopy and Gastroenterology Clinic, ‡Department of Gastroenterology, Minamata City General Hospital & Medical Center, §Hattori GI Endoscopy and Oncology Clinic, Kumamoto and ¶Department of Medical Statistics, Toho University, Tokyo, Japan

Key words
adenoma miss rate, colonoscopy, colorectal neoplasms, retroflexion.

Accepted for publication 27 July 2018.

Correspondence
Yutaka Sasaki, Department of Gastroenterology and Hepatology, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto-city, Kumamoto 860-8556, Japan.
Email: sasakiy@kumamoto-u.ac.jp

Declaration of conflict of interest: The authors declare there are no conflicts of interest for this article.

Abstract

Background and Aim: Right colon polyps can especially be overlooked when they are located on the backs of haustral folds. Previous studies have reported that repeated forward-view examinations in the right colon were effective in reducing adenoma miss rates. The aim of this study was to clarify the impact of retroflexion in the right colon after repeated forward-view examinations.

Methods: This multicenter, prospective, observational study was conducted at three institutions in Kumamoto, Japan, between February 2014 and December 2015. Subjects who were over 40 years old and scheduled for colonoscopy were recruited. For the forward view, after cecal intubation, the colonoscope was withdrawn to the hepatic flexure. The colonoscope was sequentially reinserted to the cecum and then withdrawn to the hepatic flexure. For the retroflexion view (RV), the colonoscope was reinserted to the cecum, retroflexed, and then withdrawn to the hepatic flexure. All polyps were resected at the time of detection. The primary outcome of this study was the adenoma miss rate for the repeated forward-view examinations.

Results: Of the 777 enrolled participants, retroflexion was successful in 730 (94.0%). The repeated forward-view withdrawal technique detected 291 adenomas, while the third withdrawal in the RV detected 53. The adenoma miss rate for the repeated forward-view withdrawal was 15.4%. No severe adverse events occurred during retroflexion.

Conclusion: Because adenomas located on potential blind spots can be missed when only using forward-view examinations, retroflexion in the right colon after repeated forward-view examinations might improve colonoscopy detection rates.

Introduction

Colorectal cancer (CRC) is a major cause of cancer morbidity and mortality in both Asian and Western countries.[1] Because the adenoma–carcinoma sequence is considered to be responsible for the majority of CRC, the screening and removal of adenomatous polyps can effectively prevent CRC.[2] Serrated lesions, including sessile serrated adenoma/polyp (SSA/P), which are difficult to detect endoscopically due to their low profile and pale color, have been considered to be one of the precursor lesions in the proximal colon.[3,4]

As a right-sided shift in the subtype distribution of colon cancers has been recently observed worldwide,[5] the prevention of proximal colon cancer has become an important issue. Previous studies, however, have reported that colonoscopy is less effective in preventing proximal CRC compared to distal CRC.[6,7] One of the possible explanations for these findings is that right colon lesions are more likely to exhibit a nonpolypoid appearance, thereby making it difficult to detect compared to the left-sided lesions.[8,9] Moreover, right colon lesions especially tend to be missed when they are located behind the haustral folds and anatomical flexures as these are considered to be blind spots.[10] Furthermore, as these missed lesions can potentially turn out to be interval CRCs,[11,12] reducing the adenoma miss rate in the right colon has become a pressing issue.

The use of retroflexion in the right colon makes it possible to observe the colon mucosa through a different angle. Previous studies that examined the impact of using the retroflexion view (RV) when performing second examinations from the cecum to the hepatic flexure have shown that this technique yields about an additional 10% of identified polyps. The benefit of this technique has been reported to be equal to that of performing a second examination using the forward view (FV).[10,13] Thus, these

findings confirm that it is important to undertake repeated right colon examinations, regardless of whether they are FV or RV examinations. However, it remains unclear whether all adenomas can be detected when using repeated FV.

The aim of the present study was to clarify the impact of using retroflexion in the right colon after repeated FV examinations with a high-definition, wide-angle colonoscope in Japanese subjects.

Methods

This multicenter, prospective, observational study was conducted at the Kumamoto University Hospital and at two clinical practices located in Kumamoto, Japan, between February 2014 and December 2015. This protocol was reviewed and approved by the Kumamoto University Ethics Committee (Approval Number 1729), and all study subjects provided informed consent.

Subjects. Participants who were over 40 years old and scheduled for colonoscopy for abdominal symptoms or CRC screening/surveillance were recruited. Participants with inflammatory bowel disease, polyposis, Lynch syndrome, familial adenomatous polyposis, internal anticoagulants, or a past history of colectomy were excluded from the study.

Participants were also excluded if they could not be intubated to the cecum during the colonoscopy, bowel preparation was poor, there was invasive cancer or more than 10 polyps detected in the right colon by FV, or when endoscopists judged it to be inappropriate to perform the retroflexion.

Procedures. All of the procedures were performed by 11 experienced endoscopists. Prior to the present study, these endoscopists had performed at least 2000 colonoscopy examinations.

Before undergoing the colonoscopy, all participants followed a standard bowel cleansing protocol using 1–2 L of high concentrated polyethylene glycol–electrolyte solution on the day of the examination.

All of the procedures utilized a high-definition, wide-angle (170°) colonoscope (PCF-H290I, EVIS LUCERA ELITE; Olympus Medical Systems, Tokyo, Japan). As the PCF-H290I colonoscope contains a high force transmission and passive bending section, this helps to improve insertability and operator control of the movement, including retroflexion. A soft black hood (MAJ-1990, Olympus Medical Systems, Tokyo, Japan) was attached to the tip of the colonoscope.

During the procedure, the colonoscope was inserted into the cecum without looking for lesions. After the cecal intubation, endoscopists assessed the quality of the bowel preparation in the right colon according to the following classifications: excellent (entire surface of colon mucosa was clearly seen following suction of residual fluid), good (minor amount of residual stool and opaque liquid, with most of the colon mucosa surface clearly seen), fair (surface of colon mucosa was not clearly seen due to liquid and semisolid stool that could be suctioned and/or washed out), and poor (large amounts of solid fecal matter that could not be suctioned or washed out).[14] During the standard FV, the colonoscope was withdrawn to the hepatic flexure while under meticulous observation. Sequentially, the colonoscope was reinserted into the cecum and withdrawn to the hepatic flexure in the second standard FV. Subsequently, the colonoscope was then reinserted into the cecum and retroflexed and was withdrawn to the hepatic flexure in RV. All visualized polyps were resected at the point of their first detection using either polypectomy or endoscopic mucosal resection. Principally, indigo carmine dye spraying was not used for detection in this study. However, we did not restrict its use for confirming the demarcation line of the lesion after detection. All resected tissues were collected for pathological evaluation. After the third withdrawal to the hepatic flexure, the area from the transverse colon to the rectum was examined in a standard manner.

The intubation time, withdrawal time, quality of the bowel preparation, success rate of retroflexion, polyp number, size, morphological characteristics, and histological diagnosis were recorded. In addition, the total number of advanced neoplasia (AN) found during the procedure was also recorded. AN was defined as the presence of any of the following features: adenomas larger than 10 mm, adenomas with villous histology, high-grade dysplasia including intramucosal carcinoma, and invasive cancer.[15] The withdrawal time, which included the three observations in the right colon, was calculated using the data from the participants found to have no lesions during any part of the procedure. Withdrawal times in the right colon when performing FV and RV were calculated using the same method.

Study outcomes. Recently, SSA/P has been considered to be one of the precursor lesions of the right colon.[4] The primary outcome of our study was defined as the adenoma miss rate for the repeated FV examination, which included SSA/P in the adenoma. The adenoma miss rate was calculated by determining the proportion of the number of additional adenomas found during RV to the total number of adenomas in the right colon. Secondary outcomes were defined as the success rate of the retroflexion, the AN miss rate, polyp miss rate, and the per-patient adenoma miss rate. The per-patient adenoma miss rate was calculated from the number of participants shown to have ≥1 adenoma during the retroflexion divided by the total number of participants who successfully underwent retroflexion.

Statistical analysis. As previously described,[16] a sample size of 1000 participants makes it possible to determine 95% confidence intervals for the percentage of participants with adenomas found during retroflexion. When the percentage of participants with adenomas is 10% or less, the per-patient miss rate should be less than 5%. Based on the above assumption, the present study was designed to recruit and evaluate 1000 participants. Continuous data were compared using the Mann–Whitney U test. Categorical variables were compared using either the χ^2 test or Fisher's exact test. Logistic regression analysis was utilized for the purpose of evaluating predictors of unsuccessful retroflexion and adenoma detection in RV. SPSS version 11 (SPSS, Inc., Chicago, IL, USA) was used for all the statistical analyses. All statistical tests were two tailed, with the significance defined as $P < 0.05$.

Results

The aim of the study was to enroll 1000 participants during the set registration period between February 2014 and December

Table 1 Baseline demographics

	n = 777
Gender, male/ female	352 (45.3%)/425
Age, median (years)	65 (40–85)
Body mass index, mean	23.0 (15.0–55.6)
Prior abdominal surgery, yes/ no	91 (11.7%)/686
Preparation, excellent or good/ fair	735 (94.6%)/42
Indication for colonoscopy	
Screening	372 (47.9%)
Surveillance	168 (21.6%)
Diagnostic work-up	140 (18.0%)
FIT positive	66 (8.5%)
Others	31 (4.0%)
Intubation time, mean ± SD	4.03 ± 2.37 min
Withdrawal time for total procedure, mean ± SD	8.14 ± 5.22 min
Withdrawal time for right colon with FV, mean ± SD	2.13 ± 1.37 min
Withdrawal time for right colon with RV, mean ± SD	38.28 ± 24.68 s

FIT, fecal immunochemical test; FV, forward view; RV, retroflexion view.

Table 2 Predictors of unsuccessful retroflexion

	OR (95% CI)	*P* value
Gender, male	0.97 (0.54–1.76)	N.S.
Age > 65 y	1.94 (1.05–3.57)	<0.05
BMI > 23	1.65 (0.89–3.06)	N.S.
Preparation fair	1.69 (0.58–4.97)	N.S.
Prior abdominal surgery, yes	1.60 (0.72–3.54)	N.S.
Insertion time > 4.03 min	2.14 (1.18–3.88)	<0.05

BMI, body mass index; CI, confidence interval; N.S., not significant; OR, odds ratio.

2015. However, due to poor enrollment, only 785 participants were enrolled and analyzed within this period. There were eight participants excluded after the cecal intubation. Reasons for exclusion included detection of invasive cancer during the FV in four participants, over 10 polyps during the FV in one participant, poor bowel preparation in one participant, and multiple diverticulum in the ascending colon in two participants.

Table 1 presents the baseline demographic and clinical characteristics and the analysis of the data for the remaining 777 participants. The mean withdrawal time for the total number of observations with the repeated FV in the right colon was 2.13 ± 1.37 min, while it was 38.28 ± 24.68 s in the right colon during RV and 8.14 ± 5.22 min for the total procedure.

Retroflexion was successful in 730 participants (94.0%), with only a few participants exhibiting minor bleeding (3.0%) or mucosal tear (0.8%). Perforation was not observed in any of the participants undergoing retroflexion. Logistic regression analysis showed that the significant predictors of unsuccessful retroflexion were older age (odds ratio [OR]: 1.94, 95% confidence interval [CI]: 1.05–3.57) and longer insertion time (OR: 2.14, 95% CI: 1.18–3.88) (Table 2).

Table 3 presents the characteristics of the detected adenomas in 730 participants who successfully underwent retroflexion. This study diagnosed 344 adenomas (316 conventional adenomas and 28 SSA/Ps). The adenoma miss rate during the initial FV withdrawal and repeated FV withdrawal was 35.2% and 15.4%, respectively. The polyp miss rate during the initial FV withdrawal and repeated FV withdrawal was 36.1% and 15.7%, respectively (data not shown). The adenoma miss rate during the repeated FV was similar regardless of the morphology ($P = 0.57$). In participants who underwent colonoscopy for screening ($n = 372$), the adenoma miss rate during the initial FV withdrawal and the repeated FV withdrawal was 42.2% and 18.1%, respectively (data not shown). There were 14 retrieved polyps found to be insufficient for histological evaluation, while two other polyps were diagnosed as an inflammatory and juvenile polyp, respectively. The AN miss rate during the repeated FV was 18.6%. Figure 1 shows representative images of detected adenomas during the RV. During the RV, we found not only diminutive lesions but also SSA/Ps over 10 mm and mucosal cancer over 20 mm. Table 4 showed the results of each of the endoscopists who performed more than 10 examinations. There were no significant differences in the adenoma miss rate between each of the endoscopists ($P = 0.22$). Table 5 showed the number of participants with ≥1 lesion. The per-patient adenoma miss rate was 6.7%, and the per-patient polyp miss rate was 7.7%. Logistic regression analysis showed that the significant predictors of the

Table 3 Characteristics of detected adenomas

	First (forward)	Second (forward)	First and second (forward)	Third (retroflexion)	Total
Total number	223 (64.8%)	68 (19.8%)	291 (84.6%)	53 (15.4%)	344 (100%)
Adenoma miss rate	35.2%	—	15.4%	—	—
Mean size ± SD	5.1 ± 3.1 mm	3.6 ± 1.6 mm	4.7 ± 2.9 mm	5.3 ± 3.8 mm	4.8 ± 3.0 mm
Morphology					
Nonpolypoid	71 (60.2%)	27 (22.9%)	98 (83.1%)	20 (16.9%)	118 (100%)
Polypoid	152 (67.3%)	41 (18.1%)	193 (85.4%)	33 (14.6%)	226 (100%)
Histology					
Conventional adenoma	200 (63.3%)	65 (20.6%)	265 (83.9%)	51 (16.1%)	316 (100%)
SSA/P	23 (82.2%)	3 (10.7%)	26 (92.9%)	2 (7.1%)	28 (100%)
Advanced neoplasia	30 (69.8%)	5 (11.6%)	35 (81.4%)	8 (18.6%)	43 (100%)
Advanced neoplasia miss rate	30.2%	—	18.6%	—	—

SSA/P, sessile serrated adenoma/polyp.

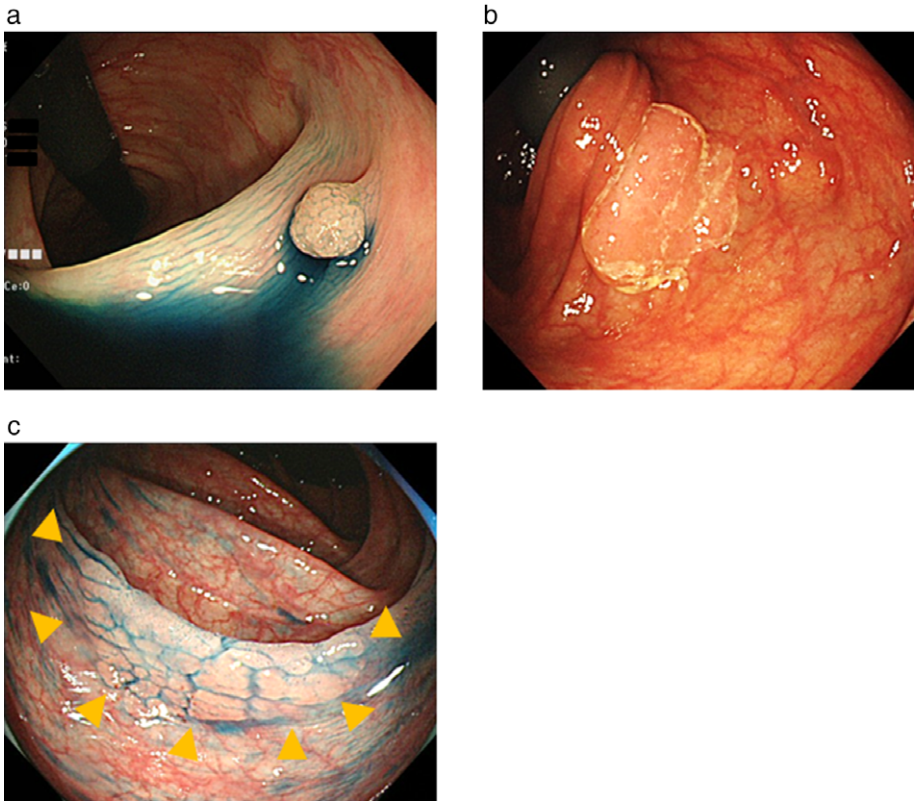

Figure 1 Representative images of detected polyps during retroflexion view. (a) 4 mm 0-Is adenoma, (b) 12 mm SSA/P, and (c) 20 mm 0-IIa mucosal cancer. The yellow arrowheads indicate the lesion boundary.

detection of at least one adenoma during the RV included older age and the presence of adenomas during the FV (Table 6).

Discussion

This study investigated the impact of retroflexion use in the right colon. After performing retroflexion in the right colon following the repeated FV examination, we then evaluated the adenoma miss rate during the repeated FV examination as the primary outcome. During the third withdrawal with RV after the repeated FV examination, we detected an additional 15.4% of adenomas in 6.7% of the participants. Significant predictors of the detection of at least one adenoma during the RV included older age and the presence of adenomas during the FV examination. Although the number of endoscopies performed by the endoscopists was not the same, there were no significant differences observed for the adenoma miss rate.

We summarized data from the previous studies on retroflexion in the right colon (Table S1, Supporting Information).[10,16–19] Four studies, except Lee's study, performed retroflexion after one-time FV observation. The rate for a successful retroflexion ranged from 82.4 to 95.9%, and the adenoma miss rate in right colon ranged from 5.1 to 18.6%. Chandran et al., who recruited the largest number of patients, conducted a prospective cohort study with 1351 patients and five experienced endoscopists.[17] They reported that the per-adenoma miss rate

Table 4 Performance of each of the endoscopists

Physicians	Retroflexion success rate	Withdrawal time for right colon		Number of detected adenomas		Adenoma miss rate for FV (%)
		FV, mean ± SD (sec)	RV, mean ± SD (sec)	FV	RV	
P1 (353)	0.946	102.14 ± 57.91	30.75 ± 18.35	97	28	22.4
P2 (140)	0.979	140.84 ± 126.44	44.31 ± 17.59	53	9	14.5
P3 (135)	0.948	169.39 ± 60.56	30.21 ± 11.88	40	4	9.1
P4 (47)	0.830	116.06 ± 66.40	33.37 ± 22.29	31	4	11.4
P5 (47)	0.894	162.44 ± 154.5	89.26 ± 20.42	35	3	7.9
P6 (19)	0.947	76.4 ± 22.83	32.88 ± 12.32	8	1	11.1
P7 (18)	0.944	178.44 ± 167.0	49.5 ± 39.3	14	2	12.5

FV, forward view; RV, retroflexion view.

Table 5 Number of participants with ≥1 lesion

	First (forward)	Second (forward)	First and second (forward)	Third (retroflexion)	Total
Number of participants with ≥1 polyp	163/730 (22.3%)	62/730 (8.5%)	203/730 (27.8%)	56/730 (7.7%)	229/730 (31.4%)
Number of participants with ≥1 adenoma	151/730 (20.7%)	54/730 (7.4%)	190/730 (26.0%)	49/730 (6.7%)	214/730 (29.3%)

was 9.8%, and retroflexion significantly increased the adenoma detection rate (ADR) from 24.6 to 26.4% ($P < 0.001$).

Kushnir et al. conducted a randomized trial that compared the second examination of the right colon when using FV and RV.[10] Their results showed a similar adenoma detection rate (46% FV and 47% RV) and number of adenomas per patient (0.9 ± 1.4 FV and 1.1 ± 2.1 RV) between the two groups.[10] These findings demonstrate that repeated right colon examinations might be important for both FV and RV. However, some adenomas could remain undetected on the proximal aspect of folds when only performing an FV examination. The fact that we detected additional adenomas in the RV after the repeated FV confirms this speculation.

Using a study design that was similar to the present study, Lee et al. recently reported on the efficacy of retroflexion following repeated FV examinations.[19] Their results are comparable to those for the present study (Table S1), even though there were several differences, such as the experience of the endoscopists, the type of scope used, and the withdrawal time. In their study, all of the endoscopic procedures were performed by three experienced physicians and eight inexperienced physicians using the CF-H260AI colonoscope, which has a standard-angle (140°) field of view. In contrast, all procedures in the present study were carried out by 11 experienced endoscopists using a PCF-H290I colonoscope, which has a wide-angle (170°) field of view.

Our study found that repeated FV examinations performed by experienced endoscopists using a wide-angle colonoscope potentially missed a considerable number of adenomas, similar to that seen for the standard-angle colonoscope. Actually, a previous study reported that the use of a wide-angle scope (170°) did not improve the adenoma miss rate compared to using a conventional scope (140°).[20] When taken together, this suggests that retroflexion might be necessary in order to thoroughly examine the right colon. Furthermore, the experience of the endoscopists might affect the success rate of the retroflexion (82.4% in their study *vs* 94.0% in the present study), which suggests that experienced endoscopists need to perform the procedure in order to be able to take full advantage of the retroflexion. Moreover, the mean withdrawal time for the right colon in the present study was about 2 min with repeated FV and about 40 s with RV. In contrast, the previous study took at least 2 min for each of the three observations, thereby taking over 6 min for the overall procedure. As the present study demonstrated a similar outcome with a shorter withdrawal time, repeated FV and sequential RV observation might be applicable for use in daily routine practices.

Table 6 Predictors of adenoma detection when using retroflexion

	OR (95% CI)	*P* value
Gender, male	1.39 (0.78–2.49)	N.S.
Age > 65 y	2.17 (1.19–4.00)	<0.05
BMI > 23	1.01 (0.98–1.03)	N.S.
Preparation poor	1.20 (0.36–4.06)	N.S.
Insertion time > 4.03 min	1.10 (0.59–2.04)	N.S.
Adenomas on forward view presence	3.26 (1.81–5.86)	<0.001

BMI, body mass index; CI, confidence interval; N.S., not significant; OR, odds ratio.

The present study further showed that the third RV observation yielded 18.6% additional AN as well as diminutive polyps (Table 3). Previous studies have reported that the presence of AN predicts a higher rate of metachronous AN and CRCs.[21] Our results suggest that retroflexion could be an efficient tool not only for detecting precancerous lesions but also for preventing interval cancers.

Novel emerging technology such as a retrograde viewing device and full-spectrum endoscopy have recently been proven to be beneficial with regard to improving the adenoma miss rate.[22] However, these new modalities are currently only available at limited facilities. In contrast, retroflexion is both simple and suitable for routine applications and, thus, can be safely used in most situations. Moreover, as endoscopists need to be skilled in the use of retroflexion when resecting a polyp from behind a fold, these endoscopists should already be familiar with performing retroflexion during routine clinical practices.

There were several limitations in the present study. First, we did not randomly compare the FV and RV during the third examination, and the same endoscopist performed the FV and RV examinations in sequence. This could have caused a bias when trying to demonstrate the benefits of the third retroflexion examination. As a result, this mental bias could cause a high adenoma miss rate during the FV. Lee et al., using a similar study design as the present study, came under criticism with regard to this issue from the author of one of four previous studies.[23] However, since the FV and RV examinations are commonly performed by the same endoscopists during routine clinical practice, the current finding might be of universal significance in the clinical setting.

The second limitation involves our quality of colonoscopy. In the current study, the yield of the first FV (64.8%) was quite low, the number of endoscopies was uneven among the participants, and the adenoma miss rate of the endoscopist who performed the largest number of colonoscopies with a shorter withdrawal time was high. The withdrawal time of first FV was an important factor contributing to poor yield of first FV. Unfortunately, we did not separately record each of the withdrawal times. However, substantially, we performed colonoscopy with sufficient quality because right colon ADR with FV and total procedure was higher than previous studies (26.0% and 29.3%, respectively) (Table S1).

The third limitation was our method of measuring the procedure time; we calculated the withdrawal time based on the data from participants who were found to have no lesions during the procedure. In order to calculate the strict observation time, it would have been better if we used a stopwatch to ensure that we excluded the mucosal washing, the diagnostic time, and the therapeutic time in all patients. However, as our study was performed within a routine clinical practice, it was unfeasible to measure all of the examination times with a stopwatch.

In conclusion, as adenomas can remain undetected on the proximal aspect of folds when only performing an FV examination, the use of retroflexion in the right colon might be able to reduce the adenoma miss rate. Careful examination of the right colon using RV should be recommended as a way of improving the overall quality of the examination and for helping to safely detect and prevent CRC.

Acknowledgment

None.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Table S1 Comparison between the current study and the past literature.