

## Colonoscopy Withdrawal Time and Adenoma Detection Rate: A Japanese Multicenter Analysis

Takuji Kawamura, Yasushi Oda, Kiyonori Kobayashi, Koji Matsuda, Mitsuhiro Kida, Kiyohito Tanaka, Yosuke Kawahara, Isao Yokota, Wasaburo Koizumi, Kenjiro Yasuda, Hisao Tajiri

Takuji Kawamura, Kiyohito Tanaka, Kenjiro Yasuda, Department of Gastroenterology, Kyoto Second Red Cross Hospital, Kyoto, Japan  
Yasushi Oda, Oda GI Endoscopy and Gastroenterology Clinic, Kumamoto, Japan

Kiyonori Kobayashi, Mitsuhiro Kida, Wasaburo Koizumi, Department of Gastroenterology, Kitasato University, Kanagawa, Japan  
Koji Matsuda, Department of Gastroenterology, St. Marianna University School of Medicine, Yokohama City Seibu Hospital, Kanagawa, Japan

Yosuke Kawahara, Hisao Tajiri, Department of Endoscopy, The Jikei University School of Medicine, Tokyo, Japan

Isao Yokota, Department of Biostatistics, Kyoto Prefectural University of Medicine, Kyoto, Japan

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**Correspondence to:** Takuji Kawamura, MD, PhD, Department of Gastroenterology, Kyoto Second Red Cross Hospital, 355-5 Haruobi-cho, Kamigyo-ku, Kyoto City, Kyoto 602-8026, Japan  
Email: [kawamurat@kyoto2.jrc.or.jp](mailto:kawamurat@kyoto2.jrc.or.jp)  
Telephone: +81-75-231-5171  
Fax: +81-75-256-3451

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### ABSTRACT

**AIM:** Limited evidence exists on the relationship between colonoscopy withdrawal time and adenoma detection rate in Japan. We aimed to clarify the clinical impact of colonoscopy withdrawal time in a Japanese setting.

**MATERIALS AND METHODS:** We recruited 6,919 consecutive patients from four Japanese endoscopic centers between April 2010 and April 2011. Colonoscopists were divided into the following groups based on the median withdrawal time of a negative colonoscopy: < 6 min (group A), 6-9 min (group B), and  $\geq$  10 min (group C). We analyzed the relationship between these withdrawal time groups and adenoma detection rate using multiple logistic regression analysis.

**RESULTS:** The final analysis included 3,862 patients. Group A included 201 (3 colonoscopists), group B included 2,741 (13 colonoscopists), and group C included 920 patients (9 colonoscopists). We found that adenoma detection rates tended to increase with longer median negative colonoscopy withdrawal times ( $p < 0.01$ ). Compared with group A, the odds ratios in group B and group C were 1.98 (95% confidence interval [CI], 1.42-2.76) and 2.51 (95% CI, 1.68-3.75), respectively.

**CONCLUSIONS:** A colonoscopy withdrawal time of over 6 min appears to be a quality indicator for colonoscopy even in a Japanese setting.

**Key words:** Colorectal neoplasms; Colonoscopy; Quality indicators

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## INTRODUCTION

According to recent global cancer statistics, colorectal cancer (CRC) is the third most commonly diagnosed cancer in men and the second in women<sup>[1]</sup>. In Japan, the incidence and mortality of CRC have increased, and it is now one of the most frequently diagnosed cancers<sup>[2]</sup>. Colonoscopic polypectomy of precancerous lesions is a beneficial procedure for preventing CRC<sup>[3]</sup>. However, considerable numbers of colorectal polyps are missed during screening and surveillance colonoscopy<sup>[4]</sup>.

Adenoma detection rate (ADR), which is defined as the proportion of individuals undergoing colonoscopy who have one or more adenomas detected, has been used as one of the reliable quality indicators for colonoscopy<sup>[5]</sup>. Several studies have suggested that interval colorectal cancer rates have been inversely linked to ADR at screening colonoscopy<sup>[6,7]</sup>.

Colonoscopy withdrawal time has been reported as a predictor of ADR in several studies<sup>[8-13]</sup>. In the majority of these studies, colonoscopy withdrawal time during negative colonoscopies (i.e., no polyps detected and/or no therapy performed) is used as a quality indicator. The landmark study by Barclay *et al.* suggests that a minimum withdrawal time of 6 min is required to gain an adequate ADR<sup>[8]</sup>. Based on these results, a withdrawal time of over 6 min during normal colonoscopy is recommended in the United States<sup>[5]</sup>, and the European guideline recommends that endoscopists should be encouraged to withdraw more slowly if adenoma detection rates are low and withdrawal times are short<sup>[14]</sup>. However, conflicting results about withdrawal time have been reported in some recent studies, which have suggested that withdrawal time should not be used as a quality indicator<sup>[15,16]</sup>.

In Japan, endoscopists have widely contributed to the development of colonoscopy; however, standardization of the basic colonoscopy technique has had limited discussion. Therefore, limited evidence exists concerning the withdrawal time of colonoscopies performed in Japan<sup>[17]</sup>. We previously reported the clinical impact of follow-up colonoscopy frequency for CRC prevention in a Japanese multicenter study<sup>[18]</sup>. Therefore, the objectives of the present study were to review the circumstances surrounding the issue of quality in our previous study, and clarify whether colonoscopists who use longer withdrawal times during negative colonoscopies can detect more adenomas.

## METHODS

### Study design

This supplementary analysis used original data, including colonoscopy withdrawal times, from a previous multicenter study (UMIN ID: 000007448)<sup>[18]</sup>. Colonoscopists who participated in the study were divided into the following three groups based on the median withdrawal time of a negative colonoscopy: < 6 min (group A), 6-9 min (group B), and ≥ 10 min (group C). A negative colonoscopy was defined as colonoscopy with no adenomas or cancers detected. Withdrawal time was defined as the duration between the time at which the cecum was reached and the time at which the scope was withdrawn from the anus<sup>[5]</sup>. Patients were also divided into three groups in accordance with the colonoscopists' groups. We analyzed the relationship between these withdrawal time groups and ADR, and advanced neoplasia detection rate (ANDR). Advanced neoplasia was defined as tubular adenomas ≥ 10 mm, adenomas with a villous histology, high-grade dysplasia, and cancer.

The protocol of the original study was approved by the institutional review board of each participating center.

### Patients

The previous study had recruited 6,919 consecutive patients from four Japanese endoscopic centers (Kyoto Second Red Cross Hospital, Oda GI Endoscopy and Gastroenterology Clinic, Kitasato University East Hospital, and The Jikei University Aoto Hospital) between April 2010 and April 2011, all of whom had provided informed consent<sup>[18]</sup>. Patients in the present study were excluded based on the following criteria: inflammatory bowel disease, observation up to the cecum was not possible, a history of colectomy, colonoscopy was performed within 6 months, inadequate/poor bowel preparation (Aronchick Scale<sup>[19]</sup> 4 and higher), age < 40 or > 75 years, an unknown colonoscopy history, an unknown family history, and an unknown colonoscopy withdrawal time. Additionally, patients who had undergone colonoscopy by a colonoscopist who had performed < 50 colonoscopies during the study period were excluded.

### Data collection

An endoscopic database (Solemio Endo<sup>®</sup>, version 3.2; Olympus Medical Systems Inc., Tokyo, Japan) was used for data collection. The withdrawal time in minutes after omitting the fraction was described by each endoscopist soon after colonoscopy by reviewing the time stamp from the endoscopic picture at the cecum and rectum. Specifically, the withdrawal time was recorded on the Solemio Endo<sup>®</sup> in 1-min increments between 1 and 9 min, with separate categories for withdrawal times ≥ 10 min. The following information was also collected for each participant: age, sex, a history of CRC, a family history of CRC, a history of colonoscopy, degree of preparation, and use of a distal attachment.

The location, size, morphology, and endoscopic diagnosis of the lesions were also described in the endoscopic report. A histological diagnosis of the resected specimen was inputted by each endoscopist after the diagnosis was made. An adenoma in this study was classified based on histopathological findings; however, if the histopathological data was missing, the diagnosis was based on the endoscopic findings using a high-definition endoscopy. Advanced neoplasia was also diagnosed based on the histological findings in addition to the endoscopic findings.

### Data analysis

As aforementioned, we analyzed the relationship between withdrawal time groups and ADR, as well as ANDR. These were defined as the rate of patients who had at least one adenoma or advanced neoplasia, respectively. Using the  $\chi^2$  test, we first analyzed differences in the patients' characteristics for each category, including the proportions of each sex, a history of invasive cancer, a family history of CRC, university hospital setting, use of a distal attachment, indications of colonoscopy, frequency of past colonoscopies, degree of preparation, and the colonoscopists' experience. Analysis of variance was instead used for continuous variables such as age. If significant differences were detected, comparisons between each group were conducted in post-hoc analysis. Second, we analyzed the relationship between withdrawal times and detection rates using the Jonckheere-Terpstra trend test. Finally, multiple logistic regression analysis was used to estimate odds ratios, which were adjusted for sex, age, a history of invasive CRC, a family history of CRC, a history of colonoscopy, hospital setting, degree of preparation, use of a distal attachment, and the colonoscopists' experience.

All statistical analyses were performed using IBM SPSS statistics, version 22 (IBM, Armonk, NY), with  $p < 0.05$  considered to be statistically significant.

## RESULTS

The final analysis included 3,862 patients (Figure 1) who underwent colonoscopies performed by 25 endoscopists (Table 1). Of 11 colonoscopists who had experience with <1,000 cases, 7 (63%) had a longer median withdrawal time of over 10 min (group C). Furthermore, only 1 of 7 colonoscopists (14%), who had experience with over 5,000 cases, was classified in group C. Group A (withdrawal time <6 min) included 201 patients (3 colonoscopists), group B (6–9 min) included 2,741 patients (13 colonoscopists), and group C ( $\geq 10$  min) included 920 patients (9 colonoscopists).

Patient characteristics are shown in Table 2. Sex, age, and a history of invasive cancer were not significantly different among the three groups; however, a family history of CRC, indications of colonoscopy, frequency of past colonoscopy, hospital setting, degree of preparation, use of a distal attachment, and the colonoscopists' experience were showed a statistically significant difference among the groups.

Overall, any adenomas and advanced neoplasia were detected in 1,776 (46.0%) and 413 (10.7%) of 3,862 patients, respectively. Histopathological confirmation of adenomas was obtained in 1,418 cases (79.8%), whereas the rest of the adenomas were diagnosed by high-definition colonoscopy. When the colonoscopists' withdrawal time increased, ADR and ANDR also tended to increase (both  $p < 0.01$ ; Figure 2). Compared with group A (<6 min), the odds ratios for ADR for colonoscopists in group B (6–9 min) and group C ( $\geq 10$  min) were 1.98 (95% confidence interval [CI], 1.42–2.76) and 2.51 (95% CI, 1.68–3.75), respectively. Regarding the detection of advanced neoplasia, the odds ratios were 1.98 (95% CI, 1.07–3.69) and 2.49 (95% CI, 1.22–5.10; Table 3), respectively. When a cutoff of 7 min was used instead, the odds ratio for ADR for colonoscopists with withdrawal times  $\geq 7$  min was 1.13 (95% CI, 0.94–1.37) compared with those whose withdrawal times were < 7 min; this did not reach statistical significance.

With regard to other factors for ADR, male sex, age, a colonoscopy frequency of 3 times or more within the past 5 years, university hospital setting, and use of a distal attachment were significantly associated with ADR, whereas a history of invasive CRC, a family history of CRC, degree of preparation, and the colonoscopists' experience were not (Table 4).

## DISCUSSION

Colonoscopy withdrawal time is widely used as an indicator of quality in Western countries; however, limited evidence of its utility exists in Asia. Insofar as we know, the present study is the first multicenter study about colonoscopy withdrawal time in Japan. The present study suggests that a longer withdrawal time contributes to a higher ADR and ANDR in a Japanese setting. Compared with patients who underwent colonoscopy performed by colonoscopists with a negative colonoscopy withdrawal time of < 6-min, ADRs were 1.98 and 2.51 times higher in patients who underwent colonoscopies performed by colonoscopists with withdrawal times of 6–9-min and  $\geq 10$ -min, respectively.

A 6-min cutoff was used in our study as Barclay *et al.* have reported that a mean withdrawal time of over 6 min is useful for maintaining colonoscopy quality<sup>[8]</sup>. However, other studies have instead used a 7-min cutoff<sup>[9,11]</sup>. In the present study, we therefore attempted to perform analysis using both a 6-min and 7-min withdrawal time cutoff. We found that when 7 min was used as the cutoff, there were no significant differences between groups.

Overall, however, our study further supports existing data show-

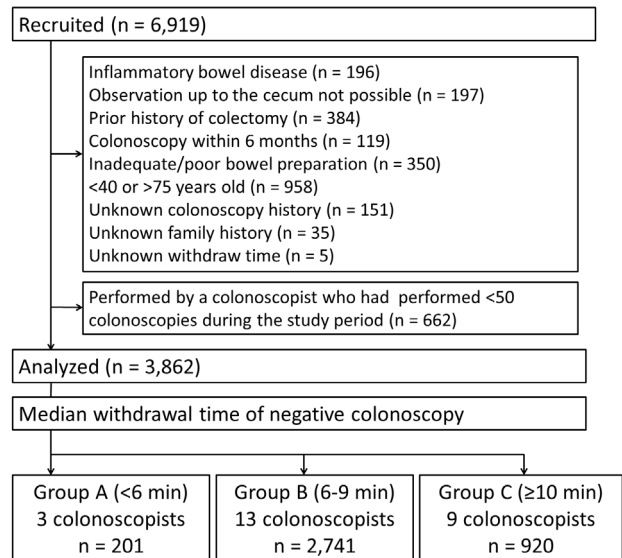


Figure 1 Study flow chart.

## Detection rate

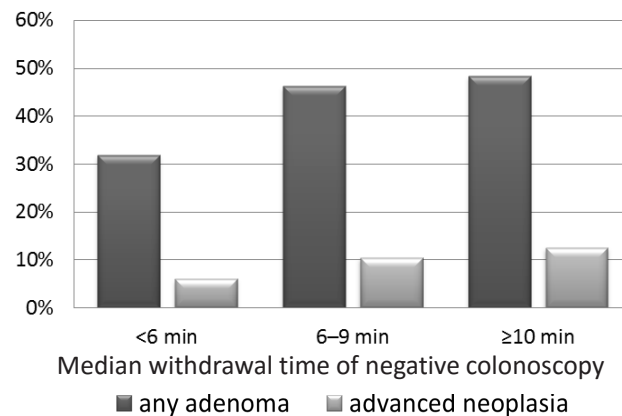


Figure 2 Relationship between the median colonoscopy withdrawal time of negative colonoscopies and adenoma detection rate (ADR), and advanced neoplasia detection rate (ANDR). ADR and ANDR tended to increase as the colonoscopists' withdrawal time increased (both  $p < 0.01$ ).

ing higher ADRs among endoscopists with longer mean colonoscopy withdrawal times<sup>[8–11,20–22]</sup>. Although withdrawal time is considered secondary to ADR as a quality measure, and would have only marginal importance for endoscopists with adequate ADRs, endoscopists with ADRs below the recommended thresholds would need to extend their withdrawal times<sup>[23]</sup>. The establishment of reliable quality indicators is particularly important for minimizing unnecessary reexamination following initial screening, as well as for addressing the issue of interval cancer. While the United States colonoscopy surveillance guideline recommends implementing a 10-year interval after a negative screening colonoscopy<sup>[24]</sup>, there is no guideline regarding re-screening after negative colonoscopies in Japan. Our results indicate that colonoscopy withdrawal time can be used as a quality indicator even in Japan, and can therefore be useful for informing surveillance screening guidelines in the Japanese population.

However, it should be noted that there have been conflicting results about withdrawal time as a quality indicator<sup>[11,15,16,25]</sup>. Although the present study suggests that a longer withdrawal time would be useful in a Japanese setting, further studies would be needed to make

**Table 1** Characteristics of the colonoscopists.

Colonoscopist	No. of colonoscopies during the study period	Cumulative volume of colonoscopy	Median withdrawal time of negative colonoscopy (min.)	Subjects with any adenomas <sup>†</sup> (%)	Subjects with advanced neoplasia (%)
A	64	<1,000	>10	46.90%	6.30%
B	60	<1,000	9	50.00%	6.70%
C	65	<1,000	9	49.20%	4.60%
D	67	<1,000	>10	61.20%	19.40%
E	94	<1,000	>10	50.00%	17.00%
F	129	<1,000	>10	41.10%	12.40%
G	129	<1,000	>10	46.50%	12.40%
H	123	<1,000	>10	54.50%	19.50%
I	164	<1,000	9	53.70%	3.00%
J	163	<1,000	8	42.90%	16.00%
K	192	<1,000	>10	53.60%	9.40%
L	61	1,000-4,999	5	24.60%	4.90%
M	57	1,000-4,999	>10	36.80%	7.00%
N	75	1,000-4,999	5	37.30%	4.00%
O	116	1,000-4,999	8	54.30%	8.60%
P	109	1,000-4,999	6	54.10%	10.10%
Q	150	1,000-4,999	7	48.70%	10.00%
R	156	1,000-4,999	7	53.80%	19.20%
S	65	>5,000	4	32.30%	9.20%
T	65	>5,000	>10	35.40%	6.20%
U	80	>5,000	6	51.30%	6.30%
V	219	>5,000	8	50.70%	17.40%
W	225	>5,000	6	48.40%	12.90%
X	281	>5,000	6	43.40%	12.80%
Y	953	>5,000	7	40.40%	7.80%

<sup>†</sup>This category includes any adenomas and cancer.

**Table 2** Patients' characteristics.

	Overall (% of total cases)	Group A (<6 min) (% of 201 cases)	Group B (6-9 min) (% of 2,741 cases)	Group C (≥10 min) (% of 920 cases)	p value
Overall, n	3,862	201	2,741	920	
Male sex, n (%)	2,118 (54.8)	116 (57.7)	1,481 (54.0)	521 (56.6)	NS
Age, years (range)	61.3 (40-75)	62.3 (41-75)	61.4 (40-75)	61.0 (40-75)	NS
History of invasive CRC, n (%)	27 (0.7)	1 (0.5)	19 (0.7)	7 (0.8)	NS
Family history of CRC, n (%)	440 (11.4)	15 (7.5)	344 (12.6) <sup>2</sup>	81 (8.8)	0.002
Indications, n (%)					<0.001
FIT positive	733 (19.0)	53 (26.4)	457 (16.7) <sup>2</sup>	223 (24.2)	
Screening	497 (12.9)	39 (19.4)	277 (10.1) <sup>2</sup>	181 (19.7)	
Temporary abdominal symptoms	697 (18.0)	22 (10.9)	606 (22.1) <sup>2</sup>	69 (7.5)	
Bloody stool	213 (5.5)	10 (5.0)	140 (5.1) <sup>3</sup>	63 (6.8)	
Surveillance after polypectomy	1,438 (37.2)	66 (32.8)	1,089 (39.7) <sup>3</sup>	283 (30.8)	
Others	284 (7.4)	11 (5.5)	172 (6.3)	101 (11.0)	
Frequency of colonoscopy within 5 years, n (%)					<0.001
None	1,784 (46.2)	105 (52.2)	1,169 (42.6) <sup>2</sup>	510 (55.4)	
Once or twice	1,449 (37.5)	66 (32.8)	1,065 (38.9) <sup>2</sup>	318 (34.6)	
Three times or more	629 (16.3)	30 (14.9)	507 (18.5) <sup>3</sup>	92 (10.0)	
University hospital setting, n (%)	1,564 (40.5)	140 (69.7) <sup>4</sup>	1,360 (49.6) <sup>4</sup>	64 (7.0) <sup>4</sup>	<0.001
Good / excellent preparation, n (%)	2,816 (72.9)	168 (83.6) <sup>4</sup>	2,007 (73.2) <sup>4</sup>	641 (69.7) <sup>4</sup>	<0.001
Use of a distal attachment, n (%)	1,520 (39.4)	1 (0.5) <sup>4</sup>	1,313 (47.9) <sup>4</sup>	206 (22.4) <sup>4</sup>	<0.001
Colonoscopists' experience <sup>1</sup> , n (%)					<0.001
<1,000 cases	1,250 (32.4)	0 <sup>4</sup>	452 (16.5) <sup>4</sup>	798 (86.7) <sup>4</sup>	
1,000-4,999 cases	724 (18.7)	136 (67.7) <sup>4</sup>	531 (19.4) <sup>4</sup>	57 (6.2) <sup>4</sup>	
≥5,000 cases	1,888 (48.9)	65 (32.3) <sup>4</sup>	1,758 (64.1) <sup>4</sup>	65 (7.1) <sup>4</sup>	

FIT, fecal immunochemical test; CRC, colorectal cancer; NS, not significant, <sup>1</sup> Cumulative volume of colonoscopy, <sup>2</sup> Significantly different from group A and C ( $p < 0.05$ ), <sup>3</sup> Significantly different from group C ( $p < 0.05$ ), <sup>4</sup> Significantly different from each of the other groups ( $p < 0.05$ ).

**Table 3** Results of multiple logistic regression analysis.

	<i>n</i>	Any adenoma <sup>1</sup>	Odds ratio (95% CI) <sup>2</sup>	Advanced neoplasia	Odds ratio (95% CI) <sup>2</sup>
Group A (<6 min)	201	64 (31.8%)	1 (ref.)	12 (6.0%)	1 (ref.)
Group B (6–9 min)	2,741	1267 (46.2%)	1.98 (1.42–2.76)	286 (10.4%)	1.98 (1.07–3.69)
Group C (≥10 min)	920	445 (48.4%)	2.51 (1.68–3.75)	115 (12.5%)	2.49 (1.22–5.10)
Overall	3,862	1776 (46.0%)		413 (10.7%)	

<sup>1</sup> This category includes any adenomas and cancer. <sup>2</sup> Odds ratios were adjusted for sex, age, a history of invasive CRC, a family history of CRC, a history of colonoscopy, hospital setting, degree of preparation, use of a distal attachment, and the colonoscopists' experience. ref, reference; CI, confidence interval; CRC, colorectal cancer.

**Table 4** Odds ratios of the other factors for the adenoma detection rate.

	Odds ratio	95% CI	<i>P</i> value
Male sex	2.2	1.92–2.52	< 0.01
Age	1.02	1.02–1.03	< 0.01
History of invasive CRC	0.89	0.39–2.01	0.78
Family history of CRC	1.11	0.90–1.36	0.34
Frequency of colonoscopy within 5 years			
None	1 (ref.)		
Once or twice	0.9	0.78–1.05	0.17
Three times or more	0.6	0.50–0.73	< 0.01
University hospital setting	1.44	1.16–1.78	< 0.01
Good / excellent preparation	0.92	0.78–1.07	0.27
Use of distal attachment	1.57	1.28–1.93	< 0.01
Colonoscopists' experience <sup>1</sup>			
<1,000 cases	1 (ref.)		
1,000–4,999 cases	1.17	0.92–1.48	0.18
≥5,000 cases	0.86	0.70–1.05	0.13

<sup>1</sup> Cumulative volume of colonoscopy; CRC, colorectal cancer; CI, confidence interval.

a conclusion. It should also be noted that while CRC screening programs in many countries begin at 50 years old<sup>[25]</sup>, we included people in their 40s in our analysis. This is because in Japan, an annual fecal immunochemical test (FIT) is recommended as a national screening program for CRC in people aged 40 and over. Therefore, most of the patients in this study underwent colonoscopy not for screening purposes, but rather because their FIT was positive, they displayed abdominal symptoms, or for surveillance after a polypectomy.

The colonoscopists' experience was also analyzed in this study. Veteran colonoscopists who had experience with over 5,000 cases had shorter withdrawal times than younger colonoscopists who had experience with < 1,000 cases; however, most of the experienced colonoscopists maintained an optimal ADR level regardless of withdrawal time. Nevertheless, the results of this study suggest that a minimum withdrawal time of 6 min would still be required for all colonoscopists.

With regard to the other factors examined, a colonoscopic intervention frequency of 3 times or more within the past 5 years was inversely linked to ADR. Although CRC can be prevented by colonoscopic intervention, more than 20% of diminutive adenomas are missed during colonoscopy<sup>[4]</sup>. It is likely that a colonoscopic intervention frequency of once or twice within 5 years was not able to prevent adenomas due to small lesions being missed.

On the other hand, a history of invasive CRC and family history of CRC, which are recognized as risk factors for CRC, were not associated ADR in this study. In this analysis, patients with a prior history of colectomy were excluded. Therefore, most of the patients with a history of CRC were also excluded. This may account for why these factors were not associated with ADR. Furthermore, degree of prepa-

ration was also not related to ADR. This could also be due to the exclusion of patients with poor/inadequate preparation from this study.

Our study has several limitations. First, this was a supplementary analysis using data from a previous study. Second, withdrawal times were inputted by colonoscopists themselves after omitting the fraction; therefore, the exact withdrawal second could not be collected in this study. Third, only three endoscopists had a median withdrawal time of < 6 min. Therefore, our results may have been affected by these three colonoscopists.

Despite these limitations, the present study provides important information about colonoscopy withdrawal times in a Japanese setting. The results of this study suggest that a longer withdrawal time contributes to a higher ADR and ANDR. A colonoscopy withdrawal time of over 6 min appears to be a quality indicator of colonoscopy even in a Japanese setting.

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