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COMPUTED TOMOGRAPHY

A novel volume-reduced CT colonography regimen using hypertonic laxative (polyethylene glycol with ascorbic acid): randomized controlled trial

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Abstract

Objectives The aim of this study is to investigate the feasibility of bowel preparation using a hypertonic laxative (polyethylene glycol with ascorbic acid, PEG + Asc) for CT colonography (CTC) and to examine the volume limit of laxative.

Methods In one institution, patients who met the indications for CTC were enrolled and randomly assigned to CTC with regimen A (800 ml PEG + Asc), B (600 ml PEG + Asc), or C (400 ml PEG + Asc). Sodium diatrizoate was given orally for fecal tagging. On the previous day, patients ate low-residue meals and took the assigned lavage solution after dinner. A reader blinded to the preparation graded residual stool/fluid and fecal tagging quality in six segments of the colorectum. The primary outcome was a proportion of colon segments without stool. One hundred twenty segments in 20 patients with each regimen were needed to show a non-inferiority margin of 15%, assuming 85% of no stool.

Results A total of 360 segments in 60 patients were analyzed. There were 83% of segments with no stool in regimen A, 89% in regimen B, and 88% in regimen C. Using the delta method, the 95% confidence interval of the risk difference (6.7%) between regimens A and B was − 2.2% to 15.6%, and the risk difference (5.0%) between regimens A and C was − 4.1% to 14%, both within the non-inferiority margin. Residual fluid and fecal tagging quality were also within the non-inferiority margin. No adverse events occurred.

Conclusions A novel CTC regimen using hypertonic laxative demonstrated optimal colon cleansing effectiveness even with the lowest volume of laxative (UMIN000022851).

Key Points

- *A novel CTC regimen using a hypertonic laxative is feasible.*
- *The lowest volume of laxative provides excellent colon imaging.*
- *However, the lowest volume of laxative did not improve patient acceptance.*

Keywords Computed tomographic colonography · Laxatives · Polyethylene glycols

Abbreviations

CI	Confidence interval
CTC	Computed tomography colonography
HU	Hounsfield unit
PEG	Polyethylene glycol

Introduction

Computed tomography colonography (CTC) has recently become established as a minimally invasive colon imaging study [1–4]. In industrialized countries, colorectal cancer is a major cause of morbidity and mortality and CTC is widely used due

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to its high diagnostic performance for the identification of colorectal neoplasms and a high rate of patient acceptance [1–6]. Due to a decreased physical burden, CTC was reported to lead to higher patient participation than colonoscopy for colorectal cancer screening [7], and serious complications associated with CTC are very rare [8]. However, all modalities for colon screening need effective bowel preparation which is another obstacle to patient acceptability. CTC also requires colon cleansing with a relatively large volume of laxative [1–5, 9]. Bowel preparation with at least 2 l of laxative solution provides excellent colon cleansing, but it is described as burdensome by most patients undergoing colon examinations [10–13].

Theoretically, CTC does not require the same complete cleansing as optical colonoscopy, because fecal tagging can differentiate polyps from stool. To reduce the volume of liquid needed for bowel cleansing, various approaches have been used to date [14–17]. A recent report on reduced-laxative CTC reported an excellent detection rate for polyps ≥ 6 mm and also high patient acceptance, but approximately 20% of participants still complained about the bowel preparation process on a post-procedure survey [6]. In other clinical trials, 20% to 30% of patients felt that even reduced-volume bowel preparation was severely burdensome [18, 19]. Further efforts are needed to reduce the burden of bowel preparation. In 2012, non-laxative CTC was initially reported to accurately detect adenomas measuring ≥ 10 mm [20], but it has the serious drawback that a dedicated computer-aided diagnosis system is essential.

A standard bowel preparation regimen for CTC has not been established to date. According to the American College of Radiology, bowel preparation for CTC should consist of a combination of dietary restriction, hydration, saline cathartics, and/or low-volume polyethylene glycol (PEG) and contact laxatives [21], but patients usually have to drink 2–4 l of lavage solution [1–5]. MoviPrep™ (EA Pharma Co., Ltd.), which contains PEG plus ascorbic acid, was developed as a volume-reduced lavage solution for optical colonoscopy. Owing to its hypertonic nature, MoviPrep™ may reduce the amount of lavage solution needed for CTC as well as optical colonoscopy. Using MoviPrep™ before CTC, the laxative volume could be reduced even more because complete bowel cleansing is not essential. This clinical trial aimed to investigate the feasibility of bowel preparation using MoviPrep™ for CTC. As a component of the trial, we attempted to determine the limit to which the volume of hypertonic laxative could be reduced without losing image quality.

Materials and methods

Study design and participants

This is a prospective, single-center, randomized control study. The study protocol was implemented according to the Declaration of Helsinki, approved by the Institutional Review Board (No. 2686) and registered at UMIN Clinical Trials Registry (ID: UMIN000022851). Enrollment was from July 2016 to November 2016. The Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed in reporting this study. Written informed consent was obtained from all patients.

Patients from 40 to 80 years old were recruited to undergo colon evaluation because of abdominal symptoms, hematochezia, or positive fecal immunochemical tests, or for surveillance due to a history of endoscopic polypectomy. Exclusion criteria included serious medical conditions associated with an increased risk of complications due to bowel preparation needed for CTC, if they had known colorectal polyps or cancers at any site at the time of enrollment, if they had a history of resection of the colon and rectum, or due to pregnancy, hyperthyroidism, or iodine contrast medium allergy. To follow the above exclusion criteria, we administered a questionnaire to the participants.

Assignment

Eligible patients were randomly assigned to one of three regimens (1:1:1): regimen A (800 ml MoviPrep™ plus 400 ml water), regimen B (600 ml MoviPrep™ plus 300 ml water), or regimen C (400 ml MoviPrep™ plus 200 ml water). Random allocation was performed by a research assistant using a computer-generated randomization sequence.

Bowel preparation

Bowel preparation started in the morning the day before CTC, when patients ate a low-residue diet. After dinner, patients drank the pre-assigned amount of MoviPrep™ with 20 ml of sodium diatrizoate (Gastrografin™; Bayer Yakuhin) to tag residual stool, followed by 10 ml of sodium picosulfate hydrate (Laxoberon™; Teijin Pharma) before bed. On the day of the examination, patients took 20 ml of sodium diatrizoate at home with water before the examination (Table 1).

CTC procedure

Patients were placed in the left decubitus position and a thin flexible rectal tube with a balloon was placed. The colon was insufflated using an automated carbon dioxide insufflator (PROTOCO2L™, E-Z-EM) at a gas pressure of 20 mmHg. CT scan was performed using an 80-row multi-detector CT (Aquilion ONE™, Canon Medical Systems) scanner in the supine and prone positions. The scanning protocol used was voltage (120 kV), rotation time (0.5 s), pitch (0.813), section thickness (1.0 mm), reconstruction interval (0.8 mm), and automatic tube current modulation system (Volume EC™, SD20, Canon Medical Systems). Spasmolytic agents and

Table 1 Bowel preparation regimen

Regimen	1 day before examination			Day of Examination
	After dinner		Before bed	
A	800 ml MoviPrep™ plus 400 ml water	20 ml Gastrografin™	10 ml picosulfate	20 ml Gastrografin™
B	600 ml MoviPrep™ plus 300 ml water	20 ml Gastrografin™	10 ml picosulfate	20 ml Gastrografin™
C	400 ml MoviPrep™ plus 200 ml water	20 ml Gastrografin™	10 ml picosulfate	20 ml Gastrografin™

intravenous contrast medium were not used during CTC, according to our previous randomized clinical trial [22].

Evaluation of residual stool, fluid, and tagging quality

CTC interpretation was performed by an experienced board-certified radiologist (KU), who was blinded to the preparation regimen used and had interpreted more than 1000 CTC examinations with endoscopic validation. All interpretations were performed using a commercially available workstation (AZE Virtual Place Raijin™, AZE) by three-dimensional primary reading (fly through), without use of software dedicated to digital subtraction bowel cleansing. Standard window settings were applied (window width, 600 Hounsfield units (HU); window level, 10 HU), but readers were permitted to adjust these settings. The interpretation time was measured. The colon was divided into six segments (cecum to rectum), and the reader graded each segment on the basis of axial images based on the protocols of previous studies [15, 23, 24]. The details of the scoring system are shown in Table 2. Supine position images were graded in this manner. Fecal tagging quality was rated by measuring the CT attenuation (HU) of residual fluid or stool in the "region of interest (10 mm^2)" representing each segment. In segments with no observed fluid or stool, fecal tagging quality and CT attenuation were not measured.

To confirm the reproducibility of this trial, an experienced radiologist (NK) in a third institution, who was blinded to the preparation regimen used and had interpreted more than 2000 CTC examinations with endoscopic validation, graded residual stool, fluid, and tagging quality of each segment on the basis of axial images in a similar manner.

Validation by colonoscopy and questionnaires

In patients identified as having a ≥ 6-mm polyp by CTC, colonoscopy was scheduled within half a year after CTC. Colonoscopists were aware of the results of the CTC. A lesion found during CTC was matched to the corresponding lesion at colonoscopy when it was located in the same or an adjacent colon segment and when its size was within 50% of the lesion seen on CTC [1].

To assess the patients' acceptance and preferences regarding the preparation and examinations, questionnaires were given to all patients on the day after CTC examination.

Outcome measurements

The primary outcome was residual stool (proportion of colon segments with "score 0" meaning no stool). Secondary outcomes were residual fluid (proportion of colon segments with score 0 or "score 1," meaning no/minimal fluid), tagging quality (proportion of colon segments with "score 4," meaning excellent tagging), adverse events, incomplete examinations, lesion detection rate, CTC reading time, and survey data of the patient experience with the preparation.

Statistical analysis

The hypothesis of this study was that regimen B (600 ml MoviPrep™) is inferior to regimen A (800 ml MoviPrep™) with regard to the proportion of colon segments with score 0 (no stool) by 15%. We regarded a non-inferiority margin of 15% as appropriate. If the hypothesis was not rejected, we determined in advance that the subsequent comparison between regimens C (400 ml MoviPrep™) and A would not be conducted. Otherwise, a comparison between regimens C and A was planned, assuming similar hypotheses. In analyzing two secondary outcomes (residual fluid and tagging quality), a similar assumption using 15% as the non-inferiority margin was applied.

Sample size was calculated based on six segments (cecum to rectum) between regimens A and B. Since the assessment for each colon segment was made independently in this trial, we expect that the outcomes will not vary among colon segments. Assuming no difference between regimens A and B in the proportion of colon segments with score 0, we calculated that 190 colon segments (95 in each regimen) were required to ensure with 80% confidence that the lower limit of the two-sided 95% confidential interval (CI) would exclude a difference in favor of "regimen A" of more than 15%. An additional assumption for this estimate was an expected 85% occurrence of score 0. Assuming 20% of dropouts, we need 119

Table 2 Scoring system of residual stool, fluid, and fecal tagging quality

Parameter	Score	Criteria
Residual stool	0	No stool
	1	Small stool (< 6 mm)
	2	Moderate size stool (6 to 9 mm)
	3	Large stool (≤ 10 mm)
Residual fluid	0	No fluid
	1	Minimal fluid (depth < 6 mm)
	2	Moderate fluid (depth ≤ 6 mm, depth < 50% of the luminal circumference)
	3	Substantial fluid (depth ≥ 50% of the luminal circumference)
Fecal tagging quality*	0	No tagging (tagging < 25%)
	1	Poor tagging (25% ≤ tagging < 50%)
	2	Inhomogeneous tagging (50% ≤ tagging < 75%)
	3	Good tagging (75% ≤ tagging < 100%)
	4	Excellent tagging (100%)

*Fecal tagging quality was assessed based upon the proportion of residual feces/fluid well mixed with contrast medium. Colon segments with no residual feces/fluid were not assessed

colon segments in each regimen. Therefore, we aimed to recruit 20 patients (120 segments) in each regimen.

We analyzed the proportion of colon segments with score 0 (primary outcome), the proportion of colon segments with score 0 or score 1, and the proportion of colon segments with score 4 based on estimates of the risk difference using the delta method. To investigate the heterogeneity of these outcomes according to the colon segment, we applied the Mantel-Haenszel method. Other dichotomous variables were analyzed using the chi-square test. Discrete variables including age, number of defecations, reading time, and CT attenuation were analyzed using the Kruskal-Wallis test. Inter-rater agreement was quantified by the weighted kappa statistic (Fleiss and Cohen) which measures agreement over and above chance agreement. Kappa values of ≤ 0.4, 0.41–0.60, 0.61–0.80, and ≥ 0.81 were considered to indicate poor/slight, fair, moderate, substantial, and almost perfect agreement, respectively. The results were considered statistically significant at $p < .05$. Statistical analyses were done with Stata (version 13.1).

Results

Patient flow

A total of 62 patients who met the indications for CTC were included. Two patients withdrew informed consent for this study. After randomization, no patients dropped out. Data for the remaining 60 patients (29 men, 31 women; median age, 68.0 years) were analyzed (Fig. 1). Patient demographics did not significantly differ for age, gender, or indication between each regimen (Table 3).

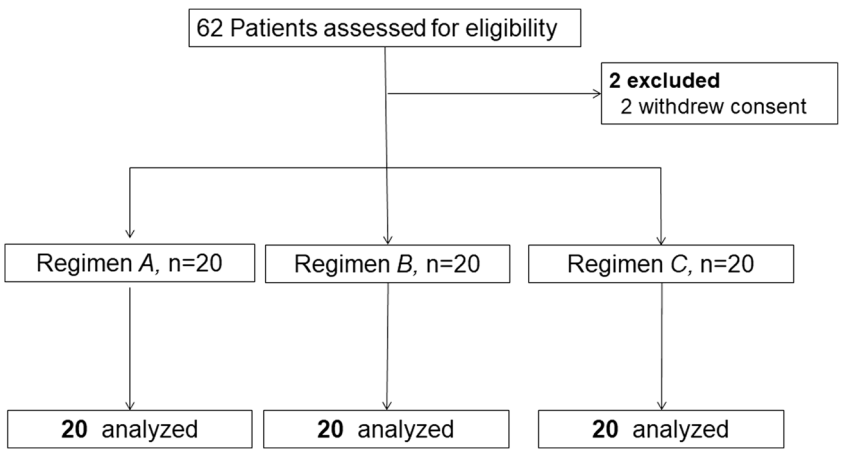

Fig. 1 Study flow diagram

Table 3 Patient background

	Regimen A (800 ml) $n = 20$	Regimen B (600 ml) $n = 20$	Regimen C (400 ml) $n = 20$	p value
Gender, n (%)				
Female	8 (40)	14 (70)	7 (35)	$p = 0.053$*
Male	12 (60)	6 (30)	13 (65)	
Age, years				
Median	68	68	68	$p = 0.69$**
Range	57–79	48–79	43–79	
Indication, n (%)				
Abdominal pain	4 (20)	1 (5)	3 (15)	$p = 0.16$*
Hematochezia	4 (20)	1 (5)	0	
FIT	10 (50)	10 (50)	8 (40)	
Survey	1 (5)	5 (25)	6 (30)	
Others	1 (5)	3 (15)	3 (15)	

FIT fecal immunochemical test (positive)

*Chi-square test

**Kruskal-Wallis test

Residual stool (primary outcome, Fig. 2a)

In all three regimens, the vast majority had score 0 (no stool). The percentage of patients with a score of 0 was 83% for regimen A, 89% for regimen B, and 88% for regimen C. The 95% CI of the risk difference (6.7%) between regimen A and regimen B was − 2.2% to 15.6% (Table 4), which were within the prespecified non-inferiority margin of − 15%. As determined in advance, a subsequent comparison between regimens A and C was conducted. The 95% CI of the risk difference (5.0%) between regimen A and regimen C was − 4.1% to 14.1% (Table 4), which were also within the prespecified non-inferiority margin of − 15%. The Mantel-Haenszel analysis did not show the heterogeneity of score 0 in colon segments ($p = 0.938$).

Residual fluid (Fig. 2b)

In all regimens, there are no remarkable tendencies. The 95% CI of the risk difference (− 8.3%) between regimen A and regimen B was − 13.5% to 11.8%, and that of the risk difference (0.8%) between regimen A and regimen C was − 11.8% to 13.5% (Table 4), which were both within the prespecified non-inferiority margin of − 15%. The Mantel-Haenszel analysis did not show the heterogeneity of score 0 or score 1 in colon segments ($p = 0.406$).

Fecal tagging (Fig. 2c)

A total of 31 colon segments with no residual stool/fluid were not assessed. In all regimens, the vast majority had a score of 4 (excellent tagging). The 95% CI of the risk difference (2.0%) between regimen A and regimen B was − 7.0% to 3.0%, and the 95% CI of the risk difference (− 5.4%) between regimen A and regimen C was − 11.4% to 5.1% (Table 4), which were both within the prespecified non-inferiority margin of − 15%. The Mantel-Haenszel analysis did not show the heterogeneity of score 4 in colon segments ($p = 0.290$). The median CT attenuation (interquartile range) for all segments was 943 (682–1073) HU for regimen A, 859 (538–1078) HU for regimen B, and 878 (608–1098) HU for regimen C. There were no significant differences between the regimens ($p = 0.495$).

Table 4 Summary of the main results

Outcomes	N (%, 95% CI)			Risk difference (% (95% CI))	
	Regimen A (800 ml) $n = 120$	Regimen B (600 ml) $n = 120$	Regimen C (400 ml) $n = 120$	Regimen A vs. B	Regimen A vs. C
Residual stool "score 0"	99 (83, 75 to 89)	107 (89, 82 to 94)	105 (88, 80 to 93)	6.7 (− 2.2 to 15.5)	5.0 (− 4.1 to 14.1)
Residual fluid "scores 0 and 1"	56 (47, 38 to 56)	55 (46, 37 to 55)	57 (48, 38 to 57)	− 0.8 (− 13.5 to 11.8)	0.8 (− 11.8 to 13.5)
Tagging quality "score 4"*	109 (97, 92 to 99)	101 (95, 89 to 98)	102 (92, 85 to 96)	− 2.0 (− 7.0 to 3.0)	− 5.4 (− 11.4 to 5.1)

CI confidence interval

*Excluding segments with no observed fluid or stool

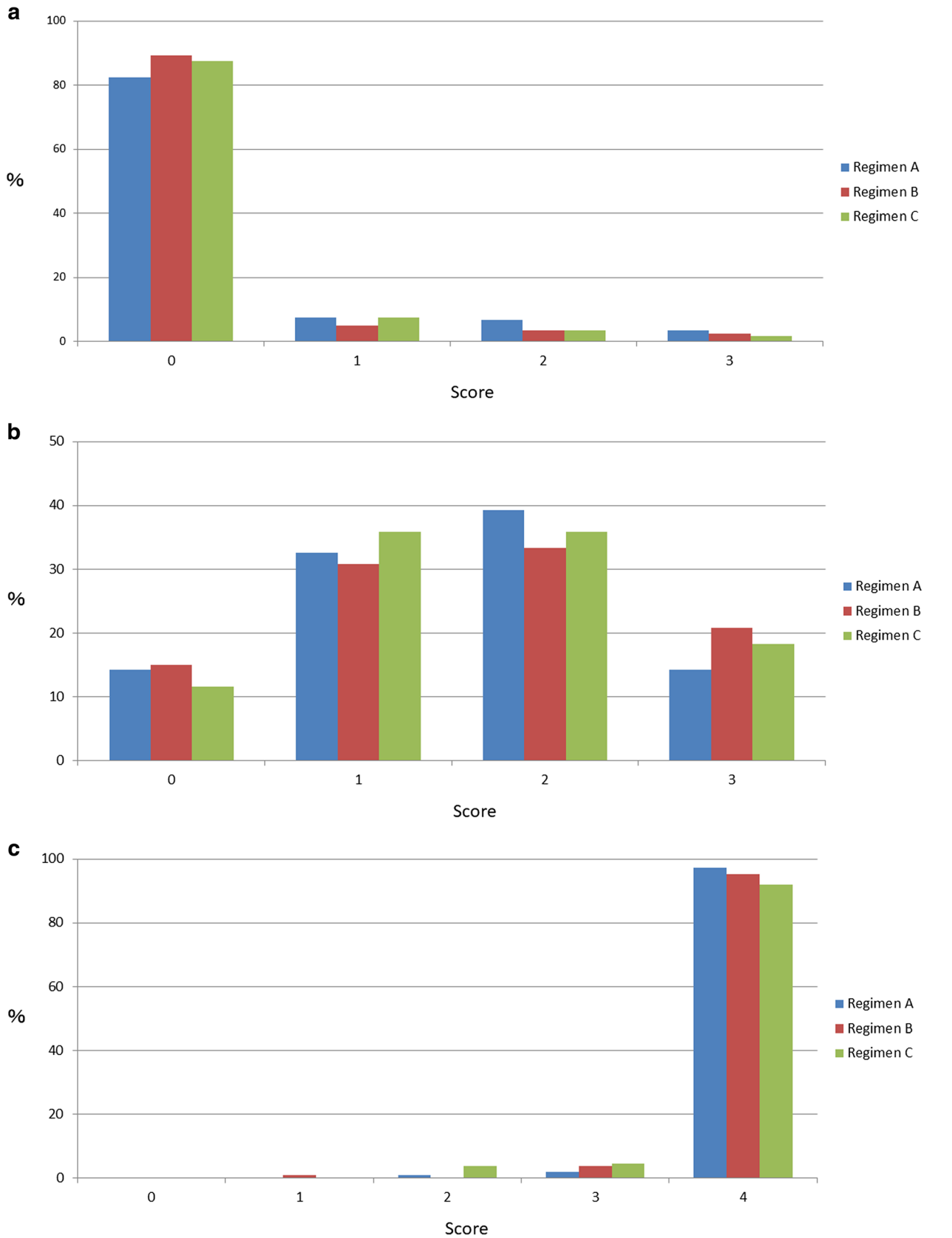

Fig. 2 Image quality according to bowel preparation regimen. **a** Residual stool scores (0 = no stool, 1 = small stool, 2 = moderate-size stool, 3 = large stool). **b** Residual fluid scores (0 = no fluid, 1 = minimal fluid, 2 = moderate fluid, 3 = substantial fluid). **c** Tagging quality scores for all colon segments in each regimen. Scoring: 0 = no tagging, 1 = poor tagging, 2 = inhomogeneous tagging, 3 = good tagging, 4 = excellent tagging

Inter-rater agreement

Weighted kappa values were 0.478 for residual stool, 0.540 for residual fluid, and 0.591 for fecal tagging, all indicating moderate agreement.

Adverse events, incomplete examination rate, lesion detection rate, and CTC reading time

No adverse events relating to bowel preparation or examinations occurred. No examination was rated technically inadequate due to bowel collapse as a C-RADS score of C0 [25]. CTC depicted small (6–9 mm) polyps (Figs. 3a–c, 4a–c, and 5a–c) in five patients and large (≥ 10 mm) polyps in three patients. The rate of detection of lesions ≥ 6 mm was 10% (2 of 20) in regimen A, 20% (4 of 20) in regimen B, and 10% (2 of 20) in regimen C, indicating similar values ($p = 0.56$, chi-square). For seven of eight patients, therapeutic colonoscopy was performed, six patients had similar polyps, and the lesions were resected endoscopically. A 10-mm flat-type lesion in the transverse colon that was found by CTC in regimen A which was not seen on colonoscopy. Total per-patient positive predictive value was 0.86 (6 of 7). The median reading time (range) was 4.0 (3.0 to 5.0) min in regimen A, 4.0 (3.0 to 5.0) min in regimen B, and 4.0 (3.5 to 5.0) min in regimen C, almost the same among regimens ($p = 0.43$).

Questionnaire (Table 5)

A review of the responses to all questions showed that either regimen C (400 ml, least amount) or regimen B (600 m) did not have better responses than regimen A (800 ml). Rather, patients had similar responses regardless of the regimen used. One exception was question 2 (amount). For patients taking regimen C, there was less tendency to report that the amount of laxative was too much ($p = 0.093$). Although the number of defecations slightly increased with a larger amount of laxative, a few participants complained of sleep disturbances. It is noted in question 5 (future preference) that a majority of patients preferred CTC to colonoscopy for a future examination.

Discussion

MoviPrep™ is a hypertonic laxative, including twice the concentration of PEG found in conventional isotonic laxatives, which is an already well-established bowel cleansing method for optical colonoscopy. The ascorbic acid cannot be absorbed

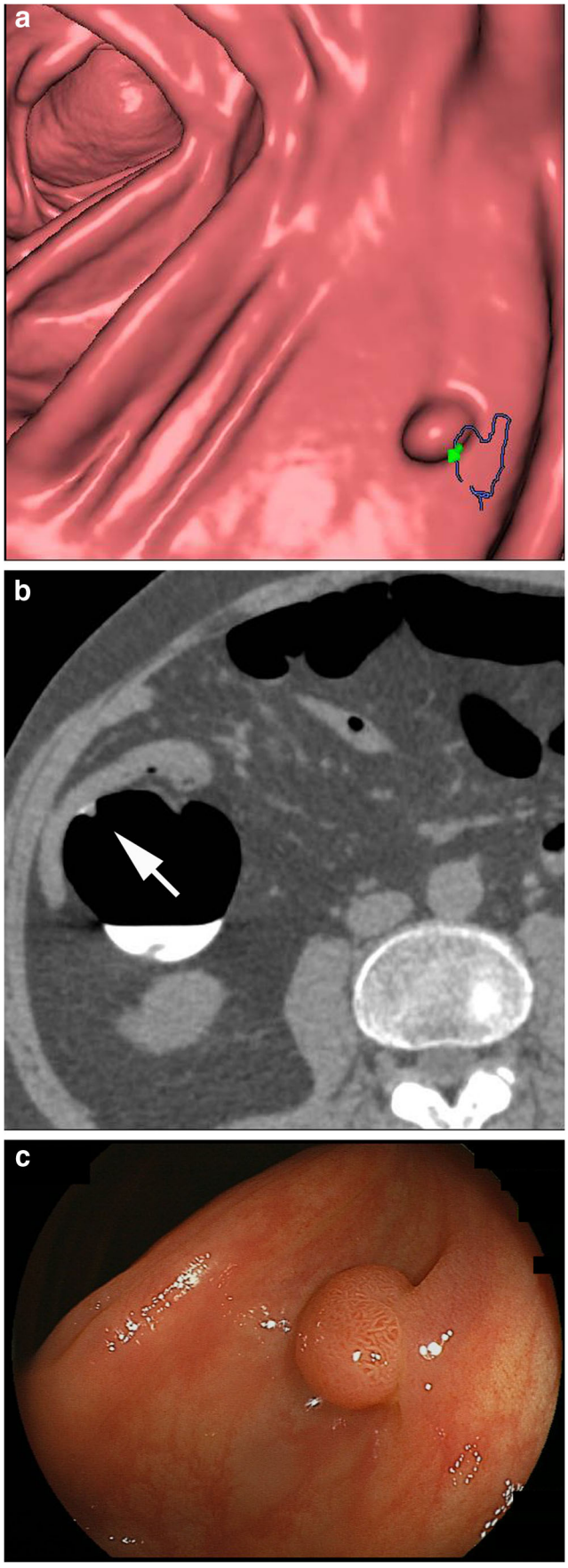

Fig. 3 Regimen A (800 ml), polypoid polyp, 6 mm in size, ascending colon, low-grade adenoma. No stool (score 0), moderate fluid (score 2), and excellent tagging quality (score 4). **a** Fly through image. **b** Axial image. An arrow denotes the lesion. **c** Optimal colonoscopy image

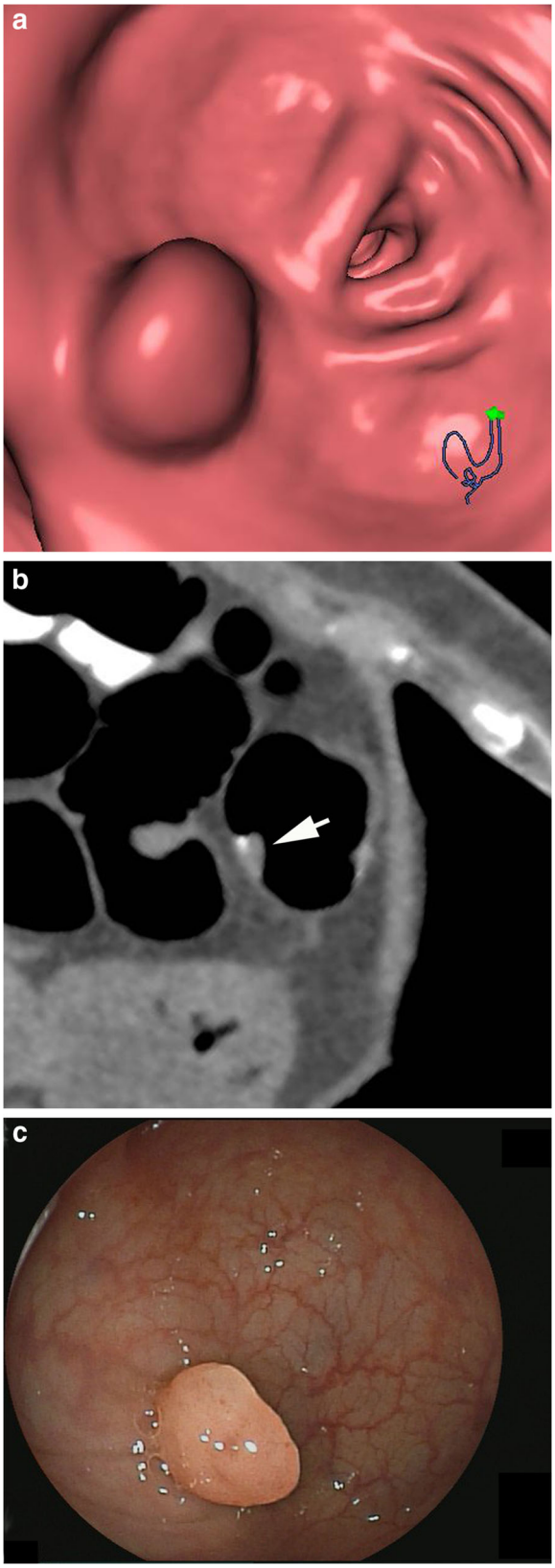

Fig. 4 Regimen B (600 ml), polypoid polyp, 8 mm in size, descending colon, low-grade adenoma. No stool (score 0), no fluid (score 0), and excellent tagging quality (score 4). **a** Fly through image. **b** Axial image. An arrow denotes the lesion. **c** Optimal colonoscopy image

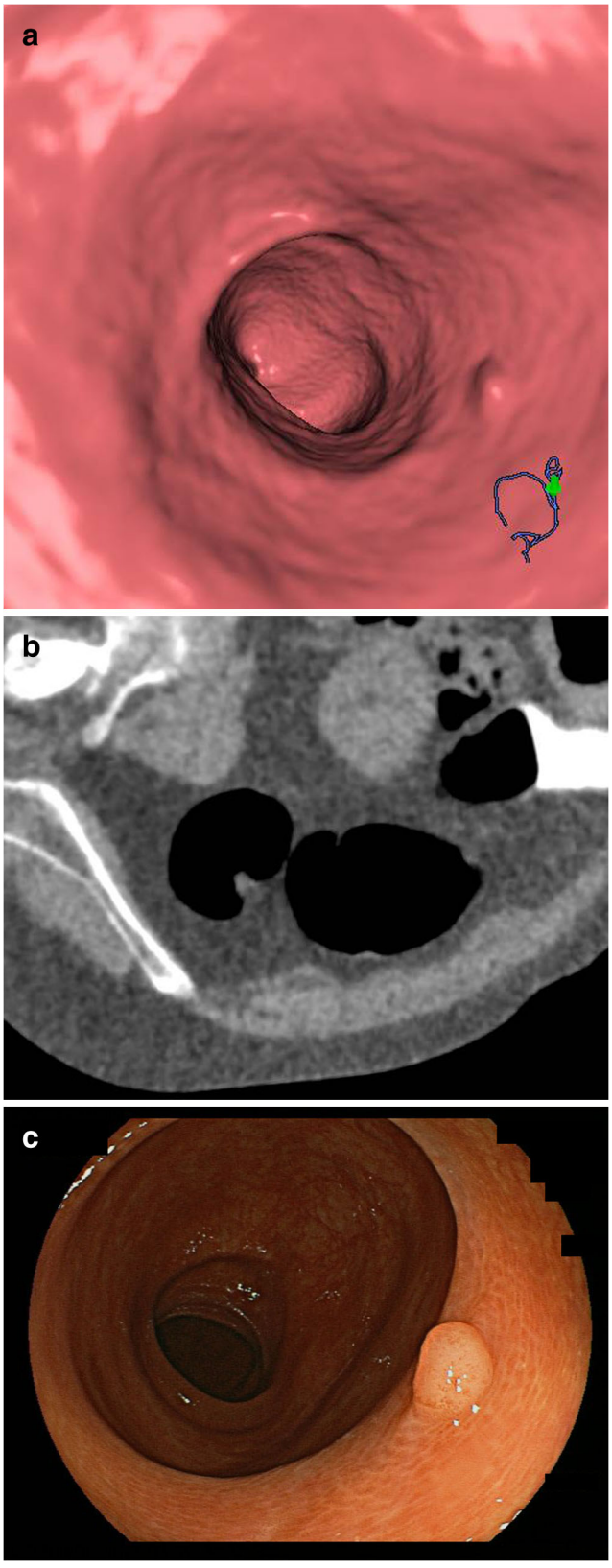

Fig. 5 Regimen C (400 ml), polypoid polyp, 6 mm in size, transverse colon, low-grade adenoma. No stool (score 0), no fluid (score 0), and excellent tagging quality (score 4). **a** Fly through image. **b** Axial image. An arrow denotes the lesion. **c** Optimal colonoscopy image

Table 5 Survey responses by the regimen

Question	Response	Regimen A (800 ml) $n = 20$	Regimen B (600 ml) $n = 20$	Regimen C (400 ml) $n = 20$	p value
Q1: How did you find swallowing the medicine?	Very easy, *n* (%)	4 (20)	1 (5)	4 (20)	0.68*
	Somewhat easy, *n* (%)	8 (40)	7 (35)	10 (50)	
	Neutral, *n* (%)	1 (5)	2 (10)	1 (5)	
	Somewhat difficult, *n* (%)	6 (30)	8 (40)	3 (15)	
	Very difficult, *n* (%)	1 (5)	2 (10)	2 (10)	
Q2: How did you feel about the amount of medicine?	Small, *n* (%)	2 (10)	1 (5)	4 (20)	0.093*
	Neutral, *n* (%)	11 (55)	11 (55)	14 (70)	
	Too much, *n* (%)	7 (35)	8 (40)	*1 (5)*	
	No answer, *n* (%)	0	0	1 (5)	
Q3: Did you experience any sleep disturbance?	No, *n* (%)	14 (70)	8 (40)	10 (50)	0.31*
	Mild, *n* (%)	4 (20)	10 (50)	7 (35)	
	Severe, *n* (%)	1 (5)	1 (5)	2 (10)	
	No answer, *n* (%)	1 (5)	1 (5)	1 (5)	
Q4: How many times did you go to the toilet after dinner?	*n* (range)	8.5 (2–19)	7 (1–28)	6 (1–12)	0.69**
Q5: Which exam would you prefer: CTC or colonoscopy?	CTC, *n* (%)	11 (55)	13 (65)	14 (70)	0.39*
	Colonoscopy, *n* (%)	3 (15)	4 (20)	1 (5)	
	Ether, *n* (%)	6 (30)	2 (10)	5 (25)	
	No answer, *n* (%)	0	1 (5)	0	

CTC CT colonography

*Chi-square test

**Kruskal-Wallis test

and exerts an osmotic effect in the colon, acting synergistically with PEG. So far, only one report employed MoviPrep™ for bowel preparation prior to CTC [26]. The present study demonstrates that the image quality of CTC using 400 ml/600 ml of MoviPrep™ was not inferior to that of 800 ml of MoviPrep™. Indeed, there was no residual stool in 80% to 90% of segments using each regimen, unexpectedly indicating that the image quality in this trial compares favorably to that in previous similar reports [15, 23, 24]. Although residual stool was well labeled with contrast media, no residual stool is best for CTC reading because specific expertise in two-dimensional interpretation is required to distinguish polyps from tagged solid stool. A large amount of residual colonic fluid may obscure polypoid lesions because the tissue under water is blind if there is a great deal of residual fluid. Since CTC is normally taken in two positions, it does not interfere with interpretation unless the fluid depth is ≥ 50% of the luminal circumference. In this clinical trial, the percentage of segments with no or minimal fluid was almost 50% to 60% in each regimen, suggesting optimal conditions for CTC reading. The quality of fecal tagging was excellent in almost all segments. Few procedures were interrupted by beam-hardening artifact which occurs with barium-based tagging regimens [27]. These results would contribute to high diagnostic accuracy and shorter reading time.

In the protocol used in this study, less volume of contrast medium was used in comparison with previous non-laxative studies or reduced-laxative studies [16, 17, 19, 20, 24, 27]. In laxative-free CTC reported by Fini et al [28], per-patient sensitivity and specificity for advanced neoplasms ≥ 6 mm were 0.89 and 0.96, respectively. However, this laxative-free method required patients to adhere to a low-fiber diet for 1 week. Furthermore, patients had to drink iodinated contrast agent at each of four main meals starting 36 h before the CTC examination. Such major dietary restrictions could change a patient's daily life considerably. In contrast, the present regimen should have a minimal effect on daily life because the bowel preparation starts after dinner on the day before the examination, and the duration of dietary restrictions is shorter than in previous reports [17, 20, 28]. This suggests that the volume-reduced laxative protocol for CTC used in the present trial may be suitable for busy people, fragile patients, and elderly patients.

In the questionnaire after the CTC examination, the majority of patients chose CTC for a future examination regardless of the regimen assigned. However, patient acceptance did not improve significantly, similar to previous reports [6, 15, 18, 19]. In contrast, a recent study comparing reduced and full bowel preparation showed that patients who underwent full bowel preparation reported a higher prevalence of

preparation-related symptoms and also more frequent interference of the bowel preparation with daily activities [29].

Even with a non-laxative study, some patients were not satisfied with the bowel preparation regimen [20]. Recently, laxative-free and diet-free bowel preparation regimens for CTC were reported and the patient acceptability rate was better than before [30]. We should aim to develop both laxative-free and diet-free bowel preparation regimens in the future.

There are several limitations to this study. First, this is a single-center study conducted in Japan where dietary habits are different from western countries. A validation study in Europe or North America is warranted. Second, image interpretation was performed by two readers blinded to the allocation, which could affect the results [18]. Inter-rater agreement was judged as moderate. Generalizability may be limited. Third, we did not evaluate the diagnostic accuracy for colorectal polyps because all participants did not undergo colonoscopy. Image quality is a surrogate marker to compare the regimens. Fourth, multiple samples obtained from a single patient may be more similar to each other than single samples from multiple patients, although the assessment for each colon segment was made independently in this trial. Image quality might be assessed based on each individual patient.

In conclusion, a novel volume-reduced CTC regimen using MoviPrep™ demonstrated optimal colon cleansing effectiveness, and the CTC image quality using 400 ml/600 ml of MoviPrep™ was not inferior to that using 800 ml of MoviPrep™. Patient acceptance did not significantly improve, similar to previous studies. Both laxative-free and diet-free bowel preparation regimens for CTC warrant further investigation.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Kazutomo Togashi (corresponding author).

Conflict of interest The authors of this manuscript declare relationships with the company EA Pharma Co., Ltd., Tokyo, Japan.

Statistics and biometry Professor Yoshikazu Nakamura (Department of Public Health, Jichi Medical University) kindly provided the statistical advice for this manuscript.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional review board approval was obtained.

Methodology
- prospective
- randomized controlled trial
- performed at one institution

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