

Efficacy of Endocuff-assisted colonoscopy in the detection of colorectal polyps



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ABSTRACT

Background and study aims Colonoscopy is the gold standard for detecting colorectal adenomas and cancers. Endoscopic surveillance has been shown to be effective for preventing colorectal cancer. Although detection of colorectal polyps at an early stage is important, endoscopic visualization of early neoplasia can be difficult. The Endocuff

is a new device that can be attached to the tip of the colonoscope to hold the colonic folds away from the field of view during withdrawal. The aim of this study was to compare the adenoma detection rate (ADR) and the mean number of adenomas detected per patient (MAP) achieved using Endocuff-assisted colonoscopy (EAC) and standard colonoscopy (SC).

Patients and methods This randomized prospective study was conducted at two academic endoscopy departments in Japan. A total of 447 patients underwent a complete colonoscopic examination between April 2015 and September 2015. The EAC group included 239 patients. The cecal intubation rate, insertion time, withdrawal time, pain score, complications, polyp detection rate (PDR), ADR, the mean number of polyps detected per patient (MPP), and the MAP were assessed.

Results There were no differences between the EAC and SC groups in terms of cecal intubation rate, insertion time, withdrawal time, or pain scores. The PDR in patients increased by about 12% (61.9% vs. 49.2%, $P=0.013$) and ADR increased by 15% (52.5% vs. 39.2%, $P=0.001$) with the use of the Endocuff. The advanced ADR was higher in the EAC group but no statistically significant difference was found (7.7% vs. 4.6%, $P=0.17$). Both MPP and MAP were also higher in the EAC group (mean \pm SD: 1.33 \pm 1.43 vs. 0.83 \pm 0.99 per patient; $P<0.01$, 1.11 \pm 1.41 vs. 0.66 \pm 0.99 per patient; $P<0.01$, respectively). No major complications occurred.

Conclusions EAC not only enabled a higher ADR but also significantly increased the mean number of adenomas identified per patient, as compared with SC.

Introduction

Colorectal cancer (CRC) is one of the most common malignancies worldwide, with high incidence rates. Early detection and removal of adenomatous polyps using colonoscopic polypectomy has been shown to reduce risk of subsequently developing CRC by 76% to 90% [1]. Removal of adenomas also lowers incidence of CRC-related deaths [2]. Colonoscopy is the gold stand-

ard for identification and removal of colonic polyps [3]. However, despite its use, polyps can remain undetected. Studies of tandem colonoscopy have reported polyp miss rates of 5% to 32% [4–10]. Thus, improved polyp detection is a major focus of quality improvement measures in colonoscopy screenings.

Recently investigated measures with a positive effect on polyp detection have included chromoendoscopy [11]; narrow band imaging (NBI, Olympus, Tokyo, Japan) [12]; the Third Eye

Retroscope (TER, Avantis Medical Systems, Sunnyvale, California, United States) [13, 14]; full-spectrum endoscopy (FUSE, EndoChoice Inc., Alpharetta, Georgia, United States) [15]; and the extra-wide-view colonoscope (Olympus, Tokyo, Japan) [16]. Brown et al. reported that chromoscopy is likely to identify significantly more patients with at least one neoplastic lesion (odds ratio [OR]=1.61, 95% confidence interval [CI] 1.24–2.09) and significantly more patients with three or more neoplastic lesions (OR=2.55, 95%CI 1.49–4.36) [11]. Horimatsu et al. reported that the mean number of polyps per patient (MPP) was significantly higher in the NBI group than in the white-light imaging group (2.01 vs. 1.56; $P=0.032$) [12]. Way et al. reported that TER allowed for detection of 34 additional polyps (a 13.2% increase; $P<0.0001$) including 15 additional adenomas (an 11.0% increase; $P<0.0001$) [13]. Gralnek et al. reported that the adenoma miss rate was significantly lower in patients in the FUSE group than those in the standard forward-viewing procedure group: 5 of 67 (7%) vs. 20 of 49 (41%) adenomas were missed ($P<0.0001$) [15]. Uraoka et al. reported that the mean detection rate for all simulated polyps with the extra-wide-angle-view colonoscope was significantly higher than that with the standard colonoscope (68% vs. 51%; $P<0.0001$) and the detection rate for polyps behind folds was significantly higher when the extra-wide-angle-view colonoscope rather than the standard colonoscope was used (61.7% vs. 46.9%; $P=0.0009$) [16].

Endocuff (Arc Medical Design Ltd., Leeds, England) is another recently developed device. It is a 2-cm long, disposable flexible cuff with two projections. It can be attached to the tip of the colonoscope to hold the colonic folds away from the field of view during withdrawal, and has been designed to improve both the adenoma detection rate (ADR) and the user's control of the tip of the colonoscope. There are a limited number of recent publications summarizing the clinical and technical success of Endocuff in improving ADR during colonoscopy. Based on a meta-analysis, Chin et al. reported that a higher frequency of adenoma (OR=1.49, 95% CI 1.23–1.80; $P=0.03$) was observed in patients undergoing procedures with the Endocuff than in those undergoing the standard colonoscopy (SC), without any differences in cecal intubation rates [17]. The aim of this study was to compare the ADR and the mean number of adenomas detected per patient (MAP) using Endocuff-assisted colonoscopy (EAC) and standard colonoscopy (SC) performed without a plastic hood.

Patients and methods

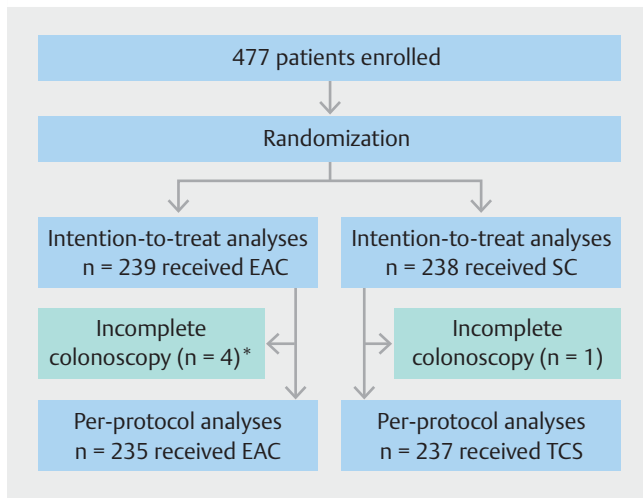
This was a prospective, randomized trial which was conducted according to the principles of the Declaration of Helsinki and registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) (registration number: UMIN 000028572). Signed informed consent was obtained from all patients. Following recruitment, patients underwent colonoscopy, with or without polypectomy, following standard institutional protocols. Patients were assigned randomly in a 1:1 ratio to undergo either EAC or SC via an envelope method before colonoscopy. In the “envelope method,” our team

placed a slip of paper with the words “EAC group” or “SC group” and related instructions into an envelope. The operator selected the envelopes sequentially and opened them immediately before endoscopy. The instructions contained in the envelope were followed consistently at the time of the procedure. Based on this method, 477 patients were randomly assigned to two groups, each consisting of almost the same number of patients. All polyps without 5 mm or less rectosigmoid hyperplastic polyps were removed. Patients receiving antiplatelet drugs or warfarin were included in this study, but such medications were appropriately discontinued prior to the endoscopic resection.

Between April 2015 and September 2015, all patients who were scheduled for routine outpatient colonoscopy at two different centers (a university hospital and an associated endoscopy clinic) were reviewed by a gastroenterologist and considered for inclusion in the current study. This study was conducted mainly at an endoscopy clinic where the operator was working on a full-time basis, as well as at a university hospital where he worked as a part-time instructor twice monthly. Thus, a single endoscopist (Y.W.) performed all the colonoscopies for all the patients included in this study. Patients who asked to undergo endoscopy at the university hospital for reasons such as proximity to their homes were referred to the university hospital and the endoscopist performed their colonoscopies on the days he was present at the institution. Exclusion criteria included previous bowel resection, inflammatory bowel disease, and/or presence of polyposis syndromes. Patients were also excluded if they were scheduled to undergo endoscopic mucosal resection for a known polyp or cancer.

Prior to colonoscopy, patients underwent bowel preparation. The procedure entailed administering sodium picosulfate the day before the colonoscopy and then 2 to 3 L of a polyethylene glycol solution the morning of the procedure. The Boston bowel preparation score (BBPS), a validated and simple-to-use scale, was applied for assessment of the cleansing effect [18]. To prevent bowel spasm, scopolamine butylbromide (20 mg) or glucagon (1.0 mg) was injected intramuscularly as an antispasmodic agent before the examination. A patient's procedural pain was evaluated using a numerical rating scale (NRS). The NRS was scaled from 0 to 10, with 0=absence of pain and 10=worst possible pain, as previously described [19]. All patients reported their respective NRS scores within 1 hour after colonoscopy to a medical assistant who was blinded to the type of instrument used. In our study, colonoscopic procedures were performed without use of sedatives because receiving the drugs would have made it difficult for a patient to assess the pain score. The colonoscopes used were PCF-H290ZI, CF-HQ290, and CF-HQ290ZI (Olympus, Tokyo, Japan).

Heart rate and pulse oximetry were monitored continuously, and blood pressure and respiration rate were recorded at 5-minute intervals. The procedures were performed by an experienced endoscopist, who has performed over 10 000 colonoscopies to date. Patient characteristics and pre-procedural measures were obtained by interview after a patient provided consent and they included age, sex, and indication for colonoscopy or abdominopelvic surgery. The duration of colonoscopy was



► **Fig. 1** Flow of patients through the study. EAC, Endocuff-assisted colonoscopy; SC, standard colonoscopy; TCS, total colonoscopy. *In 4 patients in the Endocuff-assisted colonoscopy (EAC) group, the Endocuff-assisted examination had to be stopped in the sigmoid colon due to severe stenosis caused by diverticula or cancers.

measured from insertion of the colonoscope to its final withdrawal from the anus. Total colonoscopy was identified as intubation of the cecum or ileum, which was determined by visualization of the ileocecal valve and the appendiceal orifice [20]. The polyp detection rate (PDR) or ADR was defined as the proportion of colonoscopies in which at least one polyp or adenoma was detected per colonoscopy [21, 22]. The preparation grade was measured by the BBPS [18]. The number of polyps removed and the time taken for removal were recorded. All times and measures were recorded by the attending nursing staff under the direction of the endoscopist.

The endoscopist avoided removing polyps during intubation. Polyps were removed using a variety of standard techniques, depending on size, morphology, location and the findings obtained in magnifying colonoscopy. The colorectum was divided into proximal and distal colons at the splenic flexure. Removed polyps were retrieved and sent for histopathology. Expert gastrointestinal histopathologists, who were blinded to the therapy used, reviewed the specimens. The final pathological diagnosis was made in accordance with World Health Organization guidelines [22], and classified as hyperplastic polyp, adenoma, carcinoma, or other. The definition of advanced adenoma was an adenoma 10 mm or more in diameter, a lesion with a villous component or high-grade dysplasia, or cancer. We classified the morphology of colorectal polyps according to the “General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus” of the Japanese Society for Cancer of the Colon and Rectum [23] and the Paris classification [24]. Cecal intubation rate, insertion time, withdrawal time, pain score, complications, PDR, and ADR were assessed.

Sample size and statistical analysis

The primary endpoints were the ADR and MAP. The sample size was calculated using the variable ADR data available at our centers. Our centers’ endoscopy data showed that prevalence of adenomas was 30% in patients undergoing screening surveillance or diagnostic colonoscopy. On the basis of these data, the sample size was needed to show a significant difference between the EAC and SC groups, each comprising 240 patients, at an alpha level of 0.05, with a power of 90%. Baseline and demographic data, along with the outcome variables, were compared between the EAC and SC groups using Pearson’s chi-squared tests for categorical variables and endpoints and Mann-Whitney U tests for continuous variables and endpoints. Analyses were performed using the IBM SPSS statistical software package (version 23.0, IBM Corp., Armonk, New York, United States). Two-tailed tests with a 5% level of significance were used throughout.

Results

Patients and procedure demographics

A total of 477 patients provided informed consent to be included in the study. No patient was excluded prior to randomization (► **Fig. 1**). In total, 239 patients underwent EAC and 238 underwent SC. There were no significant differences in the baseline characteristics between the EAC and SC groups (► **Table 1**). Furthermore, there were no significant differences between the EAC and SC groups in terms of cecal intubation time, withdrawal time, and quality of preparation (► **Table 2**). With respect to the cecal intubation rate, total colonoscopy was performed in almost all patients in both groups. In four patients in the EAC group, the examination had to be stopped at the sigmoid colon due to severe stenosis caused by diverticula or cancers. These examinations were completed with a standard colonoscope. The examination was incomplete in one patient in the SC group because of excessive adhesion.

Polyp and adenoma detection

Analyses regarding PDR, ADR, and the MPP and MAP were performed on the per-protocol cohort (► **Table 3**). PDRs and ADRs were higher in patients who underwent EAC than in those who underwent SC, and this difference was statistically significant (61.9% vs. 49.2% [$P=0.003$] and 55.2% vs. 39.2% [$P=0.0002$], respectively). The advanced ADR was higher in the EAC group, but no statistically significant difference was found (7.7% vs. 4.6% [$P=0.17$]). More polyps were identified in patients who underwent EAC than in those who underwent SC (mean±SD: 1.33 ± 1.43 vs. 0.83 ± 0.99 per patient; $P<0.01$). A higher number of adenomas were also identified in patients who received EAC than in those who received SC (mean±SD: 1.11 ± 1.41 vs. 0.66 ± 0.99 per patient; $P<0.01$). Both MPP and MAP were also higher in the EAC group. There were no significant differences in size, morphology, or distribution of the polyps. Cecal intubation and withdrawal times were longer and the pain scale was

► **Table 1** Baseline characteristics of all patients.

	EAC (n=239)	SC (n=238)	P value
Patients	239	238	
Age, median (IQR) (years)	61.2 (51–71)	62.2 (53–73)	0.26
Sex (M/F)	122/117	115/123	0.55
First-time colonoscopy	75	85	0.32
Abdominopelvic surgical history	89	91	0.82
BBPS (SD, IQR)	7.91 (0.94, 7–9)	7.88 (1.03, 7–9)	0.66
Indication			
▪ Screening	89	74	
▪ Polyp surveillance	24	40	
▪ Symptoms	70	65	0.39
▪ Gastrointestinal bleeding	27	31	
▪ Positive fecal occult blood test result	27	24	
▪ Unknown/other	2	4	
IQR, interquartile range; BBPS, Boston bowel preparation score; SD, standard deviation; EAC, Endocuff-assisted colonoscopy; SC, standard colonoscopy.			

higher in the EAC group, but these differences were not statistically significant. We also performed an intention-to-treat analysis (► **Table 4**). Both PDR and ADR were significantly higher in the EAC group in the intention-to-treat analysis (62.7% vs. 49.2% [$P=0.003$] and 56.1% vs. 39.1% [$P=0.0002$], respectively). MPP and MAP were also higher in the EAC group.

Adverse events

No other serious adverse events (SAEs) such as bleeding and perforation were recorded. Superficial mucosal erosions occurred in 54 patients (23.0%) during withdrawal of the colonoscope in the EAC group. Superficial mucosal erosion is a superficial scratch on the colonic mucosa, which occurs because of rubbing of the mucosal plication against the projection of the Endocuff when it is inserted or removed. It is expected to spontaneously heal over several days. In a previous meta-analysis [17], superficial mucosal erosion was found to be clinically insignificant, with no likelihood of increased frequency of perforation. No dislocation of the device occurred during any of the examinations.

Discussion

In this prospective randomized study, we compared ADR with EAC versus SC and observed that using an Endocuff during colonoscopy increased the number of adenomas detected and

► **Table 2** Colonoscopy details.

	EAC (n=239)	SC (n=238)	P value
Cecal intubation rate	235 (98.3%)	237 (99.6%)	
Cecal intubation time (min ± SD [IQR])	4.3 ± 3.0 (3–5)	4.1 ± 2.0 (3–5)	0.26
Withdrawal time (min ± SD [IQR])	8.3 ± 3.9 (6–10)	7.8 ± 2.6 (6–11)	0.11
Pain score (numerical rating scale)	2.93	2.78	0.35
SD, standard deviation; IQR, interquartile range; EAC, Endocuff-assisted colonoscopy, SC, standard colonoscopy.			

significantly increased the number of patients with at least one adenoma detected. In short, more adenomas were detected, but most were considered non-advanced lesions. However, it has been reported that colonoscopic removal of adenomatous polyps prevents death from CRC and that improved polyp detection contributes to a reduced risk of CRC [25].

The oral side of the colonic folds can be observed using an Endocuff during withdrawal of the colonoscope. Due to a reduction in the blind spots associated with the use of this device, it is reasonable that PDR, ADR, MPP, and MAP increased. Our study also showed that because the range of observation became wider, the withdrawal time tended to be longer, with no significant differences in outcomes. As for cecal insertion, the cecal intubation rates were similar in both groups. In four patients in the EAC group, the Endocuff-assisted examination had to be stopped at the sigmoid colon. Many diverticula and circumferential cancers were reported as reasons for incomplete insertion. These examinations were completed with a standard colonoscope after removal of the Endocuff. Because the hood mounted at the tip of the colonoscope increased the external diameter of the tip, careful use of the colonoscope is required in patients with stenosis of the lumen of the intestinal tract due to the presence of diverticula or tumors, or in those with anal stenosis due to hemorrhoids.

This is the first prospective, randomized controlled trial (RCT) from Japan that is adequately powered to compare ADR and MAP between EAC and SC groups. In this study, colonoscopies were performed at two academic centers by an experienced endoscopist. EAC and SC were consecutively performed in a random order, and data on polyp detection, procedure times, and bowel preparation scores were prospectively recorded, ensuring accurate and optimal collection of data from high-quality colonoscopies. Therefore, we believe that our results are reliable and applicable to daily clinical practice.

ADR is considered the most important surrogate measure for quality of colonoscopy, but has a limitation in that it does not measure the total number of adenomas detected during a procedure and thus might provoke the “one-and-done” phenomenon [26]. In the literature, it has been suggested that MAP should be reported in addition to ADR [27]. Besides avoid-

► **Table 3** Polyp detection with Endocuff-assisted colonoscopy (EAC) versus standard colonoscopy (SC): per-protocol analysis.

	EAC (n=235)	SC (n=237)	P value
All detected polyps	312	197	
Adenomas	260	158	
Patients with polyps (polyp detection rate)	148 (61.9%)	117 (49.2%)	0.003
Patients with adenomas (adenoma detection rate)	132 (55.2%)	93 (39.2%)	0.0002
Patients with advanced neoplasm	18 (7.7%)	11 (4.6%)	0.17
Patients with adenocarci- noma (Tis~)	4 (1.7%)	4 (1.7%)	0.99
Patients with adenocarci- noma (T1~)	1 (0.4%)	3 (1.3%)	0.32
Mean number of polyps per patient (SD)	1.33 (1.43)	0.83 (0.99)	<0.01
Mean number of adeno- ma per patient (SD)	1.11 (1.41)	0.66 (0.99)	<0.01
Size of polyps			
▪ 1–5 mm	186	135	
▪ 6–10 mm	99	50	0.12
▪ ≥11 mm	27	12	
Morphology of polyps			
▪ Protruded	119	72	
▪ Flat-elevated	192	122	0.61
▪ Depressed	1	3	
Distribution of polyps			
▪ Proximal	198	110	
▪ Distal	104	75	0.18
▪ Rectum	10	12	

SD, standard deviation; EAC, Endocuff-assisted colonoscopy; SC, standard colonoscopy.

► **Table 4** Polyp detection with Endocuff-assisted colonoscopy (EAC) versus standard colonoscopy (SC): intention-to-treat analysis.

	EAC (n=239)	SC (n=238)	P value
All detected polyps	315	197	
Adenomas	263	158	
Patients with polyps (polyp detection rate)	150 (62.7%)	117 (49.2%)	0.003
Patients with adenomas (adenoma detection rate)	134 (56.1%)	93 (39.1%)	0.0002
Patients with advanced neoplasm	20 (8.4%)	11 (4.6%)	0.10
Patients with adenocarci- noma (Tis~)	6 (2.5%)	4 (1.7%)	0.75
Patients with adenocarci- noma (T1~)	3 (1.3%)	3 (1.3%)	0.68
Mean number of polyps per patient (SD)	1.32 (1.43)	0.83 (0.99)	<0.01
Mean number of adeno- mas per patient (SD)	1.10 (1.41)	0.66 (0.99)	<0.01
Size of polyps			
▪ 1–5 mm	187	135	
▪ 6–10 mm	99	50	0.10
▪ ≥11 mm	29	12	
Morphology of polyps			
▪ Protruded	122	72	
▪ Flat-elevated	192	122	0.58
▪ Depressed	1	3	
Distribution of polyps			
▪ Proximal	198	110	
▪ Distal	107	75	0.21
▪ Rectum	10	12	

SD: standard deviation; EAC, Endocuff-assisted colonoscopy; SC, standard colonoscopy.

ing the “one-and-done” phenomenon, identification of every adenoma is necessary to recommend a sufficient surveillance interval. If the recommended surveillance is less intensive than it should have been had all the adenomas been detected during the initial colonoscopy, interval carcinomas could result.

In this study, we report high ADRs of 55.2% and 39.2% in the EAC and SC groups, respectively. Several RCTs and meta-analyses have compared PDRs and ADRs achieved with cap-assisted colonoscopy (CC). Although the earliest meta-analysis showed increased PDRs and improved detection of diminutive and small adenoma with CC [28], none of the meta-analyses detected a convincing increase in ADR [29, 30]. The most recent RCT conducted involved over 1000 patients and did not report a significantly higher ADR with CC [31]. Four previous studies compar-

ed ADRs between EAC and CC; however, they did report an increase in ADR with EAC [17, 32–36]. Our study also showed almost overlapping results, although in our opinion, it is preferable to compare standard colonoscopy without a plastic hood in order to evaluate the true increase in the efficacy of the Endocuff for detecting colorectal adenomas. Van Doorn, et al. reported that EAC increases detection of diminutive and flat adenomas but does not increase ADR [37]; however, withdrawal time was significantly shorter with EAC than with CC in their study. The Endocuff was designed to flatten colonic folds. Our study demonstrated that the reduction in blind spots achieved during withdrawal of the colonoscope enabled a wider range of observation, but the withdrawal time tended to be longer with EAC. Nonetheless, the prolonged observation time did not re-

sult in any significant differences. If the Endocuff can be effectively used during colonoscope withdrawal, the ADR is considered to be increased. As for colorectal polyp size, both De Palma, et al. and van Doorn SC, et al. reported that EAC improved detection of small adenomas [36,37]. EAC also improved detection of non-advanced colorectal polyps in our study.

While previous studies have described an increase in the number of polyps detected in the cecum and sigmoid colon [32,33], our study could not confirm this observation. The aim of the Endocuff is to flatten the colonic folds with its protections. The proximal colon has large folds, which would limit the observation range with standard colonoscopy, but use of the Endocuff would allow a better minimization of the blind spots. The distal colon, especially in the sigmoid colon, has overlapping folds, but using the Endocuff would also enable users to check for presence of polyps in each fold during colonoscope withdrawal. Our study resulted in an increased number of polyps being detected in the entire colon, with no bias with regard to specific sites.

The current study has a few limitations. First, patients were blinded to the allocated procedure, while the colonoscopists were not. This was a major limitation, as absence of blinding may have influenced the PDR and ADR. Second, we did not perform a tandem colonoscopy trial. Polyp and adenoma miss rates could not be calculated. Finally, this study was performed by a single experienced endoscopist who had performed over 10 000 colonoscopies at the time of this study; thus, the results may not be representative of all colonoscopy practices. Had multiple endoscopists participated in the group discussion regarding the data analysis of the single colonoscopies performed by the endoscopist, better and more convincing conclusions could have been drawn for the study. However, this study is significant for specialists or experts as it proves the role of EAC in improvement of ADR and MAP in daily clinical practice. In the future, further research is necessary to investigate whether EAC performed by non-experts also contributes to improvement in ADR and MAP, and whether there is a difference in the efficacy of Endocuff when used by experts versus non-experts.

Conclusion

EAC has enabled significantly higher PDRs and ADRs than SC in this study. No SAEs were detected. Further studies are required to confirm the current results.

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Competing interests

None

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