Endocuff vision-assisted vs. standard polyp resection in the colorectum (the EVASTA study): a prospective randomized study

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ABSTRACT

Background Cap-assisted colonoscopy is frequently used to facilitate adenoma detection during endoscopy. However, data on how cap assistance influences polyp resection are scarce. We aimed to evaluate the impact of cap assistance with the Endocuff vision device (EVD) on the resection time for colorectal polyps in patients undergoing colonoscopy.

Methods A randomized, prospective study was performed in a university hospital in Germany. A total of 250 patients were randomly assigned 1:1 to undergo either colonoscopy with the EVD (EVD arm) or standard colonoscopy without the use of a cap (standard arm). The primary outcome was the average duration of polypectomy. Secondary outcomes included adenoma detection rate, cecal and ileal intubation times, and propofol dosage.

Results The use of EVD led to a significant reduction in the median polypectomy time in the EVD vs. standard arm (54 vs. 80 seconds, respectively; \( P = 0.02 \)). This effect was strongest for polyps \( \geq 6 \) mm. Compared with the standard group, Endocuff assistance also resulted in a shorter cecal intubation time (6 vs. 8 minutes; \( P = 0.03 \)) and overall colonoscopy time (23 vs. 27 minutes; \( P = 0.02 \)). In contrast, no difference in withdrawal time was observed. The polyp and adenoma detection rates did not differ significantly between the two groups.

Conclusion Endocuff-assisted colonoscopy reduces the duration of polypectomy, which may be due to a more stable scope position during resection. Further studies are needed to investigate whether comparable effects will be seen for other interventions, such as clipping or biopsy sampling.

Clinical.Trials.gov
NCT03117114

TRIAL REGISTRATION: Prospective randomized study NCT03117114 at clinicaltrials.gov

Introduction
Detection and removal of adenomatous polyps during colonoscopy is performed to prevent the development of colorectal cancer (CRC). Cap devices, such as the Endocuff vision device (EVD), are placed over the tip of the colonoscope and consist of flexible arms that flare out during scope withdrawal, thereby stretching the colorectal mucosa. The EVD is a second-generation device that has one row of flexible arms, in contrast to the first-generation devices, which had two rows of flexible arms. The main aim of the Endocuff is to improve adenoma detection. This has been investigated in numerous studies that focused on the effect of EVDs on adenoma detection rates (ADRs) [1–6]. There is however also a notion that EVDs may facilitate withdrawal...
wal of the scope and also polyp removal by stabilizing the position of the colonoscope. Because polyp removal contributes significantly to the total procedure time, efforts to improve this process would have an enormous impact on colonoscopies. However, to our knowledge, no randomized trial has yet investigated the impact of cap assistance on polyp removal time.

The hypothesis was that cap assistance would ease polyp removal, which would result in shorter polyp removal and procedure times. In order to investigate this hypothesis, a randomized controlled trial was performed.

Methods

Patients

This clinical study was approved by the local ethics committee and initially registered at ClinicalTrials.gov (identifier: NCT03117114). Written informed consent was obtained from all patients. The study was reported in accordance with the CONSORT statement. Inpatients and outpatients aged ≥ 40 years who presented for colonoscopy at the trial site (II. Medizinische Klinik und Poliklinik, Klinikum rechts der Isar der Technischen Universität München, Munich, Germany) were consecutively screened for inclusion. Exclusion criteria were: emergency colonoscopy; ASA risk class IV, V, or VI; known adenoma/polyp scheduled for resection; known CRC or inflammatory bowel disease.

Study design

The trial was conducted at a university hospital in Germany. Patients scheduled for colonoscopy were randomized at the endoscopy unit. Colonoscopy was performed using CF-HQ 190 EVIS Exera III Advanced colonoscopes (Olympus, Tokyo, Japan). In the EVD arm, the Endocuff device (Arc Medical Design, Leeds, UK) was attached to the colonoscope before the beginning of the procedure and kept on until the end. Fig. 1 shows an exemplary image of the EVD being used during the study. In the standard arm, colonoscopies were carried out without an EVD.

Colonoscopies were performed by 14 experienced colonoscopists (> 150 performed colonoscopies) and patients underwent the procedure either without sedation or with sedation using propofol and/or midazolam depending on the patients’ preferences, comorbidities, and allergies. Sedated patients were monitored for oxygen saturation and blood pressure and received supplemental oxygen. Colonoscopists were not experienced in using the EVD prior to the study. The EVD was explained to the colonoscopists before study participation.

In both study arms, cecal intubation time, ileal intubation time, total procedure time, and polyp removal time were measured by an independent investigator (not by the colonoscopist) during the procedure. The colonoscopist indicated to the independent investigator the start and end of polyp removal during the procedure. The method of polyp resection (e.g. cold/hot snare, forceps, prior saline injection) was also recorded. For the determination of polypectomy duration, the timer was started when the first polypectomy device (e.g. forceps, snare, or injection needle) was inserted into the scope and was stopped when the polyp was resected. Polyp retrieval was not included in this time. The colonoscopist noted the size and location of each polyp.

Resected polyps were sent for histopathological evaluation at the University Hospital pathology department. Polyps were categorized depending on the pathological diagnosis as non-adenomatous (e.g. hyperplastic polyp or inflammatory polyp), adenoma (tubular, tubulovillous, or villous), clinically significant serrated lesions (sessile serrated or traditional serrated adenoma), or carcinoma.

At the end of the procedure, both the endoscopist and the patient (once awake) were asked for their satisfaction with the examination by the independent investigator. Satisfaction was evaluated on a numeric scale, ranging from 0 for minimum satisfaction to 10 for maximum satisfaction.

Randomization

Patient randomization was based on a list with randomly varying block sizes that was generated using the software nQuery Advisor version 7.0. Consecutively numbered, sealed, and opaque envelopes were used for procedure allocation.

Study endpoints

The primary endpoint was defined as polypectomy duration in both study arms. Secondary outcome measures were: number of detected polyps/adenomas, cecal and ileal intubation times, total procedure duration, patient and endoscopist satisfaction, complications, and propofol dosage.

Sample size calculation

Sample size calculation was based on data observed in the SNOWCAT study [7], in which all polypectomies were performed using the standard procedure. In the SNOWCAT data, a mean polypectomy duration of about 6 minutes per polyp was observed (unpublished data). A reduction in the average polypectomy duration of 33% to 4 minutes was considered as a rel-
relevant group difference. As polypectomy durations followed a skewed distribution, a log-transformation was intended. For the log-transformed data, a standard deviation (SD) of about 1 was observed in the SNOWCAT data and the relevant difference between the groups transformed to 0.405. Under these assumptions, a number of about 100 observations per group would be needed to detect a relevant difference, with a power of 80% using a significance level of 5% and a two-sided test (nQuery Advisor version 7.0).

As multiple polyps are resected in some patients and no polyps are resected from other patients, the sample size calculation was adapted for the presence of within-patient correlation. In the SNOWCAT study, a within-patient correlation of 0.25 was observed for polypectomy duration. About half of the patients had at least one polyp and the average number of polyps in patients with at least one polyp was about two. Considering the variance inflation factor (VIF) as described in Donner et al. [8], the sample size needed for an individually randomized trial has to be multiplied by the VIF, which is this case is $1 + (2 \text{ polyps per patient with at least one polyp} - 1) \times 0.25 = 1.25$. Consequently, 125 polyps would need to be resected in each study group. As for half of the patients at least one polyp was expected and the average number of polyps per patient with at least one polyp was assumed to be two, it was intended that 125 patients would be randomized to each arm.

Statistical analysis

For categorical data, absolute and relative frequency are presented. For continuous data, median and interquartile range (IQR) or mean and SD are shown as indicated.

For the primary analysis, the comparison of polypectomy duration between the study groups, a linear generalized estimating equation (GEE) model using log-transformed polypectomy duration as the dependent variable and study group as the independent variable was fitted to the data. An exchangeable correlation structure was assumed to account for within-patient correlation, as multiple polyps were resected for some patients. To assess treatment effect heterogeneity with regard to polyp size and polypectomy method, regression models with the relevant main effects and an interaction term with study group were fitted to the data. Logistic GEE models were used to compare proportions of polyps with multiple resections and use of methods for polyp resection (forceps vs. snare) between study groups.

For comparison of cecal intubation times, ileal intubation times, colonoscopy withdrawal times, and colonoscopy duration, t tests for independent samples were used and times were log-transformed because of the skewed distributions. The Mann–Whitney U test was used to compare propofol dosages and the distributions of the numbers of detected polyps and adenomas per patient between the groups because of the presence of zero values and for comparison of patient and endoscopist satisfaction as the data were negatively skewed.

For group comparisons of polyp detection rate (PDR) and ADR, chi-squared tests were conducted.

All statistical tests were performed two-sided and a significance level of 5% was used. Statistical analyses were performed using the statistical software R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria) and its packages gee-pack and MASS.

Results

Participants

A total of 276 patients were screened for eligibility. Of these, 26 had to be excluded either because written informed consent could not be obtained (n = 25 [specific reasons: unwillingness to participate (n = 11), language difficulties making communication impossible (n = 7), concerns regarding safety of the EVD (n = 6), or disorientation (n = 1)]) or because of active anticoagulation therapy precluding polypectomy (n = 1) (Fig. 2).

Therefore, 250 patients were randomized in a 1:1 ratio to either the EVD arm (n = 125) or standard arm (n = 125). Of these, three patients on the standard arm and seven patients on the EVD arm had to be excluded because of incomplete colonoscopy procedures. The reasons for interruption were: inadequate bowel preparation (n = 7), impassable sigmoid stenosis (n = 1), perforation (n = 1), and failed cecal intubation (n = 1).

The modified intention-to-treat (mITT) analysis therefore included 240 patients (Fig. 2). Of the 118 patients in the EVD group, three had a study protocol violation because the EVD was removed from the colonoscope during colonoscopy; how-

![Fig. 2 Flow chart of enrollment and randomization of the study participants into the standard and Endocuff vision device (EVD) arms.](image-url)
ever, according to the intention-to-treat principle, these three patients were considered in the EVD group for statistical analysis.

The age, sex, body mass index (BMI), ASA class, and smoking status of the patients, along with the presence or absence of diabetes, were evaluated. Participants had a mean (SD) age of 64.4 (11.8) years. Further characteristics of the patients and the procedures they underwent are summarized in ▶ Table 1.

### Polyp and adenoma detection

A total of 380 polyps were detected in this study. There were 20 polyps (5.3%) in two patients that were left unresected as polyposis syndromes were suspected. For a further 27 polyps (7.1%), histology was not available as the specimens were lost accidently during retrieval from the colon. Therefore, histopathological diagnoses were available in 333 polyps.

There was no difference between the study groups in terms of the PDR (54.2% vs. 52.5% for the EVD and standard groups, respectively; \(P = 0.78\)) or the ADR (38.1% vs. 42.6%, respectively; \(P = 0.48\)). Similarly, there was no difference in the distribution of the mean number of polyps detected per colonoscopy (1.4 vs 1.7 for the EVD and standard groups, respectively; \(P = 0.93\)) or the mean number of adenomas per colonoscopy (0.84 vs. 0.97, respectively; \(P = 0.51\)). Other polyp features, including size and morphology, are given in the ▶ Table 1s, see online-only Supplementary material).

### Outcomes of polypectomy

The application of different methods of polyp resection (forceps vs. snare) did not differ significantly between the EVD and standard groups (\(P = 0.27\)). A detailed summary of polyp resection methods (forceps, cold snare, or hot snare; with and without prior saline injection) can be found in ▶ Table 2s.

Information on polypectomy duration was available for 357 polyps (159 and 198 in the EVD and standard groups, respectively). The median polypectomy duration was 54 seconds (IQR 29–113) in the EVD group compared with 80 seconds (IQR 34–181) in the standard group (\(P = 0.02\) ▶ Fig. 3; ▶ Table 2).

The test for interaction between polyp size and study group revealed significant effect heterogeneity with respect to polypectomy duration (\(P = 0.047\)). The benefit of the EVD was greater for small (6–9 mm) polyps (median polypectomy duration 53 vs. 108 seconds for the EVD and standard groups, respectively; \(P = 0.001\)) and large (>9 mm) polyps (141 vs. 250 sec-
onds, respectively; \( P = 0.047 \) than for diminutive (< 6 mm) polyps (42 vs. 59 seconds, respectively; \( P = 0.28 \)) (Fig. 1s).

The test on interaction between resection method (forceps, cold snare, and hot snare) and study group showed no significant effect heterogeneity (\( P = 0.71 \)).

In the EVD group, the number of polyps requiring more than one resection was significantly lower compared with that in the standard group (17.0% vs. 28.1%, respectively, \( P = 0.02 \)) (Fig. 2s).

### Procedural outcomes

The median (IQR) cecal intubation time was significantly shorter in the EVD group than in the standard group (6 minutes [4 – 9] vs. 8 minutes [5 – 12], respectively; \( P = 0.03 \)). In contrast, the median (IQR) time required for ileal intubation did not differ significantly between the two groups (10 minutes [7 – 15] vs. 8 minutes [8 – 15], respectively; \( P = 0.45 \)). Ileal intubation was unsuccessful in 29 out of 118 patients (24.6%) in the EVD group and in 10 out of 122 patients (8.2%) in the standard group (\( P < 0.001 \)). Colonoscope withdrawal time did not differ significantly between the study groups (23 minutes [17 – 34] vs. 27 minutes [18 – 38], respectively; \( P = 0.02 \)) (Fig. 4; Table 2).

The propofol dosage was not significantly different for the EVD group vs. the standard group (175 mg [100 – 220] vs. 170 mg [120 – 238], respectively; \( P = 0.48 \)).

### Patient and endoscopist satisfaction

Patients and endoscopists evaluated the colonoscopy in terms of satisfaction after the procedure (0 for minimum satisfaction to 10 for maximum satisfaction). There was no difference between the EVD and standard groups regarding the mean patient satisfaction (8.6 vs. 8.4, respectively; \( P = 0.91 \)) or mean endoscopist satisfaction (7.6 vs. 7.6, respectively; \( P = 0.94 \)).

### Table 2 Contemporaneously collected outcomes in the two groups – modified intention-to-treat analysis.

<table>
<thead>
<tr>
<th>Factor</th>
<th>EVD arm (n = 118)</th>
<th>Standard arm (n = 122)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polypectomy duration, median (IQR), seconds</td>
<td>54 (29 – 113)</td>
<td>80 (34 – 181)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total procedure duration, median (IQR), minutes</td>
<td>23 (17 – 34)</td>
<td>27 (18 – 38)</td>
<td>0.02</td>
</tr>
<tr>
<td>Withdrawal time, median (IQR), minutes</td>
<td>12 (6 – 18)</td>
<td>12 (8 – 22)</td>
<td>0.11</td>
</tr>
<tr>
<td>Cecal intubation time, median (IQR), minutes</td>
<td>6 (4 – 9)</td>
<td>8 (5 – 12)</td>
<td>0.03</td>
</tr>
<tr>
<td>BBPS score, median (IQR)</td>
<td>6 (5 – 8)</td>
<td>6 (6 – 8)</td>
<td>0.64</td>
</tr>
<tr>
<td>Failed ileal intubation, n (%)</td>
<td>29 (24.6%)</td>
<td>10 (8.2%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

EVD, Endocuff vision device; IQR, interquartile range; BBPS, Boston bowel preparation scale.
Colonoscopy complications

There were no serious procedural complications in the EVD group. Two colorectal perforations were observed in the standard group. One perforation occurred at the end of the procedure when the colonoscope was inverted in the rectum. The other perforation occurred at the rectosigmoid junction in a patient with diverticula. Both complications were successfully managed conservatively with endoscopic clipping.

Discussion

CRC screening using colonoscopy has been shown to be an efficient method to prevent the development of CRC. The reduction of CRC incidence is achieved by endoscopic removal of colorectal adenomas, which are precursors to CRC. It is estimated that both cancer incidence and mortality is reduced by colonoscopy by about 70% [9, 10]. This success has led to a steep increase in the number of colonoscopies performed with the introduction of screening colonoscopies [11]. In addition to screening, colonoscopy is also performed for specific indications in symptomatic patients. In Germany, around 58% of the population older than 55 years have undergone a colonoscopy within the last 10 years [12]. Increasing numbers of these colonoscopy procedures are accompanied by greater efforts at polypectomy. It has been previously shown that polyp removal contributes significantly to total procedure duration [13]. Therefore, devices that could facilitate endoscopic polyp removal are of great importance to improve the efficiency of colonoscopy.

The EVD is such a device, which could potentially facilitate the polyp removal procedure. The role of Endocuff assistance has been studied extensively with regards to the efficiency of adenoma detection; however, randomized studies regarding the impact of Endocuff assistance on the duration of polypectomy procedures are missing.

The primary goal of this study was to evaluate in a randomized trial the impact of Endocuff assistance during colonoscopy on the duration of polypectomy. Polypectomy was found to be significantly faster compared with standard colonoscopy when the EVD was used. A possible explanation for this finding is that the colonoscope position is stabilized by the flexible arms of the EVD, thereby facilitating the polypectomy procedure. This may explain why the effect was particularly evident for small and large polyps where a stable colonoscope position is very important, but not for diminutive polyps. The fact that fewer resections per polyp were necessary when the EVD was being used further supports this notion. It is also conceivable that polypectomy is faster because polyp exposure is improved by the EVD. This could be particularly relevant for polyps behind mucosal folds or those located in colonic flexures. In line with this, previous studies have reported an increase in the ADR when using the Endocuff, predominantly in the left colon where mucosal folds are more prominent [4], which supports there being improved polyp visualization with the Endocuff.

EVD use reduced the median duration of polypectomy by 26 seconds, which may not be clinically relevant for a single polyp; however, this reduction equated to a reduction in polypectomy duration of >30%, which could certainly be relevant if a patient needs multiple polyps removing. The latter effect may be of particular importance when large or difficult resections need to be performed.

A limitation of this study is its non-blinded design. Obviously, the use of the EVD cannot be performed by the investigator in a blinded fashion because the flexible arms become visible upon endoscope withdrawal. Therefore, in theory, investigators could potentially advance the scope faster when using the EVD. In addition, investigators could take more time to position the scope before starting the polypectomy. However, there was no difference in the withdrawal duration between the two study groups, which is also in line with previous reports [4].

In order to achieve complete colonoscopy, cecal intubation has to be achieved. In this study, cecal intubation failed in only one of 125 patients in the EVD group and in none of 125 patients in the standard group, which is equivalent to a cecal intubation rate of >99%. Despite comparable cecal intubation rates, faster intubation of the cecum was observed with the EVD (6 vs. 8 minutes, respectively), which is in line with other studies that have reported a similar effect on cecal intubation time [4, 14]. This supports the concept that the Endocuff stabilizes the scope position and may thereby improve loop management.

In contrast to the cecal intubation time, there was no difference regarding the time required for ileal intubation. In fact, ileal intubation was unsuccessful significantly more often when using the EVD compared with the standard colonoscope. This observation is likely a consequence of the larger scope diameter when the EVD is attached, which hinders intubation of the relatively narrow ileocecal valve. As a consequence, these results suggest that the EVD should not be attached to the colonoscope when an ileal intubation is necessary.

In contrast to some previous reports using the first-generation Endocuff device, the ADR was not increased by usage of the EVD: the ADR in this study was comparably high in both groups, at approximately 40%, even without the EVD. Other studies have reported an ADR of 20.7% [3], 26.3% [2], or 28% [1] for colonoscopies without use of the Endocuff. Therefore, a possible explanation for the observation in this study is that an EVD may not increase the ADR for colonoscopists who yield high ADRs without Endocuff assistance. In fact, a large randomized controlled study using the first-generation Endocuff device with reported ADRs of 52% in the standard and Endocuff groups was also unable to replicate the beneficial impact on ADR [6]. In line with this, a meta-analysis found no benefit of EVDs for operators with high ADRs [5].

The EVD was well tolerated by the patients and their satisfaction with the procedure was not affected. In addition, no adverse events occurred when the EVD was applied. The two colonoscopies where perforations occurred in the standard group were performed by two different and experienced colonoscopists; in both cases the complication was regarded as a coincidence.

In conclusion, this study demonstrates significantly accelerated polypectomy during colonoscopies when an EVD was
used. Based on the presented data, the clinical benefit of the EVD with regard to faster polypectomy was predominantly evident in polyps ≥6mm. Future studies are needed to investigate if the EVD may also have a beneficial impact on other colonscopic interventions, such as endoscopic submucosal dissection or therapy for sources of colorectal bleeding. A limitation of this study is that it was not blinded, which is owing to the visibility of the EVD during scope insertion and withdrawal. Theoretically, an awareness of whether or not the EVD is attached could impact the performance of an individual colonoscopist; however, the absence of conflicts of interest and the number of participating colonoscopists reduces the likelihood that the lack of blinding had a relevant impact on this study.

Competing interests

None.

References


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