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ORIGINAL ARTICLE

Effect of an External Abdominal Compression Device on Polyp Detection during Colonoscopy

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ABSTRACT

AIM: ColoWrap is an external abdominal compression device applied during colonoscopy to reduce looping and procedure time. It is unclear if a shorter procedure duration or increased abdominal pressure impacts polyp detection. We determined if use of ColoWrap affected adenoma detection rate (ADR) or detection of sessile serrated polyps (SSP) compared to sham.

MATERIALS AND METHODS: At a single center, participants aged 40-80 were randomized to have ColoWrap or a sham device applied to the lower abdomen. Baseline characteristics, procedural factors, location of polyps, ADR and SSP detection rate (SSPDR) were compared between the groups. Multivariable logistic regression was performed to assess whether ColoWrap was associated with detection of adenomas and SSP.

RESULTS: Of 350 participants, 175 were assigned to each arm. Overall, there were no significant differences in ADR (43% *vs* 40%, $p = 0.52$) or SSPDR (8% *vs* 6%, $p = 0.53$) between ColoWrap and sham. In sub-group analysis, there were increased odds of adenoma detection with ColoWrap in women (OR: 2.32, 95%CI: 1.21, 4.46), participants > 60 years (OR: 2.95, 95%CI: 1.43, 6.07) and those with a BMI 30-40 (OR: 3.50, 95%CI: 1.00, 12.23). Use of ColoWrap also increased ADR in the left colon (splenic flexure to rectum) (29% *vs* 22%; $p = 0.03$) and increased SSPDR in the cecum/ascending colon (6% *vs* 2%; $p = 0.02$) compared to sham.

CONCLUSION: Use of ColoWrap during colonoscopy did not negatively impact ADR or SSPDR, and there was an apparent improvement in polyp detection in certain colon locations and patient sub-groups. These results should be interpreted with caution due to the small sample size.

Key words: Colonoscopy; Cancer screening; Adenomatous polyps

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INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer deaths in the United States[1] and screening for CRC with colonoscopy has been shown to decrease mortality through earlier detection of malignant and pre-malignant lesions[2-5]. There is evidence that removal of adenomatous polyps specifically during colonoscopy reduces the risk of CRC and CRC mortality[6-8]. Adenoma detection rate (ADR) is currently an established quality metric and is recommended by professional societies and Centers for Medicare and Medicaid services as a measure of colonoscopy quality[9,10]. Sessile serrated polyps (SSP) are histologically distinct from conventional adenomas, but are also important CRC precursor lesions that likely contribute to the problem

of "interval" or post-colonoscopy CRC[11-13]. For this reason, SSP detection rate (SSPDR) is being increasingly reported and recognized as an important measure of colonoscopy quality[14-17].

Given the importance of ADR as an indicator of colonoscopy quality, multiple interventions have been developed targeted at improving ADR. Some are procedural factors such as quality of pre-procedural bowel preparation with split dose regimens and maneuvers such as retroflexion in the cecum, withdrawal time, dynamic position changes, and ancillary maneuvers, which have all been shown to increase ADR[18-23]. Application of abdominal pressure is commonly used during colonoscopy to prevent looping and can shorten examination time and decrease patient discomfort[24,25]. It is plausible that a standardized approach to applying abdominal pressure may improve ADR and SSPDR by decreasing cecal intubation time (CIT) and allowing more time for careful withdrawal. It is also possible that abdominal pressure could reduce polyp detection due to compression of the lumen and kinking of the colon. In a previous report, we showed that application of a non-invasive abdominal compression device, ColoWrap, reduced cecal intubation time (CIT) in obese populations in particular[26]. It is unknown if a shorter procedure duration or increased abdominal pressure affects polyp detection.

The aim of this study was to determine if the use of ColoWrap affects ADR and SSPDR compared to controls. We hypothesized that use of ColoWrap would not decrease detection of adenomas and SSP compared to the sham device.

METHODS

Study Design

A randomized, blinded, sham-controlled clinical trial was performed to determine if use of the ColoWrap abdominal binder reduced insertion time and need for additional maneuvers during colonoscopy. This was a single center study conducted at multiple endoscopy facilities at the University of North Carolina Hospitals[26]. The present study is a secondary-analysis of the clinical trial data analyzing the effect of the intervention on polyp detection.

Study Population

Participants undergoing colonoscopy were enrolled between April 2013 and March 2014. Eligible participants for inclusion were between the ages of 40-80, healthy (American Society of Anesthesiologists Class I-III), completed bowel preparation prior to the procedure with at least adequate visualization for polyp detection, and were English speaking. Body mass index (BMI) was calculated using height and weight measurements. Subjects were excluded if they had a BMI > 40 kg/m^2 or waist circumference > 45 inches due to device size limitations. Additional exclusion criteria and study procedures have been described in detail previously[26].

Study Procedures

Full details of the study protocol have previously been published[26]. In brief, participants were randomized, stratified by gender, to receive ColoWrap or sham device and allocation was concealed. Study coordinators applied ColoWrap or sham external compression device and subsequently covered the abdominal area with an opaque sheet to mask treatment assignment. All procedures were performed with patients in the left lateral decubitus position and all cases, except two, used propofol for sedation. Changes in position and application of manual pressures was used at the discretion of the endoscopist during the procedure, and the external compression device was also allowed to be removed for clinical or safety reasons. The study was approved by the UNC Institutional Review Board prior to initiation, and all participants provided written informed consent. The trial was registered on clinicaltrials.gov prior to initiation (NCT0202550).

Outcome and covariate measurement

Colonoscopy and pathology reports from each case with polyps removed were reviewed individually to ascertain the number of polyps, histology, and location of each polyp. ADR and SSPDR were defined as the proportion of cases with at least one conventional adenoma or SSP respectively. We also analyzed the outcome of either a conventional adenoma or SSP, and total number of conventional adenomas per colonoscopy. Right-sided or proximal lesions were defined as polyps located in the cecum, ascending colon, hepatic flexure, or transverse colon. Left-sided lesions were polyps found in the rectum, sigmoid or descending colon, or splenic flexure. Withdrawal time was measured in standard fashion from time of cecal intubation to time that the colonoscope was removed from the patient.

Statistical analysis

Descriptive statistics and bivariate analyses were used to compare participant, procedural, and polyp characteristics between the ColoWrap and sham arms by using Student's *t* test and Wilcoxon rank sum for continuous variables and Pearson chi-squared tests for categorical variables. ADR was calculated for pre-specified groups based on age, sex, and BMI. Differences in polyp detection based on location in the colon between the two arms were also compared. Multivariable logistic regression was performed to assess whether use of ColoWrap was associated with detection of adenomas and SSP, after adjusting for a combination of variables including age, sex, bowel prep, withdrawal time, and endoscopist experience. Testing for effect measure modification for sex and age using likelihood ratios was performed. Differences were considered statistically significant at an alpha level < 0.05. All analyses were performed by using STATA 13 (StataCorp, College Station, TX).

RESULTS

Participant and procedural characteristics

Out of 350 participants, there were 175 in each arm (Table 1). Sixty-two percent of the sample was women, and there were no significant differences between the two groups in age, sex, race, and BMI. A majority underwent colonoscopy for screening or surveillance purposes. Both groups predominantly had good or excellent bowel prep and had comparable withdrawal times. Both arms had approximately 70% of the cases performed by senior faculty. Additional details regarding participant and procedural characteristics have been published previously[26].

Polyp Characteristics

Sixty-three percent of the ColoWrap group and 69% in the sham group had polyps detected on colonoscopy, $p = 0.31$ (Table 2). The sham arm had a higher percent of hyperplastic polyps detected compared to ColoWrap group, 31% *vs* 22%, $p = 0.04$. There were no differences between the groups in the number of SSP (6% *vs* 8%; $p = 0.53$) or adenomas (40% *vs* 43%; $p = 0.52$) detected. In bivariate analysis, ColoWrap was associated with increased detection of adenomas in women (40% *vs* 30%; $p = 0.12$), those older than 60 years (53% *vs* 39%; $p = 0.06$) and those with a BMI between 30-40 (53% *vs* 40%; $p = 0.26$) but these differences were not statistically significant (Figure 1).

In multivariable analysis, there was no significant difference in adenoma or SSP detection between ColoWrap *vs* sham (ORs 1.47 (95% CI: 0.91, 2.37) and 1.44 (95% CI 0.60, 3.44) respectively). In pre-specified sub-groups, women had over twice the odds of adenoma detection with ColoWrap when compared to sham (OR 2.32 (95% CI: 1.21,4.46) (Table 3). There were also increased odds of adenoma detection in people > 60 years (OR 2.95; 95% CI 1.43, 6.07) and in the obese BMI 30-40 group (OR 3.50; 95% CI 1.00, 12.23). In addition, there were increased detection rates of the combined group of adenoma or SSP in women, obese, and older participants. There was no difference in adenoma detection between ColoWrap and sham arms in men, non-obese, and younger participants. There was significant effect measure modification noted based on age with a likelihood ratio of $p = 0.02$. There was no significant effect measure modification with sex.

Table 1 Participant and Procedural Characteristics.

Characteristics	Sham (n = 175)	ColoWrap (n = 175)	p value
Age, n (%)			
< 50 years	7 (4)	13 (7)	0.24
50-60 years	63 (36)	74 (42)	
60-70 years	71 (41)	60 (34)	
≥ 70 years	34 (19)	28 (16)	
Sex. n (%)			1
Female	108 (62)	108 (62)	
Male	67 (38)	67 (38)	
BMI, n (%)			0.86
< 25	73 (42)	70 (40)	
25-30	62 (35)	67 (38)	
30-40	40 (23)	38 (22)	
Colonoscopy Indication, n (%)			0.83
Diagnostic	15 (9)	16 (9)	
Screening/Surveillance	159 (92)	157 (91)	
Aronchick bowel prep score, n (%)			0.77
Poor	4 (2)	3 (2)	
Fair	17 (10)	23 (13)	
Good	71 (41)	70 (40)	
Excellent	83 (47)	79 (45)	
Withdrawal time (min), mean ± SD	12.5 ± 5.7	11.6 ± 6.1	0.2
Endoscopist Experience, n (%)			0.79
Fellow	26 (15)	23 (13)	
Junior faculty	33 (19)	30 (17)	
Senior faculty	116 (66)	122 (70)	

Table 2 Polyp Characteristics by Treatment Group.

Characteristics	Sham (n = 175)	ColoWrap (n = 175)	p value
Adenoma, n (%)	70 (40)	76 (43)	0.52
Age ≤ 60	32 (41)	33 (35)	0.43
Age > 60	38 (39)	43 (53)	0.06
Male	38 (57)	33 (49)	0.34
Female	32 (30)	43 (40)	0.12
BMI < 30	54 (40)	56 (41)	0.88
BMI 30-40	16 (40)	20 (53)	0.26
Diagnostic	5 (33)	6 (38)	0.81
Screening/Surveillance	66 (41)	68 (43)	0.66
SSP [a], n (%)	11 (6)	14 (8)	0.53
SSP [a] or Adenoma, n (%)	78 (45)	83 (47)	0.59
Hyperplastic Polyp, n (%)	55 (31)	38 (22)	0.04
Any Polyp [b], n (%)	120 (69)	111 (63)	0.31
Polyp removed during insertion	10 (6)	11 (6)	0.82
Polyps per colonoscopy, mean ± SD	1.67 ± 1.86	1.79 ± 2.24	0.59
Adenomas per colonoscopy	1.08 ± 1.41	1.24 ± 1.26	0.36

[a] Sessile serrated polyp; [b] Does not equal sum of other categories as some patients had > 1 polyp type.

Location of detected polyps

Overall polyp detection in the right (33% *vs* 34%, $p = 0.73$) and left (40% *vs* 43%, $p = 0.93$) colon was similar in ColoWrap and sham (Table 4). Use of ColoWrap was associated with increased polyp detection in the cecum and ascending colon (24% *vs* 17%; $p = 0.02$). There was no difference in detection of right-sided adenomas; however, there was an increased proportion of participants with

Table 3 Odds of Conventional Adenomas and Sessile Serrated Polyps with ColoWrap by Gender, Age, and BMI.

Participants	Conventional Adenoma (n = 146) OR (95% CI)	Sessile Serrated Polyp (n = 25) OR (95% CI)	Conventional Adenoma or Sessile Serrated Polyp (n = 161) OR (95% CI)
Sham [a]	1.00 (ref)	1.00 (ref)	1.00 (ref)
ColoWrap [a]	1.47 (0.91, 2.37)	1.44 (0.60, 3.44)	1.51 (0.93, 2.45)
Male [b]	0.80 (0.39, 1.68)	2.32 (0.46,11.72)	0.94 (0.44, 2.00)
Female [b]	2.32 (1.21, 4.46)	1.05 (0.35, 3.18)	2.08 (1.09, 3.95)
Age <60 years [c]	0.76 (0.39, 1.46)	1.27 (0.32, 5.09)	0.82 (0.42, 1.58)
Age >60 years [c]	2.95 (1.43, 6.07)	1.48 (0.47, 4.67)	2.92 (1.39, 6.14)
BMI <30 [d]	1.24 (0.73, 2.10)	1.04 (0.42, 2.62)	1.21 (0.71, 2.06)
BMI 30-40 [d]	3.50 (1.00, 12.23) [e]	n/a [f]	5.81 (1.37, 24.69)

[a] OR adjusted for age, gender, bowel prep quality, withdrawal time, and endoscopist experience; [b] OR adjusted for age, bowel prep quality, withdrawal time, and endoscopist experience; [c] OR adjusted for gender, bowel prep quality, withdrawal time, and endoscopist experience; [d] OR adjusted for age, gender, bowel prep quality, withdrawal time, and endoscopist experience; [e] Confidence interval (1.004, 12.229), $p = 0.049$ so value interpreted as significant; [f] Too few numbers for stable estimate.

Table 4 Differences in Polyp Detection in the Right [a] and Left [b] colon with ColoWrap.

Variable	Sham (n = 175)	ColoWrap (n = 175)	p value
Any polyp			
Right	60 (34)	58 (33)	0.73
Cecum	14 (8)	20 (11)	0.17
Cecum/Ascending	29 (17)	42 (24)	0.02
Left	75 (43)	70 (40)	0.93
Adenoma, n(%)			
Right	45 (26)	42 (24)	0.96
Cecum	2 (1)	5 (3)	0.21
Cecum/Ascending	25 (14)	27 (15)	0.53
Left	38 (22)	51 (29)	0.03
SSP [c], n(%)			
Right	8 (5)	13 (7)	0.18
Cecum	2 (1)	5 (3)	0.21
Cecum/Ascending	3 (2)	11 (6)	0.02
Left	2 (1)	2 (1)	0.94
Hyperplastic Polyp, n(%)			
Right	13 (7)	13 (7)	0.83
Left	48 (27)	31 (18)	0.06

[a] Right: cecum, ascending, hepatic, and transverse colon; [b] Left: splenic flexure, descending, sigmoid, and rectum; [c] Sessile serrated polyp.

Table 5 Polyps Detected in the Right [a] and Left [b] Colon with ColoWrap *vs* Sham (Per-Polyp Analysis).

Variable	Sham	ColoWrap	p value
Any polyp, n(%)	N=245	N=240	
Right	108 (44)	107 (45)	0.91
Left	137 (56)	133 (56)	0.91
Adenoma, n(%)	N = 130	N = 138	
Right	74 (30)	68 (28)	0.68
Left	56 (23)	70 (29)	0.11
SSP [c], n(%)	N = 23	N = 28	
Right	17 (7)	21 (9)	0.46
Left	6 (2)	7 (3)	0.75
Hyperplastic Polyp, n(%)	N = 92	N = 74	
Right	17 (7)	18 (8)	0.81
Left	75 (31)	56 (23)	0.07

[a] Right: cecum, ascending, hepatic, and transverse colon; [b] Left: splenic flexure, descending, sigmoid, and rectum; [c] Sessile serrated polyp.

adenomas in the left colon (splenic flexure to rectum) with use of ColoWrap (29% *vs* 22%; p = 0.03) compared to sham. There were no differences in the location (right *vs* left colon) of SSP, but there was increased detection of SSPs in the cecum/ascending colon (6% *vs* 2%; p = 0.02). Finally, no differences in hyperplastic polyps (HP) detection were noted based on polyp location in the right *vs* left colon.

Per-polyp analysis

The number of polyps at each location of the colon was also determined between the ColoWrap and sham groups (Figure 2). There were a total of 245 polyps (130 adenomas, 23 SSP, 92 hyperplastic) in the sham group and 240 polyps (138 adenomas, 28 SSP, 74 hyperplastic) in the ColoWrap group. The per polyp analysis (Table 5) showed no significant differences in the total number of adenomas, SSP or hyperplastic polyps found in the right and left colon with use of ColoWrap.

DISCUSSION

In this study, we showed that use of an external abdominal compression device, did not decrease detection of adenomas or SSP compared to sham. ColoWrap use was independently associated with increased adenoma detection in women, those older than 60, and in moderately obese (BMI 30-40) participants; however, these associations are inconclusive given the sample size in each stratum. There was no difference in the detection of SSP but there was an increased detection of the combined outcome of conventional adenomas and SSP in the same subgroups with ColoWrap use. In addition, use of ColoWrap was associated with increased detection of left sided adenomas and increase SSPs in the cecum/ascending colon, specifically.

It is well established that removal of adenomas on colonoscopy reduces the risk of CRC, and it stands to reason that removal of SSP is also beneficial[6,11,27]. Conventional adenomas progress to colorectal cancer through the well described adenoma-carcinoma sequence[28]. In contrast, SSP carcinogenesis is thought to occur via a distinct "serrated pathway" through mechanisms such as BRAF oncogene mutations, gene promoter hypermethylation, and inactivation of DNA mismatch repair genes[29-32]. ADR, which has been shown to be correlated with SSPDR[14]. is associated with a lower risk of interval cancers as well[2,33]. More specifically ADR > 20% is associated with lower rates of interval CRC[33]. Like conventional adenomas, SSPs are also

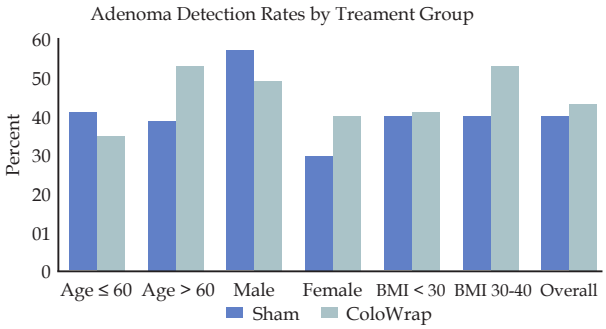

Figure 1 Adenoma detection in ColoWrap and Sham arms among pre-specified groups based on age, sex, and BMI.

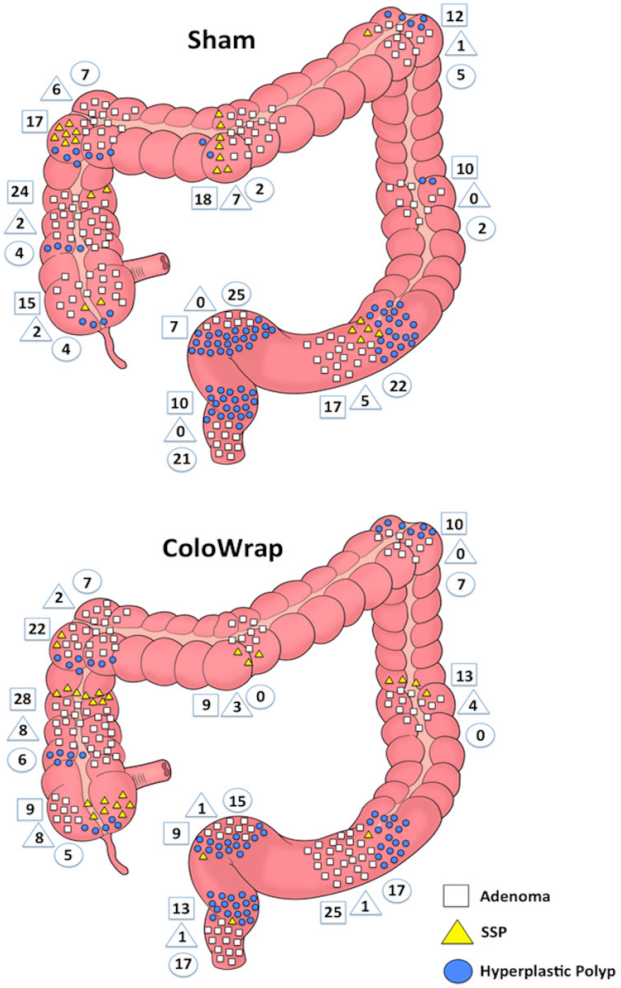

Figure 2 Location and number of adenomas, sessile serrated polyps (SSP) and hyperplastic polyps in the sham and ColoWrap groups *Note: Figure represents all polyps detected during study; some patients contributed > 1 polyp.

thought to be associated with interval cancers[34-36]. It is hypothesized that SSPs, which are predominantly right sided, tend to be missed or incompletely resected during colonoscopy[29,37,38]. In addition, SSPs with dysplasia may progress to CRC at a more rapid rate[39,40].

Increased detection of adenomas and SSPs and reduced incidence of interval cancer after screening colonoscopy have been associated with longer withdrawal times of > 6 minutes with careful mucosal inspection[14,41-44]. In our study, there was no significant difference in withdrawal times between the two groups in both intention

to treat and per-protocol analysis suggesting that differences in adenoma detection was possibly due to other factors that aid in better visualization of the colonic mucosa.

One such factor that can improve ADR is adequate luminal distention[18]. The increased left sided adenoma detection could be due to increased stability provided by ColoWrap resulting in enhanced luminal distention and straightening of the sigmoid colon. It is also possible that that the external support provided by ColoWrap can lead to decreased "fall back" of the instrument during withdrawal leading to increased mucosal visibility for identification of adenomas and SSPs. This may also explain the increased detection of SSP in the cecum and ascending colon where there is greater risk of "fall back" during withdrawal.

Despite no differences in withdrawal or cecal intubation times, women and older participants had increased ADR with use of ColoWrap. These two groups have been described to have longer and more redundant colons with sharp angulations, specifically in women[45-48]. The fact that use of ColoWrap was not associated with significant differences in looping or CIT in these subgroups in the main study, suggests that the observed increase in ADR may be due to other factors such as improved luminal distension or better instrument control during withdrawal[26].

There was also an increased proportion of cases with HPs found in the sham arm compared to ColoWrap (31% *vs* 22%, $p = 0.04$), though this difference was limited to left-sided HPs, which are felt to be of little clinical significance. Studies have shown that left-sided or distal HPs are not associated with an increased risk of proximal advanced adenomatous neoplasia or proximal advanced serrated lesions[49,50]. It is possible that providers remove distal HPs more often if they do not find any polyps proximally in an attempt to improve ADR but this needs further investigation.

Our study has multiple strengths including a randomized study design, masking of providers, and use of a sham control to reduce bias. In addition, the study was conducted at a high-volume academic medical center with multiple free-standing endoscopy facilities, and colonoscopies were performed by endoscopists with a varying range of experience. The diversity of settings and endoscopist skill level increases the generalizability of our findings to other similar arenas. However, this heterogeneity can also lead to increased variance. Since a majority of the cases used propofol, our findings are less generalizable to other centers that use alternate modalities of sedation. Another limitation of the study is that it was not designed to study differences in ADR and SSPDR, which can possibly lead to an underpowered study and a Type II error, especially for SSP that occurred with lower frequency in the study.

Overall, use of ColoWrap during colonoscopy was not associated with a deleterious effect on ADR or SSPDR. With ColoWrap there was an association with increased SSPDR in the cecum/ascending colon and ADR in the left side of the colon, in women, older participants, and those who were obese. These groups of patients have a tendency to have more difficult colons to maneuver during colonoscopy either due to looping or redundancy, and use of ColoWrap may aid in improved adenoma detection during withdrawal by providing increased stability and improved luminal distention. However, further studies are needed to confirm this benefit in other populations and to determine the exact mechanism by which the device may influence polyp detection.

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