Cold versus hot snare resection with or without submucosal injection of 6- to 15-mm colorectal polyps: a randomized controlled trial CME

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Background and Aims: Cold snare resection of colorectal lesions has been found to be safe and effective for an expanding set of colorectal lesions. In this study, we sought to understand the efficacy of simple cold snare resection and cold EMR versus hot snare resection and hot EMR for colorectal lesions 6 to 15 mm in size.

Methods: At 3 U.S. centers, 235 patients with 286 colorectal lesions 6 to 15 mm in size were randomized to cold snaring, cold EMR, hot snaring, or hot EMR for nonpedunculated colorectal lesions 6 to 15 mm in size. The primary outcome was complete resection determined by 4 biopsy samples from the defect margin and 1 biopsy sample from the center of the resection defect.

Results: The overall incomplete resection rate was 2.4% (95% confidence interval [CI], .8%-7.5%). All 7 incompletely removed polyps were 10 to 15 mm in size and removed by hot EMR (n = 4, 6.2%), hot snare (n = 2, 2.2%), or cold EMR (n = 1, 1.8%). Cold snaring had no incomplete resections, required less procedural time than the other methods, and was not associated with serious adverse events.

Conclusions: Cold snaring is a dominant resection technique for nonpedunculated colorectal lesions 6 to 15 mm in size. (Clinical trial registration number: NCT03462706.) (Gastrointest Endosc 2022;96:330-8.)

Endoscopic resection in the colorectum is undergoing a "cold revolution." Cold snaring and cold forceps both have been used effectively for diminutive polyps,[1-7] with cold forceps acceptable for lesions ≤3 mm.[5,6] Cold snaring has comparable efficacy with hot snaring for lesions ≤10 mm.[8-15] For serrated lesions ≥10 mm, piecemeal cold snare resection either after submucosal injection[16-18] or without submucosal injection[19,20] has been shown to have low recurrence rates. For adenomas ≥20 mm, piecemeal cold EMR has reduced efficacy.[21-23] Loss of efficacy may be related to a more superficial transection plane that occasionally does not remove

Abbreviations: ITT, intention to treat; VAMC, Veterans Affairs Medical Center; WRJ, White River Junction.

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the muscularis mucosa.[24] There are fewer data on the efficacy of cold resection for lesions 10 to 20 mm in size,[7,25] and at the time of study initiation, data were limited on cold snaring of lesions 6 to 9 mm in size. Available studies at that time suggested difference only for lesions 8 to 9 mm in size,[24,26] or included lesions <5 mm in size.[27] It is also unknown whether submucosal injection as the key component of an EMR improves completeness of resection and at which size threshold submucosal injection should be performed.

To further understand the efficacy of cold resection, we conducted a multicenter randomized controlled trial comparing cold versus hot snare resection with or without submucosal injection for lesions 6 to 15 mm in size. Specifically, we hypothesized that cold snaring is noninferior to alternative resection methods with regard to completeness of resection.

METHODS

This was a prospective randomized controlled clinical trial. The protocol was approved by the Institutional Review Board at Indiana University on February 6, 2018, and approved at the other sites by their local institutional review boards. The study was registered at clinicaltrials.gov on March 12, 2018 (NCT03462706).

Patients were invited to participate in the study between August 10, 2018 and March 26, 2021 as they presented for colonoscopy in one of the outpatient centers at Indiana University, Detroit Veterans Affairs Medical Center (Detroit VAMC), or White River Junction Veterans Affairs Medical Center (WRJ VAMC). Enrollment was stopped when the predetermined sample size in each arm was reached. There was 1 participating endoscopist at Indiana (D.K.R.), 3 at Detroit VAMC (S.J., F.A., K.L.), and 2 at WRJ VAMC (J.C.A., H.P.).

Eligibility criteria

Patients aged ≥40 years and willing to participate in the study by signing an informed consent form were enrolled. Presence of inflammatory bowel disease and absence of at least 1 study polyp (6- to 15-mm nonpedunculated lesions) were exclusion criteria.

Procedures

Colonoscopy was performed after split-dose bowel preparation using standard colonoscopes. After a polyp was identified and confirmed as a study candidate by measurement against an open snare of known diameter, the decision was made to randomize the patient. The endoscopist was blinded to the method to be used until after randomization. Randomization was performed using a computer-generated scheme, and patients were randomized in a 1:1:1:1 ratio. The randomization was concealed in an opaque envelope until a polyp was confirmed as a candidate and the endoscopist confirmed they had time to perform the study procedures.

Patients randomized to cold snare had immediate cold snare resection using a dedicated cold snare (Boston Cap Cold [Boston Scientific, Marlborough, Mass, USA] or Exacto Cold Snare [Steris Corporation, Mentor, Ohio, USA]). Hot snares included the 10- and 15-mm Captivator II (Boston Scientific) at Indiana University, 10-mm Snare Master (Olympus America Corporation, Center Valley, Pa, USA) at WRJ VAMC, and the 13-mm Sensation (Boston Scientific) and Lariat (Steris Corporation) at Detroit VAMC. Patients randomized to hot snare had immediate hot snare resection using electrocautery settings of the endoscopist's preference. Patients randomized to cold EMR had submucosal injection including a contrast agent, followed by snare resection with piecemeal removal as needed. Patients randomized to hot EMR had submucosal injection with a contrast agent followed by resection using electrocautery. Saline solution, hydroxyethyl starch, or any commercially available injection fluid was allowed.

Lesion resection duration was measured by a research assistant as time from the first appearance of a resection-related device (snare or injection needle) in the endoscopic field until lesion retrieval into the colonoscope. Overall removal time was the time from initial lesion identification until lesion retrieval into the colonoscope. All endoscopists used high-definition colonoscopes to assess whether resection was completed, including electronic chromoendoscopy, at their discretion.

Regardless of resection method, immediately after the endoscopist completed the removal of the polyp, biopsy samples were taken from the mucosa at the perimeter of the resection defect in 4 quadrants and placed in a single bottle for pathologic assessment. A single bite was then taken from the center of the resection defect and placed in a second separate bottle. We used the clinical pathologists' interpretation of lesions and postresection biopsy samples. The pathologists were aware that the postresection biopsy samples were for research (to avoid charging the patient) but were not aware of the study purpose or design.

Patients could have more than 1 polyp randomized, depending on the time available in the procedure. However, if a second polyp was included, the same technique used to remove the first polyp was used for the second lesion.

Outcome measures

The primary outcome of the study was efficacy of resection defined as the absence of residual polyp in either central or peripheral postpolypectomy biopsy samples. Secondary outcomes were en-bloc resection, polyp resection time, overall removal time, and intraprocedural adverse events.

Statistical methods

Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC, USA). Categorical

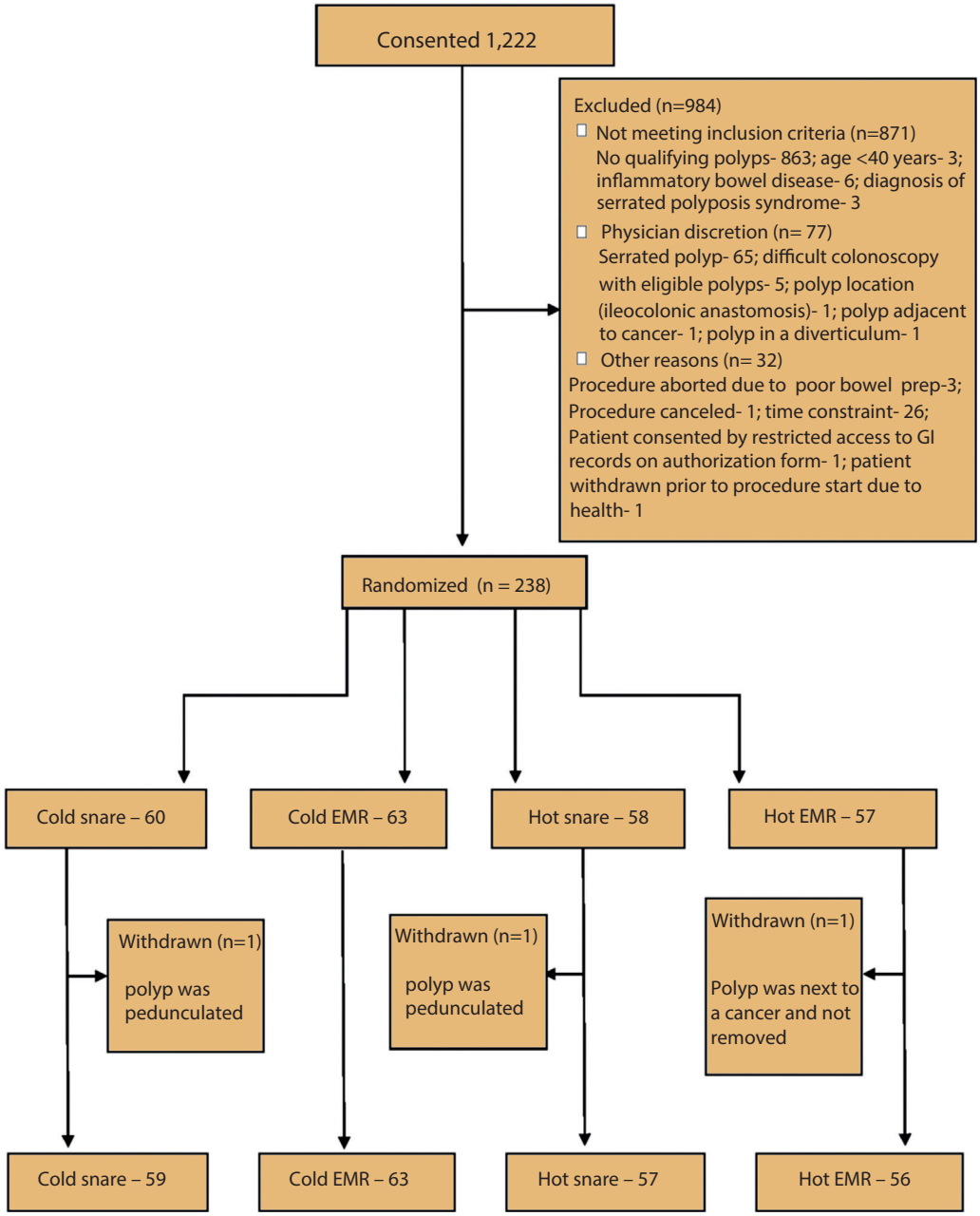

Figure 1. Flowchart showing enrollment and reasons for exclusion of patients in the study.

variables are summarized as frequencies and percentages. These were compared across treatment groups using either χ^2 tests or Fisher exact tests as appropriate. Continuous variables are summarized as mean and standard deviation. These were compared across treatment groups using the Kruskal-Wallis test. Any significant post-hoc differences among individual treatments were assessed using the Dwass-Steel-Critchlow-Fligner method. When comparing the presence of residual polyps across treatments, our interest was in the noninferiority comparison with cold snare as the reference group. To this end, 3 independent noninferiority tests, using a margin of 7%, were performed comparing cold snare with cold EMR, hot snare, and hot EMR. All tests were considered significant at $P < .05$.

Sample size

A sample size of 66 polyps per treatment was predicted to have 80% power to detect a noninferiority margin difference of 7% for the cold snare treatment compared with cold EMR, hot snare, and hot EMR treatments with an alpha of .05.

TABLE 1. Comparison of patient demographics, procedure indication, and study center between groups (n = 235)

	Cold snare (n = 59)	Cold EMR (n = 63)	Hot snare (n = 57)	Hot EMR (n = 56)	*P* value*
Mean age, y (standard deviation	66.2 (9.9)	65.0 (8.0)	66.3 (8.0)	67.0 (8.4)	.5724
Site					.3038
Detroit Veterans Affairs Medical Center	6 (10.2)	2 (3.2)	4 (7.0)	9 (16.1)	
Indiana University	44 (74.6)	47 (74.6)	41 (71.9)	37 (66.1)	
White River Junction Veterans Affairs Medical Center	9 (15.3)	14 (22.2)	12 (21.1)	10 (17.9)	
Gender					.3198
Female	25 (42.4)	28 (44.4)	19 (33.3)	17 (30.4)	
Male	34 (57.6)	35 (55.6)	38 (66.7)	39 (69.6)	
Race					.3676
African American/Black	2 (3.4)	2 (3.2)	1 (1.8)	6 (10.7)	
White	56 (94.9)	60 (95.2)	54 (94.7)	48 (85.7)	
Other/unknown	1 (1.7)	1 (1.6)	2 (3.5)	2 (3.6)	
Ethnicity					.6402
Hispanic	1 (1.7)	1 (1.6)	0 (0)	0 (0)	
Non-Hispanic	54 (91.5)	58 (92.1)	55 (96.5)	50 (89.3)	
Refused/unknown	4 (6.8)	4 (6.3)	2 (3.5)	6 (10.7)	
Indication					.2563
Diagnostic	7 (11.9)	7 (11.1)	4 (7.0)	6 (10.7)	
Screening	17 (28.8)	10 (15.9)	8 (14.0)	8 (14.3)	
Surveillance	34 (57.6)	43 (68.3)	40 (70.2)	41 (73.2)	
Therapeutic	1 (1.7)	3 (4.8)	5 (8.8)	1 (1.8)	

Values are n (%) unless otherwise defined.
*χ^2/Fisher exact test or Kruskal-Wallis test.

RESULTS

Of 1222 patients who gave consent to participate in the study, 984 were excluded, primarily because they had no polyp of appropriate size to be included in the study (Fig. 1). As the study progressed, eligible polyps that were of a serrated class were excluded by 1 endoscopist because of increasing evidence that cold resection was already established as effective for serrated lesions (Fig. 1). Some patients with eligible polyps were excluded because the endoscopist believed there was insufficient time to complete the study biopsy sampling. Table 1 shows patient demographics, study indications, and study center for the 235 patients who were enrolled and included in the intention-to-treat (ITT) analysis.

In the 235 patients included in the study, 286 polyps were included in the ITT analysis. More polyps were randomized at Indiana University (n = 210) than at WRJ VAMC (n = 52) and Detroit VAMC (n = 24). One hundred fifty-seven lesions were 6 to 9 mm in size and 129 lesions were 10 to 15 mm in size and randomized in the ITT analysis. The number of patients with >1 study polyp ranged from 13.6% to 22.2% and was not different between groups ($P = .544$).

Table 2 lists polyps per patient, bowel preparation, colonoscope insertion time to the cecum, and overall withdrawal time. Overall withdrawal time from the cecum to anus, including procedural time, was longer with hot EMR than other methods and longer with hot snaring than cold snaring (Table 2).

Table 3 compares polyp features between the study groups. Mean polyp resection time was shortest with cold snaring (60 seconds), followed by hot snaring (100 seconds), cold EMR (141 seconds), and hot EMR (174 seconds). There were similar differences in overall removal time. En-bloc resection occurred most commonly with hot EMR, followed by hot snaring, and then the cold resection techniques (Table 3). Overall, 84.1% of resections in the 6- to 9-mm group and 53.9% in the 10- to 15-mm group were en bloc. There was no difference between the study arms in the rate of en-bloc resection for 6- to 9-mm polyps.

Table 4 shows the primary outcome result of presence of residual polyp on any biopsy sample from the perimeter or center of the lesion in the ITT analysis for all study sites, for each site separately, and for polyps 6 to 9 mm and 10 to 15 mm separately. Overall, there were 7 incomplete resections (2.4%; 95% CI, .8%-7.5%). Five lesions with a postresection-positive biopsy sample

TABLE 2. Mean polyps per subject, bowel preparation scores, and insertion and withdrawal times in the intention-to-treat analysis

	Cold snare (n = 59)	Cold EMR (n = 63)	Hot snare (n = 57)	Hot EMR (n = 56)	*P* value*
No. of polyps per subject	1.2 (.4)	1.3 (.6)	1.2 (.5)	1.2 (.4)	.4933
Boston Bowel Preparation Scale score	8.5 (1.2)	8.6 (.9)	8.6 (.9)	8.4 (1.1)	.1638
Insertion time, s	454 (423)	388 (315)	413 (333)	399 (279)	.7694
Overall withdrawal time, s	1447 (586)	1672 (861)	1623 (599)	1939 (744)	.0027†

Values are mean (standard deviation).
*Kruskal-Wallis test.
†Overall withdrawal time showed a significant difference between cold snare versus hot EMR.

were from a defect margin and 4 from a central biopsy sample, including 2 lesions positive from both the margin and center. Cold snaring was noninferior to the other 3 methods with regard to efficacy of resection and was without recurrence in 68 polyps, including 41 lesions 6 to 9 mm and 27 lesions 10 to 15 mm. All 7 cases of residual polyp occurred in lesions 10 to 15 mm in size, for an overall efficacy rate of 96.8% in lesions 10 to 15 mm and 100% in lesions 6 to 9 mm in size.

There was no difference in the incidence of overall adverse events between the groups. Seven separate patients, all at Indiana, had arterial hemorrhage during the procedure after cold biopsy sampling from the center of the postresection defect and six were after hot snare resection in a lesion removed using electrocautery. All 7 episodes of bleeding were effectively controlled by snare-tip soft coagulation treatment followed by hemostatic clip placement.

One serious adverse event occurred at Indiana University. The patient had a 12-mm transverse study polyp removed by hot EMR. A 15-mm pedunculated lesion was also removed by hot snare, a 25-mm nonpedunculated lesion was removed by hot EMR, and 9 more lesions <10 mm in size were removed by cold snare. The patient restarted clopidogrel the day after the procedure and noticed rectal bleeding 2 days later. The patient was hospitalized for 3 days at an outside hospital but did not require repeat colonoscopy, transfusion, or surgery and recovered completely. The event could not be clearly attributed to the study polyp.

A second serious adverse event occurred at WRJ VAMC. The patient had a 14-mm cecal polyp removed by hot snare. The patient required hospitalization for 3 days, transfusion of 4 units of packed red blood cells, and repeat colonoscopy with clipping. At the 30-day follow-up the patient reported full recovery. All other adverse events (Table 5) were considered minor by the investigators and without difference between the study arms.

Two patients were excluded from the ITT analysis, so that the per-protocol analysis included 233 patients. One patient at Indiana was assigned to the hot snare arm, but the electrocautery unit failed and the lesion was transected cold. Both the central and periphery postresection biopsy specimens were negative. Another patient at WRJ VAMC was converted from hot snare to hot EMR to facilitate resection. Both the central and peripheral postresection biopsy samples were positive. Thus, 6 lesions with positive postresection biopsy samples were included in the per-protocol analysis. However, there was no significant difference in the study results in the per-protocol analysis (data not shown).

DISCUSSION

In this report we described a multicenter U.S. randomized trial comparing cold snare polypectomy with cold EMR, hot snaring, and hot EMR. The main result was that cold snare resection without submucosal injection dominated, because it was uniformly effective in achieving complete resection and was faster to perform than the other modalities. Thus, our results suggest that for nonpedunculated colorectal lesions up to 15 mm in size and without features suggestive of cancer, cold snare resection is noninferior to other resection techniques and could be considered as the resection method of choice. We consider it self-evident that cold snaring is less costly and produces less plastic waste than the other resection methods.

When this study was initiated, cold snare polypectomy was well established as effective for lesions 1 to 5 mm in size, but we considered that additional confirmation of its efficacy in 6 to 9 mm lesions was warranted and wanted to extend the evaluation of cold snare polypectomy to lesions 10 to 15 mm in size. Since the study was initiated, additional evidence of efficacy for lesions 6 to 9 mm in size has been reported.[8] Thus, our results are primarily confirmatory for 6- to 9-mm polyps. Fewer data from randomized controlled trials are available for lesions 10 to 15 mm in size, and our results help to extend the acceptability of cold snare polypectomy for lesions 10 to 15 mm in size.[28]

Strengths of this study include the randomized controlled trial design, the timed measurement of polypectomy, and the multicenter design. Limitations include the unequal distribution of study patients among the 3 sites (1 expert at 1 site performed 73% of the resections), although cold snare polypectomy had uniform efficacy in

TABLE 3. Polyp characteristics in the 4 study groups (n = 286)

Polyp characteristics	Cold snare (n = 68)	Cold EMR (n = 82)	Hot snare (n = 71)	Hot EMR (n = 65)	*P* value*
Location					.7647
Ascending colon	24 (35.3)	26 (31.7)	26 (36.6)	26 (40.0)	
Cecum	7 (10.3)	8 (9.8)	13 (18.3)	7 (10.8)	
Descending colon	8 (11.8)	13 (15.9)	5 (7.0)	6 (9.2)	
Hepatic flexure	5 (7.4)	3 (3.7)	6 (8.5)	4 (6.2)	
Ileocecal valve	1 (1.5)	0 (0)	1 (1.4)	0 (0)	
Rectum	2 (2.9)	1 (1.2)	2 (2.8)	2 (3.1)	
Sigmoid colon	3 (4.4)	6 (7.3)	7 (9.9)	5 (7.7)	
Transverse colon	18 (26.5)	25 (30.5)	11 (15.5)	15 (23.1)	
Shape					.3352
Paris Is	36 (52.9)	35 (42.7)	29 (40.8)	34 (52.3)	
Paris IIa	32 (47.1)	47 (57.3)	42 (59.2)	31 (47.7)	
En bloc					.0011
No	28 (41.2)	31 (38.3)	15 (21.1)	10 (15.4)	
Yes	40 (58.8)	50 (61.7)	56 (78.9)	55 (84.6)	
Predicted pathology					.2016
Adenoma	52 (76.5)	56 (68.3)	54 (76.1)	52 (80.0)	
Serrated	15 (22.1)	22 (26.8)	12 (16.9)	13 (20.0)	
Unknown	1 (1.5)	4 (4.9)	5 (7.0)	0 (0)	
Actual pathology					.4784
Adenoma	53 (77.9)	61 (74.4)	57 (80.3)	52 (80.0)	
Hyperplastic	3 (4.4)	2 (2.4)	3 (4.2)	0 (0)	
Normal mucosa	1 (1.5)	0 (0)	1 (1.4)	0 (0)	
Sessile serrated lesion	10 (14.7)	19 (23.2)	10 (14.1)	13 (20.0)	
No tissue	1 (1.5)	0 (0)	0 (0)	0 (0)	
Peripheral postresection biopsy sample					.2558
Negative	68 (100)	81 (98.8)	70 (98.6)	62 (95.4)	
Positive	0 (0)	1 (1.2)	1 (1.4)	3 (4.6)	
Central postresection biopsy sample					.1721
Negative	68 (100)	82 (100)	69 (97.2)	63 (96.9)	
Positive	0 (0)	0 (0)	2 (2.8)	2 (3.1)	
Intraprocedural adverse events					.1064
Bleeding	0 (0)	1 (1.2)	2 (2.8)	4 (6.2)	
No bleeding	68 (100)	81 (98.8)	69 (97.2)	61 (93.8)	
Mean polyp size, mm (SD)	9.4 (3.1)	9.5 (2.8)	10.1 (2.9)	10.0 (3.1)	.2608
Mean resection time, s (SD)	60 (50)	141 (92)	100 (120)	174 (113)	<.0001†
Mean overall removal time, s (SD)	127 (91)	247 (128)	191 (145)	307 (152)	<.0001‡
Mean injectate volume, mL (SD)	0 (0)	3.7 (1.7)	.0 (.4)	4.5 (2.5)	<.0001§
Mean no. of pieces (SD)	1.9 (1.7)	1.9 (1.4)	1.4 (1.2)	1.2 (.5)	.0004¶

Values are n (%) unless otherwise defined. *SD*, Standard deviation.
*χ^2/Fisher exact test or Kruskal-Wallis test.
†Resection time had a significant difference among all pairings except cold EMR vs hot EMR.
‡Overall removal time had a significant difference among all pairings.
§Injectate volume had a significant difference among all pairings except cold snare vs hot snare and cold EMR vs hot EMR.
¶Number of pieces had a significant difference among all pairings except cold snare vs cold EMR and hot snare vs hot EMR.

eliminating polyp tissue at all 3 sites. Second, the study endoscopists are experts with special interest in colorectal cancer prevention and polypectomy, which could limit the generalizability of the results. Third, some serrated lesions were included in the study, and subsequent to the design of the study, substantial efficacy has been reported

TABLE 4. Frequency of residual polyp on biopsy sampling in the 4 study arms in the intention-to-treat analysis for all sites, individual sites, and by polyp size

Residual polyp	**Cold snare (n = 68)**	**Cold EMR (n = 82)**	**Hot snare (n = 71)**	**Hot EMR (n = 65)**
All polyps, all sites (n = 286)				
No	68 (100)	81 (98.8)	69 (97.2)	61 (93.8)
95% CI	94.7-100	93.4-100	90.2-99.7	85.0-98.3
Yes	0 (0)	1 (1.2)	2 (2.8)	4 (6.2)
95% CI	0-5.3	0-6.6	.3-9.8	1.7-15.0
P value*		.0069	.0035	.0008
Residual polyp	**Cold snare (n = 51)**	**Cold EMR (n = 66)**	**Hot snare (n = 51)**	**Hot EMR (n = 42)**
Indiana University: all polyps (n = 210)				
No	51 (100)	65 (98.5)	50 (98.0)	39 (92.9)
95% CI	93.0-100	91.8-100	89.5-99.9	80.5-98.5
Yes	0 (0)	1 (1.5)	1 (2.0)	3 (7.1)
95% CI	0-7.0	0-8.2	.1-10.5	1.5-19.5
P value*		.0150	.0129	.0023
Residual polyp	**Cold snare (n = 6)**	**Cold EMR (n = 2)**	**Hot snare (n = 4)**	**Hot EMR (n = 12)**
Detroit Veterans Affairs Medical Center: all polyps (n = 24)				
No	6 (100)	2 (100)	4 (100)	12 (100)
95% CI	N/A	N/A	N/A	N/A
Yes	0 (0)	0 (0)	0 (0)	0 (0)
95% CI	N/A	N/A	N/A	N/A
P value*		N/A	N/A	N/A
Residual polyp	**Cold snare (n = 11)**	**Cold EMR (n = 14)**	**Hot snare (n = 16)**	**Hot EMR (n = 11)**
White River Junction Veterans Affairs Medical Center: all polyps (n = 52)				
No	11 (100)	14 (100)	15 (93.8)	10 (90.9)
95% CI	71.5-100	76.8-100	69.8-99.8	58.7-99.8
Yes	0 (0)	0 (0)	1 (6.3)	1 (9.1)
95% CI	0-28.5	0-23.2	.2-30.2	.2-41.3
P value*		N/A	.1008	.0788
Residual polyp	**Cold snare (n = 41)**	**Cold EMR (n = 47)**	**Hot snare (n = 36)**	**Hot EMR (n = 33)**
All polyps 6-9 mm (n = 157)				
No	41 (100)	47 (100)	36 (100)	33 (100)
95% CI	N/A	N/A	N/A	N/A
Yes	0 (0)	0 (0)	0 (0)	0 (0)
95% CI	N/A	N/A	N/A	N/A
P value*		N/A	N/A	N/A
Residual Polyp	**Cold snare (n = 27)**	**Cold EMR (n = 35)**	**Hot snare (n = 35)**	**Hot EMR (n = 32)**
All polyps 10-15 mm (n = 129)				
No	27 (100)	34 (97.1)	33 (94.3)	28 (87.5)

(*continued on the next page*)

TABLE 4. Continued

Residual Polyp	Cold snare (n = 27)	Cold EMR (n = 35)	Hot snare (n = 35)	Hot EMR (n = 32)
95% CI	87.2-100	85.1-99.9	80.8-99.3	71.0-96.5
Yes	0 (0)	1 (2.9)	2 (5.7)	4 (12.5)
95% CI	0-12.8	.1-14.9	(.7-19.2	3.5-29.0
P value*		.0440	.0253	.0068

Values are n (%) unless otherwise defined. *N/A*, Not applicable; *CI*, confidence interval.
*Three independent noninferiority tests, margin delta = 7%.

TABLE 5. Frequency of adverse events in the 4 study arms in the intention-to-treat analysis (n = 235)

	Cold snare (n = 59)	Cold EMR (n = 63)	Hot snare (n = 57)	Hot EMR (n = 56)	*P* value*
Any adverse events					.1605
None	48 (81.4)	59 (93.7)	49 (86.0)	51 (91.1)	
Serious adverse event	0 (0)	0 (0)	1 (1.8)	1 (1.8)	
Any adverse event	11 (18.6)	4 (6.3)	7 (12.3)	4 (7.1)	

Values are n (%).
*Fisher exact test.

for resection of serrated lesions using cold techniques.[16-20] Therefore, the real need is for evaluation of cold techniques[15] in adenomas. Our data do support the efficacy of cold snare polypectomy for adenomas 6 to 15 mm in size. Fourth, because all incomplete resections occurred in 10- to 15-mm lesions, a study designed for 10- to 15-mm or 10- to 20-mm lesions might be more clinically relevant at this time and appears to be warranted going forward. The observation in our study that all 10- to 15-mm cold snare resections were complete supports further study of cold snare resection for 10- to 20-mm lesions. Fifth, as in most endoscopic studies, lack of endoscopist blinding creates the potential of proceduralist bias. The high rates of complete resection in all study arms suggest such bias was insignificant. Finally, we relied on biopsy sampling of the perimeter and center of the resection defect to determine the efficacy of resection. This may not be as effective as evaluation of resection scars at surveillance colonoscopy,[16-20] but the approach of biopsy sampling of the periphery and center of the defect has been widely used as a method of evaluating resection efficacy.[3,4,6,8-10,15,29]

We encountered 2 serious adverse events, both delayed hemorrhage and both in patients undergoing resection by electrocautery. Thus, our results are consistent with the general observation that cold snare resection is nearly devoid of serious adverse events. On the other hand, the rate of delayed hemorrhage in the electrocautery arms is difficult to interpret, first because biopsy sampling of the defect center could have contributed to bleeding. Second, patients with immediate hemorrhage after resection or biopsy sampling of the lesion center underwent clip closure of the defect, which could have prevented some bleeding in the electrocautery arms.[30,31]

Our results suggest that biopsy sampling of both the periphery and defect center can contribute to counting of ineffective resections. However, biopsy sampling of the center of the defect, particularly in the case where electrocautery had been used, resulted in multiple arterial bleeds at 1 center. Fortunately, all these were easily managed endoscopically, and we did not believe it necessary to stop the center postresection biopsy sampling during the study, and this was not required by the Data Safety Monitoring Board. However, investigators using this technique should be aware that biopsy sampling of the defect center after the use of electrocautery can initiate arterial bleeding, and investigators using this technique for assessing resection efficacy should be prepared to deal with these hemorrhages.

The overall rates of complete resection in all arms of the study were very high and higher than described in an earlier study that brought awareness to the issue of ineffective resection.[29] The complete resection rates were also higher for cold snare resection in this study compared with the 81.6% reported in another recent trial comparing resection methods in 6- to 20-mm polyps.[32] This likely reflects increased awareness of the problem of incomplete resection, improved polypectomy techniques, and better colonoscopic imaging (high definition). Other recent studies performed by experts have also shown very high rates of complete resection using cold snares.[28,33]

In summary, we demonstrated in a randomized controlled trial that cold snare polypectomy is a dominant resection approach to colorectal nonpedunculated lesions 6 to

15 mm in size. Our results indicate that cold snare polypectomy is the treatment of choice for nonpedunculated lesions in this size range, because it is noninferior with regard to efficacy and more efficient than other methods.

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