A Randomized Controlled Trial of Cold Snare Polypectomy Technique: Technique Matters More Than Snare Wire Diameter

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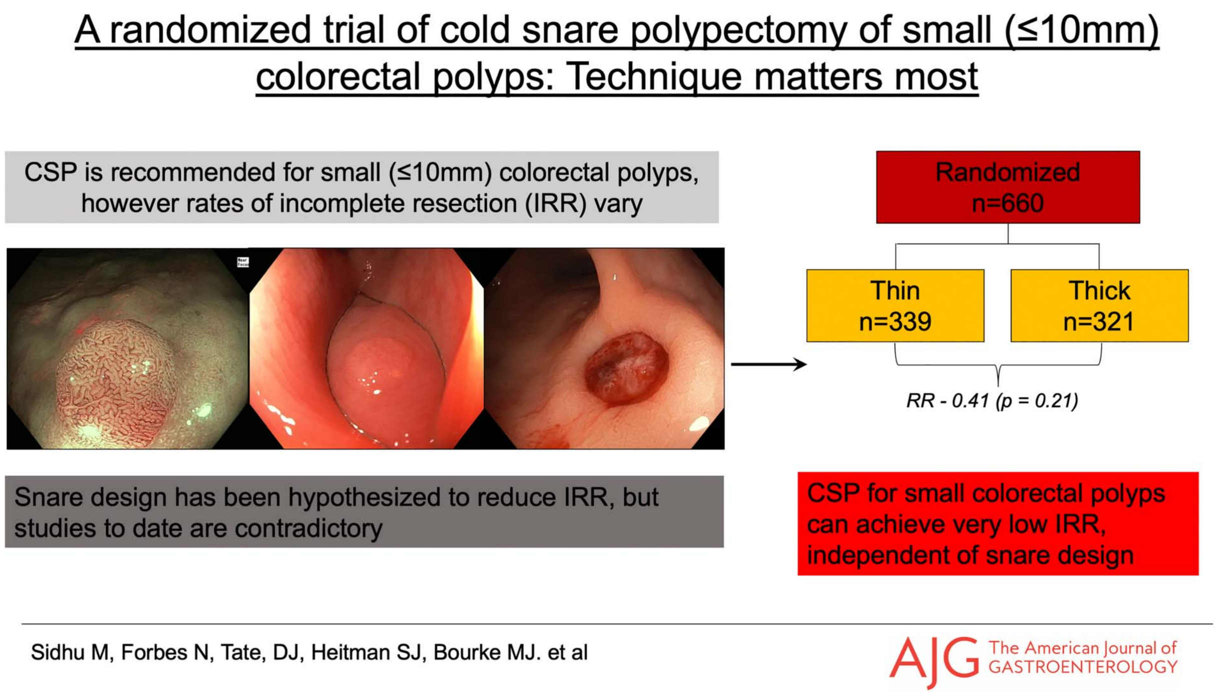
INTRODUCTION: **Cold snare polypectomy (CSP) is safe and effective for the removal of small adenomas (≤10 mm); however, reported incomplete resection rates (IRRs) vary. The optimal CSP technique, where a wide margin of normal tissue is resected around the target lesion, and snare design have both been hypothesized to reduce the IRR after CSP. We sought to investigate the efficacy of a thin-wire versus thick-wire diameter snare on IRR, using the standardized CSP technique.**

METHODS: **This was an international multicenter parallel design randomized trial with 17 endoscopists of varying experience (NCT02581254). Patients were randomized in a 1:1 ratio to the use of a thin-wire (0.30 mm) or thick-wire (0.47 mm) snare for CSP of small (≤10 mm) colorectal polyps. The primary end point was the IRR as determined by the histologic assessment of the defect margin after polypectomy.**



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Received May 17, 2021; accepted October 12, 2021; published online November 24, 2021

RESULTS: **Over 52 months to January 2020, 1,393 patients were eligible. A total of 660 patients with polyps (57.4% male) were randomized to a thin-wire (n = 339) or thick-wire (n = 321) snare. The overall IRR of the cohort was 1.5%. There was no significant difference in the IRR between the thin- and thick-wire arms; relative risk—0.41, 95% CI (0.11–1.56), *P* = 0.21. No significant differences were observed in the rate of adverse events.**

DISCUSSION: **In this multicenter randomized trial, CSP is safe and effective with very low rates of incomplete resection independent of the diameter of the snare wire used. This suggests that the optimal operator technique is more important than the snare design alone in minimizing residual adenoma after CSP.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C306, http://links.lww.com/AJG/C307, http://links.lww.com/AJG/C308, http://links.lww.com/AJG/C309, http://links.lww.com/AJG/C310

Am J Gastroenterol 2022;117:100–109. https://doi.org/10.14309/ajg.0000000000001554

INTRODUCTION

Most colorectal polyps encountered in routine endoscopic practice are small, measuring ≤10 mm in maximum diameter (1,2). Traditionally, such polyps were removed using hot snare polypectomy (HSP) (1). Although generally safe, HSP is associated with infrequent but serious adverse events including postpolypectomy bleeding (PPB) and immediate/delayed perforation (3–6). The most prevalent of these is PPB, which manifests in approximately 1%–2% of cases undergoing HSP (4,7), occurs up to 30 days after the index procedure in some instances, and is thought to be related to the formation of a sloughing eschar due to the use of electrocautery (8). PPB often results in unplanned health care utilization and, not uncommonly, repeat endoscopic intervention (9–12).

In the drive to minimize adverse events, cold snare polypectomy (CSP) has become the standard of care for small colorectal polyps (12,13). CSP is reported to have similar efficacy as compared to HSP when considering incomplete resection rates (IRRs) (14–16). Importantly, CSP avoids electrocautery and thereby the primary mechanism behind PPB (8). Reports of PPB in large studies are rare after CSP and are limited to case reports (17).

Despite the equivalent efficacy and superior safety profile of CSP versus HSP, the IRR remains a persistent problem for both techniques varying between 7% and 35% for small polyps (7,18). This is important given incomplete resection of polyps is an important cause of postcolonoscopy colorectal cancer (19,20). In an attempt to reduce the IRR after CSP, thin-wire monofilament snares have been developed, but studies on their benefit are contradictory (18,21,22). Furthermore, expert opinion strongly recommends that a wide margin of normal tissue is taken to optimize CSP performance (12,13,23). However, studies assessing the impact of optimal technique in reducing the IRR are currently lacking (24,25).

To investigate the effect of snare wire thickness on IRR, we conducted a large international multicenter randomized controlled trial, using the standardized CSP technique, of colorectal polyps ≤10 mm in size randomized to the use of a thin-wire versus thick-wire snare.

METHODS

Study design

This was a parallel design randomized controlled study with a 1:1 allocation ratio conducted at 2 tertiary referral centers in Sydney, Australia, and 1 in Calgary, Canada. The scientific protocol, data collection sheets, and patient consent forms were reviewed and approved by the institutional review board at each institution. Clinical trial registration was obtained (NCT02581254). The study was investigator initiated, and no external funding was sought. All coauthors had access to the study data and reviewed and approved the final manuscript. The manuscript was created in accordance with the Consolidated Standards of Reporting Trials guidelines for reporting randomized-control trials (26).

Participants and eligibility

Written informed consent was obtained from all participants on the day of the procedure. All patients referred for colonoscopy were eligible for inclusion if they had at least 1 polyp measuring ≤ 10 mm in size, without endoscopic evidence of suspected submucosal invasive cancer .

Exclusion criteria

1. Boston Bowel Preparation Score ≤6.
2. Cases of suspected acute upper or lower gastrointestinal bleeding.
3. Continuation of antiplatelet (aspirin excluded) or anticoagulation therapy, if not appropriately managed as per guideline recommendations (27).
4. Underlying coagulopathy (inherited or acquired).
5. Active (acute or chronic) inflammatory bowel disease .
6. Pregnancy.
7. American Society of Anesthesiologists Score ≥4.

Procedure

All patients received standardized split-dose bowel preparation using percutaneous endoscopic gastrostomy-based regimens. Intravenous procedural sedation was used administered by either the endoscopist or under direct anesthetic observation. A combination of high-definition colonoscopes (H[Q] 180/190, Olympus, Tokyo, Japan, or 90i/i10, Pentax, Tokyo, Japan) was used for all cases.

On detection of a study polyp, a 1:1 randomization to the use of a thin-wire (0.30 mm; Telemed & Exacto Cold Snare, Diagmed Healthcare) or a thick-wire (0.47 mm; SnareMaster, Olympus, Japan) snare was performed by an independent study coordinator and the appropriate snare given to the endoscopist. Polyp size was approximated by using an open snare of known dimension. For patients with multiple polyps, the study polyp was the first polyp encountered. Only the first polyp detected was included in the study. Resection of the study polyp then proceeded as above.

After complete endoscopic resection was achieved, 2 biopsies (1 from either side of the defect margin) were performed and sent to histopathology for analysis as separate specimens. Polypectomies were performed during insertion or withdrawal, at the discretion of the treating endoscopists, to minimize the polyp miss rate (28).

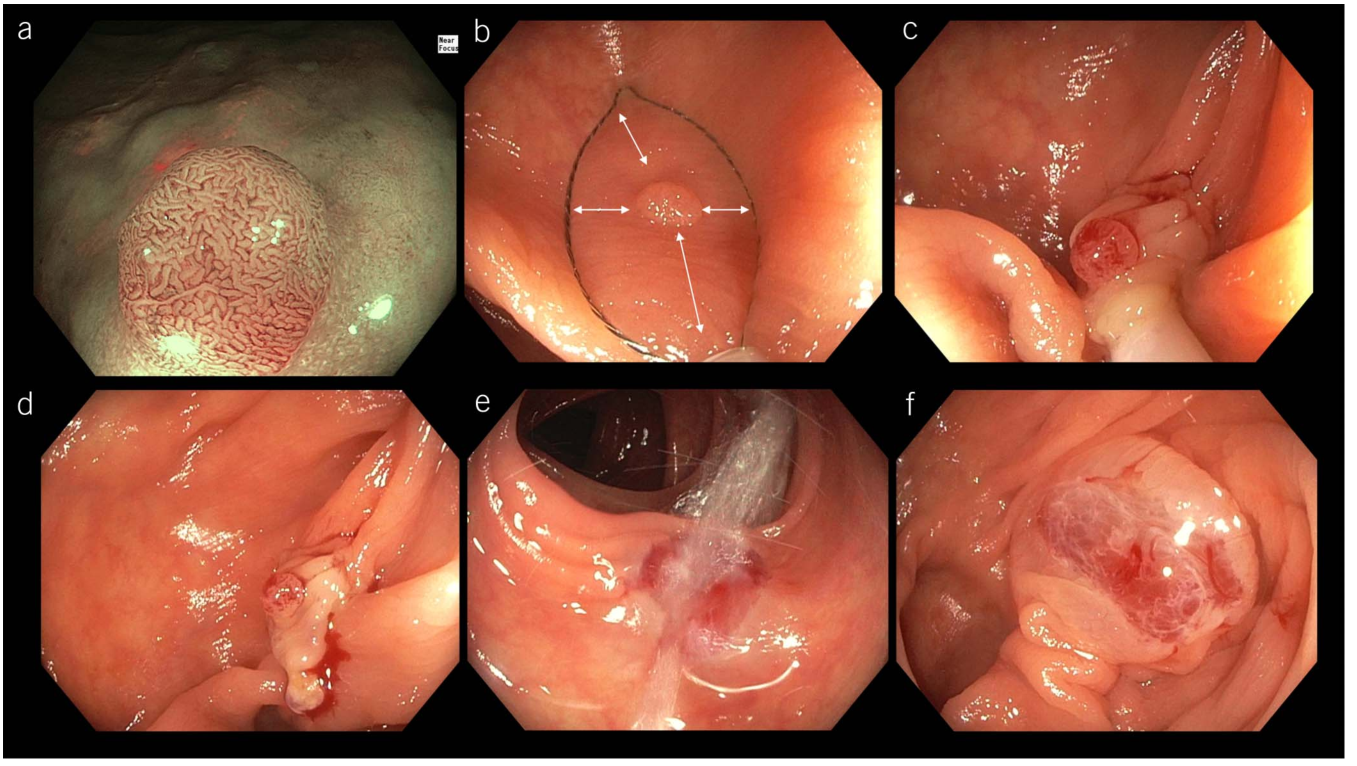

Figure 1. Cold snare polypectomy technique (left → right); (**a**) lesion suitable for cold snare polypectomy, (**b**) snare placement with a wide margin of normal mucosa around target polyp using firm downward pressure with up/down wheel on colonoscope, (**c, d**) polyp transection, (**e**) use of water pump to expand defect and evert edges, and (**f**) expanded defect to assess for residual adenoma at margin.

Randomization and blinding

Randomization was performed using computer generated blocks of 100 at each study center. Randomization tables were stored in sealed envelopes at the study centers and were known only to a study coordinator independent of the procedure.

Treatment allocation was determined and recorded by the independent study coordinator once a polyp was detected. A single polyp per patient was randomized and included in the study. The treatment allocation was not communicated to the endoscopist before polypectomy. However, endoscopist blinding was incomplete due to the different appearance of the 2 snare types. The study patient, histopathologists, and those analyzing the data were blinded to the treatment allocation. The study was, therefore, an open-label, single-blinded randomized controlled trial.

Endoscopist education

All procedures were performed by experienced endoscopists or by senior advanced endoscopy fellows under their direct supervision. All endoscopists involved in this study had performed at least 100 independent CSPs. Before patient recruitment, all study endoscopists were directed to use the standardized CSP technique as outlined below and illustrated in the following video (see Supplementary Video 1, http://links.lww.com/AJG/C309, Figure 1) (23,24,29). The CSP technique was evaluated for each endoscopist before enrollment, by the 2 senior authors, who supervised 5 polypectomies for endoscopists at their respective centers. The key aspects of the technique included the following:

1. The polyp is positioned in the 6 o'clock orientation, and the snare catheter is extended just beyond the tip of the colonoscope.
2. The snare is opened and placed over the polyp, ensuring that a ≥2 mm margin of normal mucosa is captured around the target lesion. Snare pressure on the mucosal surface is maximized by applying firm downward pressure on the mucosa with the snare using the up/down wheel on the colonoscope.
3. The snare is then closed as directed by the endoscopist. Closure should be slow to ensure adequate seating of the snare into the normal mucosa surrounding the polyp.
4. The snare is initially closed to resistance; once adequate tissue capture with a margin of normal tissue is confirmed, full closure is performed to achieve complete transection of the polyp.
5. The resected polyp is suctioned into the colonoscope.
6. Detailed inspection of the cold snare defect is performed (initially with high-definition white light [±near focus imaging]), followed by using the flushing pump to evert the edges of the defect to detect the presence of residual adenoma. If required, repeat snare resections are performed until complete endoscopic resection is achieved (as determined by the endoscopist).

Definitions

CSP—performed with a desired wide margin (≥2 mm) of normal tissue capture around the target lesion.

Study polyp—any colon polyp ≤10 mm in size, without endoscopic evidence of submucosal invasive cancer , suitable for CSP as determined by the endoscopist.

Incomplete resection (IR)—presence of any adenomatous tissue as confirmed at histopathology after complete endoscopic resection.

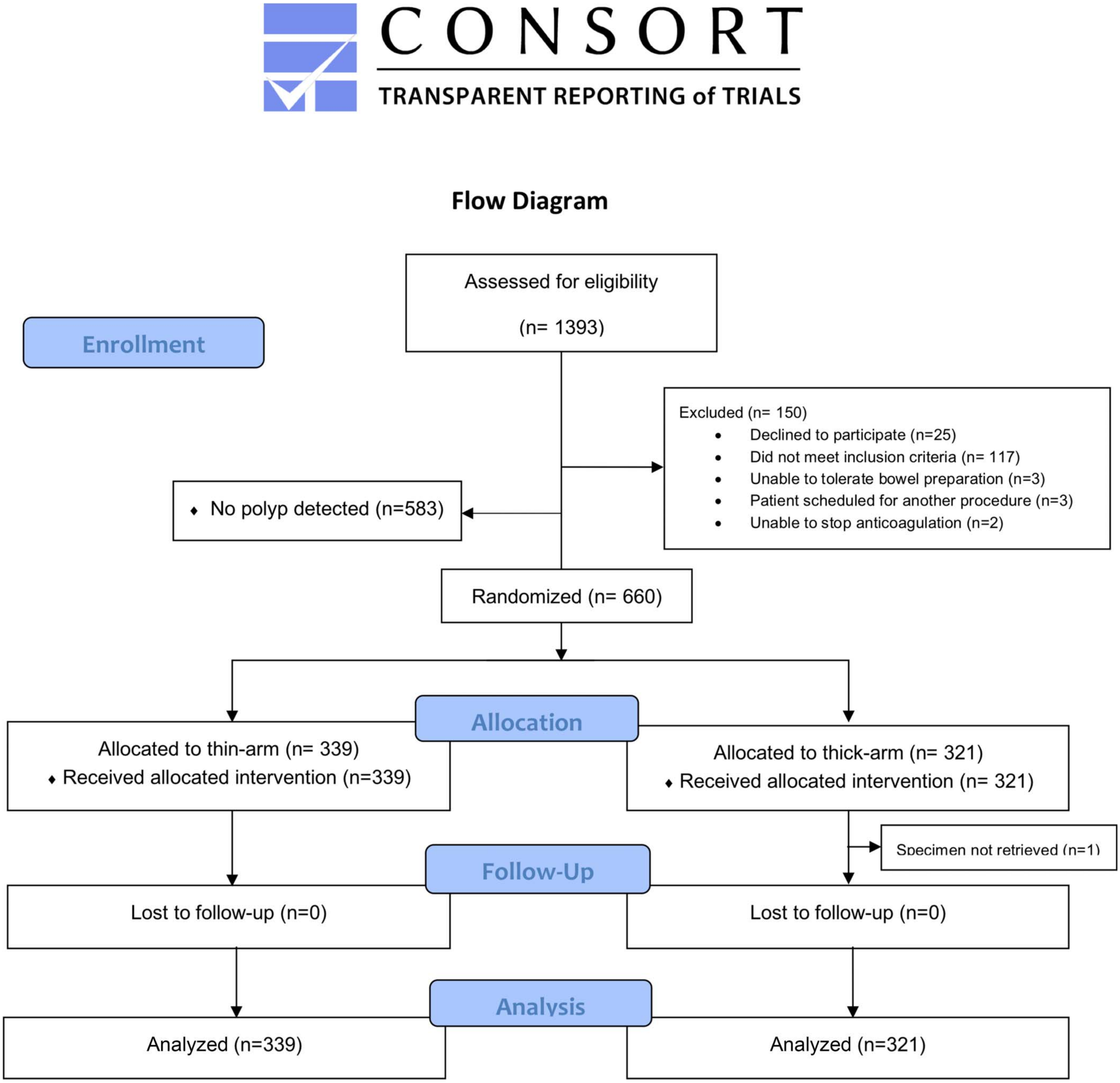

Figure 2. CONSORT flowchart—study design; IRR—complete resection rate.

Intraprocedural bleeding (IPB)—bleeding persisting for ≥ 60 seconds and requiring endoscopic treatment.

Postpolypectomy bleeding (PPB)—bleeding after the completion of the procedure and discharge from the endoscopy unit resulting in presentation to the emergency department, hospitalization, or reintervention within 14 days (30).

Major deep mural injury (DMI)–defined as per the Sydney classification (31) as a visible target sign or actual hole with or without peritoneal contamination, corresponding to type III-V.

Delayed perforation—the clinical syndrome of pain after polypectomy with imaging or surgical evidence of full-thickness injury to the colorectal wall.

Study outcomes

Primary outcome–assessment of IRR with the standardized CSP technique with a thin-wire snare compared with a thick-wire, for colorectal polyps ≤10 mm in size.

Secondary outcomes–procedural details of CSP, rate of adverse events, and the depth of excision in the resected specimens.

Adverse events

All patients enrolled in the study were contacted by the study coordinator 14 days after the procedure to record any adverse events.

Histopathological assessment

All histopathology specimens were analyzed by a specialist gastrointestinal pathologist blinded to the treatment allocation. Biopsies from

Table 1. Patient and lesion characteristics

	Thin (n = 339)	Thick (n = 321)	Total (N = 660)	*P*
Sex, n (%)				
M	195 (57.5)	184 (57.3)	379 (57.4)	0.96
F	144 (42.5)	137 (42.7)	281 (42.6)	
Mean age, yr (SD)	60.1 (9.1)	59.7(10.1)	59.9 (9.6)	0.64
Indication for colonoscopy, n(%)				
Positive FOBT (screening)	79 (23.3)	74 (23.1)	153 (23.2)	
Previous history of polyps	64 (18.9)	76 (23.7)	140 (21.2)	
Symptoms	76 (22.4)	68 (21.2)	144 (21.8)	0.71
Previous colorectal cancer	4 (1.2)	2 (0.6)	6 (0.9)	
Positive FOBT (nonscreening)	39 (11.5)	32 (10)	71 (10.8)	
Other	77 (22.7)	69 (21.5)	146 (22.1)	
ASA, n (%)				
1	104 (30.7)	113 (35.2)	217 (32.9)	
2	209 (61.7)	171 (53.3)	380 (57.6)	0.06
3	26 (7.7)	37 (11.5)	63 (9.5)	
Antithrombotic[a], n (%)				
Aspirin	28 (8.3)	29 (9.3)	57 (8.6)	
Other antiplatetet	3 (0.9)	1 (0.3)	4(0.6)	
Vitamin K antangonist	2 (0.6)	2 (0.7)	4 (0.6)	0.91
DOAC	3 (0.9)	3 (1)	6 (1)	
BBPS, median (IQR)	8 (6–9)	8 (6–9)	8 (6–9)	0.31
Location, n (%)				
R. Colon[b]	179 (52.8)	156 (48.6)	335 (50.8)	
Tranvserse	61 (18)	67 (20.9)	128 (19.4)	0.50
L. Colon	99 (29.2)	98 (30.5)	197 (29.8)	
NICE, n (%)				
Type 1	107 (31.6)	111 (34.6)	218 (33)	0.41
Type 2	232 (68.4)	210 (65.4)	442 (67)	
Size, n (%)				
<5 mm	201 (59.3)	205 (63.9)	406 (61.5)	0.23
5–10 mm	138 (40.7)	116 (11.6)	254 (38.5)	

ASA, American Society of Anesthesiologists; BBPS, Boston Bowel Preparation Score; DOAC, direct oral anticoagulant; F, female; FOBT, fecal occult blood test; IQR, interquartile range; L, left; M, male; NICE, narrow-band imaging classification of colorectal polyps; R, right.
[a]All antithrombotics (aspirin excluded) appropriately interrupted as per guideline recommendations[26]
[b]Right colon—defined as proximal to and including the hepatic flexure.

the margin were sent separately and assessed for residual adenomatous tissue. A subset of the retrieved specimens underwent repeat histopathological analysis for assessment of the depth of resection.

Statistical analysis

The IRR in the thick arm was estimated at 15% or higher, and a reduction in the IRR of 50% using a thin-wire snare was predicted (16,18). Therefore, the sample size required to detect a difference with 80% power and an alpha of 0.05 was 300 lesions in each arm.

Categorical variables were described using frequencies and percentages. Mean, median, SD, and interquartile ranges were calculated for continuous data. Statistical significance was set at a threshold of 0.05, and comparisons between different groups and outcomes were performed using the χ^2 and Fisher exact tests as appropriate. The relative risks (RRs) and associated 95% confidence intervals (CIs) of dichotomous outcomes in the active versus control arms were calculated. All data were analyzed using IBM SPSS Statistics Version 27.0 (Armonk, New York).

RESULTS

Over 52 months (September 2015–January 2020), 1,393 patients referred for colonoscopy were eligible for enrollment (Figure 2). One hundred fifty patients were excluded (declined to participate, n = 25; did not meet inclusion criteria, n = 117; unable to tolerate bowel preparation, n = 3; patient scheduled for another procedure, n = 3; and unable to stop anticoagulation, n = 2). Five hundred eighty-three patients had no polyp detected. Six hundred sixty polyps in 660 patients were randomized to the thin-wire arm (n = 339) or the thick-wire arm (n = 321) of the study.

Patient demographics

Mean patient age was 59.9 years (SD–9.6), and 57.4% were male (Table 1). The most common indication for colonoscopy was a positive screening fecal occult blood test (153, 23.2%). Most patients were American Society of Anesthesiologists Class II (380, 57.6%). The median Boston Bowel Preparation Score for the cohort was 8 (interquartile range: 6–9). Patient demographics did not differ significantly between the 2 groups.

Polyp demographics

The median polyp size was 4 mm (interquartile range: 3–5 mm). Narrow band Imaging Classification of Colorectal Polyps Type II was most commonly observed (442, 67%), and lesions were located in the right colon 50.8% (335/660) of the time. Of note, 659/660 (99.5%) specimens were retrieved for histopathological analysis. A single specimen was unable to be retrieved from the thick-wire arm (included in the intention-to-treat analysis as incompletely resected). Therefore, margin biopsies were taken in 659 (99.8%) cases (thin-wire arm; 339; thick-wire arm; 320).

Primary outcome

The overall IRR of the cohort was 1.5% (Table 2). On intention-to-treat analysis, the IRR was 3/339 (0.9%) in the thin-wire arm vs 7/321 (2.2%) in the thick-wire arm; relative risk = 0.41, 95% CI (0.12–1.56), $P = 0.21$. On per-protocol analysis, the IRR was 3/339 (0.9%) in the thin-wire arm vs 6/320 (2.2%) in the thick-wire arm; relative risk = 0.47, 95% CI (0.12–1.9), $P = 0.33$.

Secondary outcomes

Cold snare procedure. Complete endoscopic resection was achieved in all polyps (Table 3). Of note, 619/660 (93.8%) polyps (thin arm; 316, thick arm; 303) were endoscopically deemed completely resected after the first snare excision. The remainder (n = 41, 6.2%) were removed piecemeal to ensure complete excision. A cold snare protrusion was identified in 189 (28.6%) cases and was significantly more common in the thick-wire arm as compared to the thin-wire arm; 104 (32.4%) vs 85 (25.1%), $P = 0.04$.

Table 2. Primary outcome

IRR	Thin Wire	Thick Wire	Total	RR (95% CI)	*P*
All polyps					
ITT	3/339(0.9)	7/321 (2.2)	10/660 (1.5)	0.41 (0.11–1.56)	0.21
ITT[a]	3/339(0.9)	6/321 (1.9)	10/660 (1.5)	0.47 (0.12–1.88)	0.33
PP	3/339 (0.9)	6/320 (1.9)	9/659 (1.4)	0.47 (0.12–1.87)	0.33
Polyps 9–10 mm					
ITT	0/12 (0)	0/8 (0)	0/20 (0)	—	—
PP	0/12 (0)	0/8 (0)	0/20 (0)	—	—
Adenomas/SSLs only					
ITT	2/252 (0.8)	4/220 (1.8)	6/472(1.3)	0.44 (0.08–2.36)	0.42
PP	2/252 (0.8)	4/220 (1.8)	6/472(1.3)	0.44 (0.08–2.36)	0.42

CI, confidence interval; IRR, incomplete resection rate; ITT, intention to treat; PP, per protocol; RR, relative risk; SSL, sessile serrate lesion.
[a]ITT–if polyp not retrieved was completely resected.

Adverse events. Three cases of IPB were observed: thin-wire arm–1 (0.3%) vs thick-wire arm–2 (0.6%). All cases were observed as a mild ooze, and no endoscopic treatment was performed. There were no cases of PPB, major DMI, or delayed perforation attributable to CSP in either treatment arm.

Histopathology. Polyp tissue was detected in 583/659 (88.5%) of resections. Tubular adenomas were the most common histologic subtype, identified in 394/659 (59.7%) polyps; thin-wire arm–210 vs thick-wire arm–184. Low-grade dysplasia was observed in 401/659 (60.8%); thin-wire arm–212 vs thick-wire arm–189.

Table 3. Lesion outcomes

	Thin (n = 339)	Thick (n = 321)	Total (N = 660)	*P*
Complete endoscopic resection, n (%)	339 (100)	321 (100)	660 (100)	—
Complete excision at first attempt, n (%)	316 (93.2)	303 (94.4)	619 (93.8)	0.53
Endoscopic cold snare protrusion, n (%)				
Yes	85 (25.1)	104 (32.4)	189 (28.6)	0.04
Specimen not retrieved, n (%)	0 (0)	1 (0.3)	1 (0.2)	—
Margin biopsy, n (%)	339 (100)	320 (99.8)	659 (99.8)	654 (99.1)
IRR, n (%)[a]	3/339 (0.9)	6/320 (1.9)	9/654 (1.4)	0.28
Histopathology, n(%)[a]				
Hyperplastic	41 (12.1)	45 (14.1)	86 (13.1)	—
TA	210 (61.9)	184 (57.3)	394 (59.7)	—
TVA	7 (2.1)	3 (0.9)	10 (1.5)	0.43
SSL	35 (10.3)	33 (10.3)	68 (10.3)	—
Other	46 (13.6)	55 (17.2)	101 (15.3)	—
Dysplasia, n(%)[a]				
None	127 (37.5)	129 (40.3)	256 (38.8)	—
Low-grade	212 (62.5)	189 (58.9)	401 (60.8)	0.24
High-grade	0 (0)	2 (0.6)	2 (0.3)	—
Adverse events, n (%)				
IPB	1 (0.3)	2 (0.6)	3 (0.5)	0.53
Deep mural injury[b]	0 (0)	0 (0)	0 (0)	—
PPB	0 (0)	0 (0)	0 (0)	0.33
Delayed perforation	0 (0)	0 (0)	0 (0)	—

IRR, incomplete resection rate; IPB, intraprocedural bleeding; PPB, postpolypectomy bleeding; SSL, sessile serrated lesion; TA, tubular adenoma; TVA, tubular villous adenoma.
[a]Percentage calculated from retrieved specimens only.
[b]Sydney DMI Classification.[29]

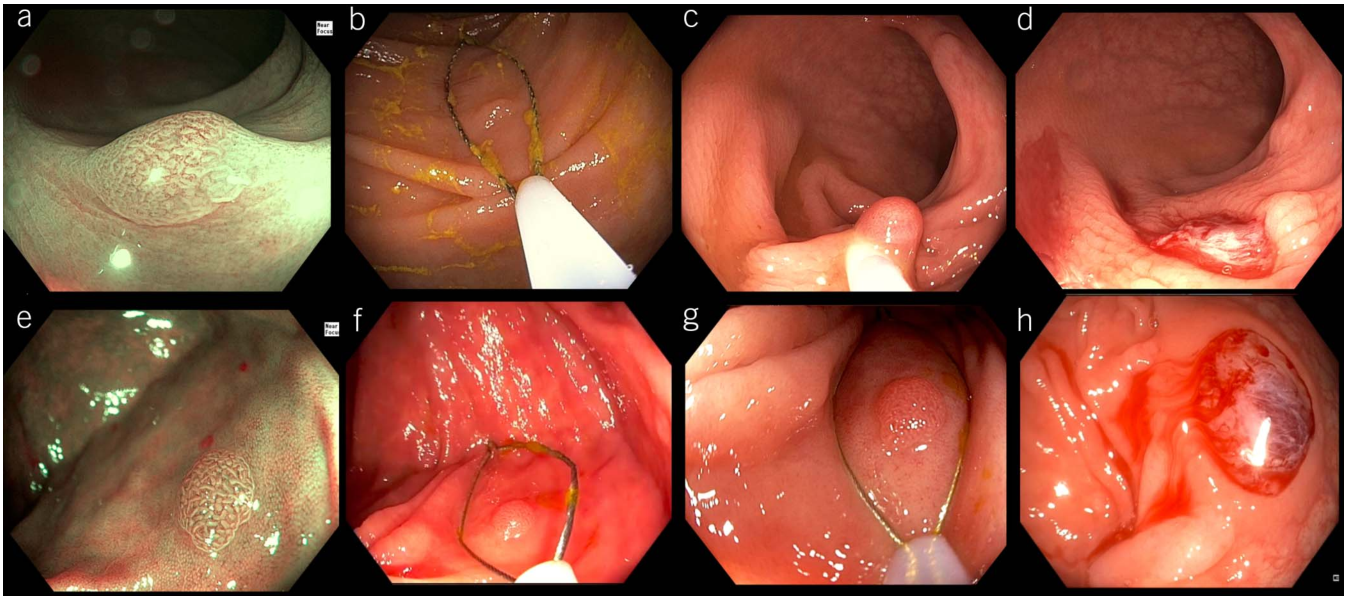

Figure 3. (**a–d**) Cold snare polypectomy using a thick-wire snare; (**e–h**) cold snare polypectomy using a thin-wire snare.

Of note, 566/659 (85.9%) polyps underwent repeat histological evaluation for the presence of submucosal tissue within the resected specimen (Supplementary Table 1, http://links.lww.com/AJG/C306). Submucosal tissue was infrequently present in CSP specimens (36, 5.8%) but was significantly more common in resections from the thin-wire arm vs thick-wire arm, 25/320 (7.8%) vs 11/303 (3.6%), $P = 0.02$.

Per endoscopist outcomes

Seventeen endoscopists were included in the study (10 senior consultants and 7 advanced endoscopy fellows) (see Supplementary Table 2, http://links.lww.com/AJG/C307). The mean polyp detection rate and adenoma detection rate were 0.52 (SD–0.13) and 0.39 (0.20), respectively. The mean number of incompletely resected polyps was similar, among individual endoscopists, in both groups; 0.01 (SD–0.09) in the thin-arm vs 0.02 (SD–0.14). There was no significant difference between the IRR of endoscopists overall ($P = 0.43$) or within either treatment arms (thin-arm; $P = 0.91$ vs thick-arm; $P = 0.16$). For detailed characteristics of IRR cases, see Supplementary Table 3, http://links.lww.com/AJG/C308.

DISCUSSION

CSP has emerged as the technique of choice for the resection of colorectal polyps ≤ 10 mm (12,13). CSP is superior to forceps (hot/cold) resection and is associated with a lower risk of adverse events as compared to HSP, by avoiding electrocautery-induced injury (32,33). In this large international multicenter randomized controlled trial of over 600 patients and colorectal polyps, we demonstrate that CSP of lesions ≤ 10 mm is extremely safe and equally efficacious whether using a thin- or thick-wire snare and results in very low (~2%) IRR among endoscopists with a broad range of experience.

Studies have historically reported higher rates of histologically confirmed IRR after CSP ranging between 7 and 35% (17,18). Although more recent publications indicate that far lower rates (< 2%) are possible (20), the factors contributing to this decrease in the IRR have not been fully explored. Because these studies often originate from single expert centers (22) and fail to either disclose the experience level of the endoscopists involved or assess the impact of the snare type used (21), their applicability in routine endoscopic practice is limited.

Previously identified factors, which may contribute to improved rates of IRR after CSP, include the following:

1. Use of a thin-wire (dedicated cold) snare (21,22).
2. Acquisition of a margin of normal tissue (at least 2 mm) around the resected polyp (24,25).
3. Endoscopic examination of the cold snare defect margin after resection (23,34).

It has been hypothesized that thin-wire monofilament snares alone reduce the IRR. Thin-wire snares allow for a quick and clean transection of polyp tissue resulting in a defect with well-defined margins that are easy to examine (8,12). However, despite these real-world benefits, studies have demonstrated contradictory outcomes, with no clear superior snare type with respect to the IRR after CSP. Horiuchi et al. (22) reported a significantly higher rate of complete histologic resection using a thin-wire compared with a thick-wire snare in a randomized study. However, their IRR was considerably higher at 9% and 21% in the thin- and thick-wire arms, respectively. Similarly, Din et al. (18) reported a lower endoscopic IRR using thin-wire versus thick-wire snares (10% vs 27%) in a small prospective study of 112 patients. Moreover, although the difference was nonsignificant, the histologic IRR was again considerably higher among both the thin- (27%) and thick-wire (35%) snare arms in comparison to our study where the histologic IRR was <2% after the use of either snare type. It is noteworthy that these earlier studies recruited patients between 2013 and 2014 and therefore employed the use of inferior endoscopic imaging technology. This combined with suboptimal CSP technique are possible explanations for the higher IRR reported in these earlier trials. In our large randomized trial, endoscopists achieved complete histologic resection of polyps in greater than

Table 4. Hot snare polypectomy vs cold snare polypectomy technique

Technique	HSP	CSP
Lesion orientation	6 o'clock	6 o'clock
Extent of tissue capture	Minimized (adapted to the size of the target lesion to minimize the risk of DMI)	Maximized/unlimited (extended beyond the target lesion to ensure margin of normal tissue and achieve complete resection)
Snare pressure on mucosal surface	Minimal (tented away from the mucosa to minimize the risk of DMI and transmural thermal injury)	Maximal (firm downward pressure using the up/down wheel to ensure adequate tissue capture)
Speed of transection	Fast (to minimize unnecessary mural thermal injury)	Not critical, but avoid rapid snare closure to ensure adequate seating of the snare into the surrounding normal mucosa during closure
Primary method of transection	Diathermy/partly mechanical	Mechanical
Depth of excision	Submucosa (6%–20%) (34)	Muscularis mucosa (common, >60%) Submucosa (uncommon, <7%)
Defect		
Protrusion	Nil	Yes (common)
Examining for residual adenoma	Challenging, limited due to diathermy-related tissue artefact	Detailed examination by using water pump to expand the defect and evert margins
Extending defect margin	Not recommended	Recommended if any suspected residual adenoma
Method of extending defect margin	EMR	CSP (piecemeal)

CSP, cold snare polypectomy; DMI, deep mural injury; EMR, endoscopic mucosal resection; HSP, hot snare polypectomy.

98% of cases regardless of snare wire thickness. Thus, it is clear from our findings that snare wire thickness alone does not explain the low observed rates of IRR found in our study.

It is important to recognize that evidence from large prospective trials assessing the impact of the standardized optimal CSP technique in reducing the IRR is currently lacking, despite expert opinion mandating its routine use (24). Two fundamental elements of this technique are hypothesized to have resulted in low overall IRRs after CSP in our study: (i) the systematic acquisition of a margin of normal tissue [at least 2 mm] and (ii) a meticulous inspection of the defect margin after CSP (Figure 3). Furthermore, this standardized CSP technique was applied throughout our trial and regardless of snare wire design. Thus, we believe that the use of the optimal CSP technique, rather than snare wire diameter, is the major driver of the low IRRs observed in our study. In addition, most previous studies examining the CSP technique have included only a small number of endoscopists (or no total number declared) and/or involved single expert centers. In contrast, our experience was across 3 large institutions in 2 countries with a clearly defined endoscopist demographic [median clinical experience 7 years, with 10 consultants and 7 advanced endoscopy fellows] who all performed similarly. This highlights that exceptional results can be achieved over a broad range of clinical experience following education and the application of the systematic, meticulous, and standardized approach we have proposed to this fundamentally important procedure during colonoscopy.

Given the relatively recent widespread adoption of CSP compared with more traditional techniques, the endoscopist technique is arguably more underdeveloped for CSP than for HSP. Although similar, important differences exist between CSP and HSP (Table 4):

1. Resection of a wide margin of normal tissue around the target polyp. Indeed, there seems to be no additional demonstrable risk imposed by an extended cold snare resection in either this or other studies (35,36). This makes the technique not only effective but appealing for a broad range of endoscopists. In contrast, this is only possible through endoscopic mucosal resection when using electrocautery and is associated with a higher risk of adverse events (3).
2. During CSP, the snare is placed on the target lesion with firm downward pressure on the mucosa using the up/down wheel on the colonoscope. In comparison, when performing HSP, the snare is tented away from the mucosa to minimize the risk of major DMI.
3. Detailed endoscopic examination for residual polyp by irrigation and expansion of the defect after CSP with an endoscope flushing pump. With HSP this is often more difficult With HSP this often more difficult due to the diathermy artefact.

Alongside these specific points, standard polypectomy techniques common to both modalities also apply, including maintaining a short colonoscope position wherever possible and ensuring 6 o'clock orientation of the polyp (37).

The adverse event profile of CSP in our study was extremely favorable regardless of snare wire thickness and in keeping with contemporary evidence (12,13). Expectedly, there were no occurrences of DMI or delayed perforation attributable to CSP in our study in either arm, given that this phenomenon is intimately linked to the use of cautery (8). One patient in the trial (thick-wire arm) presented with PPB, but on repeat endoscopy, it was determined that the culprit lesion was an HSP ulcer with a visible vessel that required endoscopic clipping. The ulcer bed of the CSP study polyp was clean based with no signs of recent bleeding. It should be emphasized that IPB during CSP is regarded as a technical interference rather than a true adverse event (6), and although rates vary in the published literature (6,8), it usually does not alter a patient's clinical course. IPB was observed at a rate of 0.3% in this study.

In this study, as lesions included were ≤10 mm and a 10-mm snare was used throughout, piecemeal CSP was required for the small subset of the polyps 9–10 mm in size. This study was not designed to address piecemeal technique, although recent data appear promising for certain types of LNPCPs (23,35,36). Piecemeal resection in this study was performed if required due to a failed

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attempt at *en bloc* resection. This occurred perhaps more frequently than would be expected (6.1%), possibly due to our requirement of meticulously visualizing the margin after CSP. We did not observe an increase in the IRR with piecemeal resection, nor was there an increase in adverse events among this small subset of patients. Nevertheless, endoscopists should strive for *en bloc* resection of polyps ≤10 mm in size whenever possible (38).

On histologic assessment of the depth of resected specimens, we found that CSP specimens very infrequently contained submucosal tissue (<6.5%), although it was more commonly observed in the thin-wire arm (Supplementary Table 2, http://links.lww.com/AJG/C307). In comparison, HSP specimens commonly contain submucosal tissue (>80%) (39). This finding intrinsically disadvantages the safety of HSP, as a deeper resection is associated with an increased risk of thermal injury to the colonic wall, whereas the exposed deep submucosal vessels significantly increase the risk of PPB. However, this also highlights an important limitation of CSP, which is in the setting of unsuspected advanced histology such as high-grade dysplasia or early cancer. As the plane of resection during CSP does not include the entire muscularis mucosa, the completeness of resection cannot be ensured, and thus, lesions with advanced histology should be re-excised by conventional polypectomy or other advanced endoscopic resection methods. Fortunately, such findings in small polyps are infrequent and occur at reported frequencies of 0.06% and 0.03%, respectively (13,40).

Despite the methodologic rigor with which our randomized trial was conducted, our study has several limitations. First, as is the case with most randomized trials assessing the efficacy of endoscopic interventions, endoscopists were not blinded to the type of snare used. Although unlikely, it is possible that this could have introduced bias. However, randomization with concealed allocation, multicenter design with involvement of a large and heterogeneous group of endoscopists, and blinding of the pathologists and data analysts all helped to mitigate potential bias. Second, in this study, we used marginal biopsies to assess IRRs. This technique is prone to sampling error and even if unlikely, the potential for introducing bias from an endoscopist systematically missing visible residual polyp according to preferred snare type. However, this approach is superior to endoscopic assessment alone and has been used in other published studies (16). Third, our sample size was informed by the existing literature at the time our trial began enrollment. Although we had expected a higher IRR, as described above, we believe that the standardized and meticulous technique used across the trial cohort substantially lowered the IRR in both arms of this trial. Although we cannot rule out that thin-wire snares may further reduce IRRs during CSP, we were underpowered to demonstrate a statistically significant reduction in IRRs of 1.2% (2.2%–0.9%). Nevertheless, such a small difference is arguably inconsequential and would have required over 4,000 randomized patients to demonstrate. Finally, lesions in the study were not randomized to the resection of a wide or minimal normal margin of tissue around the target polyp. However, based on expert opinion, the resection of a wide margin of normal tissue is now considered standard best practice and as such incorporated in international polypectomy guidelines. Thus, not only would clinical relevance be debatable as wide-margin resection is part of established practice, it would also be unethical to expose 50% of the cohort to an inferior treatment.

CONCLUSION

Our findings demonstrate the efficacy and safety of CSP for lesions ≤10 mm, regardless of whether a thin- or thick-wire snare was used. The standardized and meticulous endoscopist technique focused on acquisition of a wide margin of normal tissue followed by close inspection of the defect margin is likely to be the single most important factor in achieving technical success and optimizing resection outcomes when performing CSP.

CONFLICTS OF INTEREST

Guarantor of the article: Steven J. Heitman, MD, MSc, and Michael J. Bourke, MBBS.

Specific author contributions: M.S.: study design, collected, organized, and analyzed data, and drafted and revised the manuscript after review by the coauthors. N.F.: performed procedures, collected data, codrafted the manuscript, and revised the manuscript after review by the coauthors. D.J.: study design, collected and analyzed data, and assisted in writing and revising the manuscript after review by the coauthors. L.D.: study design, identified and recruited patients, performed procedures, and reviewed the manuscript. E.Y.T.L.: identified and recruited patients, performed procedures, and reviewed the manuscript. N.B.: identified and recruited patients, performed procedures, collected data, and reviewed the manuscript. A.v.H.: identified and recruited patients, performed procedures, collected data, reviewed histopathology specimens, and reviewed the manuscript. D.M.: review of histopathology specimens and reviewed the manuscript. E.C.: performed procedures, collected data, and reviewed the manuscript. S.C.: recruited patients, collected data, and reviewed the manuscript. A.S.: review of histopathology specimens and reviewed the manuscript. R.J.H.: performed procedures, collected data, and reviewed the manuscript. S.J.H.: study design, performed procedures, collected data, co-led the study, and critically reviewed the manuscript. M.J.B.: conceived, designed and led the study, and critically reviewed and approved the final manuscript.

Financial support: The Cancer Institute New South Wales and the N.B. Hershfield Chair in Therapeutic Endoscopy provided funding for a research nurse to assist with the administration of the study in Sydney, New South Wales, and Calgary, Alberta, respectively. Neither funder had any input regarding study design or conduct, data collection, management, analysis or interpretation, or preparation, review, or approval of the manuscript

Potential competing interests: N. Forbes: Boston Scientific—consultant; Pentax medical—research support and speaker's honoraria. S.J. Heitman: Pendopharm—consultant. M.J. Bourke: Olympus, Cook Medical, and Boston Scientific—research support. The remaining authors report no conflicts of interest.

Study Highlights

WHAT IS KNOWN

- ✓ Cold snare polypectomy (CSP) is safe and effective for the removal of small adenomas.
- ✓ IRRs vary. Dedicated CSP snares (thin-wire) have been hypothesized to reduce incomplete resection rates (IRRs).
- ✓ We sought to investigate the efficacy of thin-wire versus thick-wire snares on IRR.

WHAT IS NEW HERE

- ✓ CSP is safe and effective with very low rates of IRR, independent of the diameter of the snare wire used.
- ✓ The optimal operator technique is more important than the snare design in minimizing residual adenoma after CSP.

REFERENCES

1. Zauber AG, Winawer SJ, OBrien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012;366:687–96.
2. O'Brien MJ, Winawer SJ, Zauber AG, et al. The National Polyp Study. Patient and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. Gastroenterology 1990;98:371–9.
3. Heitman SJ, Tate DJ, Bourke MJ. Optimizing resection of large colorectal polyps. Curr Treat Options Gastroenterol 2017;15:213–229.
4. Rabeneck L, Paszat LF, Hilsden RJ, et al. Bleeding and perforation after outpatient colonoscopy and their risk factors in usual clinical practice. Gastroenterology 2008;135:1899–906.
5. Burgess NG, Metz AJ, Williams SJ, et al. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014;12:651–61.
6. Papastergiou V, Paspatis GA, Paraskeva KD. Immediate intraprocedural bleeding: True 'complication' of cold snare polypectomy? Endosc Int Open 2019;07:E1031–E1032.
7. Pohl H, Srivastava A, Bensen SP, et al. Incomplete polyp resection during colonoscopy - results of the complete adenoma resection (CARE) study. Gastroenterology 2013;144:74–80.
8. Tolliver KA, Rex DK. Colonoscopic polypectomy. Gastroenterol Clin North Am 2008;37:229–51.
9. Liaquat H, Rohn E, Rex DK. Prophylactic clip closure reduced the risk of delayed postpolypectomy hemorrhage: Experience in 277 clipped large sessile or flat colorectal lesions and 247 control lesions. Gastrointest Endosc 2013;77:401–7.
10. Hilsden RJ, Dube C, Heitman SJ, et al. The association of colonoscopy quality indicators with the detection of screen-relevant lesions, adverse events, and postcolonoscopy cancers in an asymptomatic Canadian colorectal cancer screening population. Gastrointest Endosc 2015;82:887–94.
11. Bahin FF, Rasouli KN, Byth K, et al. Prediction of clinically significant bleeding following wide-field endoscopic resection of large sessile and laterally spreading colorectal lesions: A clinical risk score. Am J Gastroenterol 2016;111:1115–22.
12. Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. 2017.
13. Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic removal of colorectal lesions—recommendations by the US multi-society task force on colorectal cancer. Gastroenterology 2020;158:1095–129.
14. Kawamura T, Takeuchi Y, Asai S, et al. A comparison of the resection rate for cold and hot snare polypectomy for 4-9 mm colorectal polyps: A multicentre randomised controlled trial (crescent study). Gut 2018;67:1950–7.
15. Jegadeesan R, Aziz M, Desai M, et al. Hot snare vs. cold snare polypectomy for endoscopic removal of 4–10 mm colorectal polyps during colonoscopy: A systematic review and meta-analysis of randomized controlled studies. Endosc Int Open 2019;07:E708–E716.
16. Qu J, Jian H, Li L, et al. Effectiveness and safety of cold versus hot snare polypectomy: A meta-analysis. J Gastroenterol Hepatol 2019;34:49–58.
17. Chang L-C, Shun C-T, Hsu W-F, et al. Risk of delayed bleeding before and after implementation of cold snare polypectomy in a screening colonoscopy setting. Endosc Int Open 2019;07:E232–E238.
18. Din S, Ball AJ, Riley Sa, et al. Cold snare polypectomy: Does snare type influence outcomes? Dig Endosc 2015; 27:603–8.
19. Anderson R, Burr NE, Valori R. Causes of post-colonoscopy colorectal cancers based on world endoscopy organization system of analysis. Gastroenterology 2020;158:1287–99.
20. Belderbos TDG, Pullens HJM, Leenders M, et al. Risk of post-colonoscopy colorectal cancer due to incomplete adenoma resection: A nationwide, population-based cohort study. United Eur Gastroenterol J 2017;5:440–7.
21. Dwyer J, Tan J, Urquhart P, et al. A prospective comparison of cold snare polypectomy using traditional or dedicated cold snares for the resection of small sessile colorectal polyps. Endosc Int Open 2017;05:E1062–E1068.
22. Horiuchi A, Hosoi K, Kajiyama M, et al. Prospective, randomized comparison of 2 methods of cold snare polypectomy for small colorectal polyps. Gastrointest Endosc 2015;82:686–92.
23. Tate DJ, Awadie H, Bahin FF, et al. Wide-field piecemeal cold snare polypectomy of large sessile serrated polyps without a submucosal injection is safe. Endoscopy 2018;50:248–52.
24. Hewett DG. Cold snare polypectomy: Optimizing technique and technology (with videos). Gastrointest Endosc 2015;82:693–96.
25. Abe Y, Nabeta H, Koyanagi R, et al. Extended cold snare polypectomy for small colorectal polyps increases the R0 resection rate. Endosc Int Open 2018;06:E254–E258.
26. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. Plos Med 2010;7:1–7.
27. Acosta RD, Abraham NS, Chandrasekhara V, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. Gastrointest Endosc 2016;83:3–16.
28. Wildi SM, Schoepfer AM, Vavricka SR, et al. Colorectal polypectomy during insertion and withdrawal or only during withdrawal? A randomized controlled trial. Endoscopy 2012;44:1019–23.
29. Burgess NG, Bahin FF, Bourke MJ. Colonic polypectomy. Gastrointest Endosc 2014.
30. Burgess NG, Williams SJ, Hourigan LF, et al. A management algorithm based on delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. Clin Gastroenterol Hepatol 2014;12:1525–33.
31. Burgess NG, Bassan MS, McLeod D, et al. Deep mural injury and perforation after colonic endoscopic mucosal resection: A new classification and analysis of risk factors. Gut 2017;66(10):1779–89.
32. Lee CK, Shim J-J, Jang JY. Cold snare polypectomy vs. cold forceps polypectomy using double-biopsy technique for removal of diminutive colorectal polyps: A prospective randomized study. Am J Gastroenterol 2013;108:1593–600.
33. Metz AJ, Moss A, McLeod D, et al. A blinded comparison of the safety and efficacy of hot biopsy forceps electrocauterization and conventional snare polypectomy for diminutive colonic polypectomy in a porcine model. Gastrointest Endosc 2013;77:484–90.
34. Tutticci NJ, Kheir AO, Hewett DG. The cold revolution: How far can it go? Gastrointest Endosc Clin N Am 2019;29:721–36.
35. Tutticci NJ, Hewett DG. Cold EMR of large sessile serrated polyps at colonoscopy (with video). Gastrointest Endosc 2018;87:837–42.
36. Hattem WAV, Shahidi N, Vosko S, et al. Piecemeal cold snare polypectomy versus conventional endoscopic mucosal resection for large sessile serrated lesions: A retrospective comparison across two successive periods. Gut 2020:1–7.
37. Burgess NG, Bahin FF, Bourke MJ. Colonic polypectomy (with videos). Gastrointest Endosc 2015;81:813–35.
38. Belderbos T, Belderbos TDG, Leenders M, et al. Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: Systematic review and meta-analysis. Endoscopy 2014;46:388–402.
39. Suzuki S, Gotoda T, Kusano C, et al. Width and depth of resection for small colorectal polyps: Hot versus cold snare polypectomy. Gastrointest Endosc 2018;87:1095–103.
40. Lieberman D, Moravec M, Holub J, et al. Polyp size and advanced histology in patients undergoing colonoscopy screening: Implications for CT colonography. Gastroenterology 2008;135(4):1100–5.