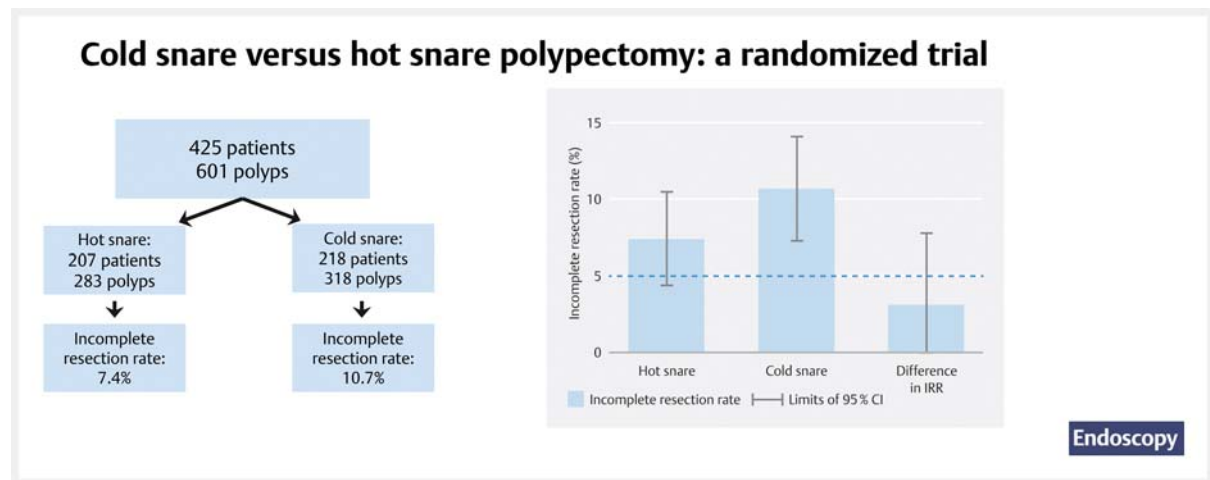


# Complete polyp resection with cold snare versus hot snare polypectomy for polyps of 4–9 mm: a randomized controlled trial

## INFOGRAPHIC



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**ABSTRACT**

**Background** Endoscopic screening with polypectomy reduces the incidence of colorectal cancer (CRC). Incomplete polyp removal may attenuate the effect of screening. This randomized trial compared cold snare polypectomy (CSP) with hot snare polypectomy (HSP) in terms of complete polyp resection.

**Methods** We included patients  $\geq 40$  years of age at eight hospitals in four countries who had at least one non-pedunculated polyp of 4–9 mm detected at colonoscopy. Patients were randomized 1:1 to CSP or HSP. Biopsies from the resection margins were obtained systematically after polypectomy in both groups. We hypothesized that CSP would be non-inferior to HSP, with a non-inferiority margin of 5%.

Logistic regression models were fitted to identify the factors explaining incomplete resection.

**Results** 425 patients, with 601 polyps, randomized to either CSP or HSP were included in the analysis. Of 318 polyps removed by CSP and 283 polyps removed by HSP, 34 (10.7%) and 21 (7.4%) were incompletely resected, respectively, with an adjusted risk difference of 3.2% (95% CI  $-1.4\%$  to  $7.8\%$ ). There was no difference between the groups in terms of post-polypectomy bleeding, perforation, or abdominal pain. Independent risk factors for incomplete removal were serrated histology (odds ratio [OR] 3.96; 95%CI 1.63 to 9.66) and hyperplastic histology (OR 2.52; 95%CI 1.30 to 4.86) in adjusted analyses.

**Conclusion** In this randomized trial, non-inferiority for CSP could not be demonstrated. Polyps with serrated histology are more prone to incomplete resection compared with adenomas. CSP can be used safely for small polyps in routine colonoscopy practice.

## Introduction

Endoscopic screening for colorectal cancer (CRC) has been shown to reduce the incidence of CRC in randomized controlled trials [1–4]. This effect is due to removal of possible CRC precursors, polyps, by polypectomy. However, some individuals are diagnosed with CRC after colonoscopy (so-called “post-colonoscopy cancer”) [5, 6]. Several mechanisms may explain this phenomenon: the lesion (CRC or polyp) was missed at the previous endoscopic examination; the CRC is new and rapidly growing; the cancer develops in an incompletely removed polyp. In 2013, Pohl et al. showed that 10% of sessile or flat polyps are incompletely removed; in 2020, we showed an incomplete resection rate of 15.9% [7, 8]. It is estimated that incomplete polyp removal may account for 19%–27% of post-colonoscopy CRCs [5, 6].

Polypectomy is usually performed by snare removal, as recommended by European Society of Gastrointestinal Endoscopy (ESGE) guidelines [9]. For polyps smaller than 10 mm in diameter, either hot snare polypectomy (HSP) using electrocautery or cold snare polypectomy (CSP) without electrocautery may be applied. The most serious complication associated with polypectomy is perforation [10]. These perforations most often result from electrocautery [11], which is avoided with CSP [12, 13].

Bleeding complications after HSP or CSP have been well studied, and rates are comparable. There have been no perforations in comparative studies, but one study found that HSP was more often associated with post-procedural abdominal complaints than CSP [14, 15]. Because polyps  $< 10$  mm are numerous (90% of all polyps) [11], management of these polyps is important.

Many endoscopists have endorsed CSP as it is quicker and associated with a lower risk of perforation. However, reports of

its efficacy with respect to complete polypectomy have been conflicting. Some studies have reported comparable resection rates [16–18], while others have found HSP to be favorable to CSP [19, 20]. A recent meta-analysis showed that the risk of incomplete resection does not differ between HSP and CSP, but there was significant heterogeneity between the trials [21]. Also, in some randomized trials and retrospective reports, CSP was performed with the use of dedicated cold snares, which may have influenced the results [17, 18]. Finally, most of the studies were performed in Asian populations and most were single center.

The aims of this international multicenter randomized trial were to compare HSP and CSP in terms of the rate of incomplete polyp resection and risk of complications, and to identify factors that could predict incomplete resection.

## Methods

### Setting

This randomized trial was conducted at five different hospitals in Norway, one hospital in Poland, one hospital in Denmark, and one hospital in the USA from August 2015 to January 2020.

### Population

Patients aged  $\geq 40$  years undergoing an outpatient colonoscopy with one or more non-pedunculated polyps sized 4–9 mm in diameter were eligible for the trial. We excluded patients with previous biopsy or attempted polypectomy of the polyp triggering inclusion in the trial, those who had used clopidogrel or other non-aspirin platelet inhibitors within 5 days before the scheduled colonoscopy, had an INR  $> 1.8$ , failure to pause other oral anticoagulants, or severe co-morbidity defined as a New York Heart Association class  $\geq 3$ .

All potentially eligible patients were approached and informed about the study prior to their colonoscopy and prior to knowledge of their polyp status. Those willing to participate signed the consent form before the procedure. If no eligible polyps were found, the signed consent form was discarded.

### Randomization and assignment

We applied block randomization using varying block sizes (4, 6, and 8). Randomization to CSP or HSP was performed 1:1 at the patient level and stratified by the study site. Randomization was performed using sealed opaque envelopes that were opened by the study nurse after an eligible polyp had been detected. If a patient had more than one eligible polyp, the same polypectomy method was used for all polypectomies. The endoscopists were not blinded to the polypectomy technique, but they were unaware of the block size. Patients were not told which group they had been randomized to, but no other attempts were made to obscure assignment.

### Interventions and assessment of complications

Bowel cleansing and colonoscopy were performed according to local routines at the participating centers. All endoscopists had access to an instructional video on how to perform HSP and CSP before participating in the trial. For the CSPs, the snare was placed around the polyp, ensuring that there was a rim of free margin (1–2 mm) around the polyp. The snare was closed without tenting (pulling the polyp into the lumen), and the polyp was guillotined. For the HSPs, the snare was placed around the polyp. After the snare had been closed, the polyp was tented (pulled into the lumen), and insufflation gas was exsufflated. Electrocautery was then applied.

When a polyp eligible for inclusion was detected, the polyp size was measured using a biopsy forceps or the snare as reference.

CSPs were performed using a dedicated cold snare (Exacto cold snare, size 9 mm; US Endoscopy, Mentor, Ohio, USA), and HSPs were performed with the standard hot snare and diathermy equipment available at the centers.

After polypectomy, the endoscopist rinsed the polypectomy site with water and inspected the polypectomy site with white light and, if available, narrow-band imaging (NBI). Any visible remaining polyp tissue was removed. When complete visual polypectomy had been achieved, biopsies were taken from the resection margins using a 2.2-mm biopsy forceps. Two biopsies were taken for polyps 4–6 mm in size and three for those 7–9 mm in size. The polyp and the margin biopsy specimens were deposited in separate formaldehyde containers and submitted for histopathological examination. The same pathologist examined both polyp and margin biopsy specimens.

Immediately after the colonoscopy, the endoscopist completed a study data collection form regarding patient-related variables (age, sex, indication for colonoscopy [i.e. screening, symptoms, or other]), immediate complications, and endoscopist ID, and polyp-related variables (i.e. size [in mm], location [colon segment], and en bloc or piecemeal resection).

### Outcomes

The primary outcome of interest was the proportion of incompletely resected polyps, defined as polyp tissue present in the resection margin biopsies obtained after polypectomy. Secondary outcomes included complications (defined as bleeding, perforation, or other complications registered during colonoscopy and until follow-up at 30 days), and risk factors for the primary outcome.

Early/immediate bleeding was defined as bleeding that occurred during colonoscopy after the polypectomy or biopsies that needed intervention in terms of clips, epinephrine injection, or electrocautery. No specific time limit was applied for observation of the polypectomy site before intervention was deemed necessary.

All patients received a phone call from designated study personnel 30 days after the colonoscopy, during which they were asked about symptoms related to delayed post-polypectomy bleeding, defined as bleeding occurring between day 2 and 30 after polypectomy, or perforation. The patients were asked if they had observed blood in their stool, experienced stomach pain, and been admitted to the hospital. The study personnel were unaware of the randomization group.

### Statistics

The primary aim of the study was to evaluate whether CSP was non-inferior to HSP for complete polyp resection. The rate of incomplete resections varies in different studies and settings [20, 22, 23]. We predicted incomplete resection rates of 5% in both groups for the sample size calculation. If there was no difference in the rate of incomplete resection between CSP and HSP (5% in both groups), then a total of 600 polyps would be required to be 80% sure that the upper limit of a two-sided 95% CI would exclude a difference in favor of the hot snare group of more than 5%. This non-inferiority limit was decided after thorough discussion among the investigators; 5% was regarded as the upper limit of what the authors thought was a clinically acceptable difference. For the main analysis, to evaluate non-inferiority, we calculated the difference (with 95%CI) in the proportions of positive margins between the two groups: an upper boundary of the 95%CI less than 5% would indicate non-inferiority.

We used a modified intention-to-treat approach, where randomized patients with missing histology reports ( $n = 3$ ) or non-polyp histology ( $n = 1$ ) were excluded from all analyses. The patients we were unable to reach for the 30-day follow-up ( $n = 22$ ) were excluded from the analyses of late complications but were included in all other analyses.

For the secondary analyses, we first calculated the association between incomplete polyp resection and patient/polyp characteristics (i.e. age, sex, indication for colonoscopy, Boston Bowel Preparation Scale score, morphology, location, resection, histology, and dysplasia), fitting a univariate logistic regression model. We then fitted a multivariable logistic regression model including the arm and adjusting for those factors that were associated with the outcome of interest on the univariate analysis ( $P$  value  $< 0.10$ ).

To take into account the fact that each individual possibly had more than one polyp (i. e. clustered data), we used the generalized estimating equations (GEE) method with a compound-symmetry covariance structure in all analyses, both primary and secondary, both univariate and multivariable.

All analyses were conducted with Stata software, version 14.2 (StataCorp, College Station, Texas, USA) and SAS software, version 9.4 (SAS Institute, Cary, North Carolina, USA), and two-sided *P* values <0.05 were considered statistically significant. We used the online service Sealed Envelope for sample size calculation.

The study was approved by the relevant ethics committee responsible for the participating centers. Written informed consent was obtained from all participants before inclusion in the trial.

## Results

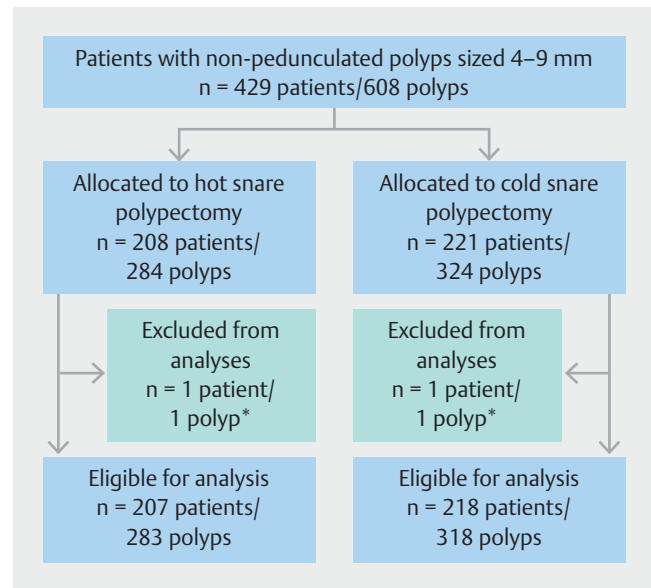
A total of 429 patients with 608 polyps were randomized and eligible for the study according to polyp findings. Four patients with seven total polyps were excluded from analyses owing to either non-adenomatous or non-serrated histology, or absence of histology report (either because no specimen was sent to the pathologist, or the report was missing). Accordingly, 425 patients with 601 polyps were eligible for analyses (► Fig. 1). Of these, 207 patients with 283 polyps had been randomized to HSP, and 218 patients with 318 polyps had been randomized to CSP.

There were no significant differences in the baseline characteristics of the patients or polyps between the two intervention groups (► Table 1 and ► Table 2). The mean ages were 61.9 and 63.1 years in the HSP and CSP groups, respectively. En bloc polypectomy (vs. piecemeal) was similar in the two groups: 309 (97.2%) and 280 (98.9%) polyps were removed en bloc with CSP and HSP, respectively.

### Complete resection rate

In the CSP group, 34 polyps (10.7%, 95%CI 7.3% to 14.4%) were incompletely resected, and 21 polyps (7.4%, 95%CI 4.4% to 10.5%) were incompletely resected in the HSP group. The difference, taking into account that some patients had more than one polyp removed, was 3.2% (95%CI -1.4% to 7.8%) (► Fig. 2). In the CSP group, the incomplete resection rate for adenomas was 7.5% (95%CI 3.8% to 11.1%), for sessile serrated lesions (SSLs) 27.3% (95%CI 8.7% to 45.9%), and for hyperplastic polyps 14.3% (95%CI 7.1% to 21.5%). In the HSP group, the incomplete resection rate for adenomas was 4.1% (95%CI 1.3% to 6.9%), for SSLs 16.7% (95%CI 0.0% to 33.9%), and for hyperplastic polyps 13.4% (95%CI 5.3% to 21.6%).

Overall, the incomplete resection rate for adenomas was 5.8% (95%CI 3.5% to 8.1%), for SSLs 22.5% (95%CI 9.6% to 35.4%), and for hyperplastic polyps 13.9% (95%CI 8.5% to 19.3%). In total for all polyps, regardless of method of resection, the incomplete resection rate was 9.2% (95%CI 6.9% to 11.9%).



► Fig. 1 Flow chart of patients through enrollment, randomization, and analysis.

\* Excluded from analysis owing to missing histology reports or no polyp tissue having been reported on histology (e. g. normal colonic mucosa).

► Table 1 Characteristics of the 425 patients who underwent snare polypectomy and were analyzed in the study.

	Patients randomized to hot snare polypectomy (n=207)	Patients randomized to cold snare polypectomy (n=218)
Sex, n (%)		
▪ Male	121 (58.5)	137 (62.8)
▪ Female	86 (41.6)	81 (37.2)
Age, mean (range), years	61.9 (40–82)	63.1 (42–83)
Indication for colonoscopy, n (%)		
▪ Screening	71 (34.3)	77 (35.3)
▪ Symptoms	87 (42.0)	83 (38.1)
▪ Other	49 (23.7)	58 (26.6)
Quality of bowel preparation, n (%)		
▪ BBPS < 6	9 (4.3)	12 (5.5)
▪ BBPS ≥ 6	198 (95.7)	206 (94.5)

BBPS, Boston Bowel Preparation Scale.

In multivariable analyses, only polyp histology SSL (odds ratio [OR] 3.96, 95%CI 1.63 to 9.66) and hyperplastic polyp (OR 2.52, 95%CI 1.30 to 4.86) were independent predictors for incomplete resection (► Table 3).

► **Table 2** Characteristics of the 601 polyps removed in this study.

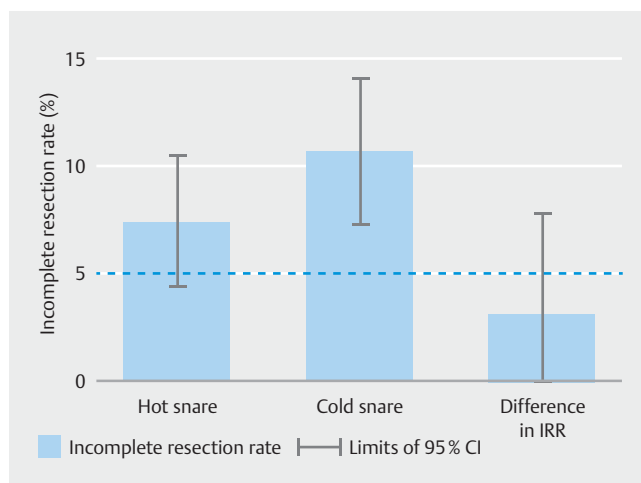
	Polyps removed by hot snare polypectomy (n=283)	Polyps removed by cold snare polypectomy (n=318)
Size, n (%), mm		
▪ 4–6	241 (85.2)	258 (81.1)
▪ 7–9	42 (14.8)	60 (18.9)
Morphology, n (%)		
▪ Flat	68 (24.0)	89 (28.0)
▪ Elevated	215 (76.0)	223 (70.1)
▪ Uncertain	0 (0.0)	6 (1.9)
Location, n (%)		
▪ Proximal colon <sup>1</sup>	103 (36.4)	113 (35.5)
▪ Distal colon <sup>2</sup>	180 (63.6)	205 (64.5)
Resection, n (%)		
▪ En bloc	280 (98.9)	309 (97.2)
▪ Piecemeal	3 (1.1)	9 (2.8)
Histology, n (%)		
▪ Tubular adenoma	191 (67.5)	195 (61.3)
▪ Tubulovillous adenoma	5 (1.8)	6 (1.9)
▪ Sessile serrated lesion	18 (6.4)	22 (6.9)
▪ Hyperplastic polyp	67 (23.7)	91 (28.6)
▪ Unclassified serrated polyp	2 (0.6)	4 (1.3)
Dysplasia, n (%)		
▪ No dysplasia	85 (42.3)	116 (57.3)
▪ Low grade dysplasia	197 (49.4)	202 (50.6)
▪ High grade dysplasia	1 (100.0)	0 (0.0)

<sup>1</sup> The proximal colon includes both flexures.  
<sup>2</sup> The distal colon is defined as distal to the left flexure.

## Complications

During the colonoscopy, seven patients (1.6%) had bleeding that needed intervention: five were related to the polypectomy and two to the study biopsies. Four of the bleeds related to polypectomy occurred after CSP (1.8%), and one after HSP (0.5%;  $P=0.70$ ). All bleeds were successfully treated endoscopically during the same procedure.

A total of 411 out of 433 participants (95%) were contacted by phone after 30 days. The remainder were unreachable despite multiple attempts. There were no serious adverse events. Eight patients (1.9%), five (2.4%) in the CSP group and three (1.5%) in the HSP group ( $P>0.99$ ), reported visible blood in the stool within 30 days after the procedure, but none of them were admitted to hospital. There were no perforations. Two pa-



► **Fig. 2** Proportion of incomplete polyp resections (incomplete resection rate [IRR]) in the hot snare and cold snare groups, and the difference in proportions between the two groups with 95%CI (the red line indicates the non-inferiority margin).

tients, one in the CSP group and one in the HSP group, reported that they experienced abdominal pain after the procedure. There were no hospital admissions in either group.

## Discussion

In this randomized controlled trial of polyps sized 4–9 mm, 7.4% and 10.7% were incompletely resected by HSP and CSP, respectively. We could not reject the non-inferiority of CSP, but the incomplete resection rate and complications did not differ between the two groups in secondary analyses.

Our observed difference between the CSP and HSP groups of 3.2% in the incomplete resection rate is in line with previous trials and a recent meta-analysis, which reported rate differences of between 0.5% and 7.0% [16–19, 24–26].

In earlier studies investigating the difference between CSP and HSP [16–19, 25], the incomplete resection rates in both the CSP and the HSP groups were lower than in our study. The meta-analysis, including eight studies, by Shinozaki et al. [21] showed an incomplete resection rate of 5.0% in the HSP group and 6.0% in the CSP group, both lower than our results. Two of the studies in this meta-analysis were performed as dual- or multicenter studies [17, 18], whereas the six other studies were single center. One of the studies [19] was performed in a tertiary-care referral center. There were also differences in how complete resection was measured: three studies used the same methodology as our study (negative margin biopsies) [15, 27–29], whereas four others used the pathologist's examination of the resection margin to confirm complete resection [17–19]. This might explain the lower rate of incomplete resection compared with this present study that was performed in both community and university hospitals and in different countries.

Another interesting difference in methodology is that in two of the studies using margin biopsies, five biopsies were taken after each polypectomy: four quadrant biopsies from the mar-

► **Table 3** Number of incomplete resections and odds ratios for incomplete resection.

	Total number of polyps	Incomplete resections, n (%)	P value <sup>1</sup>	OR (95%CI) <sup>2</sup>
Snare type				
▪ Hot	283	21 (7.4)	0.18	Reference
▪ Cold	318	34 (10.7)		1.41 (0.77 to 2.58)
Sex				
▪ Female	224	30 (13.4)	0.01	Reference
▪ Male	377	25 (6.6)		0.55 (0.30 to 1.02)
Age, years				
▪ <65	359	32 (8.9)	0.84	
▪ ≥65	242	23 (9.5)		
Indication for colonoscopy				
▪ Screening	217	20 (9.2)	0.97	
▪ Symptoms	224	21 (9.4)		
▪ Other	160	14 (8.8)		
Quality of bowel preparation				
▪ BBPS <6	31	2 (6.5)	0.39	
▪ BBPS ≥6	569	53 (9.3)		
Size, mm				
▪ 4–6	499	41 (8.2)	0.09	Reference
▪ 7–9	102	14 (13.7)		1.89 (0.95 to 3.78)
Morphology				
▪ Elevated	438	34 (7.8)	0.20	
▪ Flat	157	20 (12.7)		
▪ Uncertain	6	1 (16.7)		
Location				
▪ Proximal colon	216	20 (9.3)	0.97	
▪ Distal colon	385	35 (9.1)		
Resection				
▪ En bloc	589	54 (9.2)	0.92	
▪ Piecemeal	12	1 (8.3)		
Histology				
▪ Tubular adenoma	386	22 (5.7)	0.01	Reference
▪ Tubulovillous adenoma	11	1 (9.1)		1.27 (0.17 to 9.21)
▪ Sessile serrated lesion	40	9 (22.5)		<b>3.96 (1.63 to 9.66)</b>
▪ Hyperplastic polyp	158	22 (13.9)		<b>2.52 (1.30 to 4.86)</b>
▪ Unclassified serrated polyp	6	(16.7)		2.22 (0.12 to 39.7)

► **Table 3** (Continuation)

	Total number of polyps	Incomplete resections, n (%)	P value <sup>1</sup>	OR (95%CI) <sup>2</sup>
Dysplasia				
▪ No dysplasia	201	32 (15.9)	0.001	
▪ Low grade dysplasia	399	23 (5.8)		
▪ High grade dysplasia	1	0 (0.0)		

BBPS, Boston Bowel Preparation Scale.  
<sup>1</sup> From univariate analysis.  
<sup>2</sup> From multivariable logistic regression, including the factors associated with the outcome of interest on univariate analysis (*P* value < 0.10); dysplasia was not entered in the model as it was highly correlated with histology.

gins and one from the base [18, 19]. In our study, we took a maximum of three biopsies. One would expect that taking more biopsies would enhance the risk of discovering incomplete resection, so the reason for the lower incomplete resection rates in the other studies remains unknown. However, these results confirm the need for adequate training and quality control of polypectomy.

We found that sessile serrated histology and hyperplastic histology were independent risk factors for incomplete resection in multivariable analysis. Hyperplastic histology was also an independent risk factor for incomplete polyp resection in the NORPOL trial from 2020 [8], with an incomplete resection rate of 18.9%, but only 3.1% of the hyperplastic polyps were incompletely resected in the CARE study from 2013 [23]. Both of these studies included, in addition to the small polyps, larger polyps (> 1 cm), so the results are not directly comparable with our study. The results for SSLs correlate with the results from a recent study on polypectomy, where the OR for incomplete resection for SSLs compared with adenomas was 8.5 [8], but this study also included polyps of larger size (up to 40 mm).

The incomplete resection rates in the CSP and HSP groups for adenomas and hyperplastic polyps were relatively similar in our trial, while those for SSLs seemed to give a larger difference, favoring HSP. However, the trial was not powered for subgroup analyses, and these results should be interpreted with caution. Other studies have shown no difference in incomplete resection of SSLs between the CSP and HSP groups [16, 17]. Because SSLs are believed to be the precursor of up to 35% of CRCs [30], it is important to be aware of the potential of incomplete resection.

The incomplete resection rates in the CSP and HSP groups for adenomas, SSLs, and hyperplastic polyps also show that the differences between CSP and HSP are small. The risk of incomplete resection is substantially larger for SSLs and hyperplastic polyps compared with adenomas.

Removal of polyps with endoscopic injection of submucosal fluid (EMR) may be an important adjunct. An Italian report published in 2017 showed an incomplete resection rate of SSLs of only 1.2% [31]. These polyps were all ≥ 10 mm in size and were removed by cold snare EMR. In another trial that compared hot snare EMR in polyps < 10 mm with CSP, EMR was superior to CSP when removing small polyps of 6–10 mm [19] and, in the study by Papastergiou et al. [18], cold snare EMR of small polyps was

non-inferior to hot snare EMR. Unfortunately, we have no data on the use of EMR in our study, so we are not able to compare the incomplete resection rates with or without EMR.

An important finding in this study was that piecemeal polyp resection did not correlate with the method of polyp resection, so the use of CSP does not increase the risk of piecemeal polypectomy.

The complication rate was very low in this study, as in other studies of polypectomy for small colorectal polyps [8, 16–19, 23, 25]. In our study, as in others [17–19], there was no difference between the CSP and HSP groups. There were no perforations and no difference in terms of immediate or delayed bleeding. When the patients were contacted 30 days after the colonoscopy, only two patients, one in each group, reported that they had experienced abdominal pain after the procedure. Both HSP and CSP of small polyps are therefore safe procedures with very low complication rates.

Cold snares are commonly used for polypectomies of small polyps < 10 mm in size [16–19, 24], but there are also studies reporting the use of cold snares for larger polyps. Kimoto et al. found that only 0.2% of large SSLs ≥ 20 mm were incompletely resected, and they had an intraprocedural bleeding rate of 3.0%, all treated within the same colonoscopy [32]. CSP also seems to be a safe and feasible procedure for larger polyps, but more randomized studies are needed to confirm this.

The strengths of this study are first and foremost the inclusion of hospitals from four different countries and the randomized design. This mixture of different hospitals from different countries makes our results generalizable to everyday practice. The use of the same dedicated cold snare for all the CSPs is also a strength of this study, as it contributes to standardization of the cold snare technique in this study. One could argue that the use of the standard hot polypectomy snare at the different centers is a limitation; however, as electrocautery is the mode of removal in the HSP group, the snare itself may be less important. Another strength is the high rate of 30-day follow-up (95%).

One point that should be mentioned, is the inclusion time in this study, which was quite long. The reasons for this are diverse, but differences in when the centers entered the trial and stopped inclusion are important reasons: not all hospitals included patients during the entire period. Even if there was no consecutive inclusion of patients, due to time restrictions and

local circumstances, the randomized design of the trial hindered any selection bias.

A limitation to this study is the missing data for the patients with no histology report, and for the patients we were not able to reach for the 30-day follow-up phone call. However, the number of patients with missing histology was very few ( $n = 3$ ), and we believe a response rate of 95% for assessment of late complications is acceptable. A selection bias due to very serious complications is unlikely in this trial.

Another limitation is that there is, as of now, no standardized method for calculating the incomplete resection rate. We used margin biopsies to measure this, but the number of biopsies is not validated, and the gold standard would probably be polyp recurrence by surveillance colonoscopies. Furthermore, the level of clinically relevant incomplete resection rate and its implication are unknown in terms of the risk of subsequent CRC. Corley et al. showed that each 1% absolute increase in adenoma detection rate (ADR) was associated with a 3% decrease in the risk of post-colonoscopy CRC [33]. Assuming an ADR of 25% in a population of 400 individuals, 100 adenomas are detected. A difference in incomplete resection rate of 3 percentage points (from 7% to 10%) equates to a difference in ADR of 0.8% ( $3/400$ ); assuming that an incompletely removed adenoma has the same risk of developing into CRC as an unremoved adenoma). This number is quite low (knowing that post-colonoscopy CRCs comprise about 7% of all CRCs [34]), but not negligible.

In conclusion, CSP for polyps of 4–9 mm is a safe and technically easy procedure with a very low complication rate. We could not, however, prove non-inferiority compared with the standard HSP technique in this study. More high quality evidence, standardizing the number of margin biopsies and including findings at surveillance colonoscopy, is needed.

## Competing interests

The authors declare that they have no conflict of interest.

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## Clinical trial

Trial Registration: ClinicalTrials.gov | Registration number (trial ID): NCT02484079 | Type of study: Randomized, Multi Center Study

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