Introduction

Colorectal cancer (CRC) is the third most common cancer in the US with 135–420 new cases per year [1]. Screening colonoscopy with polypectomy substantially reduces CRC incidence and mortality [2, 3]. However, an unexpected high rate of incomplete resection of colon polyps has been reported in some recent studies, and this has in turn been related to a higher risk of post-colonoscopy interval CRC [4].

Diminutive (< 5 mm) and small (6–9 mm) polyps represent the vast majority of polyps removed at screening colonoscopy [5]. In theory, two major techniques are available for these lesions:

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

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ABSTRACT

Introduction In recent years, cold snare polypectomy (CSP) has increasingly been used over hot snare polypectomy (HSP) for the removal of colorectal polyps (4–10 mm in size). However, the optimal technique (CSP vs. HSP), in terms of complete polyp resection and complications, is uncertain. Our aim was to compare incomplete resection rate (IRR) of polyps and complications using CSP vs. HSP. Methods Randomized controlled studies (RCTs) comparing CSP and HSP for removal of 4–10 mm colorectal polyps were considered. Studies were included in the analysis if they obtained biopsy specimens from the resection margin to confirm the absence of residual tissue and reported complications. IRR and complication rate were the outcome measures. Pooled rates were reported as Odds Ratios (OR) or risk difference with 95 % Confidence Interval (CI). Results In total, three RCTs were included in the final analysis. A total of 1051 patients with 1485 polyps were randomized to either HSP group (n = 741 polyps) or CSP group (n = 744 polyps). The overall IRR did not differ between the two groups (HSP vs. CSP: 2.4 % vs. 4.7 %; OR 0.51, 95 %CI 0.13–1.99, P = 0.33, I² = 73 %). The HSP group had a lower rate of overall complications compared to the CSP group (3.7 % vs. 6.6 %; OR 0.53, 95 % CI 0.3–0.94, P = 0.03, I² = 0 %). Polyp retrieval rates were not different between the two groups (99 % vs. 98.1 %). Conclusion Our results suggest that HSP and CSP techniques can be effectively used for the complete removal of 4–10 mm colorectal polyps; however, HSP has a lower incidence of overall complications.
polyps were included in our study. Such submucosal injection) for removal of 4
(RJ and MA) individually searched the databases for article
ed data suggested by PubMed were also searched. Two authors
Only English language and human studies were searched. Relat-

mucosal resection

snare polypectomy

pared the efficacy of HSP with CSP for colorectal polyps ranging
although evidence comparing efficacy with HSP is lacking [18].

Jegadeesan Ramprasad et al. Hot snare vs. cold polypectomy: a meta-analysis of available evidence with the objective to
compare the IRR and adverse events between CSP and HSP
when removing polyps between 4 and 10mm in size.

Materials and methods
A comprehensive search was performed using PubMed, Em-
base, and abstracts of conferences presented at Digestive Dis-
eses Week and the United European Gastroenterology Week. These sources were searched using the keywords “polypec-
tomy”, “cold polypectomy”, “cold snare polypectomy”, “hot
snare polypectomy”, “remnant adenoma”, and “endoscopic mucosal resection” to extract studies up to December 2017. Only English language and human studies were searched. Relat-
ed data suggested by PubMed were also searched. Two authors
(RJ and MA) individually searched the databases for article
screening. The abstracts were not blinded for authors, institu-
tions or journals during review. Only data from randomized
controlled trials comparing the efficacy of and adverse events
related to the use of CSP with those of HSP (with or without
submucosal injection) for removal of 4–10mm colorectal polyps
were included in our study. Such ‘4–10 mm’ definition was preferred over the generally reported ‘6–9 mm’ for small
polyps, in order not to exclude relevant studies, and also in-
clude 4-, 5- or 10-mm polyps. In addition, we limited our inclu-
sion to only those studies where biopsy specimens were obtain-
ed from the post-polypectomy resection margin to confirm the
absence of any residual polypoid tissue (i.e. endoscopic and
histologic radical resection). If multiple articles were found
from the same institution, then the most recent article was
used for analysis. Letters to editors, case reports, case series,
case-control, and cohort studies were excluded.

Data collection and bias assessment
Baseline demographic data (age, gender), number of study par-
ticipants, number of polyps examined, morphology of polyps,
histology of polyps, location of polyps, IRR, type of snare used,
procedure time, and complication rates were extracted from
each study. Paris classification [22] and Vienna classification
[23] systems were used to assess the morphology and histology
of polyps, respectively. Polyps were classified as either right-si-
ded (if found in the cecum, ascending colon or transverse co-
on) or left-sided (if found in the descending colon, sigmoid co-
on, or rectum). IRR was defined as the presence of any residual
polypoid tissue in biopsied specimen post-polypectomy with
either technique. Procedure time was defined as the time re-
quired from identification of polyp to complete resection of
the polyp using either technique [19, 21].

Complications included immediate bleeding during the pro-
cedure, delayed bleeding after the procedure, and perforations
of the intestinal wall. Immediate bleeding was defined as con-
tinuous hemorrhage usually for ≥30 seconds immediately after
polypectomy [19]. Delayed bleeding was defined as hemor-
rhage after colonoscopy requiring endoscopic hemostasis. All
three studies have excluded patients who were treated with an-
thrombotic agents.

Outcome measures
The primary outcome of our study was IRR and secondary out-
comes were complication rates, polyp retrieval rates, and pro-
cedure time.

Risk of bias assessment
The risk of bias was evaluated based on guidelines from the Co-
chrane Handbook for Systematic Reviews of Interventions [24]
using the following: adequacy of random sequence generation,
allocation concealment, blinding of the participant, blind out-
come assessment, incomplete outcome data, and selective
outcome reporting.

Statistical analysis
Pooled odds ratio (OR) and 95% confidence interval (CI) were
calculated for primary and secondary outcomes. For pooled an-
alysis of rare events, risk difference was used as an estimate
to compare any possible detectable difference, when applic-
able. Heterogeneity of the study was assessed using the I² sta-
tistic [25]. Percentages of 25% (I² = 25), 50% (I² = 50), and 75%
(I² = 75) were considered to be a low, moderate, and high de-
gree of heterogeneity, respectively. In the presence of substan-
tial heterogeneity (I² > 50%), a random effect model was used
as the pooling method; otherwise, a fixed effect model was
adopted as the pooling method. Statistical software used was

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tial heterogeneity (I² > 50%), a random effect model was used
as the pooling method; otherwise, a fixed effect model was
adopted as the pooling method. Statistical software used was
Results

A total of 244 studies were retrieved using the databases (Fig. 1). After screening through the title, abstracts, and full texts, a total of three RCTs were selected [19–21]. All three studies were published between April 2017 and August 2017 (Table 1). A total of 1051 patients were found to have 1485 small polyps (4–9 mm in size) which were randomized to either the HSP group (n = 741 polyps) or the CSP group (n = 744 polyps). Of 1485 colorectal polyps, 1266 polyps were included in the final analysis with 630 polyps in the HSP group and 636 polyps in the CSP group. Two RCTs [19, 21] included only neoplastic polyps for the final analysis while one RCT [20] included all colorectal polyps which were excised. The mean age of patients randomized to the CSP group was 64.1 years old, while those randomized to the HSP group was 65.3 years old, as described in two studies [20, 21]. The mean percentages of males were 55.5% in the CSP group and 56.8% in the HSP group.

The risks of bias assessment are reported in Fig. 2.

Type of snare

The snares used in these studies were: Captivator II 10 mm (Boston Scientific, Natick, MA, United States) [19, 20], the Acusnare (Cook Medical, Bloomington, IN, USA) [20], SnareMaster 10 mm (Olympus Medical, Tokyo, Japan) [20, 21] and Exacto/9 mm (US Endoscopy, Mentor, OH, United States) [19]. For HSP, electro-cautery was performed with the ERBE ICC 200 electrosurgical generator (ERBE Electromedizin, Tübingen, Germany) [20, 21]. Only one study mentioned the setting for cautery as fractionated cutting mode ENDO CUT Q (effect 3; cut duration 1; cut interval 3) [20]. Sub-mucosal injection before polypectomy was performed for both groups in one study [19], however, it was only performed for the HSP group in the other two studies [20, 21].

Polyp characteristics

Based on the morphology of polyps, 436 out of 691 (63.1%) and 432 out of 685 (63.1%) were classified as type 0–I polyps, while 255 out of 691 (36.9%) and 263 out of 685 (38.4%) were classified as type 0–II in the CSP and HSP group, respectively. On a histological basis, the following polyps were removed: 1152 (78.1%) tubular adenomas, 111 (7.5%) advanced adenomas (prominent villous component and high grade dysplasia), 86 (5.8%) sessile serrated polyps/adenoma, 83 (5.6%) hyperplastic polyps and 43 (2.9%) polyps without histological diagnosis. The locations of polyps were reported in all studies with a total of 757 out of 1485 (51%) found to be right-sided. All three studies reported the average polyp sizes which were not significantly different on comparison. The size averaged between 5.4 and 8.3 mm as provided in Table 1.

Endoscopic mucosal resection

Submucosal injection before polypectomy for endoscopic mucosal resection (EMR) was performed for both groups in one study [19]; however, it was only performed for selected polyps in the HSP group in the other two studies based on endoscopist preference [20, 21]. The injected submucosal solution included
Table 1  Details of the three studies included.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patient age, mean ± SD, years</th>
<th>Gender male, %</th>
<th>No. of polyps, n</th>
<th>Polyp size, mean ± SD, mm</th>
<th>Macroscopic appearance, n</th>
<th>Histological findings, n</th>
<th>Location of the polyp, n</th>
<th>No. of all adverse events, n</th>
<th>Incomplete resection rate, %</th>
<th>Complete retrieval rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawamura et al., 2017 [19]</td>
<td>NA</td>
<td>NA</td>
<td>341</td>
<td>NA</td>
<td>234</td>
<td>107</td>
<td>333</td>
<td>10</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>Zhang et al., 2017 [21]</td>
<td>64.5 ± 7.7</td>
<td>96 (53.6 %)</td>
<td>267</td>
<td>7.4 ± 1.4</td>
<td>164</td>
<td>81</td>
<td>189</td>
<td>45</td>
<td>46</td>
<td>25</td>
</tr>
<tr>
<td>Papastergiou et al., 2018 [20]</td>
<td>63.1 ± 10.3</td>
<td>46 (59.7 %)</td>
<td>83</td>
<td>8.2 ± 1.6</td>
<td>38</td>
<td>45</td>
<td>59</td>
<td>0</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>Zhang et al., 2017 [21]</td>
<td>65.8 ± 9.4</td>
<td>101 (56.4 %)</td>
<td>258</td>
<td>7.7 ± 1.5</td>
<td>164</td>
<td>74</td>
<td>175</td>
<td>41</td>
<td>49</td>
<td>26</td>
</tr>
<tr>
<td>Papastergiou et al., 2018 [20]</td>
<td>64.1 ± 10.9</td>
<td>45 (57.7 %)</td>
<td>81</td>
<td>8.3 ± 1.4</td>
<td>34</td>
<td>47</td>
<td>60</td>
<td>0</td>
<td>8</td>
<td>13</td>
</tr>
</tbody>
</table>

NA, not available; TA, tubular adenoma; AA, advanced adenoma; HP, hyperplastic polyps; SSP, sessile serrated polyps; OP, other polyps.

In Table 1, we summarize the details of three studies included in the analysis, focusing on patient age, gender distribution, number of polyps, polyp size, macroscopic appearance, histological findings, location of the polyp, number of adverse events, incomplete resection rate, and complete retrieval rate. The studies were conducted using Cold snare polypectomy and Hot snare polypectomy techniques, with results indicating varying effectiveness and outcomes.

The table highlights the diversity in study populations and methodologies, emphasizing the importance of detailed documentation for accurate clinical comparisons.
1:10 000 epinephrine in one of the studies that allowed submucosal injection for HSP only [21] while the other two studies did not use any epinephrine in the injected submucosal solution.

Incomplete resection rate

IRR was assessed via four-quadrant biopsy along with biopsy of the base of the post-polypectomy site in two studies [19,20] and biopsy of the left and right lateral margins in one study [21]. IRR was collectively found to be 2.4% (15/630) and 4.7% (30/636) for HSP and CSP group, respectively. The study heterogeneity was substantial ($I^2 = 73\%$), hence a random effects model was used to assess the difference in incomplete resection. The pooled odds ratio was 0.51 (95% CI 0.13–0.99, $P=0.33$). The difference in IRR between HSP and CSP was not statistically significant (Fig. 3).

Adverse events

All three studies reported adverse events (immediate procedural bleeding, delayed bleeding, and perforations). A total of 741 polyps were removed using HSP and 744 polyps were removed employing CSP. Clinically and statistically, a lower rate of overall adverse events was observed with HSP compared to CSP (20/546 [3.7\%] vs. 36/545 [6.6\%], pooled OR 0.53, 95% CI 0.3–0.94, $P=0.03$; $I^2 = 0\%$) (Fig. 4a).

When assessing adverse events separately, immediate bleeding rate was lower in the HSP group (18/546 [3.3\%]) compared to the CSP group (36/545 [6.6\%]), yielding a pooled OR 0.48 (95% CI 0.27–0.86, $P=0.01$; $I^2 = 0\%$) (Fig. 4b). All patients with immediate post-polypectomy bleeding required endoscopic hemostasis to control bleeding and was clinically successful in all three studies. Two studies used hemostatic clip placement for endoscopic hemostasis [20,21] while one study did not mention the technique used for endoscopic hemostasis [19].

The delayed bleeding rates were not different between the two groups (2/546 [0.4\%] vs. 0/545 [0\%]) (Fig. 4c). Delayed bleeding occurred in only two patients who underwent HSP in one of the studies [19] while the other two studies did not have any occurrence of delayed bleeding in either group. Since delayed bleeding was considered a "rare event" among the studies included, we used pooled risk difference as pooled estimate to detect if any difference existed between the groups. Pooled risk difference was zero and results were not statistically significant ($P=0.45$).

No case of perforation was reported in either group in any of the three studies. Preventive hemostasis, defined as prophylactic coagulation of vessels or red spots in the ulcer or clipping of a non-bleeding post-polypectomy mucosal defect, was allowed in the HSP group, but not in the CSP group in one study [19].

Polyp retrieval rate

The polyp retrieval rate was not clinically or statistically significantly different between the two groups. Collective retrieval rates were 99\% for the HSP group and 98.1\% for the CSP group.
yielding a pooled OR of 1.9 (95% CI 0.74–4.83, \(P=0.18\); \(I^2=0\%\)) as shown in ▶ Fig. 5.

### Procedure time

Procedural time was defined as the time required from identification of polyp to complete resection of the polyp using either technique [19,21]. Only two studies reported procedural time for polypectomies. Kawamura et al. reported median times of 83 seconds and 60 seconds for the HSP and CSP group, respectively [19]. Zhang et al. had comparatively longer times for their polypectomies with mean procedural times of 330 seconds and 282 seconds, respectively for the HSP and CSP group [21].

### Discussion

The results of this meta-analysis suggest that there is no significant difference between cold and hot snare in achieving a complete resection of 4–10 mm colorectal polyps, but there is a higher rate of adverse events with cold snare, albeit this is limited to immediate post-polypectomy bleeding that was amenable to endoscopic treatment in all of the cases.

The main result of our analysis is the equivalence between the two techniques in achieving a complete endoscopic resection. This is clinically relevant as completeness of resection represents by far the dominant end point when approaching the risk/benefit ratio of endoscopic resection for sub-centimetric lesions. Our meta-analysis, however, showed that there is residual uncertainty on the equivalence between the two techniques, as shown by the very high heterogeneity level in this estimate. In detail, in two of the three studies, the rate of incomplete resection was 2- to 6-fold higher with cold snare than hot...
served in previous prospective studies were 0.6–15%. That spontaneously stops and does not need intervention [13]. The rate for immediate bleeding has been reported to be 0% using HSP and 0% with CSP [30, 31]. The overall adverse events for our meta-analysis were lower for the HSP group compared to CSP, with sub-analysis revealing immediate post-procedural bleeding to be lower for the HSP group. Clinically, this does not have any major significance as immediate bleeding is usually self-limiting and managed with observation on the majority of occasions or with post-procedural clipping immediately after polyp removal [10, 32]. Since all three studies excluded patients treated with antithrombotic agents, the use of antithrombotic agents did not have any influence on post-polypectomy bleeding.

Several factors pose limitations to our meta-analysis. Firstly, despite a wide literature search on the main electronic databases, only three RCTs were available in the literature which were evaluated and compared in this systematic review and meta-analysis. Secondly, there was no follow-up colonoscopy for these patients to confirm “true” complete resection as polyps may recur in previously biopsied negative margin sites. Further studies are needed that not only biopsy the resection margins to confirm complete removal but also assess the patients at a follow-up surveillance colonoscopy and biopsy the scar area to determine the IRR. The post-polypectomy sites can also be evaluated by performing endoscopic mucosal resection of the 1–3 mm margin around the resection site to determine IRR as suggested by Matsuura et al. [33]. Third, the rates of incidence of colon cancer and mortality from colon cancer were not assessed in these studies which undermines the true efficacy of removing small colorectal polyps. Large, multicenter long-term studies are needed to assess the incidence of colon cancer when comparing the two techniques in removing small colorectal polyps.

Moreover, two studies reported four-quadrant biopsy along with biopsy of base of polypectomy site compared to one study that biopsied only left and right resected margins to display any residual polypoid tissue. This can imply potential bias and possibly false IRR. There is potential bias involved with different physicians as each endoscopist has a different skill set with different procedural times. There was also substantial heterogeneity noted between the three included studies which could be partially explained by different types of snare used between studies for polypectomy and the difference in the utility of submucosal injection between CSP and HSP groups in the included studies. Also, immediate bleeding was only defined in one study, while the other studies used the term “intra-procedural
bleeding” that was summed together as “immediate bleeding” for our systematic review. Finally, we only searched articles published in the English language and may have missed relevant studies published in other languages.

Despite the above limitations, the main strength of this meta-analysis is the fact that all three studies being compared were randomized controlled trials (RCTs) with a low risk of bias based on the Cochrane risk of bias assessment scale that demonstrated incomplete resection rate (IRR) using post-polyectomy biopsy to confirm residual tissue. Furthermore, all RCTs assessed polyp size between 4 and 10 mm which is in accordance with our study objective and further decreased the bias associated with the size of polyps.

In conclusion, our study findings show that there is no statistically significant difference between the two techniques, although the rate of overall complications is higher with CSP; however, this is self-limiting. Based on currently available RCTs, we suggest that, clinically, either CSP or HSP can be safely used as one of the standard techniques for the resection of 4–10 mm colorectal polyps. More studies are needed in future to assess recurrence of polyps and incidence of cancer to further gauge the efficacy of these two techniques.

Competing interests

None

References


