AG-2018-70
dx.doi.org/10.1590/S0004-2803.201800000-79

Best polypectomy technique for small and diminutive colorectal polyps: a systematic review and meta-analysis

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Received 14/6/2018
Accepted 13/7/2018

ABSTRACT – **Background** – Polypectomy of colorectal polyps is the mainstay of colorectal cancer prevention. Identification of the best polypectomy technique is imperative. **Objective** – This review aims at comparing efficacy of nine different resection methods for small colorectal polyps (<10 mm). **Methods** – We searched and selected only randomized controlled trials. Primary outcome was complete resection rates of small polyps by histological eradication. Secondary outcomes were: adverse events, retrieval tissue failures rates and duration of procedure. **Results** – Eighteen trials including 3215 patients and 5223 polyps were analysed. Overall, cold polypectomy had a significantly shorter time of procedure than hot polypectomy (RD -5.92, 95%CI -9.90 to -1.94, $P<0.05$), with no statistical difference on complete histological eradication (RD 0.08, 95%CI -0.03 to 0.19, $P>0.05$). Regarding cold polypectomy techniques, cold snare was found superior to cold forceps on complete and en-bloc resection rates and less time consuming. When comparing endoscopic mucosal resection (EMR) with hot-snare and cold-snare, the latter showed no-inferiority on histological eradication, adverse events or retrieval tissue failure rates. **Conclusion** – Cold polypectomy is the best technique for resection of small colorectal polyps. Among cold methods, dedicated cold snare was found superior on histological eradication. Cold snare endoscopic mucosal resection might be considered an option for polyps from 5 to 9 mm.

HEADINGS – Colonic polyps, surgery. Endoscopic mucosal resection. Follow-up studies.

INTRODUCTION

Colorectal cancer is the third most common cancer and the fourth most common cause of death worldwide[1]. The development of such neoplasms occurs as a consequence of multi-step genetic mutations from normal colonic epithelium to a pre-malignant lesion (adenoma) and adenocarcinoma ultimately[2,3]. Resection of pre-malignant lesions, generally found as polyps, is considered the mainstay of the colorectal cancer prevention[4].

The endoscopic polypectomy is a minimally invasive procedure for removal of colorectal polyps. Currently, there are many techniques and, usually, endoscopists choose based on personal preferences and polyp size. Small polyps, defined as those smaller than 10 mm, are the most common findings on screening colonoscopy[5,6]. Consequently, the employment of an effective and safe polypectomy technique specific for small lesions is imperative.

Polyps smaller than 3 mm are usually resected with a biopsy forceps; for polyps from 4 mm to 9 mm, the endoscopist normally opts for hot or cold snare[7]. However, delimitation and snaring of flat and depressed lesions may be challenging[8]. Such cases render the endoscopic mucosal resection (EMR) a useful option.

Previous meta-analyses only compared diminutive polyps or no more than four polypectomy techniques[9-11]. Therefore, the literature lacks an updated and high-quality study regarding outcomes of resection methods for small polyps. This systematic review and meta-analysis aims at comparing all available techniques reported on randomized clinical trials to determine the best therapeutic option for this subgroup of polyps.

METHODS

Protocol and registration

This protocol was outlined and registered prior to the beginning of the study. We specified eligibility criteria and methods of analysis on the International Prospective Register of Systematic Reviews –University of York (PROSPERO) (http://www.crd.york.ac.uk/PROSPER) under registration number CRD42017068726)[12]. Also, it was approved by our institution's Internal Review Board (IRB number 293/17). Finally, we conducted this study in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) recommendations[13].

Eligibility criteria

- **Participants**

All participants were adults (≥18yo). There were no restrictions as to gender or number of polyps per patient. Studies with patients diagnosed with familial polyposis syndrome, inflammatory bowel disease or incomplete colonoscopy were excluded.

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
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• Intervention

Different endoscopic polypectomy methods for colorectal polyps smaller than 10mm. We included studies comparing two or more different techniques in spite of the outcomes assessed. Techniques compared were: cold snare polypectomy (CSP), cold forceps polypectomy (CFP), standard forceps polypectomy (SFP), hot snare polypectomy (HSP), hot forceps polypectomy (HFP), suction pseudopolyp technique (SPT), jumbo forceps polypectomy (JFP), endoscopic mucosal resection (EMR), cold snare EMR (CS-EMR) and hot snare EMR (HS-EMR).

Hot procedures were those which electrical current was used to resect the polyp, cold procedures were those performed without it and EMR were those in which a submucosal injection was made before polypectomy.

• Outcomes

- histological complete resection rates (complete resection confirmed by pathologist by the specimen examination);
- *en-bloc* resection rates (visual polyp eradication judged by endoscopist's experience and discretion);
- early and delayed bleeding (intraprocedural bleeding which required hemostatic treatment and bleeding within 2 weeks after polypectomy requiring endoscopic intervention, respectively);
- perforation;
- retrieval tissue failure rates (failure to retrieve a polyp after its resection);
- duration of the procedure (time for polypectomy only).

• Studies

This systematic review included only randomized controlled trials providing outcomes of diverse colorectal polypectomy techniques for polyps smaller than 10 mm. Non-comparative studies and abstracts were excluded. There were no restrictions regarding language or publication date.

Sources of information

We searched Medline/PubMed, Cochrane Central Register of Randomized Controlled Trials/CENTRAL, LILACS, and EMBASE from inception to November 1st, 2017.

Our search strategies were:

- Medline / PubMed: (adenomatous OR adenoma OR adenomatosis OR polyps OR polyp) AND (colon OR colorectal OR colonic OR rectal OR rectum OR colorectum OR intestinal OR intestine) AND (surgery OR snare OR forceps OR resection OR surgical instruments OR polypectomy) AND random*;
- Lilacs: (adenoma OR polyp) AND (endoscopy OR endoscopic) AND polypectomy;
- Cochrane/CENTRAL: (adenoma OR polyp) AND (endoscopy OR endoscopic);
- Embase: (adenomatous OR adenoma OR adenomatosis OR polyps OR polyp) AND (colon OR colorectal OR colonic OR rectal OR rectum OR colorectum OR intestinal OR intestine) AND (surgery OR snare OR forceps OR resection OR surgical instruments OR polypectomy) – only randomized controlled trials

Study selection

Two reviewers (TCV and BWM) independently searched titles and abstracts to assess eligibility. Then, a full-text evaluation confirmed that studies fulfilled all eligibility criteria. Results from individual assessment were then confronted and any disagreement was resolved by consensus with a third researcher (MEGH).

Data collection process and data items

The main author extracted the absolute numbers from the eligible full-text articles. The second researcher (BWM) verified the extracted data. These results were then stratified by polypectomy technique and by outcome. Data collected from the studies included: patients' demographics, endoscopic procedures, number of lesions, lesion size and location, incomplete resection rates, retrieval tissue failure rates, immediate or delayed bleeding and perforation; procedure duration time.

Risk of bias in individual studies

The risk of bias of the studies was assessed with The Cochrane Risk of Bias tool[14] following pre-determined parameters: adequacy of random sequence generation; allocation concealment; double-blinding; incomplete outcome data and selective outcome reporting.

Summary measures and planned methods of analysis

The analyses were carried out using the Review Manager 5.3 software (RevMan 5.3 − Cochrane Informatics & Knowledge Management Department)[15]. We employed risk differences for dichotomous variables using a fixed-effects model to provide forest and funnel plots for each comparison. Data on risk difference and 95 % confidence interval (CI) for each outcome were calculated using the Mantel−Haenszel test, and inconsistency (heterogeneity) was assessed using the Chi-square (Chi^2) and the Higgins method (I^2)[16]. We calculated the number needed to treat or to harm (NNT or NNH) if the difference achieved statistical superiority.

Risk of bias across studies and additional analyses

We assessed publication bias using a funnel plot analysis. Asymmetry may result from the non-publication of small trials with negative results (supporting the null hypothesis) or from missing data in the published studies (selective reporting bias). If the heterogeneity (I^2) was higher than 50%, we considered reports outside the funnel plot as outliers and excluded them from the analysis. Then, we performed another meta-analysis and reassessed heterogeneity. We considered true heterogeneity if I^2 was higher than 50% and outliers could not be detected. We acknowledge that other factors might produce asymmetry in funnel plots leading to a high heterogeneity (true study heterogeneity), such as differences in trial quality or differences in the population studied. In these cases, we changed the effect from fixed to random.

Forest plots exhibit the risk differences and their confidence intervals for each comparison group. Specific forest and funnel plots assessed each outcome. An additional forest plot was designed if high heterogeneity demanded exclusion of outliers.

RESULTS

Study selection

The initial search identified 1470 studies that were screened through title and abstract evaluation. Among them, twenty-five articles were selected for full-text assessment. Subsequently, we excluded seven studies that either compared obsolete cauterization techniques or were meta-analyses/abstract-only papers. Finally, eighteen studies were selected for this meta-analysis. (FIGURE 1).

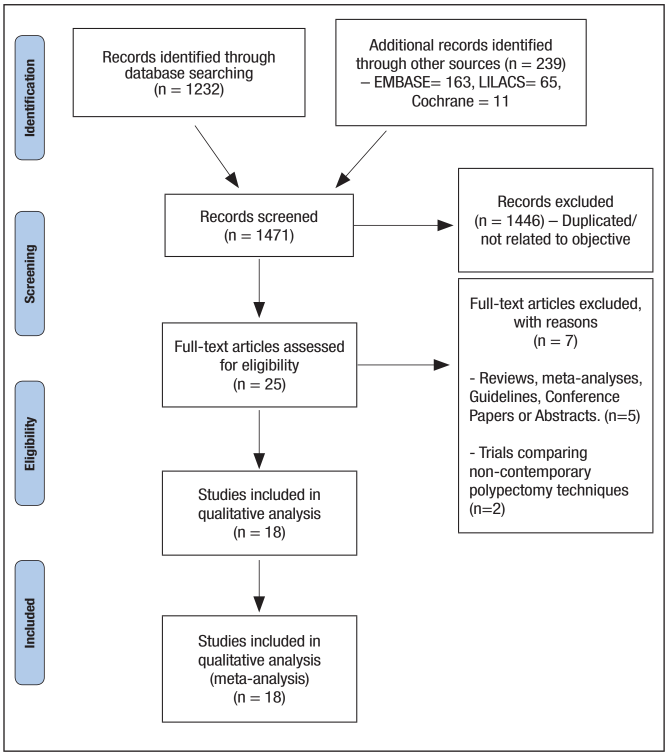


FIGURE 1. Study selection flowchart. Adapted from references 13 and 36.

Study characteristics

All eighteen studies were randomized controlled trials published in English. A total of 3215 patients accounted for 5223 polypectomies. All patients were adults diagnosed with polyps smaller than 10 mm. The exclusion criteria of the RCTs were similar (familial polyposis syndrome, inflammatory bowel disease and/or incomplete colonoscopy). One study included patients specifically under anticoagulation therapy[17].

Eleven direct comparisons were analysed. If a trial used three arms in the study (e.g. cold snare vs hot snare vs cold forceps polypectomy) we extracted individual data and analysed three separate comparisons.

Most studies assessed our primary and secondary outcomes: complete resection rate, adverse events, retrieval tissue failure rate and duration of procedure; however, the definition of latter differed significantly among studies: some trials started the stopwatch when they initiated the exam; others started during the withdraw; yet, a few timed only the polypectomy procedure.

A summary of the characteristics of the included trials is shown in TABLE 1.

Risk of bias within studies

FIGURE 2 summarizes the risk of bias within the studies according to the Cochrane Risk of Bias tool. There was no double-blind trial, which is classified as a potential source of bias. Most trials randomized each polyp separately. Yet, some studies used only one polypectomy technique in the same patient, independent of number and size of polyps removed.

TABLE 1. Characteristics of the included trials.

Author, Year	Polyp size criteria (mm)	Mean polyp size (mm)	Males (%)	Age (yr)	Polypectomy method comparisons	No. of polyps	Histology – adenoma (%)
Papastergiou V, 2017[33]	6–9 mm	8.2	58.7	63.6	CS-EMR X HS-EMR	164	72.6
Zhang Q, 2017[32]	6–9 mm	7.6	55.0	64.9	CSP X EMR	525	69.3
Komeda Y, 2017[23]	3–5 mm	4.0	69.0	69.0	CSP X HFP	283	93.6
Kawamura T, 2017[18]	4–9 mm	5.4	68.2	66.0	CSP X HSP	687	87.2
Park SK, 2016[24]	<5 mm	NA	73.3	56.0	CSP X CFP	231	79.6
Kim H-S, 2016[31]	5–9 mm	6.3	61.3	64.1	HSP X EMR	353	89.8
Horiuchi A, 2015[28]	< 10 mm	6.4	87.4	67.7	CSP X DCSP	210	70.9
Din S, 2015[27]	3–7 mm	4.0	65.2	63.5	CSP X DCSP	161	67.6
Aslan F, 2015[29]	3–5 mm	4.4	64.2	60.6	SFP X JFP	263	68.4
Kim JS, 2015[8]	≤ 7 mm	4.4	81.0	62.0	CSP X CFP	145	88.3
Gomez V, 2015[19]	< 6 mm	3.6	57.0	60.4	CSP X HSP X CFP	62	60.0
Din S, 2015[26]	3–7 mm	4.0	67.9	63.7	CSP X SPT	148	67.5
Horiuchi A, 2014[17]	< 10 mm	6.3	70.0	67.2	CSP X HSP	159	91.8
Aslan F, 2014[20]	5–10 mm	8.7	70.1	58.9	CSP X HSP	149	81.7
Lee CK, 2013[25]	< 5 mm	3.7	53.7	57.2	CSP X CFP	117	69.9
Draganov PV, 2012[30]	≤ 6 mm	NA	45.7	60.0	SFP X JFP	305	39.3
Paspatis GA, 2011[21]	3–8 mm	5.5	56.0	60.4	CSP X HSP	1083	80.7
Ichise Y, 2011[22]	< 8 mm	5.6	66.0	65.3	CSP X HSP	205	91.2

EMR: endoscopic mucosal resection; CS-EMR: cold snare EMR; HS-EMR: hot snare EMR; CSP: cold snare polypectomy; HFP: hot forceps polypectomy; HSP: hot snare polypectomy; CFP: cold forceps polypectomy; DCSP: dedicated cold snare polypectomy; SFP: standard forceps poly-pectomy; SPT: suction pseudopolyp technique; JFP: jumbo forceps polypectomy.

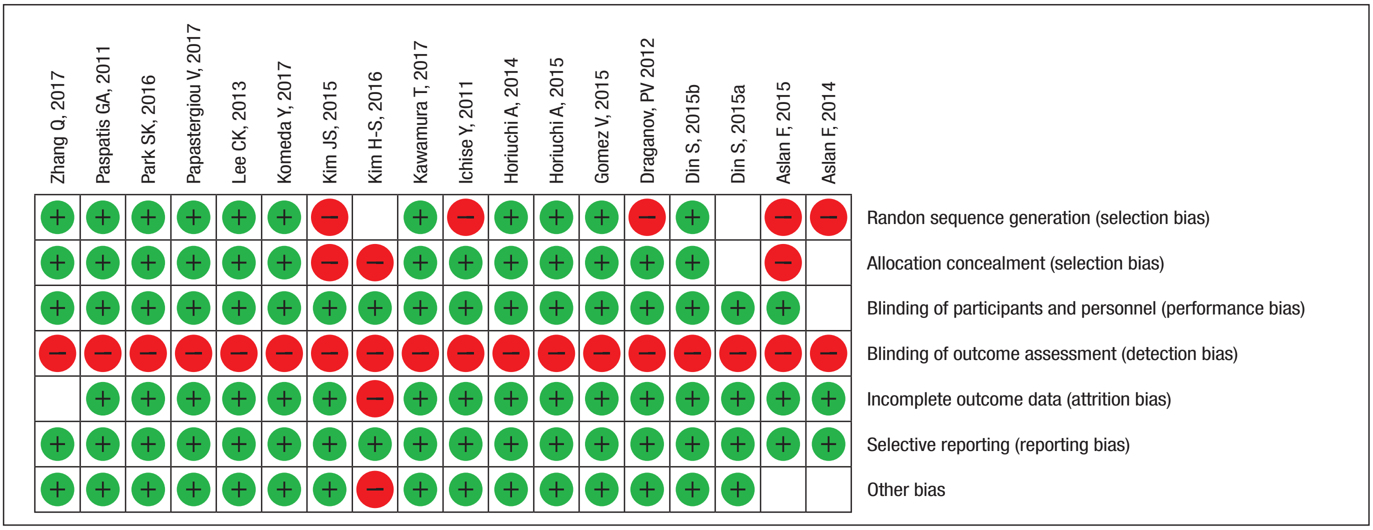


FIGURE 2. Summary of risk of bias appraisal for individual studies.

Synthesis of results and risk of bias across studies

Among eighteen analysed trials, 3215 patients and 5223 polypectomies were assessed. In summary, our analyses entailed ten different comparisons. Additionally, we created two more groups that were confronted: all cold versus all hot procedures.

The comparisons are outlined next:

1. cold snare versus hot snare
2. cold snare versus hot forceps
3. cold forceps versus hot snare
4. cold snare versus cold forceps
5. cold snare versus suction pseudopolyp technique
6. cold snare versus dedicated cold snare
7. standard forceps versus jumbo forceps
8. EMR versus hot snare
9. EMR versus cold snare
10. EMR + cold snare versus EMR + hot snare
11. hot polypectomy versus cold polypectomy

We summarized all favourable results of these comparisons in TABLE 2.

1. Cold snare vs hot snare

Three studies compared complete resection rates between cold and hot snare polypectomy[18–20] cold snare, and cold biopsy forceps. Kawamura et al.[18] and Gómez et al.[19] confirmed complete resection by obtaining biopsies from the resection margins after polypectomy, whereas Aslan et al.[20] only confirmed it from the polyp examination. The mean risk difference [RD] was 0.01 (95% CI, -0.02 to 0.03) with I^2=0%, meaning absolute homogeneity. Hence, this analysis showed equivalence of methods (FIGURE 3A).

Although all four studies[17,18,21,22] assessed bleeding, only Horiuchi A et al.[17] and Kawamura T et al.[18] observed this adverse event (AE). Both used the same methodology. Seven patients presented delayed bleeding amongst 437 allocated for the hot snare group while none of the 376 in the cold snare group did. However, this finding did not achieve statistical difference rendering these methods equally safe. The I^2 values for immediate and delayed bleeding and total AEs were higher than 50%, that is, highly heterogeneous. Since this comparison entailed only two trials, an outlier exclusion was inappropriate. Therefore, this analysis considered true heterogeneity and demanded adoption of the random effect model. None of the trials reported perforations. (FIGURE 3B).

TABLE 2. Summary of favourable results.

	Complete resection	En-bloc resection	Retrieval tissue failure	Adverse events	Duration of procedure
CSP x HSP	=	O	=	=	CSP
CSP x HFP*	CSP	CSP	=	O	=
CSP x CFP	CSP	CSP	CFP	O	CSP
CSP x SPT*	=	=	=	O	O
CSP x DCSP	DCSP	DCSP	=	O	=
CFP x HSP*	=	O	O	O	O
SFP x JFP*	JFP	JFP	O	=	JFP
EMR x HSP*	=	=	=	EMR	=
EMR x CSP*	EMR	EMR	O	=	CSP
CS-EMR x HS-EMR*	=	O	=	=	O

CSP: cold snare polypectomy; HSP: hot snare polypectomy; HFP: hot forceps polypectomy; CFP: cold forceps polypectomy; SPT: suction pseudopolyp technique; DCSP: dedicated cold snare polypectomy; SFP: standard forceps poly-pectomy; JFP: jumbo forceps polypectomy; EMR: endoscopic mucosal resection; CS-EMR: cold snare EMR; HS-EMR: hot snare EMR. O: not analysed. = No statistical difference. * Only one trial analysed.

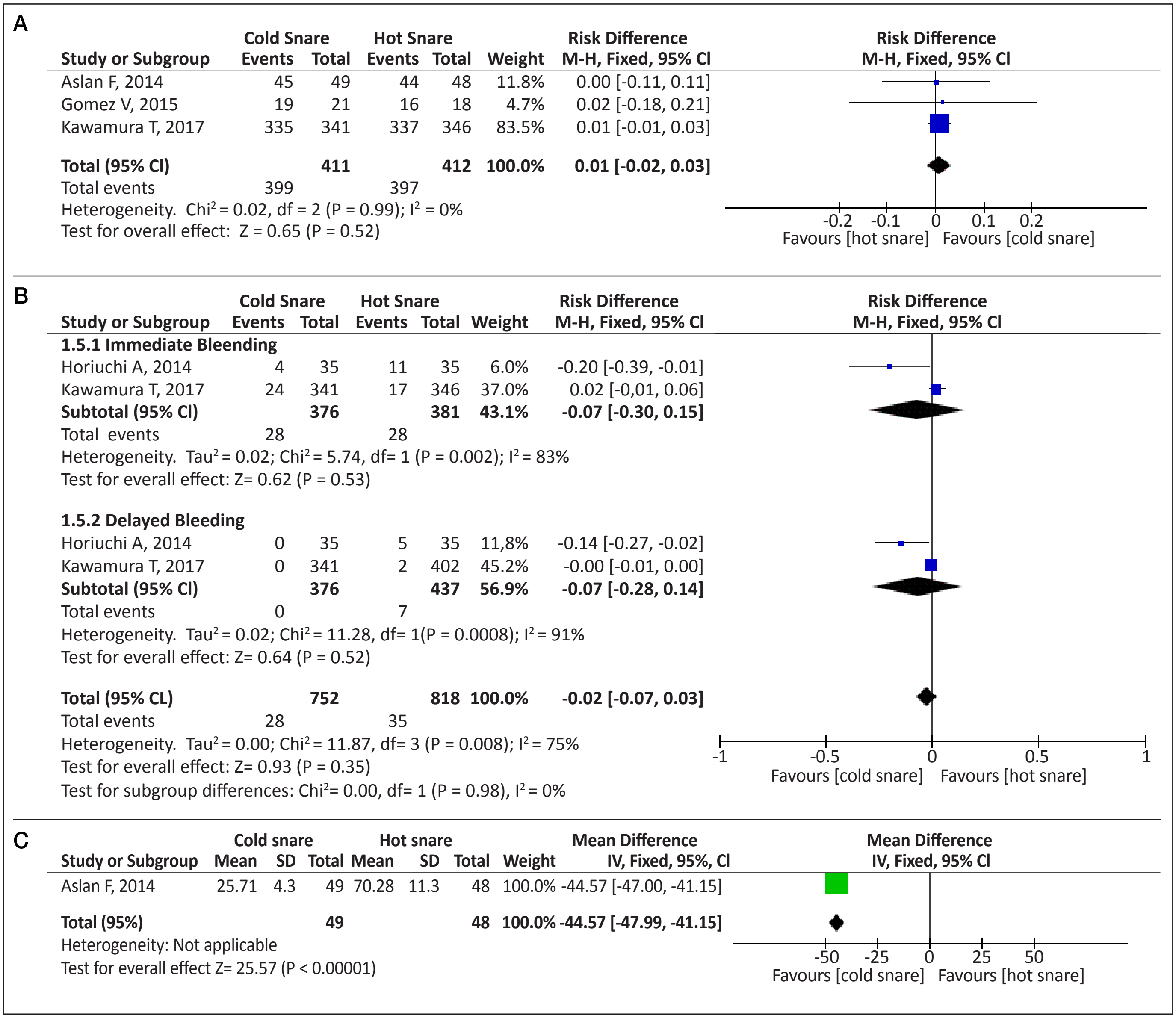


FIGURE 3. Cold snare vs Hot Snare forest plots. **(A)** Complete histological eradication. **(B)** Adverse events. **(C)** Duration of procedure.

Only Aslan et al.[20] assessed duration of procedure by the time of polypectomy itself. In this trial, cold snare polypectomy was significantly faster than hot. Accordingly, the risk difference for duration of procedure was -44.57 (95% CI, -47.99 to -41.15). (FIGURE 3C).

Four studies compared failure on retrieving the specimen[17,18,21,22]. None of them showed difference between methods. The pooled mean risk difference was 0.00 (95 % CI, -0.03 to 0.03), with the I^2=0%.

2. Cold snare vs hot forceps

Cold snare polypectomy was significantly superior to hot forceps regarding complete and *en-bloc* resection rates (RD 0.33, 95%CI 0.22 to 0.44 and RD 0.19, 95%CI 0.12 to 0.26, respectively) as compared on the single study performed by Komeda et al.[23]. The NNT for complete resection was 3. That is, for every three cold snare polypectomies, one would have been incomplete if performed with hot forceps. On the other hand, there was no statistical difference between those techniques regarding negatives outcomes (retrieval tissue failure rate: RD 0.03, 95%CI, -0.01 to 0.07 and adverse events: RD 0.01, 95%CI, -0.06 to 0.07).

3. Cold forceps vs hot snare

On this subgroup of a single study[19], we analysed cold forceps versus hot snare. Gomez et al.[19] assessed only complete resection rate and found no statistical difference between the afore mentioned methods (RD -0.06, 95%CI, -0.28 to 0.17).

4. Cold snare vs cold forceps

Four studies assessed complete resection rates, with no difference between methods, to compare cold snare and cold forceps[8,19,24,25]. The cold snare was significantly superior (*P*=0.0007) with an NNT of 11. The risk difference was 0.09 (95%CI, 0.04 to 0.14) and the I^2=49% (FIGURE 4A). Only Lee CK et al.[25] assessed *en-bloc* resection rate and also found cold snare to be significantly better than cold forceps (NNT 4, RD 0.23, 95% CI, 0.09 to 0.36) (FIGURE 4A).

Three authors compared the retrieval tissue failure rates[8,24,25]. Despite lacking statistical difference on the first two studies, the pooled analysis favoured the cold forceps (RD 0.06, 95% CI, 0.03 to 0.10). There was no heterogeneity according to the Higgins test for this comparison group (FIGURE 4B).

The analysis of duration of procedure was also highly homogenous and found statistical difference favouring the cold snare technique (RD -0.70, 95% CI, -1.16 to -0.24) (FIGURE 4C).

5. Cold snare vs suction pseudopolyp technique

The pseudopolyp suction technique (SPT) consists in aspirating the polyp into the suction channel and rapidly excising the lesion with a cold snare before it restores the original shape.

A single trial performed by Din S et al.[26] compared cold snare to SPT and found equivalence between methods regarding complete and en-bloc resection rates and retrieval tissue failure rate. Complete resection rate: RD -0.12, 95%CI -0.29 to 0.04; En-bloc resection rate: RD: -0.06, %95CI: -0.13 to 0.01; Retrieval tissue failure rate: RD 0.01, 95%CI: -0.09 to 0.11.

6. Cold snare vs dedicated cold snare

Din S et al. and Horiuchi A et al.[27,28] compared two types of snares for cold polypectomy. The standard one versus another specially designed for cold resection. The so-called dedicated cold snare has a thinner braided wire and is smaller than the traditional snare. Also, it is not insulated.

The pooled analysis concerning complete resection rates significantly favoured the DCS (P=0.02, RD 0.10, 95%CI, 0.02 to 0.19) with I^2=0%. The calculated NNT was 10 (FIGURE 5). Furthermore, based on Horiuchi A et al. data[28], it was possible to sub-classify the polyps according to their size. Then, histological eradication was found to be significantly higher only when polyps were larger than 8 mm (RD 0.38, 95%CI, 0.11 - 0.65) (FIGURE 5). Both confirmed complete resection by absence of residual tissue at resection margin.

A single trial assessed *en-bloc* resection and the results favoured the dedicated cold snare polipectomy (DCSP) (NNT=4.5, RD 0.22, 95%CI 0.08 to 0.36)[28].

Concerning adverse events and duration of procedure, there was no difference between techniques (RD= -0.02, 95%CI -0.12 to 0.09 and RD -1.00, 95% CI -4.82 to 2.82, respectively). Although, the duration of procedure was measured as the whole procedure, not only the polypectomy itself.

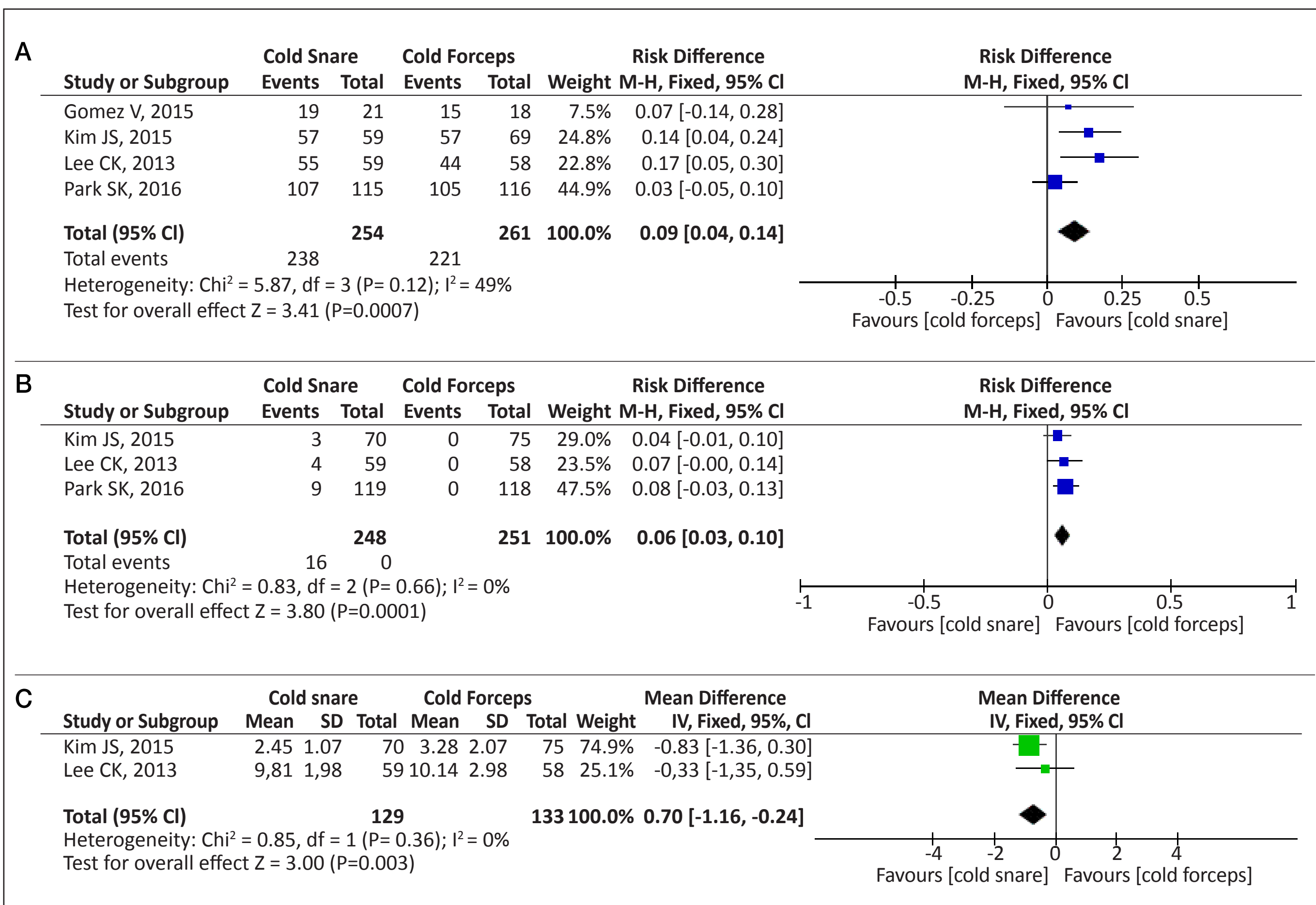
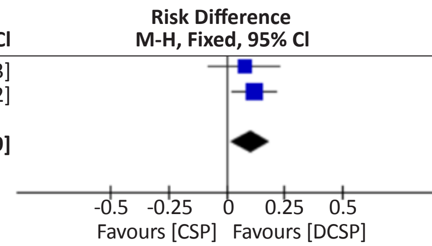


FIGURE 4. Cold Snare vs Cold Forceps forest plots. **(A)** Complete resection rates. **(B)** Retrieval tissue rate failure. **(C)** Duration of procedure.

Study or Subgroup	dedicated cold snare Events	Total	cold snare Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Din S, 2015b	44	89	30	72	43.2%	0.08 [-0.08, 0.23]
Horiuchi A, 2015	89	98	88	112	56.8%	0.12 [0.03, 0.22]
Total (95% CI)		**187**		**184**	**100.0%**	**0.10 [0.02, 0.19]**
Total events	133		118			

Heterogeneity: Chi² = 0.26, df = 1 (P= 0.61); I² = 0%
Test for overall effect: Z = 2.36 (P=0.02)



Study or Subgroup	dedicated cold snare Events	Total	cold snare Events	Total	Weight	Risk Difference M-H, Random, 95% CI
5.1.1 < 5 mm						
Horiuchi, A 2015	35	38	41	45	39.9%	0.01 [-0,11, 0.13]
Subtotal (95% CI)		38		45	39,9%	0.01 [-0.11, 0.13]
Total events	35		41			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.16 (P = 0.87)						
5.1.2 6-7 mm						
Horiuchi, A 2015	39	42	37	45	37.7%	0.11 [-0.03, 0.24]
Subtotal (95% CI)		42		45	37,7%	0.11 [-0.03, 0.24]
Total events	39		37			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.53 (P = 0.13)						
5.1.3 8-10						
Horiuchi, A 2015	15	18	10	22	22.4%	0.38 [-0,11, 0.65]
Subtotal (95% CI)		**18**		**22**	**22,4%**	**0.38 [-0.11, 0.65]**
Total events	15		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.75 (P = 0.006)						
Total (95% CI)		**98**		**112**	**100.0%**	**0.13 [-0.04, 0.30]**
Total events	89		88			

Heterogeneity: Tau² = 0.02; Chi² =6.83, df =2 (P=0.03); I² = 71%
Test for overall effect: Z = 1.46 (P = 0.14)
Test for subgroup differences: Chi² = 6.16; df = 2 (P= 0.05), I² = 67.5%

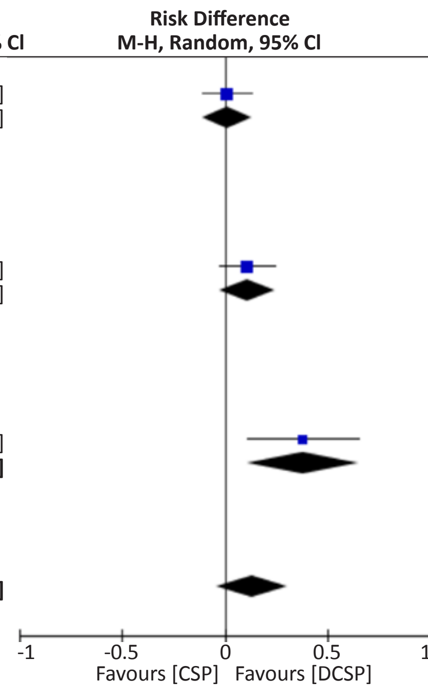


FIGURE 5. Forest plot analyses comparing standard and dedicated cold snare for complete histological eradication.

Again, only Din S et al.[27] evaluated retrieve tissue failure rates and showed the equivalence of methods (RD -0.05, 95%CI -0.17 to 0.07).

7. Standard forceps vs jumbo forceps

The risk difference regarding complete resection rate of jumbo forceps versus standard forceps was 0.09 (95% CI 0.04 to 0.15). The number needed to treat was 11, with I^2=0% (FIGURE 6). Aslan et al.[29] confirmed the complete resection with biopsies of the resected margins and Draganov et al.[30] by the specimen analyses.

Only Draganov et al.[30] compared *en-bloc* resection rates between these methods and showed statistical difference favouring the jumbo forceps with an NNT of 3.5 (RD -0.28, 95% CI -0.38 to -0.18).

Concerning adverse events, we found equivalence of methods despite high heterogeneity (RD=0.01, 95% CI -0.05 to 0.07; I^2=59%).

Study or Subgroup	J umbo Forceps Events	Total	Standard Forceps Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Aslan F, 2015	102	102	144	161	79.4%	0.11 [0.06, 0.16]
Draganov, PV, 2012	28	34	24	31	20.6%	0.05 [-0.15, 0.24]
Total (95% CI)		**136**		**192**	**100.0%**	**0.09 [0.04, 0.15]**
Total events	130		168			

Heterogeneity: Chi² = 0.41, df = 1 (P= 0.52); I² = 0%
Test for overall effect: Z = 3.26 (P=0.001)

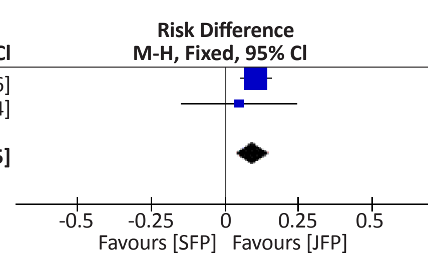


FIGURE 6. Forest plot comparing jumbo forceps and standard forceps for complete resection rate.

8. EMR vs hot snare

Only Kim H-S et al.[31] compared endoscopic mucosal resection and hot snare polypectomy. There were no differences regarding complete resection rate and *en-bloc* resetion (RD=0.04, 95% CI -0.02 to 0.11 and RD -0.01, 95%CI -0.08 to 00.05, respectively) but EMR was superior in terms of adverse events with an NNH of 20 (RD= -0.05, 95% CI -0.08 to -0.01).

9. EMR vs cold snare

Only Zhang Q et al.[32] compared endoscopic mucosal resection and cold snare polypectomy. Considering complete and *en-bloc* resection rates, EMR was superior to CSP both with a NNT of 14 (RD 0.07, 95 % CI 0.03 to 0.11 and RD 0.07, 95% CI 0.03 to 0.12, respectively). There was no difference in adverse event rates between groups (RD= -0.01, 95% CI -0.04 to 0.02). Regarding duration of procedure, CSP was faster than EMR (RD 0.8, 95% CI 0.28 to 1.32).

10. CS-EMR vs HS-EMR

Papastergiou V et al.[33] compared cold (CS-EMR) versus hot endoscopic mucosal resection (HS-EMR) for small polyps in a non-inferiority trial. The risk difference was -0.04 (95% CI, -0.11 to 0.04) concerning complete histological eradication. Accordingly, adverse events and retrieval tissue rate failures were similar between methods (RD 0.02, 95% CI -0.02 to 0.07 and RD 0.02, 95% CI -0.05 to 0.10, respectively).

11. Hot polypectomy vs cold polypectomy

We created this subgroup analysis comprising six studies to compare all cold polypectomy techniques versus all hot procedures[18-20,23,32,33].

Concerning complete resection rates, our meta-analysis showed no statistical difference between the two techniques (RD 0.08, 95% CI -0.03 to 0.19). Also, there was no change in results when diminutive polyps were analysed separately from small polyps (RD=0.20, 95% CI -0.08 to 0.48). Nevertheless, this analysis found true high heterogeneity (I^2>90%). (FIGURE 7A).

Only two trials compared *en*-bloc resection rate[23,32]. This analysis also found high heterogeneity (I^2=97%) and no statistical difference between cold and hot polypectomy (RD=0.06, 95% CI -0.20 to 0.32) (FIGURE 7B).

Four trials evaluated adverse events[17,18,23,32]. The initial result found high heterogeneity (I^2=80%) (FIGURE 7C). The sensitivity analysis through a funnel plot identified an outlier study (FIGURE 7D)[18]. After removing the outlier, we found absolute homogeneity and no statistical difference between groups (RD 0.02, 95 % CI -0.00 to 0.04) (FIGURE 7E).

Six trials assessed retrieval tissue failure rate[17,18,21-23,33]. Our meta-analysis showed equivalence of methods (RD 0.01, 95% CI -0.01 to 0.02) with I^2=0% (FIGURE 7F).

Finally, cold polypectomy was statistically faster than hot procedures. Concerning the duration of procedure, the risk difference was -44.60 (95% CI -48.00 to -41.19) with no heterogeneity (FIGURE 7G).

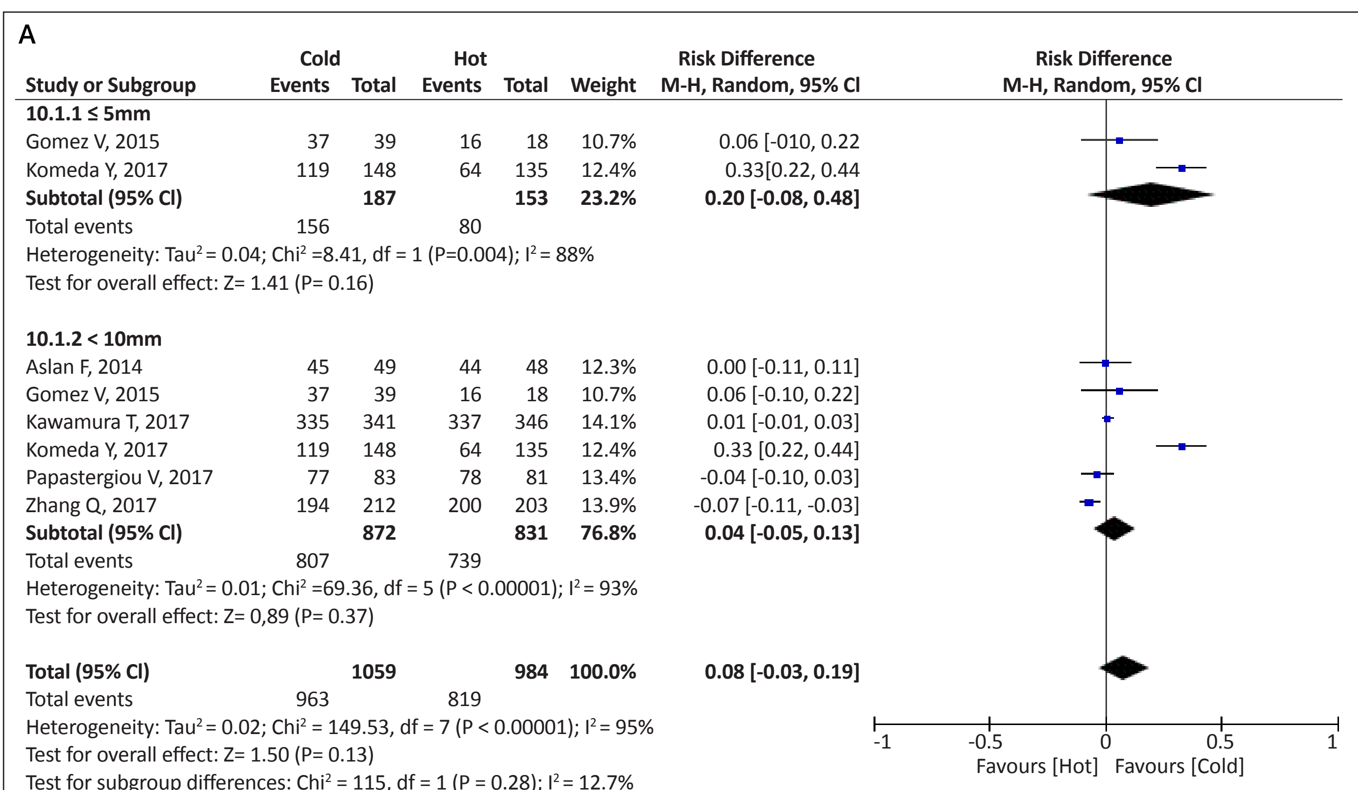
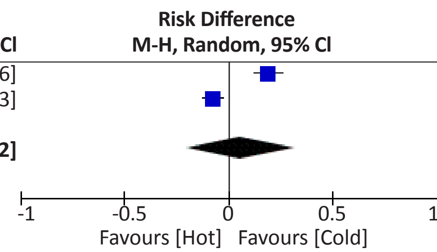


FIGURE 7. Pooled analyses of cold polypectomy techniques vs hot methods. (**A**) Forrest plot analysis for complete histological eradication rate. (**B**) Forrest plot analysis for *en-bloc* resection rate. (**C**) Forrest plot analysis for adverse events rate. (**D**) Funnel plot analysis for adverse events. (**E**) Forrest plot for adverse event after excluding the outlier. (**F**) Forrest plot for retrieval tissue rate failure rate. (**G**) Forrest plot for duration of procedure.

B

Study or Subgroup	Cold Events	Cold Total	Hot Events	Hot Total	Weight	Risk Difference M-H, Random, 95% CI
Komeda Y, 2017	147	148	108	135	49.6%	0.19 [0.12, 0.26]
Zhang Q, 2017	234	267	245	258	50.4%	-0.07 [-0.12, -0.03]
Total (95% CI)		**415**		**393**	**100.0%**	**0.06 [-020, 0.32]**
Total events	381		353			

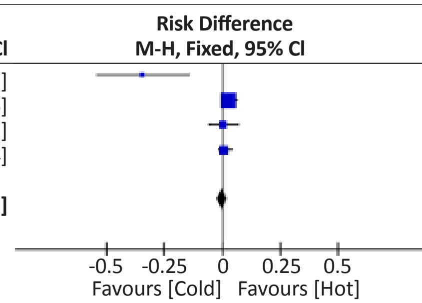
Heterogeneity: Tau² = 0.03; Chi² = 39.09, df = 1 (P < 0.00001); I² = 97%
Test for overall effect: Z= 0.44 (P= 0.66)



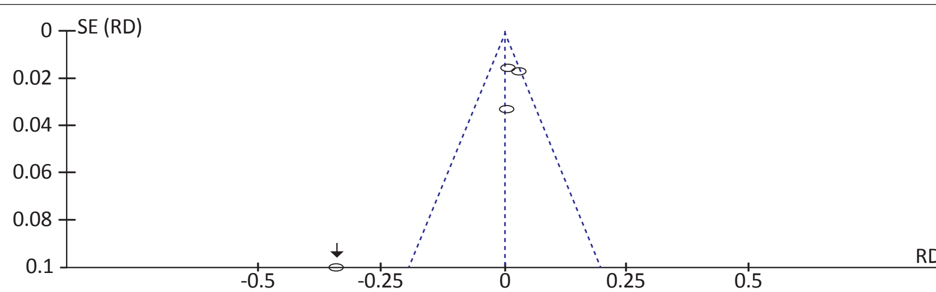
C

Study or Subgroup	Cold Events	Cold Total	Hot Events	Hot Total	Weight	Risk Difference M-H, Fixed, 95% CI
Horiuchi A, 2014	4	35	16	35	4.8%	-0.34 [-0.54, -0.15]
Kawamura T, 2017	24	341	17	402	51.0%	0.03 [-0.01, 0.06]
Komeda Y, 2017	13	148	11	135	19.5%	0.01 [-0.06, 0.07]
Zhang Q, 2017	5	179	3	179	24.7%	0.01 [-0.02, 0.04]
Total (95% CI)		**703**		**751**	**100.0%**	**0.00 [-0.02, 0.03]**
Total events	46		47			

Heterogeneity: Chi² = 14.65, df = 3 (P = 0.002); I² = 80%
Test for overall effect: Z= 0.14 (P= 0.89)



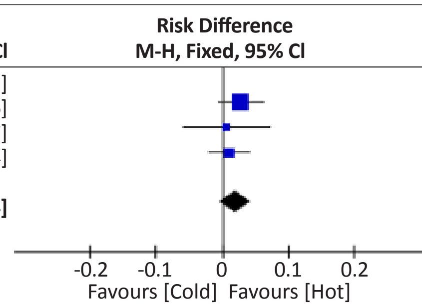
D



E

Study or Subgroup	Cold Events	Cold Total	Hot Events	Hot Total	Weight	Risk Difference M-H, Fixed, 95% CI
Horiuchi A, 2014	4	35	16	35	0.0%	-0.34 [-0.54, -0.15]
Kawamura T, 2017	24	341	17	402	53.5%	0.03 [-0.01, 0.06]
Komeda Y, 2017	13	148	11	135	20.5%	0.01 [-0.06, 0.07]
Zhang Q, 2017	5	179	3	179	26.0%	0.01 [-0.02, 0.04]
Total (95% CI)		**668**		**716**	**100.0%**	**0.02 [-0.00, 0.04]**
Total events	42		31			

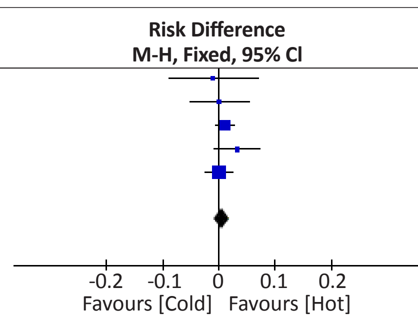
Heterogeneity: Chi² = 0,69.65, df = 2 (P = 0.71); I² = 0%
Test for overall effect: Z= 1.59 (P= 0.11)



F

Study or Subgroup	Cold Events	Cold Total	Hot Events	Hot Total	Weight	Risk Difference M-H, Fixed, 95% CI
Horiuchi A, 2014	5	78	6	81	6.3%	- 0.01 [-0.09, 0.07]
Ichise Y, 2011	4	101	4	104	8.1%	0.00 [-0.05, 0.05]
Kawamura T, 2017	7	394	3	402	31.5%	0.01 [-0.01, 0.03]
Komeda Y, 2017	7	148	2	135	11.2%	0.03 [-0.01, 0.07]
Paspatis GA, 2011	21	530	22	553	42.9%	- 0.00 [-0.02, 0.02]
Total (95% CI)		**1251**		**1251**	**100.0%**	**0.01 [-0.01, 0.02]**
Total events	44		37			

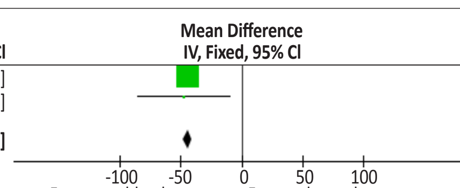
Heterogeneity: Chi² = 2.42, df = 4 (P = 0.66); I² = 0%
Test for overall effect: Z= 0.90 (P = 0.37)



G

Study or Subgroup	Cold Polypectomy Mean	Cold Polypectomy SD	Cold Polypectomy Total	Hot Polypectomy Mean	Hot Polypectomy SD	Hot Polypectomy Total	Weight	Mean Difference IV, Fixed, 95% CI
Aslan F, 2014	25.71	4.3	49	70.28	11.3	48	99.2%	-44.57 [-47.99, -41.15]
Zhang Q, 2017	282	204	179	330	162	179	0.8%	-48.00 [-86.16, -9.84]
Total (95% CI)			**228**			**227**	**100.0%**	**-44.60 [-48.00, -41.19]**

Heterogeneity: Chi² = 0.03, df = 1 (P = 0.86); I² = 0%
Test for overall effect: Z= 25.69 (P < 0.00001)



DISCUSSION

This meta-analysis is the largest regarding treatment of the most common kind of colonic polyps. The strength of this review is the use of only RCTs including more than 5000 polypectomies. Also, our study presents the greatest number of comparisons currently available in the literature.

Comparing methods with electrocautery (hot polypectomy) versus without it (cold polypectomy) we found no statistical difference in complete resection, adverse event or retrieval tissue rates. However, cold polypectomy was time-saving compared to diathermy, which may favour cold techniques. Yet, our results are in accordance with several independent articles suggesting that cold polypectomy presents at least the same curability rates as hot polypectomy whereas the same risk of adverse events[9,23,32,33]. Thus, complete resection rates among diminutive polyps (<5 mm) and small polyps (<10 mm) are similar, showing that using electrocautery does not improve the resection rate but carries the hypothetical drawback of increased perforation and bleeding risks.

Among cold polypectomy techniques, the cold snare was superior to forceps in terms of complete and *en-bloc* resection (9% vs 23% incomplete resection rates, respectively), possibly because it may resect 2 mm to 3 mm of normal mucosa around the base of the polyp leading to greater complete resection rates[34]. Furthermore, it is faster than forceps[8,25]. Despite the absence of statistical difference in failure to recover resected polyp in Lee CK et al.[25] and Kim JS et al.[8], the pooled analysis favoured forceps technique. Even though some experts with large experience in NBI advocate for selective 'resect and discard' strategy for diminutive polyps, most guidelines recommend retrieval of all resected polyps[10,35]. Therefore, the higher failure to retrieve rate of cold snare may be considered its major drawback.

The comparison of cold snare versus pseudopolyp suction technique in a single trial showed no difference regarding complete resection, *en-bloc* resection or retrieval tissue failure rates[26]. Duration of procedure and costs were not assessed but the latter demands employment of a dedicated cap which inevitably renders SPT more time consuming and more expensive.

Another comparison group evaluated the two types of snare: the standard one (with or without electrocautery) versus a dedicated cold snare which has no input port for electrocautery. Two articles[27,28] were included and demonstrated that the (DCSP) was significantly superior in terms of complete and *en bloc* resection rates. A subgroup analysis showed statistical significance exclusively for polyps larger than 8mm in Horiuchi's et al.[28] trial. Nevertheless, these techniques presented similar adverse event rates and duration of procedure. Jung et al.[11] suggested that the superiority of the DCSP could be due to the thinner wire and its shield shape. On the other hand, they also suggested that using a limited cold snare would probably increase the overall polypectomy cost since the examiner would need to change devices if a larger or pedunculated polyp was detected. Since few studies adequately evaluated this device, further randomized trials are needed to correctly assess cost-effectiveness and convenience of DCSP.

The pooled analysis enrolling results from Aslan et al.[29] and Draganov et al.[30] compared jumbo to standard forceps. The first was significantly superior to the latter regarding curability rate while carrying the same risk of adverse events. Duration of procedure could not be analysed because Draganov et al.[30] measured the exam duration and the whole procedure, not the time of polypectomy itself. As discussed by Raad D et al.[10], JFP has a wider opening diameter and, therefore, needs fewer bites to achieve complete resection.

Although no trial confronted JFP to CSP head-to-head, Jung YS et al.[11] performed a network meta-analysis to indirectly compare them and showed no statistical difference on histological eradication.

Three trials evaluated the EMR technique for polyps from 5 to 9mm: Kim et al., Zhang et al., and Papastergious et al.[31-33]. However, each trial had a distinct control group. Kim H-S et al.[31] compared EMR to hot snare alone and found no statistical difference on complete resection rates, although the latter presented a higher risk of adverse events. Zhang et al.[32] compared EMR to cold snare alone and showed that EMR is superior in terms of histological and endoscopic complete resection regardless of the same adverse event rate. The major drawback was the extended duration of the procedure. Finally, Papastergiou et al.[33] compared injection in submucosa followed by cold snaring or by hot snaring and showed that these methods are both effective and safe.

Our study is not free of limitations. Firstly, despite the great number of randomized controlled trials included, no comparison group had more than six studies at the same analysis and some of the groups had only one study analysed. Secondly, most studies had a considerable variety of polyp sizes but only a few categorized by size; that fact precluded a strong statistical analysis for polyps <5 mm separately from 5 to 10 mm. Thirdly, there were no follow-up colonoscopies to assess recurrence rates. Finally, one-quarter of the articles had low methodological quality, which might somehow impair reliability.

Despite these limitations, we were able to reach important conclusions. Also, this is the largest and most updated meta-analysis available in the literature to support the daily practice of endoscopists.

CONCLUSION

This meta-analysis shows that cold polypectomy techniques have equivalent curability rate and is as safe as hot polypectomy techniques for resection of polyps smaller than 10mm. Cold snaring is the best option for resection of such polyps. The use of electrocautery seems to be unnecessary. Further studies are needed to compare cold snare alone versus EMR.

ACKNOWLEDGEMENTS

We thank Mariana Bertoncelli Tanaka, Galileu Farias, Thiago Visconti, Martin Andrés Coronel Cordero and Nelson Miyajima for comments that greatly improved the manuscript.

Authors' contributions

Tranquillini CV and Bernardo WM: search, data collection, writing of the manuscript. Brunaldi VO: writing and correction of the manuscript. Moura ET, Marques SB, Moura EGH: review and correction of the manuscript.

Tranquillini CV, Bernardo WM, Brunaldi VO, Moura ET, Marques SB, Moura EGH. Revisão sistemática e meta-análise sobre técnicas de polipectomia de pólipos colorretais pequenos e diminutos. Arq Gastroenterol. 2018;55(4):358-68.

RESUMO – **Contexto** – A polipectomia de pólipos colorretais é a base da prevenção do câncer colorretal. A identificação da melhor técnica de polipectomia é imperativa. **Objetivo** – Esta revisão tem como objetivo comparar a eficácia de nove diferentes métodos de ressecção para pólipos colorretais pequenos (<10 mm). **Métodos** – Pesquisamos e selecionamos apenas ensaios clínicos randomizados. O desfecho primário foi taxas de ressecção completa de pólipos pequenos por confirmação histológica. Os desfechos secundários foram: eventos adversos, taxas de falha de recuperação do espécime e duração do procedimento. **Resultados** – Dezoito estudos, incluindo 3215 pacientes e 5223 pólipos foram analisados. No geral, a polipectomia a frio teve um tempo de procedimento significativamente menor do que a polipectomia a quente (RD -5,92; IC 95% -9,90 a -1,94; $P<0{,}05$), sem diferença estatística na erradicação histológica (RD 0,08; IC 95% -0,03 a 0,19; $P>0{,}05$). Em relação às técnicas de polipectomia a frio, a alça fria foi considerada superior ao uso de pinça fria nas taxas de ressecção completa e em bloco, além de um menor tempo de procedimento. Ao comparar a ressecção endoscópica da mucosa utilizando alça quente ou alça fria, esta última mostrou não-inferioridade na erradicação histológica, eventos adversos ou taxas de falha do tecido de recuperação. **Conclusão** – A polipectomia a frio mostrou ser a melhor técnica para ressecção de pequenos pólipos colorretais. Entre os métodos frios, a alça fria dedicada foi considerada superior na erradicação histológica. ressecção endoscópica da mucosa com alça fria pode ser considerado uma opção para pólipos de 5 a 9 mm.

DESCRITORES – Pólipos do colo, cirurgia. Ressecção endoscópica de mucosa. Seguimentos.

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