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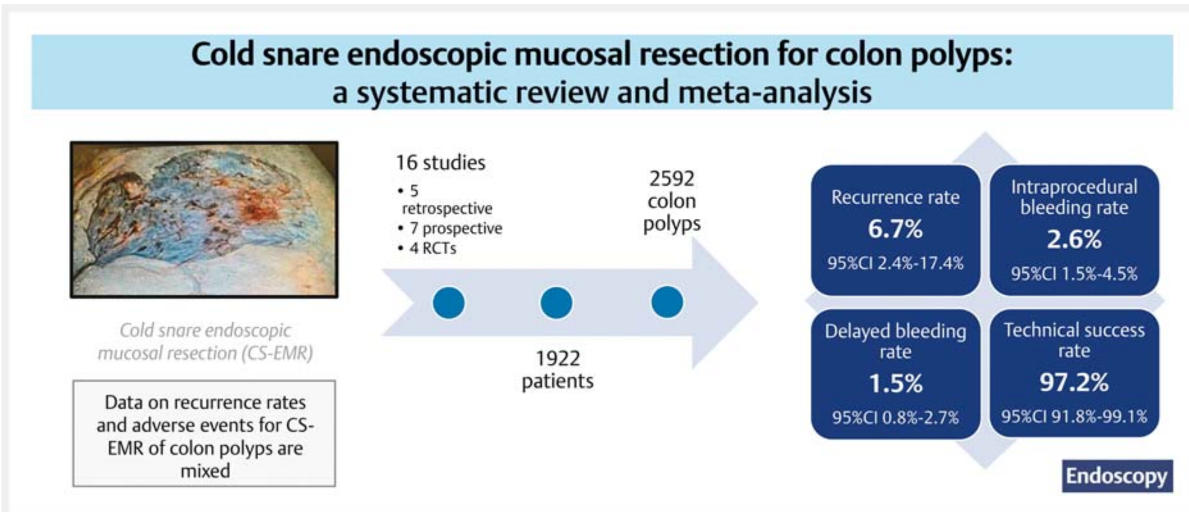
Cold snare endoscopic mucosal resection for colon polyps: a systematic review and meta-analysis

GRAPHICAL ABSTRACT



Authors

Mohamed Abdallah[1], Khalid Ahmed[2], Daniyal Abbas[3], Mouhand F. H. Mohamed[4], Gaurav Suryawanshi[1], Nicholas McDonald[1], Natalie Wilson[1], Shifa Umar[5], Aasma Shaukat[6], Mohammad Bilal[1]

Institutions

1 Department of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis, Minnesota, United States
2 Department of Internal Medicine, The Wright Center for Graduate Medical Education, Scranton, Pennsylvania, United States
3 Department of Internal Medicine, East Carolina University, Greenville, North Carolina, United States
4 Brown University, Warren Alpert Medical School, Providence, Rhode Island, United States
5 Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, United States
6 Division of Gastroenterology, Department of Medicine and Population Health, NYU Grossman School of Medicine, New York, New York, United States

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Corresponding author
Mohamed Abdallah, MD, Department of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, 406 Harvard St SE, MMC36 Minneapolis, MN 55455, United States
abdal088@umn.edu

ABSTRACT

Background Cold snare endoscopic mucosal resection (CS-EMR) can reduce the risks associated with electrocautery during colon polyp resection. Data on efficacy are variable. This systematic review and meta-analysis aimed to estimate the pooled efficacy and safety rates of CS-EMR.

Methods We conducted a comprehensive literature search of multiple databases, from inception to March 2023, for studies addressing outcomes of CS-EMR for colon polyps. The weighted pooled estimates with 95 %CIs were calculated using the random effects model. I^2 statistics were used to evaluate heterogeneity.

Results 4137 articles were reviewed, and 16 studies, including 2592 polyps in 1922 patients (51.4 % female), were included. Overall, 54.4 % of polyps were adenomas, 45 % were sessile serrated lesions (SSLs), and 0.6 % were invasive carcinomas. Polyp recurrence after CS-EMR was 6.7 % (95 % CI 2.4 %–17.4 %, I^2 = 94 %). The recurrence rate was 12.3 % (95 %CI 3.4 %–35.7 %, I^2 = 94 %) for polyps ≥ 20 mm, 17.1 % (95 %CI 4.6 %–46.7 %, I^2 = 93 %) for adenomas, and 5.7 % (95 %CI 3.2 %–9.9 %, I^2 = 50 %) for SSLs. The pooled intraprocedural bleeding rate was 2.6 % (95 %CI 1.5 %–4.5 %, I^2 = 51 %), the delayed bleeding rate was 1.5 % (95 %CI 0.8 %–2.7 %, I^2 = 18 %), and no perforations or post-polypectomy syndromes were reported, with estimated rates of 0.6 % (95 % CI 0.3 %–1.3 %, I^2 = 0 %) and 0.6 % (95 %CI 0.3 %–1.4 %, I^2 = 0 %), respectively.

Conclusion CS-EMR demonstrated an excellent safety profile for colon polyps, with variable recurrence rates based on polyp size and histology. Large prospective studies are needed to validate these findings.

Introduction

Cold snare endoscopic mucosal resection (CS-EMR) is a technique used for the resection of colon polyps where submucosal injection is performed and the polyp is then removed using a smaller diameter snare without the use of electrocautery [1]. It has been gaining popularity as an alternative technique to hot snare EMR [2].

Cold snare polypectomy remains the primary endoscopic technique for removing most small and diminutive polyps [3]. However, for nonpedunculated polyps measuring 10–19 mm, and polyps ≥ 20 mm with no submucosal invasion, hot snare polypectomy and hot snare EMR are more frequently employed [3, 4]. These techniques, however, are associated with higher rates of adverse events compared with cold snare polypectomy [5].

CS-EMR potentially has a lower risk for adverse events compared with other advanced endoscopic resection techniques because electrocautery is not used [6]. Electrocautery, which is used to facilitate transection through polyp tissue and minimize intraprocedural bleeding, is associated with adverse events such as post-polypectomy syndrome, delayed post-polypectomy bleeding, and perforation [5, 7]. This is postulated to result from the sloughing of the eschar, which exposes the partially coagulated submucosal blood vessels and causes necrosis of the edges of the mucosal defect and tissue damage from thermal energy [8].

CS-EMR has gained popularity over recent years for the resection of larger colon polyps. However, data on the recurrence rate and adverse events associated with CS-EMR are variable [6, 9–11]. This systematic review and meta-analysis of the available literature aims to estimate the pooled rates of efficacy and safety of CS-EMR for colon polyps.

Methods

Search strategy and study selection for analysis

A comprehensive literature search was conducted in MEDLINE via Ovid, EMBASE via Ovid, Scopus, ClinicalTrials.gov, and the Cochrane registry from inception to March 2023 for studies that reported on the efficacy and safety of CS-EMR for colon polyps. An experienced medical librarian conducted the literature search; the search strategy is provided in the online-only Supplementary material. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify full-length articles in the English language [12, 13]. In this PRISMA-compliant meta-analysis, all types of studies, including case–control, cross-sectional, or cohort studies published in the English language were screened. A PRISMA checklist is provided in the Supplementary material. Reviews, case reports, and letters to the editor were excluded from the database results before screening using Scottish Intercollegiate Guidelines Network (SIGN) filters.

The title/abstract screening was performed independently by three investigators (M.A., K.A., and D.A.) using the following inclusion criteria: 1) studies that reported polyp recurrence or adverse event rates following CS-EMR for colon polyps (polypoid and nonpolypoid lesions); 2) included adult patients aged ≥ 18 years; 3) published in the English language; and 4) reported as full papers. Exclusion criteria were studies that: 1) included fewer than 10 patients; 2) did not provide data on the outcomes of interest; 3) reported the use of cold snare polypectomy without submucosal injection; 4) reported CS-EMR on the upper gastrointestinal tract; and 5) did not meet ≥ 1 inclusion criterion. References of selected retrieved articles were manually reviewed for additional potentially relevant articles.

All results were downloaded into EndNote X9 (Thompson ISI ResearchSoft, Philadelphia, Pennsylvania, USA). Any duplication was identified and removed. In the case of duplicate studies from the same institution/database, the latest study with the largest number of patients was included to avoid duplication. Any discrepancy among investigators was resolved by consensus among all the investigators.

Study outcomes

The primary outcomes of this study were the rates of recurrence following CS-EMR and associated adverse events. The secondary outcome was the technical success rate, which was defined as the ability to reach and resect the intended lesion. Polyp recurrence was defined as macroscopic or microscopic evidence of an adenoma or sessile serrated lesion (SSL) on the first follow-up colonoscopy. Subgroup analyses of data based on polyp histology (adenoma vs. SSL) and polyp size (<20 mm and ≥20 mm) were performed. Adverse events included immediate intraprocedural bleeding, delayed post-polypectomy bleeding, perforation, and post-polypectomy syndrome, up to 30 days following the index colonoscopy.

Data extraction and quality assessment

Data from studies selected for analysis were extracted independently by three authors (M.A., K.A., D.A.): study characteristics (sample size, study population); study design; demographics; lesion size; morphology of colon lesions according to the Paris classification [14]; type of injectate and snares used; location of colon polyps (right colon was defined as proximal to the splenic flexure); technical success; adverse events; and data on follow-up and recurrence. The Newcastle–Ottawa Scale for cohort studies was used to assess the quality of studies [15]. This quality score consists of questions about the representativeness of the cohort, assignment of exposure, outcomes not present at the start of the study, assignment of outcomes, and adequate follow-up. Disagreements were resolved by discussion or, if necessary, a fourth reviewer (N.M.). Scores of >5, 3–5, and <3 were considered suggestive of a high, medium, and low quality, respectively.

Statistical analysis

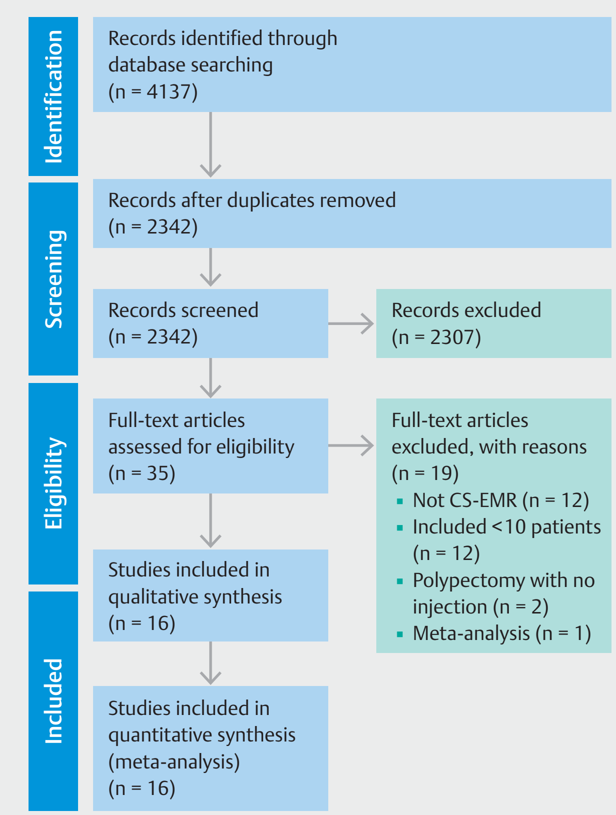
Data analysis was performed using Comprehensive Meta-Analysis (CMA 3.0) software (Biostat, Englewood, New Jersey, USA). The pooled rates and 95 %CIs were calculated using the Der Simonian and Laird method to pool the data using the random effects model. The I^2 statistic was used to determine the heterogeneity between studies, with significant heterogeneity defined with a value above 50 % or *P* value <0.1 [16]. Sensitivity analysis was conducted in the case of substantial heterogeneity by excluding one study at a time from the overall analysis using the "leave-one-out method" to explore the potential source of substantial heterogeneity. Publication bias was assessed using funnel plots if more than 10 eligible studies were included in the meta-analysis, otherwise, the use of funnel plots is inappropriate, given that the power of the test is too low to distinguish chance from actual funnel plot asymmetry [17].

Results

Baseline characteristics

The PRISMA flow diagram and results based on the search strategies and selection criteria described above are outlined in ▶ **Fig. 1**. Of the 4137 articles in the initial search, 1795 were duplicates. Title and abstract screening of the remaining 2342 was conducted, and 35 full-text studies were assessed for eligibility. Of 35 studies of interest, 16 met the inclusion criteria and were selected for the final meta-analysis (▶ **Fig. 1**) [2, 6–11, 18–26].

Four studies were randomized controlled trials, seven were prospective studies, and five were retrospective. Six studies were from the USA, three from Australia, two each from China and Japan, and one each from the UK, South Korea, and Greece. There were 1922 patients (52.4 % females) with 2592 polyps (74.1 % in the right colon and 25.8 % in the left colon) (▶ **Table 1**). In addition, 1374 of the polyps (54.4 %) were adenomas, 1136 (45 %) were SSLs, and 15 (0.6 %) were invasive carcinoma on the final histology. The morphology of lesions using the Paris classification were as follows: 548/907 (60.4 %) were of protruded morphology (Ip, Isp, Is), 346/907 (38.2 %) were superficially elevated (IIa, IIa + c, IIa + s, IIa + IIb), and 13/907 (1.4 %) were reported as flat (IIb, IIc, III) (▶ **Table 1**). Piecemeal CS-EMR was reported in all polypectomies in seven studies (▶ **Table 2**). The composition of injectates and the type of snare used for CS-EMR are outlined in ▶ **Table 2**.



▶ **Fig. 1** Literature review process using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for studies included in the analysis. CS-EMR, cold snare endoscopic mucosal resection.

Recurrence rate

The pooled polyp recurrence rate, reported in seven studies, was 6.7 % (95 %CI 2.4 %–17.4 %, I^2 = 94 %) (▶ **Fig. 2a**). The recurrence rate was 17.1 % (95 %CI 4.6 %–46.7 %, I^2 = 93 %) for adenomas (▶ **Fig. 2b**), and 5.7 % (95 %CI 3.2 %–9.9 %, I^2 = 50 %) for SSLs (▶ **Fig. 2c**). For polyps <20 mm, the recurrence rate was reported in only one study, by Piraka et al., and it was 0 %. For polyps ≥20 mm, the recurrence rate was 12.3 % (95 %CI 3.4 %–35.7 %, I^2 = 94 %) (▶ **Fig. 2 d**).

▶ **Table 1** Baseline characteristics of studies included in the systematic review of cold endoscopic mucosal resection for colon polyps.

First author Year [ref] Country	Study period	Study design	No. of patients/polyps	Age, years	Female sex, n/N (%)	Lesion size, mm	Lesion location	Lesion histology, n/N (%)	Shape characteristics, n/N (%)[1]
Choksi 2015 [18] USA	Feb 2012 – May 2013	Retrosp.	15/15	68 (IQR 49–85)	6/15 (40 %)	Mean 20 (range 10–45)	N/A	Adenoma: 15/15 (100 %)	N/A
Papastergiou 2018 [2] Greece	Jan 2016 – Oct 2016	Dual center RCT	77/83	63.1 (SD10.3)	31/77 (40.3 %)	Mean 8.2 (SD 1.6)	Right colon: 43/83 (51.8 %) Left colon: 40/83 (48.2 %)	Adenoma: 65/83 (78.3 %) SSL: 17/83, (20.5 %)	Is: 38/83 (45.8 %) IIa: 45/83 (54.2 %)
Piraka 2017 [22] USA	Oct 2013 – Sep 15	Single center, retrosp.	73/94	64 (IQR 43–86)	39/73 (53.4 %)	Mean 22.3 (range 12–60) <20 mm: 35 >20 mm: 37	Right colon: 78/94 (83.0 %) Left colon: 16/94 (17.0 %)	Adenoma: 89/94 (94.7 %) SSL: 5/94 (5.3 %)	N/A
Rameshshanker 2018 [23] UK	NI	Single center, prosp.	10/29	51 (range 29–77)	N/A	Mean 15 (range 10–30)	Right colon: 29/29 (100 %)	SSL: 29/29 (100 %)	N/A
Tutticci 2018 [11] Australia	Nov 2015 – May 2016	Cohort, prosp.	99/163	57	69/99 (69.7 %)	Mean 17.5 (range 10–40)	Right colon: 159/163 (97.5 %) Left colon: 4/163 (2.4 %)	SSL: 163 (100 %)	N/A
Li 2020 [20] China	Jul 2017 – Mar 2019	Single center, prosp.	132/252	51.8 (range 18–75)	59/132 (44.7 %)	Mean 12.0 (SD 3.36) 6–10 mm: 87 11–15 mm: 123 16–20 mm: 42	Right colon: 133/252 (52.8 %) Left colon: 119/252 (47.2 %)	Adenoma: 232/252 (92.1 %) SSL: 19/252 (7.5 %) Adenocarcinoma: 1/252 (0.4 %)	Ip: 48/252 (19.0 %) Isp: 81/252 (32.1 %) Is: 90/252 (35.7 %) IIa: 33/252 (13.1 %)
Mangira 2020 [21] Australia	Jan 2016 – Dec 2017	Cohort, retrosp.	186/204	68 (range 21–91)	123/186 (66.1 %)	Mean 25.5	Right colon: 189/204 (92.6 %) Left colon: 15/204 (7.4 %)	Adenomas: 67/204 (32.8 %) SSL: 134/204 (65.7 %)	Is: 3/164 (1.8 %) IIa: 134/164 (81.7 %) IIa + IIb: 9/164 (5.5 %) IIb: 13/164 (7.9 %) N/A: 5/164 (3.0 %)
Shimodate 2020 [24] Japan	Nov 2017 – Sep 2019	RCT	97/97	68	NI	Median 5	Right colon: 50/97 (51.5 %) Left colon: 47/97 (48.5 %)	Adenoma: 92/97 (94.8 %) SSL: 2/97 (2.1 %)	N/A

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▶ **Table 1** (Continuation)

First author Year [ref] Country	Study period	Study design	No. of patients/ polyps	Age, years	Female sex, n/N (%)	Lesion size, mm	Lesion location	Lesion histology, n/N (%)	Shape characteristics, n/N (%)[1]
van Hattem 2021 [6] Australia	Apr 2016 – Jan 2020	Multicenter, retrosp.	121/156	60 (range 50–72)	85/121 (70.2 %)	Median 25 (range 20–30) <25 mm: 65 25–34 mm: 64 >35 mm: 27	Right colon: 146/156 (93.6 %) Left colon: 10/156 (6.4 %)	SSL: 156 (100 %)	N/A
Yabuuchi 2020 [7] Japan	Mar 2018 – Dec 2018	Observational study, prosp.	72/80	68.5 (IQR 63–75)	25/72 (34.7 %)	Median 12 (IQR 11–12)	Right colon: 51/80 (63.8 %) Left colon: 29/80 (36.3 %)	Adenoma: 70/80 (87.5 %) Adenocarcinoma: 10/80 (12.5 %)	0-IIa: 45/80 (56.3 %) 0-IIa + Is: 2/80 (2.5 %) 0-Is: 24/80 (30.0 %) 0-Isp: 9/80 (11.3 %)
McWhinney 2021 [9] USA	Feb 2016 – Dec 2019	Retrosp.	312/566	62.5 (SD10.5)	218/312 (69.9 %)	Mean 17.2 (SD 6.5)	Right colon: 500/566 (88.3 %) Left colon: 66/566 (11.7 %)	Adenoma: 8/566 (1.4 %) SSL: 522/566 (92.2 %)	N/A
Song 2021 [25] USA	Sep 2018 – Apr 2019	Single center, prosp.	27/50	67.50 (SD 7.38)	3/58 (5.2 %)	Mean 6.5 (SD 1.36)	Right colon: 24/50 (48.0 %) Left colon: 26/50 (52.0 %)	Adenoma: 42/50 (84.0 %) SSL: 5/50 (10.0 %) Others: 3/50 (6.0 %)	Is, Isp, Ip: 30/50 (60.0 %) IIa: 20/50 (40.0 %)
Suresh 2021 [10] USA	Jan 2015 – Jul 2019	Single center, retrosp.	310/310	66.5 (range 41–90)	154/310 (49.7 %)	Mean 29.4 (range 20–80)	Right colon: 256/310 (82.6 %) Left colon: 54/310 (17.4 %)	Adenoma: 249/310 (80.3 %) SSL: 60/310 (19.4 %) Adenocarcinoma: 1/310 (0.3 %)	N/A
Guo 2022 [19] China	Jan 2017 – Dec 2019	Single center, retrosp.	162/201	60.12 (SD 10.7)	48/162 (29.6 %)	Mean 6.58 (SD 0.85)	Right colon: 73/201 (36.3 %) Left colon:128/201 (63.7 %)	Adenoma: 182/201 (90.5 %) Inflammatory: 6/201 (3.0 %) Proliferative: 9/201 (4.5 %) Hamartoma: 4/201 (2.0 %)	0-Ip: 14/201 (7.0 %) 0-Is: 96/201 (47.8 %) 0-Isp: 80/201 (39.8 %) 0-IIa: 11/201 (5.5 %)
Rex 2022 [8] USA	Aug 2018 – Mar 2021	Multicenter, RCT	63/82	65 (SD 8)	28/63 (44.4 %)	Mean 9.5 (SD 2.8)	Right colon: 62/82 (75.6 %) Left colon: 20/82 (24.4 %)	Adenoma: 61/82 (74.3 %) SSL: 19/82 (23.2 %) Hyperplastic: 2 /82 (2.4 %)	Is: 35/82 (42.7 %) II a: 47/82 (57.3 %)

▶ Table 1 (Continuation)

First author Year [ref] Country	Study period	Study design	No. of patients/ polyps	Age, years	Female sex, n/N (%)	Lesion size, mm	Lesion location	Lesion histology, n/N (%)	Shape characteristics, n/N (%)[1]
Kim 2023 [26] South Korea	Jan 2018 – Feb 2021	Multicenter, RCT	166/210	62.0 (SD11.1)	55/166 (33.1 %)	Mean 7.2 (SD 1.4) 6–8 mm: 169 (80.5 %) 9–10 mm: 41 (19.5 %)	Right colon: 117/210 (55.7 %) Left colon: 93/210 (44.3 %)	Adenoma: 202/210 (96.2 %) SSL: 5/210 (2.4 %) Adenocarcinoma: 3/210 (1.4 %)	N/A
Totals			1922/2592		943/1846 (51.1 %)		Right colon: 1910/2577 (74.1 %) Left colon: 667/2577 (25.9 %)	Adenoma: 1374/2525 (54.4 %) SSL: 1136/2525 (45.0 %) Adenocarcinoma: 15/2525 (0.6 %)	Protruded (Ip, Isp, Is): 548/907 (60.4 %) Superficially elevated (IIa, IIa + c, IIa + s, IIa + IIb): 346/907 (38.2 %) Flat (IIb, IIc, III): 13/907 (1.4 %)

EMR, endoscopic mucosal resection; IQR, interquartile range; N/A, not available; prosp., prospective; RCT, randomized controlled trial; retrosp., retrospective; SSL, sessile serrated lesion. [1]Paris classification.

Intraprocedural bleeding, delayed bleeding, perforation, and post-polypectomy syndrome

The pooled intraprocedural bleeding rate, reported in 14 studies, was 2.6 % (95 %CI 1.5 %–4.5 %, I^2 = 51 %) (▶ **Fig. 3a**), and the pooled delayed bleeding rate, reported in 13 studies, was 1.5 % (95 %CI 0.8 %–2.7 %, I^2 = 18 %) (▶ **Fig. 3b**). No perforation or post-polypectomy syndrome was reported in 13 studies and 11 studies, with estimated rates of 0.6 % (95 %CI 0.3 %–1.3 %, I^2 = 0 %) and 0.6 % (95 %CI 0.3 %–1.4 %, I^2 = 0 %), respectively (▶ **Fig. 3c,d**).

Technical success

The technical success for CS-EMR, reported in six studies, was 97.2 % (95 %CI 91.8 %–99.1 %, I^2 = 79 %) (▶ **Fig. 4a**). Three studies evaluated the technical success for polyps < 20 mm, and it was 93.2 % (95 %CI 83.0 %–97.5 %, I^2 = 76 %) (▶ **Fig. 4b**). Technical success for polyps ≥ 20 mm was reported to be 100 % in two studies by van Hattem et al. and Tutticci et al. [6, 11]. For SSLs, the technical success was reported in three studies and was 99.5 % (95 %CI 97.3 %–99.9 %, I^2 = 0 %) (▶ **Fig. 4c**).

Sensitivity analysis

Due to the substantial heterogeneity, sensitivity analysis was performed for recurrence rate using the “leave-one-out method” (**Fig. 1 s**).

Quality of studies and risk of bias

The quality of studies was assessed using the Newcastle–Ottawa Scale. A total of 14 studies were considered high quality, one medium, and one low quality. The detailed assessment of study quality is summarized in **Table 1 s**. The funnel plot showed asymmetry, suggesting publication bias (**Fig. 2 s**).

Discussion

This meta-analysis pooled data from studies that reported outcomes of CS-EMR for colon polyps. We found CS-EMR to be safe and effective in removing colon polyps, especially for smaller polyps and SSLs. CS-EMR was utilized equally on adenomas and SSLs, and was more commonly performed for polyps in the right colon and those with protruding morphology (Ip, Isp, Is). The technical success rate of CS-EMR was high at 97.2 %. In addition, the polyp recurrence rate following CS-EMR was 6.7 %. The recurrence rate was lower for SSLs compared with adenomas, and was higher for polyps ≥ 20 mm compared with polyps < 20 mm. The pooled intraprocedural bleeding rate was 2.6 %, and the pooled delayed bleeding rate was 1.5 %. There were no reports of perforation or post-polypectomy syndrome.

It is hypothesized that the lower rate of adverse events with CS-EMR is because electrocautery was not used [20]. The excellent safety profile of CS-EMR has been demonstrated in our meta-analysis, with no reports of post-polypectomy syndrome or perforations. Intraprocedural bleeding can be treated immediately during the procedure, thereby also reducing the risk of delayed post-polypectomy bleeding. In addition, our analysis demonstrated only a few instances of delayed bleeding follow-

▶ **Table 2** Characteristics of cold snare endoscopic mucosal resection.

First author, year	Injected solution	Snare used	Lesion size, mm	Piecemeal resection, n/N (%)	Mean, or median follow-up
Choksi 2015	Submucosal injection of 1:60 000 epinephrine in saline combined with methylene blue	Exacto snare (US Endoscopy, Mentor, OH, USA), Mini snare or Hexagonal snare (Cook Medical Inc., Bloomington, IN, USA)	20 (range 10–45)	N/A	N/A
Papastergiou 2018	Methylene blue tinted normal saline solution	Snaremaster snare (Olympus, Tokyo, Japan), Ascus-Snare, Captivator (Boston Scientific, Marlborough, MA, USA), Exacto snare (US Endoscopy, Mentor, OH, USA)	8.2 (SD 1.6)	0/83 (0 %)	N/A
Piraka et al. 2017	Dilute epinephrine mixed with saline and methylene blue or indigo carmine dye	Exacto snare (US Endoscopy, Mentor, OH, USA), Captivator snare (Boston Scientific, Marlborough, MA, USA), Hexagonal snare (Cook Medical Inc., Bloomington, IN, USA)	Mean 22.3 (range 12–60) < 20 mm: 35 > 20 mm: 37	94/94 (100 %)	2–10 months
Rameshshanker 2018	0.1 % hyaluronate and methylene blue	Exacto snare (US Endoscopy, Mentor, OH, USA)	Mean 15 (range 10–30)	29/29 (100 %)	9 months
Tutticci 2018	Succinylated gelatin and dilute methylene blue	Exacto (US Endoscopy, Belrose, Australia), Captivator II (Boston Scientific, Mascot, Australia), or AcuSnare (Cook Medical, Eight Mile Plains, Australia)	Mean 17.5 (range 10–40)	163/163 (100 %)	154 days
Li 2020	Mixed normal saline solution, epinephrine (1:100 000), and methylene blue	Captivator (Boston Scientific, Marlborough, MA, USA)	Mean 12.0 (SD 3.36) 6–10 mm: 87 11–15 mm: 123 16–20 mm: 42	41/252 (16.3 %)	N/A
Mangira 2020	Dilute methylene blue 121 or 0.4 % indigo carmine mixed with succinylated gelatin 10	Exacto snare (US Endoscopy, Mentor, OH, USA) or SnareMaster Plus (Olympus, Tokyo, Japan)	Mean 25.5	204/204 (100 %)	Median 150 days for SC1. Median 18 months for SC2
Shimodate 2020	Normal saline solution mixed with indigo carmine (0.04 %) and epinephrine (1:10 000)	Exacto snare (US Endoscopy, Mentor, OH, USA) or SnareMaster Plus (Olympus, Tokyo, Japan)	Median 5	0/97 (0 %)	N/A
van Hattem 2021	Succinylated gelatin w 0.4 % indigo carmine and 1:100 000 epinephrine	Captivator (Boston Scientific, Marlborough, MA, USA), TeleMed, Hexagonal, Exacto snare (US Endoscopy, Mentor, OH, USA), AcuSnare mini hexagonal (Cook Medical, Bloomington, IN, USA)	Median 25 (range 20–30) < 25 mm: 65 25–34 mm: 64 > 35 mm: 27	156/156 (100 %)	SC1 (6 months): 92/96 (95.8 %) SC2 (18 months): 51/59 (86.5 %)
Yabuuchi 2020	Indigo carmine-tinged glycerol solution	SnareMaster Plus (Olympus, Tokyo, Japan)	Median 12 (IQR 11–12)	3/80 (3.8 %)	28 days
McWhinney 2021	Hydroxyethyl starch mixed with a contrast agent (indigo carmine or methylene blue) or Eleview (Aries Pharmaceutical, San Diego, CA, USA)	Exacto snare (US Endoscopy, Mentor, OH, USA) and Captivator (Boston Scientific, Marlborough, MA, USA)	Mean 17.2 (SD 6.5)	566/566 (100 %)	Median 12.4 months
Song 2021	Saline-containing injection of indigo carmine	Exacto snare (US Endoscopy, Mentor, OH, USA)	Mean 6.5 (SD 1.36)	2/50 (4.0 %)	N/A

▶ **Table 2** (Continuation)

First author, year	Injected solution	Snare used	Lesion size, mm	Piecemeal resection, n/N (%)	Mean, or median follow-up
Suresh 2021	Dilute epinephrine in normal saline with either methylene blue or indigo carmine	10 mm thin and stiff snare (no information on the manufacturer)	29.4 (range 20–80)	310/310 (100 %)	3–6 months
Guo 2022	Submucosal injection with normal saline	N/A	Mean 6.58 (SD 0.85)	N/A	N/A
Rex 2022	N/A	Captivator (Boston Scientific, Marlborough, MA, USA) or Exacto snare (Steris Corporation, Mentor, OH, USA)	Mean 9.5 (SD 2.8)	31/82 (37.8 %)	N/A
Kim 2023	Normal saline solution mixed with indigo carmine (0.04 %) and epinephrine (1:10 000)	Traditional oval snare (SGO-1622S; Endo-Therapeutics, Seoul, Korea)	Mean 7.2 (SD:1.4) 6–8 mm: 169 (80.5 %) 9–10 mm: 41 (19.5 %)	N/A	N/A

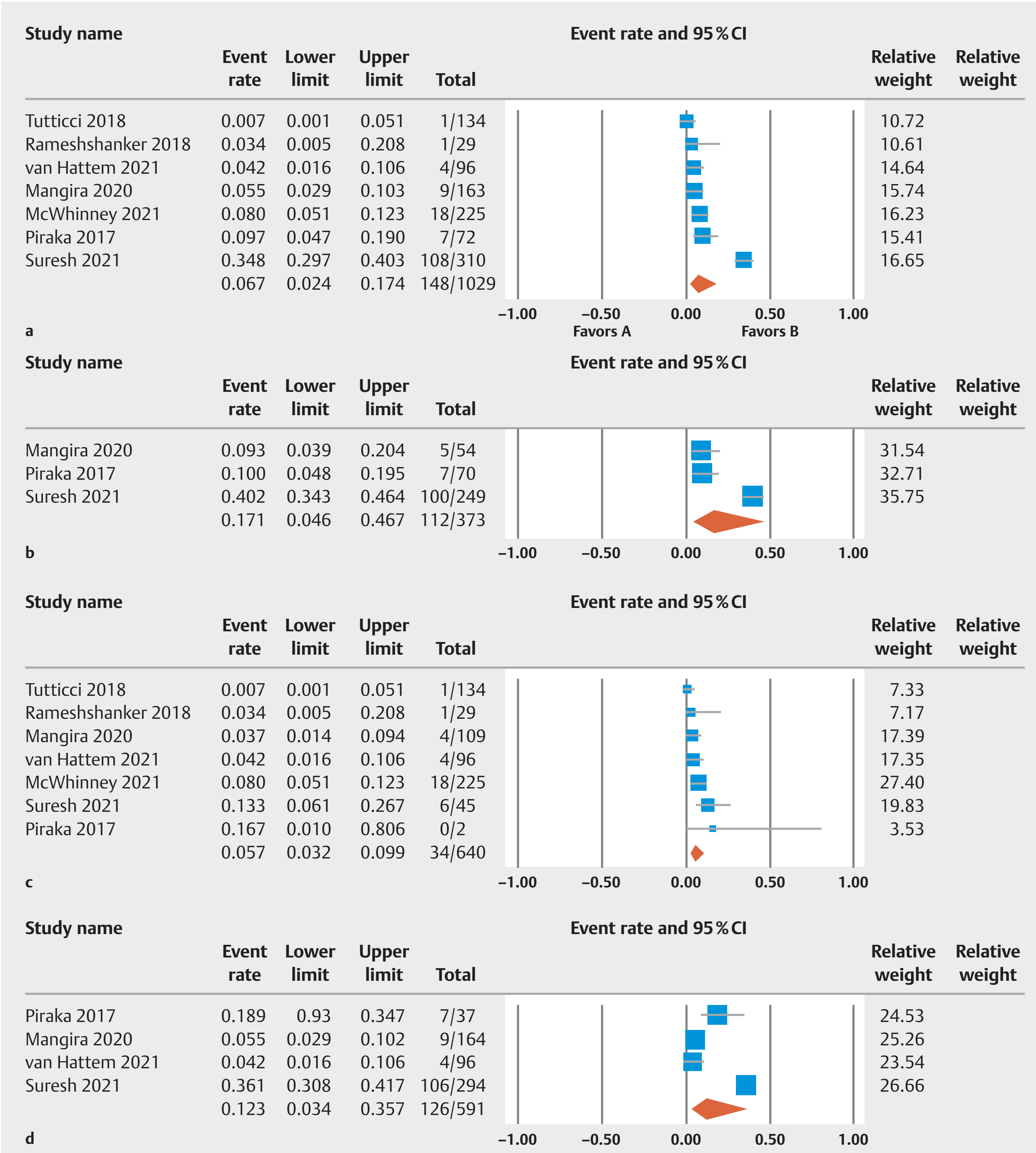
IQR, interquartile range; N/A, not available; SC1, first surveillance colonoscopy; SC2, second surveillance colonoscopy.

ing CS-EMR, which further validates the safety of CS-EMR. These findings have also been shown in several studies and meta-analyses comparing different polypectomy techniques, such as hot snare polypectomy, EMR, cold snare polypectomy, and CS-EMR [27, 28]. However, more data are needed to evaluate the safety of CS-EMR in patients at higher risk for bleeding, such as patients on antiplatelet or anticoagulation therapy.

In addition to an excellent safety profile, some studies have shown that CS-EMR was associated with shorter procedure time, shorter inpatient stay, and lower cost than conventional EMR [19, 20,29]. The main question that arises with the widespread adoption of CS-EMR is the recurrence rate. Our analysis found the pooled polyp recurrence rate to be 6.7 % (95 %CI 2.4 %–17.4 %, I^2 = 94 %). The recurrence rate for SSLs was 5.7 % (95 %CI 3.2 %–9.9 %, I^2 = 50 %) in our analysis. Despite the reported acceptable efficacy of CS-EMR, especially for SSLs [6, 9, 11, 23], other studies have shown a high recurrence rate with CS-EMR [10]. For example, Suresh et al. reported a recurrence rate as high as 34.8 % following CS-EMR of 310 polyps [10]. For polyps ≥ 20 mm in our study, the recurrence rate was 12.3 % (95 %CI 3.4 %–35.7 %, I^2 = 94.9 %), and it was 17.1 % (95 %CI 4.6 %–46.7 %, I^2 = 93 %) for adenomas. In the study by Suresh et al., all resected polyps were ≥ 20 mm, and most of the recurrences occurred in adenomatous polyps. Multivariate analysis demonstrated that risk factors for recurrence included older age, large polyp size, and advanced polyp histology, including tubulovillous adenoma or high grade dysplasia [10]. Although Suresh et al. reported this high recurrence rate, all the other included studies in our meta-analysis reported a recurrence rate well below 10 % [10]. Therefore, more studies are required to support or refute the high recurrence rate.

The limitations of our study are those inherent to a meta-analysis. The study heterogeneity was high. We hypothesize that heterogeneity in the study outcomes was due to the difference in resection techniques, study population, polyp size and characteristics, and experience of the participating endoscopists. Given this heterogeneity, we conducted subgroup analyses based on histology and size of the resected lesions. In addition, we performed a sensitivity analysis. However, heterogeneity remained in these additional analyses and still limits the generalizability of the results of this review. In addition, a wide variation was noted in the type of snares and submucosal injectates used, as well as in the resection technique. Furthermore, adoption of the CS-EMR technique is influenced by institution, volume, and endoscopists' experience. Few studies in our meta-analysis included polyps < 10 mm, which are typically resected using cold snare polypectomy. The dissimilarity in the research methodologies, along with the incongruities in the proportion of studies conducted prospectively versus retrospectively and the inclusion of both single-center and multicenter studies in the review, collectively contribute to the heterogeneity observed between the studies. We also found evidence of publication bias. Owing to the limited number of studies and the high likelihood of selection bias introduced by the inclusion of non-randomized studies, we could not compare cold and hot snare EMR. Despite these limitations, a strength of the study is that we were able to conduct a meta-analysis of multiple studies to increase the sample size and produce a high level of evidence for an important clinical question [2, 20–22]. Moreover, we conducted subgroup analyses to evaluate the efficacy of CS-EMR with regard to polyp size and histology, which provides endoscopists with valuable information on the most appropriate resection technique for managing colon polyps.

In conclusion, the data from this systematic review and meta-analysis of the literature demonstrate that CS-EMR is an effective technique for managing colon polyps in selected pa-

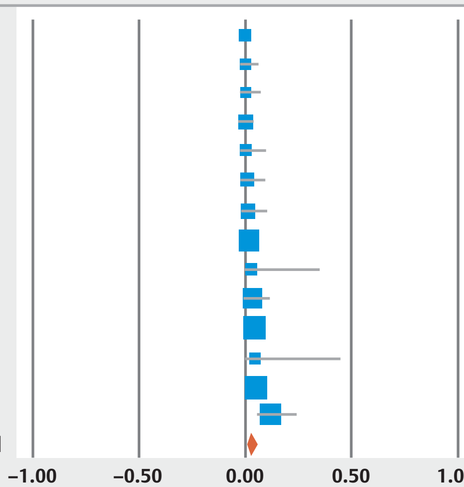


▶ **Fig. 2** Forest plots for the recurrence rate after cold snare endoscopic mucosal resection for different colon polyps. **a** All polyps. **b** Adenomas. **c** Sessile serrated lesions. **d** Polyps ≥ 20 mm.

tients. Our analysis showed that CS-EMR has an excellent safety profile and variable recurrence rates based on polyp size and histology. Patients with a higher risk of developing adverse events from resection of large polyps, such as patients on anti-coagulation/antiplatelet therapy, may benefit from CS-EMR [30]. There is a need for prospective, large, randomized controlled trials to better evaluate the efficacy of CS-EMR, especially for adenomas and for polyps ≥ 20 mm. In addition, studies are needed to compare CS-EMR with other endoscopic resection techniques, such as hot snare EMR and underwater EMR.

Study name	Event rate	Lower limit	Upper limit	Total	Relative weight	Relative weight
McWhinney 2021	0.002	0.000	0.025	0/312	3.42	
van Hattem 2021	0.004	0.000	0.062	0/121	3.41	
Shimodate 2020	0.005	0.000	0.076	0/97	3.41	
Tutticci 2018	0.006	0.001	0.042	1/163	5.71	
Yabuuchi 2020	0.007	0.000	0.100	0/72	3.40	
Piraka 2017	0.014	0.002	0.091	1/73	5.68	
Rex 2022	0.016	0.002	0.104	1/63	5.67	
Mangira 2020	0.022	0.008	0.056	4/186	11.55	
Choksi 2015	0.022	0.008	0.350	0/15	3.33	
Papastergiou 2018	0.039	0.013	0.114	3/77	10.27	
Kim 2023	0.043	0.022	0.080	9/210	14.26	
Rameshshanker 2018	0.045	0.003	0.448	0/10	3.29	
Guo 2022	0.049	0.025	0.096	8/162	13.90	
Song 2021	0.120	0.055	0.242	6/50	12.70	
	0.026	0.015	0.045	33/1611		

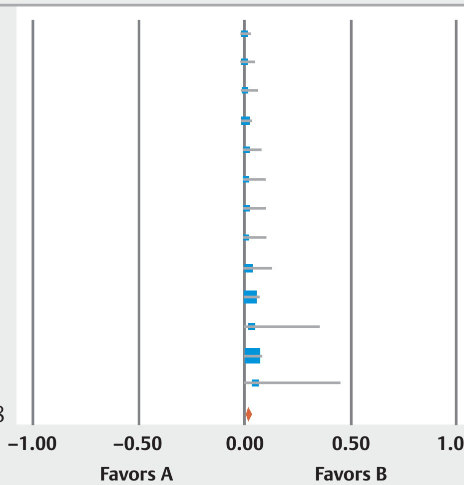
Event rate and 95 % CI



a

Study name	Event rate	Lower limit	Upper limit	Total	Relative weight	Relative weight
McWhinney 2021	0.002	0.000	0.025	0/312	4.21	
Tutticci 2018	0.003	0.000	0.047	0/163	4.20	
van Hattem 2021	0.004	0.000	0.062	0/121	4.20	
Kim 2023	0.005	0.001	0.033	1/210	7.70	
Shimodate 2020	0.005	0.000	0.076	0/97	4.19	
Papastergiou 2018	0.006	0.000	0.094	0/77	4.19	
Piraka 2017	0.007	0.000	0.099	0/73	4.19	
Yabuuchi 2020	0.007	0.000	0.100	0/72	4.19	
Song 2021	0.020	0.003	0.129	1/50	7.60	
Guo 2022	0.025	0.009	0.064	4/162	20.41	
Choksi 2015	0.031	0.002	0.350	0/15	4.09	
Mangira 2020	0.038	0.018	0.077	7/186	26.78	
Rameshshanker 2018	0.045	0.003	0.448	0/10	4.04	
	0.015	0.008	0.027	13/1548		

Event rate and 95 % CI



b

▶ **Fig. 3** Forest plots for adverse events of cold snare endoscopic mucosal resection for colon polyps. **a** Intraprocedural bleeding. **b** Delayed bleeding.

Competing Interests

The authors declare that they have no conflict of interest.

References

[1] Kwok K, Tran T, Lew D. Polypectomy for large polyps with endoscopic mucosal resection. Gastrointest Endosc Clin N Am 2022; 32: 259–276

[2] Papastergiou V, Paraskeva KD, Fragaki M et al. Cold versus hot endoscopic mucosal resection for nonpedunculated colorectal polyps sized 6–10 mm: a randomized trial. Endoscopy 2018; 50: 403–411

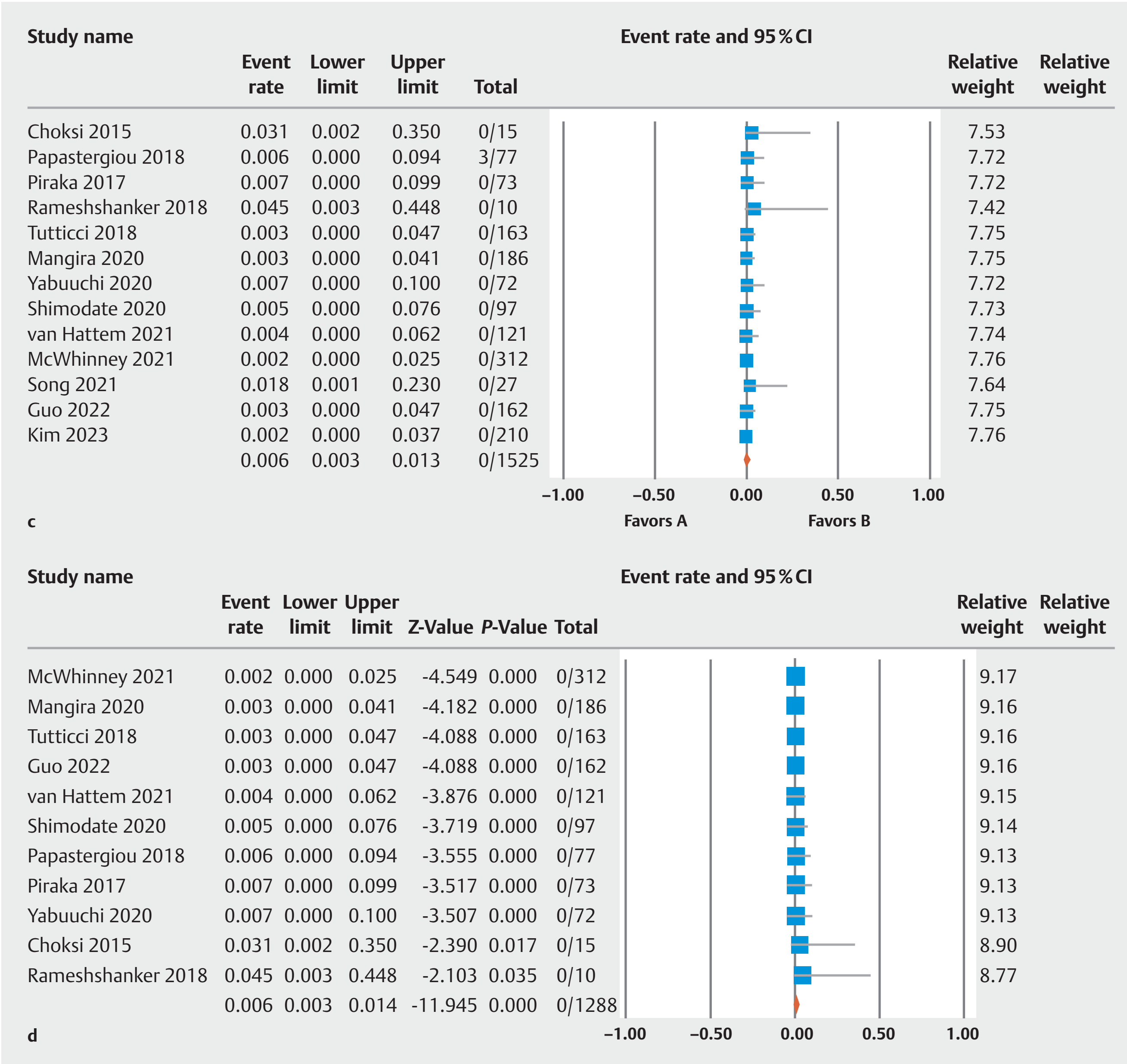
[3] Kaltenbach T, Anderson JC, Burke CA et al. Endoscopic removal of colorectal lesions – recommendations by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020; 158: 1095–1129

[4] Shaukat A, Kaltenbach T, Dominitz JA et al. Endoscopic recognition and management strategies for malignant colorectal polyps: recommendations of the US Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc 2020; 92: 997–1015.e1

[5] Yamashina T, Fukuhara M, Maruo T et al. Cold snare polypectomy reduced delayed postpolypectomy bleeding compared with conventional hot polypectomy: a propensity score-matching analysis. Endosc Int Open 2017; 5: E587–e94

[6] van Hattem WA, 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 2021; 70: 1691–1697

[7] Yabuuchi Y, Imai K, Hotta K et al. Efficacy and safety of cold-snare endoscopic mucosal resection for colorectal adenomas 10 to 14 mm



▶ **Fig. 3** Forest plots for adverse events of cold snare endoscopic mucosal resection for colon polyps. **c** Perforation. **d** Post-polypectomy bleeding. *Kim 2023, Song 2021, and Tutticci 2018 reported events per polyps.

in size: a prospective observational study. Gastrointest Endosc 2020; 92: 1239–1246

[8] Rex DK, Anderson JC, Pohl H et al. Cold versus hot snare resection with or without submucosal injection of 6- to 15-mm colorectal polyps: a randomized controlled trial. Gastrointest Endosc 2022; 96: 330–338

[9] McWhinney CD, Vemulapalli KC, El Rahyel A et al. Adverse events and residual lesion rate after cold endoscopic mucosal resection of serrated lesions ≥10 mm. Gastrointest Endosc 2021; 93: 654–659

[10] Suresh S, Zhang J, Ahmed A et al. Risk factors associated with adenoma recurrence following cold snare endoscopic mucosal resection of polyps ≥ 20 mm: a retrospective chart review. Endosc Int Open 2021; 9: E867–e73

[11] Tutticci NJ, Hewett DG. Cold EMR of large sessile serrated polyps at colonoscopy (with video). Gastrointest Endosc 2018; 87: 837–842

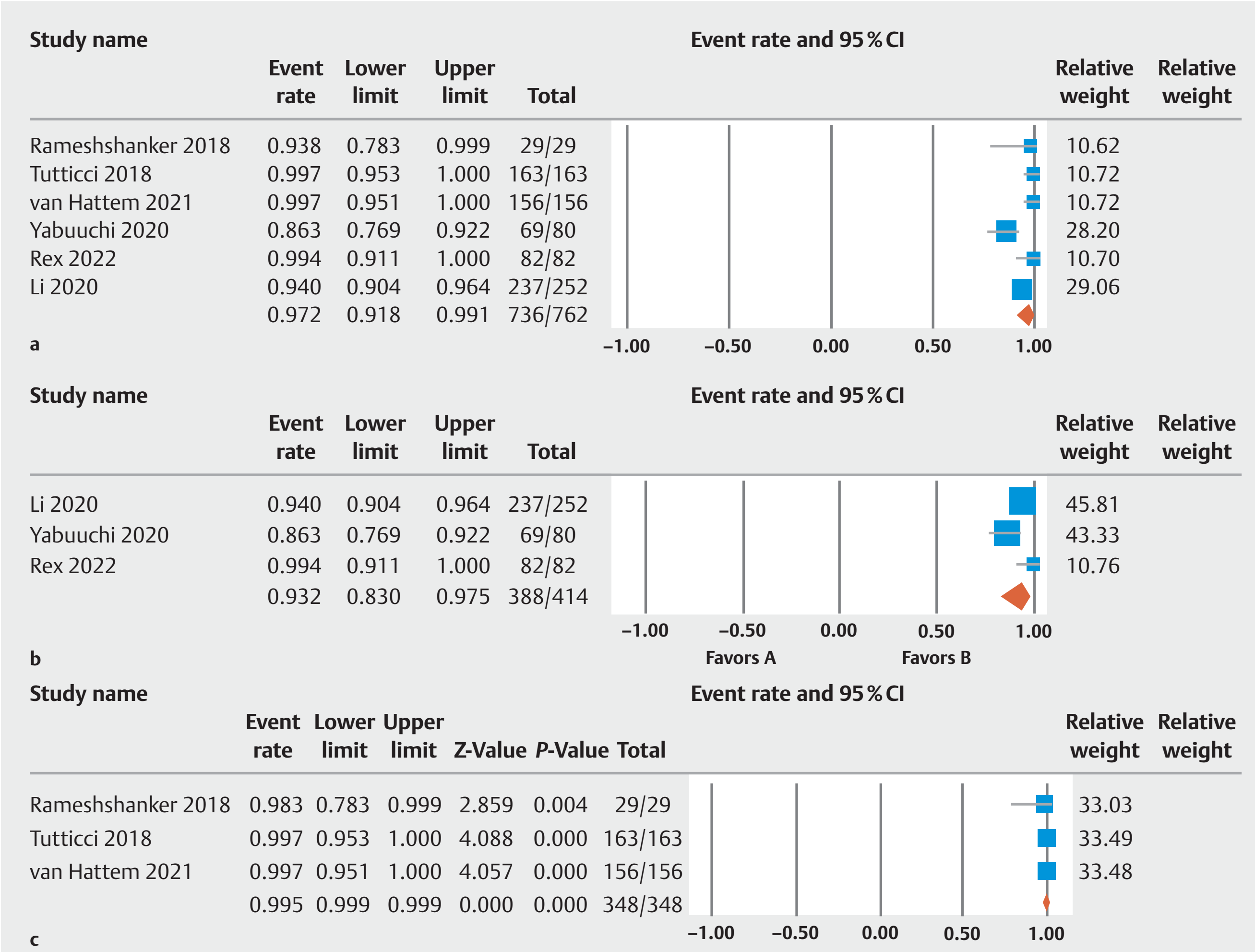
[12] Moher D, Liberati A, Tetzlaff J et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009; 62: 1006–1012

[13] Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71

[14] The Paris endoscopic classification of superficial neoplastic lesions. esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58: (Suppl. 06): S3–43

[15] Stang A. Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010; 25: 603–605

[16] Higgins JP, Thompson SG, Deeks JJ et al. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557–560



► **Fig. 4** Forest plots for the technical success rate of cold snare endoscopic mucosal resection for different colon polyps. **a** All polyps. **b** Polyps < 20 mm. **c** Sessile serrated lesions (SSLs).

[17] Lau J, Ioannidis JP, Terrin N et al. The case of the misleading funnel plot. BMJ 2006; 333: 597–600

[18] Choksi N, Elmunzer BJ, Stidham RW et al. Cold snare piecemeal resection of colonic and duodenal polyps ≥1 cm. Endosc Int Open 2015; 3: E508–513

[19] Guo Y, Li HM, Zhu WQ. Cold or hot snare with endoscopic mucosal resection for 6–9 mm colorectal polyps: a propensity score matching analysis. J Laparoendosc Adv Surg Tech A 2022; 32: 158–164

[20] Li D, Wang W, Xie J et al. Efficacy and safety of three different endoscopic methods in treatment of 6–20 mm colorectal polyps. Scand J Gastroenterol 2020; 55: 362–370

[21] Mangira D, Cameron K, Simons K et al. Cold snare piecemeal EMR of large sessile colonic polyps ≥20 mm (with video). Gastrointest Endosc 2020; 91: 1343–1352

[22] Piraka C, Saeed A, Waljee AK et al. Cold snare polypectomy for non-pedunculated colon polyps greater than 1 cm. Endosc Int Open 2017; 5: E184–e9

[23] Rameshshanker R, Tsiamoulos Z, Latchford A et al. Resection of large sessile serrated polyps by cold piecemeal endoscopic mucosal resection: Serrated COld Piecemeal Endoscopic mucosal resection (SCOPE). Endoscopy 2018; 50: E165–e7

[24] Shimodate Y, Itakura J, Takayama H et al. Impact of submucosal saline solution injection for cold snare polypectomy of small colorectal polyps: a randomized controlled study. Gastrointest Endosc 2020; 92: 715–722.e1

[25] Song JH, Friedland S. Is submucosal injection helpful in cold snare polypectomy for small colorectal polyps? Clin Endosc 2021; 54: 397–403

[26] Kim MJ, Na SY, Kim JS et al. Cold snare polypectomy versus cold endoscopic mucosal resection for small colorectal polyps: a multicenter randomized controlled trial. Surg Endosc 2023; 37: 3789–3795

[27] Yuan X, Gao H, Liu C et al. Effectiveness and safety of the different endoscopic resection methods for 10- to 20-mm nonpedunculated colorectal polyps: a systematic review and pooled analysis. Saudi J Gastroenterol 2021; 27: 331–341

[28] Thoguluva Chandrasekar V, Spadaccini M, Aziz M et al. Cold snare endoscopic resection of nonpedunculated colorectal polyps larger than 10 mm: a systematic review and pooled-analysis. Gastrointest Endosc 2019; 89: 929–936.e3

[29] Mehta D, Loutfy AH, Kushnir VM et al. Cold versus hot endoscopic mucosal resection for large sessile colon polyps: a cost-effectiveness analysis. Endoscopy 2022; 54: 367–375

[30] McDonald N, Chandan S, Bilal M. Colonoscopic polypectomy in patients on anticoagulation: time to embrace the cold revolution? Gut 2022; 71: 653

