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Snare tip soft coagulation (STSC) after endoscopic mucosal resection (EMR) of large (>20 mm) non pedunculated colorectal polyps: a systematic review and meta-analysis

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ABSTRACT

Background and study aims Endoscopic mucosal resection (EMR) of laterally spreading tumors (LSTs) >20 mm in size can be challenging. Piecemeal EMR of these lesions results in high rates of adenoma recurrence at first surveillance colonoscopy (SC1). Snare tip soft coagulation (STSC) of post resection margins is a safe and effective technique to prevent adenoma recurrence. We conducted a systematic review and meta-analysis to evaluate the effectiveness and safety of this technique.

Patients and methods Multiple databases were searched through April 2021 for studies that reported on outcomes of post EMR STSC for LSTs >20 mm in size. Meta-analysis was performed to determine pooled odds of adenoma recurrence as well as pooled proportion of adverse events including intraprocedural and delayed bleeding as well as intraprocedural perforation events.

Results Six studies including two randomized controlled trials (RCT) and four cohort studies with 2122 patients were included in the final analysis. Overall pooled odds of adenoma recurrence at SC1 with post EMR STSC compared to no STSC was 0.27 (95 % 0.18–0.42; I2 = 0 %), P < 0.001. Pooled rate of adenoma recurrence at SC1 in post EMR STSC cohort was 6 %. Rates of intraprocedural bleeding, delayed bleeding and intraprocedural perforation were 10.3 %, 6.5 % and 2 % respectively.

Conclusions Our results show that thermal ablation of resection margins with STSC in LSTs >20 mm is a safe and effective technique in reducing the incidence of adenoma recurrence.

Introduction

Colorectal cancer (CRC) is the third most common cause of cancer worldwide and the third leading cause of cancer deaths in Western countries [1]. Colonoscopy remains a commonly performed screening test for CRC as it has both diagnostic and therapeutic capabilities. It is estimated that endoscopic removal of adenomatous polyps can reduce CRC-related mortality by more than 50 % [2]. Most polyps are small (< 10 mm) and easily managed with conventional polypectomy techniques such cold snare excision [3, 4]. A subset of colorectal lesions, termed as laterally spreading tumors (LSTs) are non-protruding lesions, >10 mm in size, that spread laterally and circumferentially instead of vertically along the colonic wall. These account for 3 % to 5 % of polyps detected by colonoscopy and in comparison, with small polyps, large LSTs (> 20 mm), particularly non-granular type, have a much greater risk of submucosal invasive cancer [5, 6].

Endoscopic mucosal resection (EMR) is the preferred treatment method for large (20 mm) non-pedunculated colorectal lesions with low risk of severe adverse events (1 %) and low rates of local recurrence (14 %) [7–9]. While en-bloc resection of large LSTs can be challenging, piecemeal resection of these lesions has been shown to be significantly associated with recurrent disease at first surveillance colonoscopy (SC1) [10]. Endoscopic submucosal dissection (ESD) may overcome this problem, allowing dissection of larger lesions in one piece. However, the procedure is technically difficult, time-consuming, associated with hospital admission and has an increased risk of complications such bleeding or perforation [11]. A recent review evaluating the efficacy of EMR and ESD for LSTs noted that overall polyp recurrence occurred more frequently with EMR (12.6%) compared to ESD (1.1 %). While the majority of recurrences were amenable to successful endoscopic treatment, timing of endoscopic surveillance was heterogeneous between the studies, which may have affected the rate of early recurrence [12].

The US Multi-Society Task Force on Colorectal Cancer recommends against use of ablative techniques such snare tip soft coagulation (STSC) or argon plasma coagulation (APC) on endoscopically visible residual tissue of a lesion, as this has been associated with an increased risk of recurrence. Based on moderate-quality evidence, use of adjuvant thermal ablation of the post-EMR margin, where no endoscopically visible adenoma exists, is conditionally recommended [3]. There is, however, insufficient evidence to recommend a specific modality (ie, APC or STSC).

Thermal ablation using STSC is a novel approach with promising results, allowing operator-controlled applications with controlled depth of coagulation. We conducted a systematic review and meta-analysis to evaluate the effectiveness and safety of STSC after EMR of large (> 20 mm) colorectal polyps.

Patients and methods

Search strategy

The published English literature was searched by an experienced librarian and two other individuals, SC and SD, for studies that reported on post EMR STSC in colorectal lesions. A comprehensive search of several databases from inception to April 2021 was performed. The databases included ClinicalTrials.gov, Ovid EBM Reviews, Ovid Embase (1974 +), Ovid Medline (1946 + including epub ahead of print, in-process & other non-indexed citations), Scopus (1970 +) and Web of Science (1975 +). Manual search for studies of interest was performed by two authors (SC, BPM). Controlled vocabulary supplemented with keywords was used to search for studies of interest. The search strategies were created using a combination of keywords and standardized index terms. Keywords included “endoscopic mucosal resection”, “EMR”, “colorectal lesions” and “snare tip soft coagulation” along with phrases associated with the procedure such as “colonoscopy”. Results were limited to English language. All results were exported to Endnote where 24 obvious duplicates were removed leaving 49 citations. Details of study selection are provided in PRISMA Flow Chart – **Supplementary Fig. 1**. The full search strategy is available in **Supplementary Appendix-1**. The MOOSE checklist was followed and is provided as **Supplementary Appendix-2**. Reference lists of evaluated studies were examined to identify other studies of interest.

Study selection

In this meta-analysis, we included all randomized clinical trials (RCTs) and retrospective/prospective cohort studies where outcomes of performing STSC after EMR of LST > 20 mm were reported, either by itself or in comparison to no STSC or other thermal ablation technique such as Argon Plasma Coagulation (APC). Studies were included irrespective of inpatient/outpatient setting, follow-up time, geography and whether published as full manuscripts or abstracts, as long as they provided the clinical outcomes data needed for the analysis.

Our exclusion criteria were as follows: (1) studies reporting outcomes of STSC for non-colonic lesions (2) studies that reported alternative post-EMR ablation techniques such as APC (3) studies performed in the pediatric population (age < 18 years), and (4) studies not published in English language. In cases of multiple publications from a single research group reporting on the same patient, same cohort and/or overlapping cohorts, data from the most recent and/or most appropriate comprehensive report were retained. Additionally, authors were contacted via email to clarify if patient cohort overlap was present or not. The retained studies were then decided by two authors (SC, BPM) based on the publication timing (most recent) and/ or the sample size of the study (largest).

Data abstraction and quality assessment

Data on study-related outcomes from the individual studies were abstracted independently onto a standardized form by at least two authors (SC, DR). Author SD cross-verified the collected data for possible errors and two authors (SC, BPM) did the quality scoring independently [13]. The quality of evidence

presented in the RCTs and risk of bias in all included studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. (**Supplementary Fig. 2**). [13] The Newcastle-Ottawa scale for cohort studies was used to assess the quality of other studies [14]. This quality score consisted of 8 questions, the details of which are provided in **Supplementary Table 1**.

Outcomes assessed

Main Outcomes

The main outcomes addressed wree pooled odds of adenoma recurrence at SC1 after post EMR STSC compared to no STSC and pooled rate of adenoma recurrence at SC1 after post EMR STSC

Supplementary outcomes

The supplementary outcomes were as follows:

1. Pooled incidence of intraprocedural bleeding (IPB) after STSC – defined as bleeding that persisting for 30 seconds and requiring endoscopic control, achieved with snare tip soft coagulation (STSC) or coagulation graspers, [15] or mechanical hemostasis [16] or as oozing or spurting of blood persisting for longer than 60 s and not responding to water jet irrigation [17]
2. Pooled incidence of delayed bleeding (DB) after STSC – defined as any bleeding which occurred after the procedure and required emergency room presentation, hospitalization, or re-intervention (endoscopy, angiography, surgery) within 14 days [15, 16] or passage of fresh blood per rectum within the following 2 weeks after the procedure [18].
3. Pooled incidence of intra-procedural perforation events after STSC – defined as incidence of target sign or actual hole in the colonic wall (types III–V deep mural injury as per the Sydney Classification of Deep Mural Injury) [15, 16]. or presence of free air on plain abdominal film and/or abdominal computed tomography scan with associated abdominal pain, leukocytosis and elevated C-reactive protein [18].
4. Pooled incidence of post polypectomy syndrome after STSC – defined as transmural thermal injury with resultant serosal inflammation characterized by localized abdominal pain, leukocytosis and occasionally fever [18].

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates and 95 % CIs (confidence intervals) in each case following the methods suggested by DerSimonian and Laird using the random-effects model [19]. When the incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis [20]. The Mantel-Haenszel-type method was used to estimate the pooled odds ratio (OR) for all outcomes [21]. Heterogeneity between studies was assessed by means of a χ^2 test (Cochran Q statistic) and quantified with the I^2 statistic. In this, values of <30 %, 30 %–60 %, 61 %–75 %, and >75 % were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively. Publication bias was ascertained, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test [22]. When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie's 'Trim and Fill' test was used to ascertain the impact of the bias [23]. $P<0.05$ was used 'a-priori' to define significance between the groups compared. All analyses were performed using RevMan version 5 from the Cochrane collaboration (the Cochrane Collaboration, Copenhagen, Denmark) and OpenMeta [Analyst] software [24].

Results

Search results and population characteristics

From an initial pool of 73 studies, 49 records were screened after reduplication, 21 full-length articles were assessed. Six studies including two RCTs, [15, 25] and four cohort studies [16–18, 26] with 2122 patients were included in the final analysis. In four studies, STSC post EMR was compared to EMR without STSC [15, 17, 25, 26], whereas STSC was compared to APC in another study [18]. There were a total of 1096 men and 1026 women in our analysis. Mean age ranged from 64.1 to 67.3 years. Further details along with population characteristics as well as further details like the polyp size, location and histology are described in ▶ **Table 1** and ▶ **Table 2**.

Characteristics and quality of included studies

Three of the included studies were retrospective [17, 18, 26] and the others were prospective in design. Two studies included in our analysis were only published as abstracts, but data on outcomes was clearly reported [25, 26]. Three studies originated from USA, one from Greece and two from Australia. Both studies from Australia were multicenter prospective trials with different study periods i. e. July 2013 – May 2016 [15] and May 2016 – August 2020 [16]. There was no overlap of patient cohorts in these studies as confirmed by the study authors. Based on Newcastle-Ottawa scale, all cohort studies were considered high quality.

Meta-analysis outcomes

Main and supplementary outcomes as mentioned below, were calculated at SC1 for patient cohorts that underwent EMR with STSC and those without STSC. Additionally, individual outcomes in patients undergoing post EMR STSC were calculated.

Main outcomes

The overall pooled odds of adenoma recurrence at SC1 with post EMR STSC compared to no STSC was 0.27 (95 % 0.18–0.42; $I^2=0$ %), $P<0.001$ (▶ **Fig. 1**). The overall pooled rate of adenoma recurrence at SC1 in post EMR STSC cohort was 6 % (95 % CI 2.6–9.4; $I^2=78.7$ %) (▶ **Fig. 2**).

Supplementary Outcomes

The overall pooled incidence of intraprocedural bleeding after STSC was 10.3 % (95 % CI 3.3–17.4; $I^2=93.3$ %) (**Supplementary Fig. 3**). The overall pooled incidence of delayed bleeding after STSC was 6.5 % (95 % CI 5.2–7.8; $I^2=0$ %) (**Supplementary Fig. 4**). The overall pooled incidence of perforation events after

▶ **Table 1** Study details and population characteristics.

Study	Design	Morphology/size	Patients		Age ± SD (Range)		Male/female		Polyp size mean (SD); median (range)	
			STSC	Others	STSC	Others	STSC	Others	STSC	Others
Kandel 2019	Retrospective, single center, November 1, 2016, to November 30, 2017, USA	NR/ >20 mm	60	60 (No STSC)	66 (49–81)	65 (45–83)	25/35	31/29	28 ± 11; 25 (20–60)	28 ± 11; 25 (20–60)
Katsinelos 2019	Retrospective, Single center, January 2006 and December 2014, Greece	LST/ >20 mm	51	50 (APC)	64.11 ±21	64.27 ±12.41	28/23	30/20	38.6 ± 12.6	42.7 ± 12.5
Klein 2019	Prospective, Multicenter, 1:1 Randomized, July 2013 – May 2016, Australia	LST/ >20 mm	210	206 (No STSC)	66.1 ± 11.6	67.0 ± 13.1	101/109	102/104	30 (25–40)	30 (25–45)
Wehbeh 2020 (abs)	Retrospective, Single center, January 2016 and July 2019, USA	LST/ >20 mm	148	140 (No STSC)	65.9 (8.7)	66.6 (10.8)	78/70	79/61	32.5 (13.7)	30.4 (10.9)
Senada 2020 (abs)	Multicenter, Randomized Controlled Trial, USA	LST/ >20 mm	73	75 (No STSC)	65.5 (9.1)	66 (10.5)	33/40	35/40	30 ± 11.1	33.3 ± 16.7
Sidhu 2021	Multicenter, Prospective Trial, May 2016 – August 2020	LST/ >20 mm	1049	–	67.3 (10.9)	–	554/495	–	35 (25–45	–

NR, not reported; LST, laterally spreading tumor; APC, argon plasma coagulation; STSC, snare tip soft coagulation

STSC was 2 % (95 % CI 0.2–4.2; I^2 = 83.4 %) (**Supplementary Fig. 5**). The overall pooled incidence of post polypectomy syndrome after STSC was 2.4 % (95 % CI 2.2–7; I^2 = 54.5 %) (**Supplementary Fig. 6**).

Validation of meta-analysis results

Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. We found no significant difference in the pooled outcomes was noted with the exclusion of any one study.

Heterogeneity

We assessed dispersion of the calculated rates using the confidence interval (CI) and I^2 percentage values. The CI gives an idea of the range of the dispersion and I^2 tells us what proportion of the dispersion is true vs chance [27]. Overall, low to moderate heterogeneity was noted in pooled odds of adenoma recurrence, pooled rates of delayed bleeding and post polypectomy syndrome and considerable heterogeneity was noted in pooled rates of intraprocedural bleeding and perforation events. The latter can be likely be explained by the variation in the definition of these adverse events among studies.

Assessment of bias

Based on visual inspection of the funnel plot as well as quantitative measurement that used the Egger regression test, there was no evidence of publication bias (funnel plot, **Supplemental Fig. 7 a–c**, Eggers two-tailed P = 0.2). Further statistical analysis using the fail-Safe N test and Duval and Tweedie's "Trim and Fill" test revealed that the reported pooled results would not be significantly affected by the unpublished studies.

Based on Newcastle-Ottawa Scale for study quality assessment, all the included cohort studies were considered of high quality. Based on GRADE methodology, while the pooled odds of adenoma recurrence was graded as high for certainty of evidence, all other outcomes were graded as low for certainty of evidence due to observational design of the included studies.

Discussion

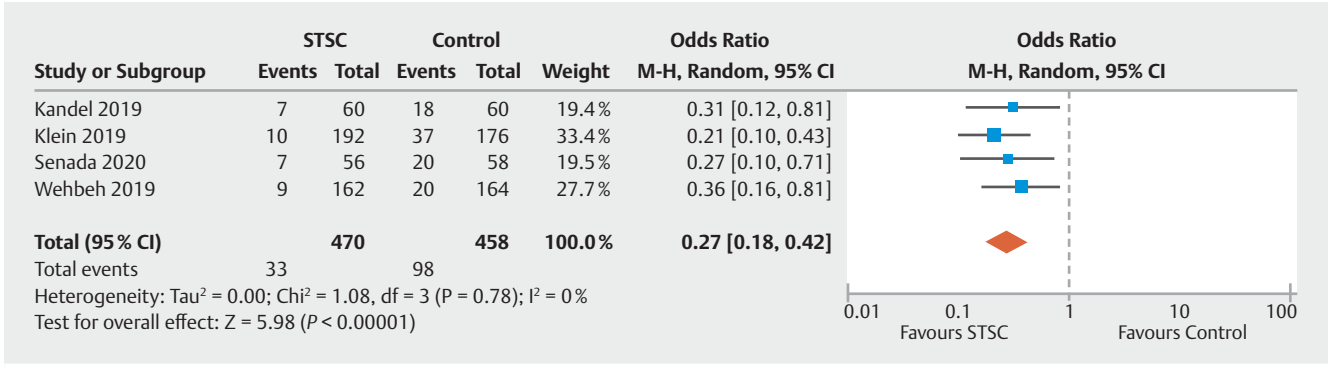
Our analysis shows that performing snare tip soft coagulation at the resection margins post EMR of large (>20 mm) laterally spreading tumors results in a statistically significant lesser incidence of adenoma recurrence at follow up surveillance colonoscopy as compared to EMR alone. STSC is a safe and effective technique resulting in an adenoma recurrence rate of 6 % at first surveillance colonoscopy.

Endoscopic mucosal resection is widely performed and successful technique for treatment of colorectal lesions [28, 29]. While en-bloc EMR can be safely performed for lesions ≤20mm

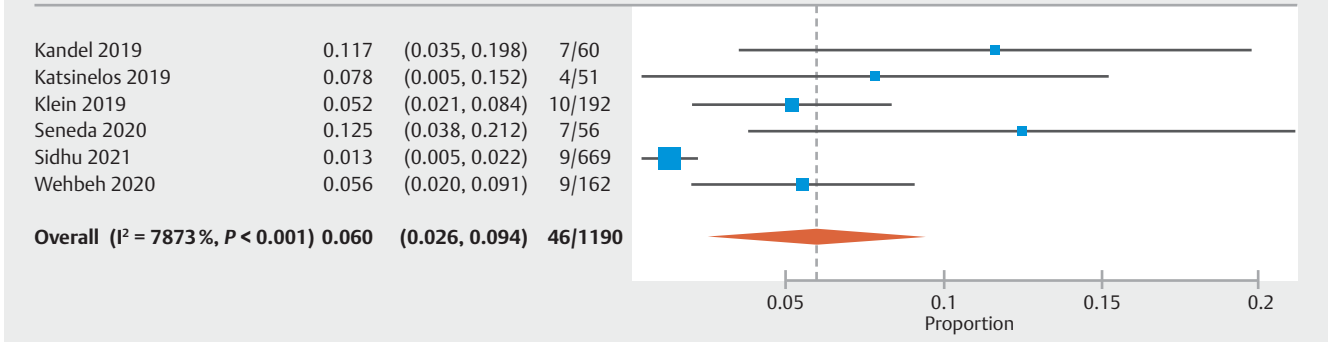
▶ **Table 2** Study outcomes.

Study	Polyp histology		Polyp location		PP syndrome		Perforation		Intraprocedural bleeding		Delayed bleeding		Adenoma recurrence (SC1)	
	STSC	Others	STSC	Others	STSC	Others	STSC	Others	STSC	Others	STSC	Others	STSC	Others
Kandel 2019	SSA 27, SSA w/ HGD 1, TA 14, TA w/ HGD 2, TVA 10, TVA w/HGD 7, ImCa 3	SSA 19, TA 21, TA w/HGD 2, TVA 16, TVA w/HGD 1, ImCa 1	P 50, D 10	P 48, D 12	0/60	0/60	NR	NR	9/60	12/60	2/60	3/60	7/60 (5–6 mo)	18/60 (5–6 mo)
Katsinelos 2019	V 15, TVA 26, TA 9, CIS 1	V 18, TVA 20, TA 10, CIS 2	C 5, A 1, T 1, D 2, S 10, Re 32	C 6, A 3, T 0, D 0, S 7, Re 34	3/51	5/50	4/51	3/50	NR	NR	5/51	4/50	4/51 (3 mo)	5/50 (3 mo)
Klein 2019	TA 43, TVA 116, SSP 51, IC 7, HGD 46, LGD 123	TA 35, TVA 124, SSP 47, IC 9, HGD 47, LGD 127	R 106, L 104	R 109, L 97	NR	NR	1/210	3/206	49/210	47/206	13/210	12/206	10/192 (5–6 mo)	37/176 (5–6 mo)
Wehbeh 2020 (abs)	NR	NR	R 105, T35, L 22	R 90, T 40, L 28	NR	NR	NR	NR	NR	NR	NR	NR	9/162 (7.1 mo)	23/164 (7.4 mo)
Senada 2020 (abs)	TA 37, TVA 20, SSA 15, IC 1	HP 1, TA 32, TVA 27, SSA 10, TSA 1, IC 2	R 65, L 8	R 40, L 35	NR	NR	NR	NR	9/73	19/75	NR	NR	7/56 (6.7 mo)	20/58 (6.7 mo)
Sidhu 2021	TA 254, TVA 616, SSL 117, Ca 62, LGD 672, HGD 232	–	R 561, L 488	–	–	–	27/1037	–	62/1037	–	71/1037	–	9/669 (6 mo)	–

SSA, sessile serrated adenoma; HGD, high-grade dysplasia; TA, tubular adenoma; TVA, tubulovillous adenoma; IC, invasive cancer; LGD, low-grade dysplasia; V, villous; SSL, sessile serrated lesion; P, proximal; D, distal; R, right; L, left; C, cecum; A, ascending Colon; T, transverse colon; D, descending colon; Re, rectum; abs, abstract; Ca, cancer; ImCa, intramucosal cancer.



▶ **Fig. 1** Forest Plot of pooled odds of adenoma recurrence.



▶ **Fig. 2** Forest Plot of pooled proportion of adenoma recurrence.

in the proximal colon and ≤ 25 mm in the rectosigmoid colon, curative resection with EMR becomes more challenging in LSTs > 20 mm. Risk of intraprocedural perforation is also higher with larger LSTs [4, 30]. The inability to perform en bloc resection of larger LSTs is the main limitation of EMR compared to endoscopic submucosal dissection (ESD). Furthermore it has been estimated that adenoma recurrence rate after piecemeal EMR for LST > 20 mm may be as high as 22 % [31]. Limitations of ESD include requirement of additional endoscopic training, increased procedure time with specialized instruments and multi-day hospital admission [32]. Studies comparing ESD to EMR have also shown higher risk of perforation events with ESD without a significant difference in the risk of major bleeding events [12, 33].

Intraprocedural bleeding (IPB) and clinically significant delayed bleeding (DB) are considered significant limitations of EMR. Due to variability in definitions, with some studies not specifically defining IPB, whereas others only reporting procedural bleeding not responding to immediate endoscopic hemostasis, incidence rates of IPB reported in literature are highly variable, ranging from 0 % to 38 %.[29, 34–36]. Incidence of DB is estimated to be 2.6 % to 9.7 % for colorectal lesions larger than 2 cm [8, 37]. Similar to these reports, in our analysis, the pooled incidence of IPB and DB was 10.3 % and 6.5 %, respectively.

Snare tip soft coagulation (STSC) was first described by Fahrtash-Bahin et al as a technique to control intraprocedural bleeding following wide field resection of large colonic lesions [38]. The technique requires the use of a microprocessor-controlled generator capable of delivering fixed low-voltage output that is capped at 190 Volts to prevent deep tissue injury (SOFT COAG mode, 80 W Effect 4; ERBE Electromedizin, Tubingen, Germany). The energy is applied systematically to the entire margin of the post-EMR mucosal defect using a light touch with 1 to 2 mm of exposed snare tip aiming to create a 2- to 3-mm rim of completely ablated tissue (complete whitening of the tissue) around the entire circumference of the resection defect. The US Multi-Society Task Force on Colorectal Cancer recommends that all grossly visible tissue of a lesion be resected in a single colonoscopy session and in the safest minimum number of pieces [3]. Ablative techniques, such as snare tip and argon plasma coagulation (APC) for the ablation of residual grossly visible tissue is not recommended as this has been associated with an increased risk of adenoma recurrence thought to be due to incomplete treatment of deeper layers [39–41]. Adjuvant thermal ablation of the post-EMR margin with STSC offers a more cost-effective alternative to APC as no additional equipment/catheters are needed.

Data regarding the use of STSC are still emerging, and to date, there is no systematic review and meta-analysis on this topic. Our study is the first in the literature to evaluate the ef-

fectiveness and safety of this technique in a large cohort of patients. There are several strengths to our review including systematic literature search with well-defined inclusion criteria, careful exclusion of redundant studies, inclusion of good quality studies with detailed extraction of data, rigorous evaluation of study quality, and statistics to establish and/or refute the validity of the results of our meta-analysis. We included only those studies in which STSC was performed for LSTs >20 mm. To calculate the pooled odds of adenoma recurrence with STSC, we only included those studies in which the technique was compared to EMR performed without STSC. Studies without a comparator group [16] and those in which post EMR thermal ablation using APC [18] was performed were excluded for assessing our main outcomes. There are also several limitations to this study, most of which are inherent to any meta-analysis. First and foremost, two of the included studies in our analysis were published only as abstracts. While interim results were available for one study, the outcomes of interest were clearly presented. Details on patient selection, statistical methodology, polyp location and histology were not presented and could not be assessed. Second, in one of our included studies, in addition to thermal ablation of the resection margins, any area suspicious for residual adenomatous tissue was also ablated [18]. There was also considerable heterogeneity in some of our secondary outcomes, which is likely due to inclusion of retrospective and prospective studies, in addition to RCTs, in our analysis resulting in selection bias. One of the included RCT in our analysis was only published as an abstract [25], as a result we were unable to assess selection, detection and performance bias for this study given lack of information provided. Additionally, due to lack of blinding reported by Klein et al, there is likelihood of detection bias in our outcomes. There was insufficient data to assess outcomes of cohort studies and RCTs separately. Thirdly, there was variability in the time to first surveillance colonoscopy, ranging from 3 months to 7 months. Finally, we were unable to assess the outcomes of STSC based on polyp/lesion location.

Conclusions

Our analysis shows that post EMR thermal ablation of resection margins with snare tip soft coagulation in LSTs >20 mm results in significantly lesser rate of adenoma recurrence compared to EMR alone. The overall rate of adenoma recurrence at first surveillance colonoscopy appears to be low at 6 %. In terms of safety, we found that the rates of intraprocedural bleeding, delayed bleeding and intraprocedural perforation were 10.3 %, 6.5 % and 2 % respectively. Further randomized trials comparing EMR with STSC and ESD are needed to validate our findings.

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Competing interests

Peter Draganov: Consultant: Olympus, Boston Scientific, Cook endoscopy, Fuji Film, Medtronic, Merit, Lumendi, Steris, Microtech.
Mohamad Othman: Consultant: Abbvie, Boston Scientific, Olympus, Lumendi, Conmed.
Other authors declare no COI.

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