Cold snare piecemeal EMR of large sessile colonic polyps ≥20 mm (with video) CME

Dileep Mangira, MBBS, FRACP,[1,2] Karla Cameron, MBBS,[1] Koen Simons, PhD,[3,4] Simon Zanati, MBBS, FRACP,[1] Richard LaNauze, MBBS, FRACP,[5] Spiro Raftopoulos, MBBS, FRACP,[6] Gregor Brown, MBBS, FRACP, PhD,[7] Alan Moss, MBBS, MD, FRACP, FASGE[1,2]

Melbourne, Australia

Background and Aims: Conventional EMR using a hot snare is the standard of care for resection of large (≥20 mm) nonmalignant sessile colonic polyps. Serious adverse events are predominantly because of electrocautery. This could potentially be avoided by cold snare piecemeal EMR (CSP-EMR). This study aimed to evaluate the safety and efficacy of CSP-EMR of sessile colonic polyps sized ≥20 mm.

Methods: All cases of CSP-EMR at 5 Australian academic hospitals for sessile polyps ≥20 mm over a 2-year period, from January 2016 to December 2017, were identified retrospectively. Efficacy was defined as the absence of residual or recurrent polyp tissue during the first surveillance colonoscopy (SC1) and second surveillance colonoscopy (SC2). Clinically significant intraprocedural or delayed adverse events and surveillance colonoscopy findings were assessed by reviewing medical records.

Results: CSP-EMR was performed on 204 polyps sized ≥20 mm in 186 patients (men, 33.8%; median age, 68 years). SC1 for 164 polyps (80.4%) at a median interval of 150 days showed residual or recurrent polyp in 9 cases (5.5%; 95% confidence interval, 3%-11%). SC2 for 113 polyps (72.9%) at a median interval of 18 months showed late residual or recurrent polyp in 4 cases (3.5%; 95% confidence interval, .9%-8.5%) after a normal SC1. Intraprocedural bleeding was successfully treated in 4 patients (2.2%), whereas 7 patients (3.8%) experienced self-limited clinically significant post-EMR bleeding and 1 patient (.5%) required overnight observation for nonspecific abdominal pain that resolved spontaneously. None experienced other adverse events.

Conclusions: CSP-EMR of sessile colonic polyps ≥20 mm is technically feasible, effective, and safe. The adverse event rate and polyp recurrence rate were low. Randomized or large prospective trials are required to confirm the noninferiority and improved safety of CSP-EMR compared with conventional EMR and to further determine the polyp morphologies that are best suited for CSP-EMR. (Gastrointest Endosc 2020;91:1343-52.)

(footnotes appear on last page of article)

EMR is a minimally invasive endoscopic technique for the removal of large laterally spreading colorectal tumors.[1-3] At most Western academic endoscopy centers, EMR is the standard of care for noninvasive colonic polyps ≥20 mm.[4,5] The conventional EMR technique uses submucosal fluid injection to expand the plane between the mucosa and submucosa, followed by hot snare polypectomy, either en bloc or piecemeal, via cauterization with high-frequency current.[3,6] Thermal energy is used to facilitate transection through dense polyp tissue and to minimize intraprocedural bleeding (IPB). However, the electrosurgical current delivered through the snare is the main cause for adverse events post-EMR.

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Conventional "hot" EMR has risks of clinically significant post-EMR bleeding, possibly because of sloughing of the eschar exposing partially coagulated submucosal blood vessels. Additionally, electrocautery thermal energy can cause postpolypectomy syndrome (PPS) or perforation.[7,8] Modern microprocessor-controlled electrosurgical units use alternate cycles of cutting and coagulating current to minimize deep thermal injury. Despite these advances in electrosurgical units, the rates of clinically significant post-EMR bleeding range from 6% to 15%[9] and perforation rates vary from 1% to 2%.[10-12]

Although polyp resection performed with the EMR technique is a cost-effective and safe alternative to surgery,[13] residual or recurrent polyp at the EMR site is a major limitation of EMR.[14] Rates of early recurrence vary from 16% to 55%.[15,16] However, a recent Australian publication by Klein et al[17] established a new benchmark, with a recurrence rate of 5.2% after EMR of large colorectal polyps sized ≥20 mm. Such a low recurrence rate was achieved by soft coagulation thermal ablation of the post-EMR mucosal defect margin.[17] Although adenoma recurrence is usually diminutive, unifocal, and easily managed by EMR,[16] it requires additional surveillance colonoscopies, causing an increase in financial burden, and the inconvenience of additional colonoscopy may reduce patient acceptance of the procedure.[14]

Cold snare polypectomy has rapidly gained international acceptance as an effective and safe technique for resection of small polyps sized <10 mm.[4,18,19] For medium-sized polyps measuring 10 to 19 mm, limited but promising evidence supports the safety of this technique without compromising the efficacy of polypectomy, in particular for serrated polyps.[20,21] However, for polyps sized ≥20 mm, the evidence for cold snare resection is limited. Although conventional EMR is the current standard of care for polyps ≥20 mm,[4] we have increasingly performed cold snare piecemeal EMR (CSP-EMR) for sessile polyps ≥20 mm as an alternative modality to conventional EMR technique, with the potential benefit of reduced adverse events. However, the main concern with CSP-EMR for this indication is the potential for reduced efficacy, with the possibility of obviously incomplete resection at the index procedure or suspected complete resection but with higher rates of polyp recurrence observed at surveillance colonoscopy. The aim of this multicenter study was to evaluate the efficacy and safety of CSP-EMR for sessile colonic polyps sized ≥20 mm.

METHODS

This study was approved by the Western Health Research Ethics Committee. We performed a retrospective multicenter review of all CSP-EMR procedures at 5 Australian academic hospitals for sessile polyps ≥20 mm over 2 years, from January 2016 to December 2017. Lesions were assessed using high-definition white-light imaging (HD-WLI) and narrow-band imaging (NBI). We recorded polyp overall morphology using the Paris classification,[22] surface morphology (granular, nongranular, or mixed),[23] and Kudo pit pattern.[24] Any lesion suspicious for submucosal invasion (eg, Kudo V or Paris 0-IIa+c with nongranular surface) was excluded. In addition, any lesion with a large (>10 mm) Paris 0-Is component where en bloc cold snare resection of the 0-Is component would be difficult to achieve because of the inability to cut through the thick polyp base was also excluded from CSP-EMR. Other exclusion criteria were pedunculated polyps, active/quiescent colitis, patients with other lesions resected by hot snare during the same procedure, and rectal lesions. In addition to suspected tubular or tubulovillous adenomas, sessile serrated adenomas (SSAs) were also included in the study and were endoscopically suspected according to traditional features such as adherent surface mucus, cloud-like surface, interruption of mucosal vessels, and Kudo 2 open pit pattern. Final diagnosis of adenoma or SSA and dysplasia extent was made histologically on the CSP-EMR specimens. Relevant patient and procedure-related data were obtained from electronic medical records.

All CSP-EMRs were performed in day-procedure units within academic hospitals by 1 of 5 gastroenterologists or by an endoscopy fellow under direct supervision. All proceduralists were trained in EMR at high-volume centers. The colonoscopes were CF-HQ190L/PCF-H190L (Olympus, Tokyo, Japan) with carbon dioxide insufflation. A short distal transparent cap was used at endoscopist discretion for cases where this was believed likely to be useful based on images obtained from the referring endoscopist. Patients received instructions for a low-residue white diet[25] for 2 days before the procedure and for split-dose bowel preparation, consisting of 1 sachet of polyethylene glycol and 2 sachets of sodium picosulfate with magnesium citrate. Propofol sedation was administered by anesthesiologists. Antiplatelet and anticoagulants were withheld as per American Society for Gastrointestinal Endoscopy antithrombotic management guidelines for patients undergoing therapeutic endoscopic procedures.[26] Aspirin was always continued.

An opened snare of known dimensions (9 mm or 10 mm) was used to assess polyp size. Pit pattern was examined using HD-WLI and NBI. Polyps were excised using the CSP-EMR technique, with most resected after submucosal injection. The injectate comprised dilute methylene blue or .4% indigo carmine mixed with succinylated gelatin (Gelofusine; BBraun, Crissier, Switzerland). Dilute (1:100,000) epinephrine was added to the injectate at endoscopist discretion. Submucosal injection was performed with a 23-gauge injector (NM-6108-0423; Olympus). Exacto 9-mm cold snare (REF-00711115; US Endoscopy, Mentor, Ohio, USA) or SnareMaster Plus 10 mm hot/cold snare (SD-400U-10; Olympus) were the most commonly used snares. A limited number of cases

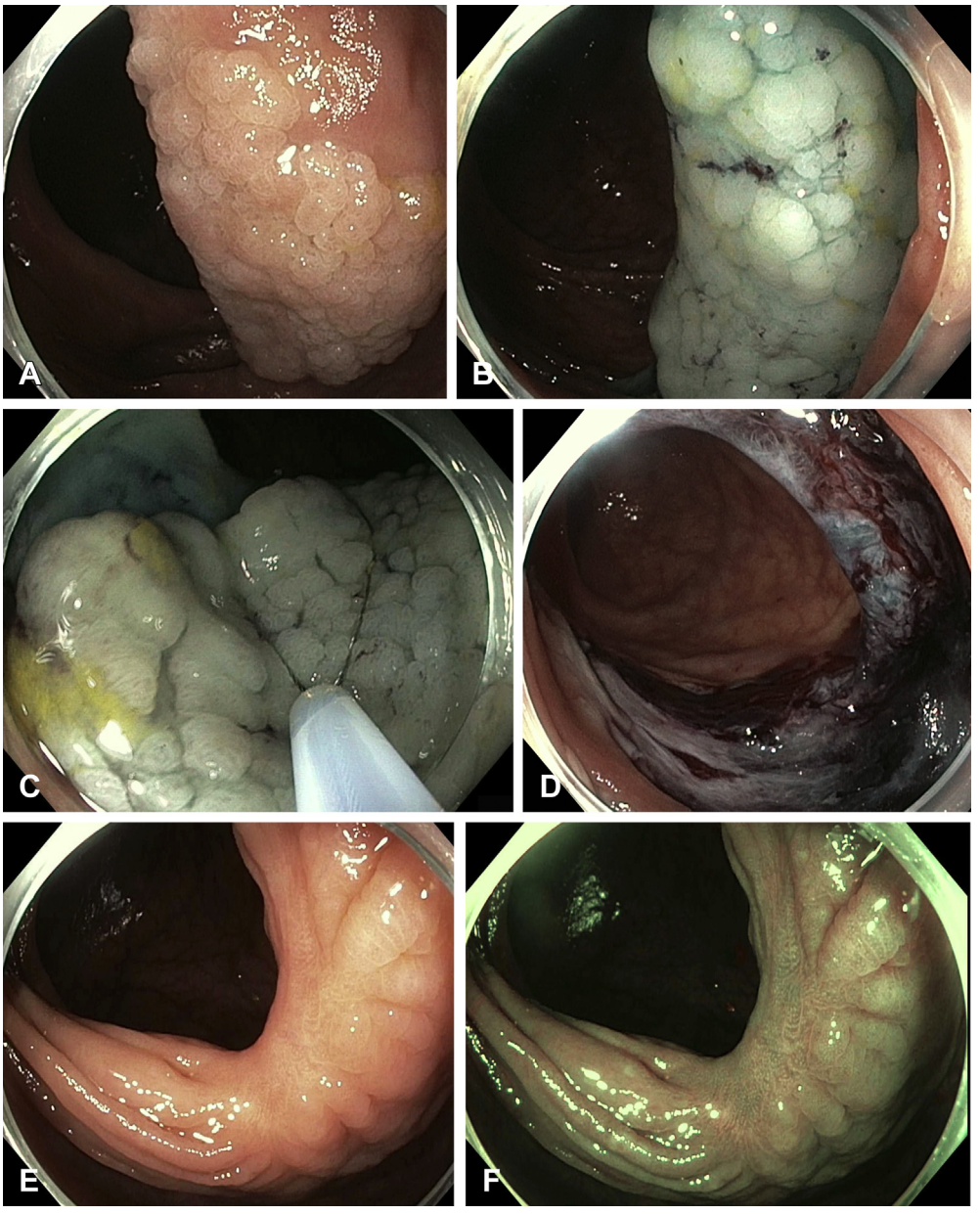

Figure 1. A, A 30-mm Paris 0-IIa granular lesion located in the proximal ascending colon. **B,** The polyp is elevated with submucosal injection. **C,** Cold snare placement of the 10-mm snare. **D,** The EMR site at the conclusion of the procedure. Histology returned as tubular adenoma with low-grade dysplasia. **E,** EMR scar at first surveillance colonoscopy (white-light view). **F,** EMR scar at first surveillance colonoscopy (narrow-band imaging view).

were performed without submucosal injection but with expansion of the submucosa achieved by flushing the mucosal defect with water via the auxiliary foot pump after the first cold snare resection was performed.

A meticulous CSP-EMR resection technique was used (Fig. 1 and Video 1, available online at www.giejournal.org). The technique was similar to conventional EMR, with resection commencing at 1 edge of the lesion, followed by sequential inject and resect technique.[3,6] Compared with conventional EMR, the cold snare was deliberately positioned over a slightly wider margin (eg, 2 mm) of normal adjacent colonic mucosa. Downward angulation of the instrument tip and gentle suction enabled effective tissue capture. Care was taken to achieve contiguous resections by placing the snare edge onto 1 to 2 mm of resected submucosa within the resection defect. After each resection, exposed submucosa was irrigated with water with the auxiliary water channel to expand the submucosal plane to reduce the risk of deep mural injury. Overlapping resections were performed until all visible polyp tissue was excised with clear margins. HD-WLI and NBI were used to interrogate the EMR defect and margins. Any suspected residual polyp tissue was further excised using the cold snare. All excised tissue fragments were retrieved through the suction channel for histology. Minor ooze of blood is

frequently observed after CSP-EMR and nearly always settles spontaneously. If bleeding persisted beyond 2 minutes, endoscopic clips were applied at endoscopist discretion. Wherever possible, complete endoscopic resection was achieved and then the clip(s) placed at the conclusion, so the clip(s) would not interfere with the EMR. Clips were only placed on the bleeding vessel, with no attempt made to close the EMR site completely. A SPOT tattoo (G44-018Rev-08; GI Supply) was injected 3 cm distal to EMR site. Histologic assessment was by expert GI anatomic pathologists at each site.

Postprocedure care was at the discretion of the proceduralist. In most cases, patients remained fasted for 2 hours followed by clear fluids for 1 hour. If tolerated, patients were then discharged home on either a clear fluid diet for the remainder of the day and overnight with regular diet resumed the following day or on regular diet the same day. Patients were considered to have clinically significant post-EMR bleeding if they had any bleeding after the procedure that resulted in a deviation from the expected usual post-EMR clinical course. This included the patient returning to the hospital emergency department or requiring admission to the hospital or any medical intervention to manage bleeding. Management of clinically significant post-EMR bleeding was at the discretion of the endoscopist. All patients were reviewed in the outpatient clinic in 4 to 6 weeks. Follow-up appointments were focused on discussing histology results, identifying delayed adverse events, and planning surveillance colonoscopy. The post-EMR surveillance intervals were for first surveillance colonoscopy (SC1) at 4 to 6 months and second surveillance colonoscopy (SC2) at 16 to 18 months after the index EMR.[4]

At surveillance, the CSP-EMR site was interrogated with HD-WLI and NBI. The EMR scar was photographed, and if no recurrent polyp was identified, the EMR scar underwent biopsy sampling for histologic confirmation. Any recurrent/residual adenoma suspected at the surveillance colonoscopy was recorded as such, and the area was completely excised with either cold snare, cold biopsy sampling with soft coagulation thermal ablation, hot snare resection, or hot avulsion based on endoscopist preference.

Statistical analysis

Statistical analysis involved reporting results for continuous variables as a mean (standard deviation) or median (interquartile range [IQR]) for skewed data. Frequencies (%) were used for incidence and for categorical variables, and 95% confidence intervals (CIs) were calculated when pertinent. Potential risk factors for residual/recurrent polyp were identified by univariate analysis using the Student t test to compare means and the Fisher exact test to compare categorical variables. Multiple logistic regression analysis was performed for factors associated with recurrent/residual adenoma with $P \leq .10$ on univariate analysis to identify independent associations. Statistical analyses were performed using the "R" software program.[27]

RESULTS

Over a 24-month period (January 2016 to December 2017), CSP-EMR was performed on 204 lesions (mean, 25.5 mm [standard deviation, 8.4]; median, 20 mm [IQR, 20-30]) in 186 patients (63 men [33.8%]; median age, 68 years [range, 21-91]). Ninety-two polyps (44%) were ≥25 mm, 61 (29.6%) ≥30 mm, and 19 (9.2%) ≥40 mm. One hundred eighty-nine polyps (92.6%) were from the proximal colon (proximal to the splenic flexure) and 15 polyps (7.4%) were from the distal colon (distal to the splenic flexure). The histology analysis of the EMR specimens showed 134 SSAs (65.6%), 45 tubular adenomas (21.8%), 22 tubulovillous adenomas (10.8%), and 3 other (1.5%) (hyperplastic, 2; hamartoma, 1). Cytologic dysplasia was absent in 128 polyps (62.7%), low-grade dysplasia was present in 72 polyps (35.3%), and high-grade dysplasia was present in 4 polyps (1.9%). At the end of the initial study data collection period (August 2018), 164 of 204 polyps (80.4%) underwent SC1 at a median interval of 150 days (mean, 180 days). At SC1, biopsy samples were taken of the EMR scar for histologic confirmation in the absence of residual/recurrent polyp for 89 polyps (54.3%). An additional data collection period extended to October 2019 was used to capture SC2 results. Of the 164 polyps with SC1 results, 117 (71.3%) underwent SC2 at a median interval of 18 months from the index colonoscopy.

Efficacy

Of 164 lesions, residual/recurrent polyp was found at the EMR site of 9 lesions (5.5%; 95% CI, 3%-11%) at SC1. Cases with residual/recurrent polyp detected at SC1 had a median initial polyp size of 25 mm (mean, 28.5 mm; IQR, 20-30 mm; range, 20-50 mm) compared with a median of 20 mm (mean, 25.6 mm; IQR, 20-30 mm; range, 20-50 mm) in those without residual adenoma; however, this was not statistically significant ($P = .18$). All lesions that had recurrence at SC1 were in the proximal colon, with 6 of 9 (66.7%) in the cecum, 2 of 9 (22.2%) in the ascending colon, and 1 of 9 (11.1%) in the transverse colon. All residual lesions were deemed to have been successfully fully resected at SC1 based on the endoscopists' assessment. Treatment of recurrent polyp at SC1 was with the cold resection technique using cold snare, cold biopsy sampling, or a combination in 7 of 9 lesions (77.8%), whereas a combination of cold resection along with hot snare or snare tip soft coagulation was used in 2 lesions (22.2%).

Univariate analysis (Table 1) with odds ratios (ORs) revealed that cecal location ($P = .003$; OR, 9.1; 95% CI, 2.1-38.5) and involvement of an endoscopy fellow ($P =$

.04; OR, 4.2; 95% CI, 1.0-16.6) were associated with recurrence at SC1. Lesion size was not a significant risk factor for recurrence on univariate analysis. *P* values for adrenaline use in injectant and involvement of an endoscopy fellow during the procedure were .07 and .05, respectively. Including these predictors in a multiple logistic regression model resulted in an adjusted OR of 8.0 ($P = .006$; 95% CI, 1.8-35.3) for cecal location, indicating low sensitivity to the inclusion of these potential risk factors. In contrast, associations weakened further for adrenaline use (adjusted OR, .3; $P = .12$; 95% CI, .1-1.4) and endoscopy fellow involvement (adjusted OR, 2.8; $P = .17$; 95% CI, .6-12.7) when adjusted for 1 another and for cecal location. Of the 9 cases with recurrent polyp at SC1, 4 underwent SC2 and all 4 cases had normal EMR scars at SC2.

One hundred thirteen of 155 polyps (72.9%) with a normal SC1 underwent SC2. Four cases of late recurrence were identified at SC2 (3.5%; 95% CI, .9%-8.5%). Three of these recurrences were completely excised using a cold snare, but 1 required a combination of cold snare and hot snare for complete resection. The histology of these 4 cases of late recurrence was 2 SSA, 1 tubular adenoma with low-grade dysplasia, and 1 tubulovillous adenoma with low-grade dysplasia.

Safety

Ten of 186 patients (5.4%; 95% CI, 2.6%-9.7%) experienced an adverse event. Persistent IPB was noted in 4 patients (2.2%; 95% CI, .6%-5.4%). None of these patients was on antiplatelet or anticoagulant medications at any time. Bleeding was successfully treated by placement of hemostatic clips with immediate success in 2 patients. One patient was not treated with clips but rather with snare tip soft coagulation of the bleeding vessel. One patient was treated first with snare tip soft coagulation but when bleeding persisted was treated with hemostatic clips. Treatment of IPB in all 4 patients was successful.

Clinically significant post-EMR bleeding was observed in 7 patients (3.8%; 95% CI, 1.5%-7.6%). Of these 7 patients, 4 presented within 24 hours post-EMR, 1 between 24 to 48 hours, and 2 between 8 and 14 days. Six were managed conservatively. Of these 6 patients, 1 was discharged home from the emergency department observation ward after an overnight stay. The other 5 (2.7% of all study patients) were admitted to the hospital ward for up to 2 days of observation, but none of them required blood transfusion or colonoscopy. Only 1 patient underwent colonoscopy because of ongoing bleeding. However, that patient was found to have a clean-based post-EMR ulcer that was no longer bleeding, and because there was no visible vessel, it did not warrant endoscopic intervention.

One patient (.5%) developed post-EMR generalized abdominal pain and was admitted to the hospital for observation overnight. The pain settled spontaneously, and the patient was discharged from the hospital the following day. None experienced PPS, deep mural injury, or perforation.

DISCUSSION

Colorectal EMR is a safe, effective, and less-invasive alternative to surgery.[1,28] However, electrocautery use during EMR exposes patients to risks, including perforation, PPS, and clinically significant post-EMR bleeding. Avoidance of thermal energy when feasible can reduce these risks. To our knowledge, this is the largest study investigating safety and efficacy outcomes for CSP-EMR of large sessile (≥20 mm) colonic polyps. Our study of 186 patients with 204 polyps demonstrates that CSP-EMR is safe. It was free of adverse events for 94% of patients, with only 2.2% of patients experiencing IPB that was always successfully managed endoscopically. A small number of patients (3.8%) experienced clinically significant post-EMR bleeding, but none warranted therapeutic intervention; .6% experienced nonspecific abdominal pain that required overnight hospital observation with discharge home next day. No patients experienced PPS or perforation.

Improved safety with CSP-EMR is important, but it is essential not to compromise efficacy. A large prospective observational study from the Australian Colonic EMR group assessed adenoma recurrence after conventional EMR for polyps ≥20 mm. The early recurrence rate at 4 months post-EMR was 16%.[16] A recent randomized trial (Soft Coagulation for the Prevention of Adenoma Recurrence [SCAR]) compared the efficacy of conventional EMR with conventional EMR plus thermal ablation of the post-EMR mucosal margin.[17] Although the latter group had a recurrence rate of 5.2% (relative risk, .25; 95% CI, .13-.48), which sets a new benchmark for adenoma recurrence post-EMR, it is important to note that the standard therapy arm of conventional EMR had a 21% recurrence rate.[17] In comparison, in our study, the recurrence rate was 5.5% at SC1, which is comparable with the interventional arm of the SCAR study. Furthermore, at SC2 at a median of 18 months in our study, the late recurrence rate was 3.5%, which almost exactly corresponds to the late recurrence rate of 4% for conventional EMR at 16 months in the Australian Colonic EMR study.[16] In addition, for the limited number of cases (n = 4) where recurrence at SC1 was treated and then SC2 data were also available, the endoscopic treatment applied at SC1 was effective in all cases, again reflecting our experience in conventional EMR studies of a high rate of successful endoscopic treatment of polyp recurrence at the EMR site.

We acknowledge significant limitations to our study that make direct comparison with the randomized SCAR study problematic, including large Paris 0-Is polyps excluded, absence of randomization, smaller median polyp size, and the retrospective nature of our study. Nonetheless,

TABLE 1. Factors associated with recurrence at first surveillance colonoscopy (univariate analysis)

	No recurrence (n = 155)	Recurrence (n = 9)	*P* value
Age, y			.36
Mean	62.9 (16.1)	67.4 (13.9)	
Gender			.27
Male	53 (34.2)	1 (11.1)	
Female	102 (65.8)	8 (88.9)	
Size, mm			.81
Mean	25.6 (8.0)	26.1 (5.5)	
Endoscopy fellow involved			.05
No	130 (83.9)	5 (55.6)	
Yes	25 (16.1)	4 (44.4)	
Location			.17
Cecum	28 (18.1)	6 (66.7)	
Ileocecal valve	2 (1.3)	0 (0)	
Ascending colon	48 (31)	2 (22.2)	
Hepatic flexure	27 (17.4)	0 (0)	
Transverse colon	39 (25.2)	1 (11.1)	
Splenic flexure	3 (1.9)	0 (0)	
Descending colon	5 (3.2)	0 (0)	
Sigmoid colon	3 (1.9)	0 (0)	
Paris classification			.28
0-Is	3 (1.9)	0 (0)	
0-IIa	128 (82.6)	6 (66.7)	
0-IIa+0-IIb	8 (5.2)	1 (11.1)	
0-IIb	11 (7.1)	2 (22.2)	
Not available	5 (3.2)	0 (0)	
Surface morphology			.43
Granular type	33 (21.3)	4 (44.4)	
Nongranular type	33 (21.3)	1 (11.1)	
Mixed	1 (0.6)	0 (0)	
Likely sessile serrated adenoma	88 (56.8)	4 (44.4)	
Kudo classification			.30
Kudo I	0 (0)	0 (0)	
Kudo II	83 (64.3)	3 (42.9)	
Kudo III	31 (24)	2 (28.6)	
Kudo IV	13 (10.1)	2 (28.6)	
Not available	2 (1.6)	0 (0)	
Ease of polyp access			.23
Easy to access	110 (84.6)	5 (71.4)	
Easy to reach but difficult to position	8 (6.2)	0 (0)	
Difficult to reach but easy to position	8 (6.2)	2 (28.6)	
Difficult to reach and position	4 (3.1)	0 (0)	

(*continued on the next page*)

despite these limitations, it is reasonable for us to suggest that CSP-EMR is effective, at least in a subset of patients. We believe that CSP-EMR shows similar outcomes to best practice conventional EMR for appropriately selected lesions. Prospective studies are required to validate our findings. From a safety perspective, CSP-EMR had fewer

TABLE 1. Continued

	No recurrence (n = 155)	Recurrence (n = 9)	*P* value
Submucosal lift			.52
Saline solution	4 (2.6)	0 (0)	
Gelofusine	121 (78.1)	6 (66.7)	
No injection	30 (19.4)	3 (33.3)	
Dye included in submucosal injectate			.28
None	30 (19.4)	3 (33.3)	
Indigo carmine	9 (5.8)	1 (11.1)	
Methylene blue	116 (74.8)	5 (55.6)	
Adrenaline included in submucosal injectate			.07
No	53 (34.2)	6 (66.7)	
Yes	102 (65.8)	3 (33.3)	
Polyp lift			.56
Lifted well	121 (78.1)	6 (66.7)	
Partially lifting	3 (1.9)	0 (0)	
Nonlifting	1 (.6)	0 (0)	
Lifting not attempted	28 (18.1)	3 (33.3)	
Not available	2 (1.3)	0 (0)	
Snare type			.11
Exacto	97 (74.6)	3 (42.9)	
Olympus Snaremaster Plus	10 (7.7)	2 (28.6)	
Not available	22 (16.9)	2 (28.6)	
Additional modalities used to complete resection			.17
None	154 (99.4)	9 (100)	
Cold biopsy forceps	1 (.6)	0 (0)	
All adverse events			.37
No adverse events	148 (95.5)	8 (88.9)	
Adverse events	7 (4.5)	1 (11.1)	
Histology			.20
Tubular adenoma	37 (23.9)	3 (33.3)	
Tubulovillous adenoma	12 (7.7)	2 (22.2)	
Sessile serrated adenoma/polyp	105 (67.7)	4 (44.4)	
Other	1 (.6)	0 (0)	
Dysplasia			.26
None	97 (62.2)	5 (50)	
Low grade	56 (35.9)	4 (40)	
Focal high grade	3 (1.9)	1 (10)	
Diffuse high grade	0 (0)	0 (0)	
Carcinoma	0 (0)	0 (0)	

Values are n (%) unless otherwise defined.

adverse events than that shown for conventional EMR. In the SCAR study, the adverse event rates for the control arm were 23% IPB, 6% clinically significant post-EMR bleeding, 1.5% intraprocedural perforation, and .5% delayed perforation.[17] Once again, the limitations of our study design in comparison must be acknowledged, but the impression of lower adverse events with CSP-EMR is present. Prospective assessment of safety could be combined with the evaluation of efficacy in a randomized trial.

Only a limited number of small studies have assessed safety and efficacy of cold snare for large polyps.[29,30] Table 2 summarizes the evidence. Previously, the largest study for cold snare EMR of large polyps that included conventional adenomas (and not only SSAs) was by

TABLE 2. Studies assessing safety and efficacy of cold snare for large polyps

Study reference	Study design	Patients (total)	Polyps (total)	Polyps (≥20 mm) n (%)	Polyp characteristics	Intraprocedural bleeding	Clinically significant postpolypectomy bleeding	Recurrence rate (%)
Choksi et al[18] (2015)	Retrospective observational	15	15	11 (73)	Adenomas	0/11	0/11	N/A
Piraka et al[29] (2017)	Retrospective observational	73	94	37 (39)	Adenomas and SSA/Ps	1/37	0/37	18.4
Muniraj et al[30] (2015)	Retrospective observational	30	30	15 (50)	Adenomas and SSA/Ps	NA	0/15	N/A
Tutticci et al[20] (2018)	Prospective observational	99	163	74 (45)	SSA/Ps	0/74	0/74	0

SSA/Ps, Sessile serrated adenomas/polyps; *NA*, not available.

Piraka et al[29] with a retrospective study of 37 patients with polyps ≥20 mm, with no major adverse events and an adenoma recurrence rate of 18% noted. In a large prospective observational cohort study of SSA polyps, successful CSP-EMR was performed on 163 SSAs with 74 polyps (45%) sized ≥20 mm.[20] At a median follow-up of 154 days, no recurrence (0/74) was seen in the subgroup of larger SSAs.[20] In a recent systematic review and pooled analysis of cold snare endoscopic resection of nonpedunculated polyps >10 mm, a subgroup analysis on safety and efficacy for polyps ≥20 mm was performed.[31] The pooled rates of IPB, clinically significant post-EMR bleeding, and PPS were 1.3%, 0%, and 1.2%, respectively. However, the pooled recurrent adenoma rate for larger (≥20 mm) polyps in the systematic review was 15%, which is substantially higher than the 5.5% recorded in our study.

We believe that our study of CSP-EMR for large polyps has demonstrated enhanced safety compared with conventional EMR without compromising efficacy. We believe that efficacy was achieved with appropriate lesion selection and by making minor modifications to the conventional EMR technique, which are possible because of the intrinsic safety afforded by cold snaring. During cold snare resection, a greater emphasis was placed on overlapping the snare relative to the previous resection to enhance tissue capture and facilitate complete resection without being concerned about the possibility of deep mural injury. Second, we widely resected the polyp margins to be sure of complete resection of lateral polyp margins without being concerned that further resections would increase the risk of thermal snare–related injury. Furthermore, if there was doubt as to whether a prominent area within the EMR site represented residual polyp or merely bunched-up normal submucosa, this area was irrigated with water to expand it and then cold snare excised again. This cannot be recommended if hot snare resection is used. Furthermore, a thin, stiff, monofilament cold snare was used. The snare base was pressed down onto the colonic wall to enhance tissue capture until the snare had fully closed and resected the tissue, which is different from the conventional EMR technique whereby the closed snare is lifted away from the underlying colonic wall before applying electrocautery to reduce the risk of deep thermal injury. These differences between CSP-EMR and conventional EMR techniques mean that traditional risk factors for polyp recurrence after conventional EMR, including multiple piecemeal resections, may not necessarily apply to CSP-EMR in the same manner, and further study is required to elucidate the strongest risk factors for recurrence after CSP-EMR.

Although submucosal injection is not universally accepted as a requirement for CSP-EMR, it confers several benefits as suggested by Tutticci and Hewett[20] and Piraka et al.[29] First, submucosal injection expands the submucosa, making resection easier by reducing snare stalling on dense submucosal tissue. Second, the dye within the injectate defines polyp margins accurately and assists in detecting residual polyp islands within the EMR defect. Third, submucosal injection reduces IPB by a direct tamponade effect and is enhanced by the addition of epinephrine. Although IPB during CSP-EMR is nearly always self-limiting, reducing IPB avoids delays while waiting for the bleeding to subside and also provides a clear working view. This is important, as we know from a previous conventional EMR study that IPB is a risk factor for higher recurrence rates after EMR,[16] likely because of impaired visibility.

In addition to the limitations we described earlier, our study has several additional limitations that must be acknowledged. First, rectal lesions were excluded from our study, because rectal lesions were not resected with CSP-EMR during this study period. This is because rectal lesions are at low risk of perforation during EMR, which reduces the potential safety benefit of the cold snare. Furthermore, the efficacy of cold snare EMR was not previously proven for large lesions, and because inadequate oncologic resection in the rectum can potentially lead to major surgical intervention with significant lifestyle implications for the patient, we believed it was not appropriate to pursue rectal CSP-EMR until its efficacy was proven in the colon. Conversely, some studies

have shown rectal lesions to be at an increased risk of bleeding after EMR,[32] so potentially CSP-EMR could be of benefit to reduce the likelihood of clinically significant post-EMR bleeding.[32] However, this will need to be assessed in future studies that could include appropriately selected rectal lesions considered to be at low risk for submucosal invasion. Second, our procedures were performed by 5 experienced endoscopists at tertiary academic endoscopy centers, potentially limiting the generalizability of these results to community endoscopists. Indeed, current European Society of Gastrointestinal Endoscopy guidelines strongly recommend that endoscopic removal of large laterally spreading colorectal tumors should be performed by appropriately trained endoscopists at tertiary care facilities.[4] However, the enhanced safety of CSP-EMR may allow for expansion of EMR into community facilities because the risk of perforation is significantly reduced with cold snare EMR. We believe that with suitable training in CSP-EMR, its enhanced safety will allow for many large lesions, such as Paris 0-IIa lesions sized 20 to 30 mm with granular surface morphology, to be managed by suitably trained endoscopists at community facilities. Third, our data are limited by not having surveillance colonoscopy results for all patients. Fourth, the histopathology analysis of CSP-EMR specimens may potentially be more limited than conventional EMR specimens. This is because conventional EMR specimens are likely to be larger and may also potentially contain a greater depth of submucosa. Therefore, although not ever proven, it may theoretically be possible to miss early or subtle lymphovascular invasion in CSP-EMR specimens. Because cold snare EMR for larger polyps is nearly always a multiple piecemeal resection, it is critical to appropriately select lesions suitable for this technique, and we must be vigilant to not perform cold snare EMR for lesions with a high risk of containing covert malignancy. Our careful lesion selection is reflected in the fact that none of our patients had carcinoma in this series and only 1.9% had high-grade dysplasia. Finally, we did not record the duration of CSP-EMR procedures, which would have been of interest to compare with conventional EMR for similarly sized lesions.

In conclusion, this study is, to the best of our knowledge, the largest study of the safety and efficacy of CSP-EMR technique for large sessile laterally spreading colorectal tumors ≥20 mm. Furthermore, a large proportion of our cases were adenomas, suggesting that CSP-EMR is feasible, safe, and effective not only for SSAs but also for tubular and tubulovillous adenomas. Our adverse event and adenoma recurrence rates were both lower than shown in previous studies of the conventional EMR technique. Even allowing for the limitations of our retrospective study design, our data provide a strong indication that CSP-EMR should be considered a viable technique for excision of large sessile colonic polyps and is worthy of further study to define the lesions best suited to the CSP-EMR technique and to determine the place of CSP-EMR within our EMR armamentarium.

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Abbreviations: CI, confidence interval; CSP-EMR, cold snare piecemeal EMR; HD-WLI, high-definition white-light imaging; IPB, intraprocedural bleeding; NBI, narrow-band imaging; PPS, postpolypectomy syndrome; SC1, first surveillance colonoscopy; SC2, second surveillance colonoscopy; SCAR, Soft Coagulation for the Prevention of Adenoma Recurrence; SSA, sessile serrated adenoma.

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Current affiliations: Department of Gastroenterology, Western Health, Melbourne, Australia (1), Department of Medicine, Western Health, Melbourne Medical School (2), School of Population and Global Health (4), The University of Melbourne, Melbourne, Australia; Western Health Office for Research, Western Health, Melbourne, St Albans, Australia (3), Department of Gastroenterology, Peninsula Health, Melbourne, Australia (5), Department of Gastroenterology, Sir Charles Gairdner Hospital, Perth, Australia (6), Department of Gastroenterology, The Alfred Hospital and Monash University, Melbourne, Australia (7).

Reprint requests: Alan Moss, Department of Gastroenterology, Western Health, Footscray, Melbourne, Victoria 3011, Australia.

If you would like to chat with an author of this article, you may contact Dr Moss at Alan.Moss@wh.org.au.