Recurrence rates after piecemeal endoscopic mucosal resection of large colorectal laterally spreading tumors

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Abstract

Background Piecemeal endoscopic mucosal resection (pEMR) is routinely employed for large laterally spreading tumors (LSTs). Recurrence rates following pEMR are still unclear, especially when cap-assisted EMR (EMR-c) is performed. We assessed the recurrence rates and recurrence risk factors post-pEMR for large colorectal LSTs, including both wide-field EMR (WF-EMR) and EMR-c.

Methods This was a single-center, retrospective study of consecutive patients who underwent pEMR for colorectal LSTs ≥20 mm at our institution between 2012 and 2020. Patients had a post-resection follow-up period of at least 3 months. A risk factor analysis was carried out using the Cox regression model.

Results The analysis included 155 pEMR: 51 WF-EMR and 104 EMR-c, with a median lesion size of 30 (range: 20-80) mm and a median endoscopic follow up of 15 (range: 3-76) months. Overall, disease recurrence occurred in 29.0% of cases; there was no significant difference in recurrence rates between WF-EMR and EMR-c. Recurrent lesions were safely managed by endoscopic removal, and at risk analysis lesion size was the only significant risk factor for recurrence (mm; hazard ratio 1.03, 95% confidence interval 1.00-1.06, P=0.02).

Conclusions Recurrence of large colorectal LSTs after pEMR occurs in 29% of cases. This rate is mainly dependent on lesion size, and the use of a cap during pEMR has no effect on recurrence. Prospective controlled trials are needed to validate these results.

Keywords Piecemeal endoscopic mucosal resection, laterally spreading tumors, cap, recurrence, risk factors

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Introduction

Endoscopic resection techniques have made outstanding advances in the last few years and have been proven to be more cost-effective and safer than surgery for non-malignant colorectal polyps [1]. Laterally spreading tumors (LSTs) are challenging to remove because of their flat shape and large size, with a more than 9% risk of submucosal invasive cancer or lesions ≥20 mm [2,3].

Piecemeal endoscopic mucosal resection (pEMR) has been successfully employed for LSTs up to 100-120 mm in diameter, but with initial major concerns about the high recurrence rate, which ranges from 2.2% to 21% [4-6]. However, these data are derived from heterogeneous series that also included sessile polyps and *en bloc* resections, and had only short follow-up periods. Larger prospective studies [5], improved endoscopic resolution, and the introduction of modified pEMR modalities have all helped to progressively mitigate the initial concerns about the use of pEMR. Cap-assisted EMR (EMR-c) has been extensively used as a backup technique for flat colorectal lesions not suitable for standard pEMR [7-10]. However, there has never been a direct comparison of recurrence rates between standard pEMR (also defined as “wide-field” EMR; WF-EMR) and EMR-c for large LSTs.

This study sought to investigate the recurrence rates and recurrence risk factors following pEMR (including EMR-c) for the removal of large colorectal LSTs.

Patients and methods

Patient selection and endpoints

This was a single-center, retrospective study with prospective data collection. We included consecutive patients undergoing pEMR for large (≥20 mm) colorectal LSTs (years: 2012-2020), with a minimum follow-up period of 3 months.

The primary endpoints were to describe recurrence rates in the overall population post-pEMR and to identify any risk factors for disease recurrence. The secondary endpoint was to compare WF-EMR and EMR-c in terms of recurrence rates, recurrence-free survival analysis, efficacy, and safety.

The study protocol complied with the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008), as reflected in the *a priori* approval by the institution’s human research committee (No. 621/2021, 05.14.2021). Informed consent was obtained from each patient included in the study.

Data collection

Patient data were prospectively gathered and stored in a dedicated electronic database at the time of EMR. The variables included age, sex, use of anticoagulants or antiplatelet agents (suspended as needed in accordance with guideline recommendations), prior attempted resection of the lesion, submucosal lifting, histological report, hospital stay, adverse events, detection of recurrence, and follow-up data.

LSTs were classified according to the Paris and LST classifications for endoscopic morphology [11,12], as well as the Kudo and Japan Narrow-Band Imaging Expert Team (JNET) optical classifications [13,14].

Complete endoscopic resection rate, R0 resection, and the occurrence of adverse events were used to assess the efficacy and safety of the EMR techniques. Endoscopic complete resection was defined by the absence of residual tissue on final inspection at the end of index EMR. R0 resection was defined as a deep margin free from adenomatous tissue at histological evaluation.

Procedure time was calculated from the patient’s admission to the operative endoscopy room up to the time of exit.

Adverse events were assessed for all the procedures and included: (a) intraprocedural bleeding: bleeding that occurs during EMR and requires endoscopic hemostasis with snare tip coagulation or coagulation forceps; (b) delayed bleeding: passage of fresh blood or dark stools after the procedure; (c) deep mural injury (as per Sydney classification) [15]: muscular layer exposure (Grade I), muscular layer defect uninterpretable due to fibrosis (Grade II), target sign (Grade III) or full-thickness perforation (Grade IV) detected during EMR; and (d) post-polypectomy syndrome: abdominal pain (with or without fever) without overt signs of perforation presenting after the procedure.

EMR techniques and histological evaluation

The procedures were all performed by endoscopists with experience in advanced endoscopic resection, under conscious sedation (midazolam and meperidine or fentanyl), with pre-2013 standard endoscopes (CFQ-180AI, GIF-1T140, PCF-Q180AI; Olympus) and high-definition endoscopes from 2013 to 2020 (CF-HQ190I, PCF-H190I, GIF-HQ190I, GIF-1TH190; Olympus).

The endoscopist chose the appropriate resection technique based on a case-by-case meticulous evaluation of the lesion’s characteristics, including its location in the colon, the morphology, pit pattern and lifting sign, in accordance with previous publications [5]. WF-EMR and EMR-c procedures were performed in accordance with other studies found in the literature [5,16] and were carried out at our institution as per standard protocol, that is, requiring submucosal injection with a long-lasting solution (saline, methylene blue, epinephrine, and methylcellulose gel).

In the case of WF-EMR, a conventional lift-and-cut hot snare resection was carried out; the choice of snare type (standard, barbed, or single filament) was left to the endoscopist’s discretion. For the cap-assisted technique, a dedicated cap was attached to the distal end of the scope (Distal Attachment, Olympus). Three caps with different diameters were routinely used: 13.9 mm (MH-594) for standard and operative gastroscopes, 14.9 mm (MH-595) for pediatric colonoscopes, and 17.2 mm (MH-597) for regular colonoscopes. The choice of endoscope was left to the endoscopist’s discretion, depending on the lesion and patient characteristics.

After submucosal injection of the solution under the lesion, a crescent snare was fitted into the cap’s circumferential rim. This process was aided by aspirating the adjacent normal mucosa to create a dome-like inner fold that prevents the snare from dislodging and slipping into the lumen. Once the snare was correctly deployed, the lesion was gently suctioned within the cap (with a lower aspiration setting) and cut in a piecemeal fashion using an electrocautery snare.

Irrespective of the EMR technique used, the endoscopist decided to attempt the closure of the mucosal defect with clips and the thermal ablation of its margins with snare tip coagulation, as recommended in the literature [17]. It should be noted that margin thermal treatment of the margins had not been employed in the initial years of our retrospective analysis. Finally, the resected fragments were retrieved using a snare net (Meditalia; Italy), and all the specimens were pinned and oriented for histological examination.

After the procedure, patients were hospitalized at the endoscopist’s discretion, and in the absence of complications, a one-day liquid diet was followed by the gradual resumption of oral intake.

Colorectal neoplastic lesions were classified according to the modified Vienna Criteria [18]. All histological specimens were reevaluated by 2 expert gastrointestinal pathologists (CS and NLD).

Endoscopic follow up

Following the EMR, the first surveillance colonoscopy (SC1) and second surveillance colonoscopy (SC2) were scheduled at 3 to 6 months and 12 to 18 months, respectively. Subsequent colonoscopies were planned at 3- to 6-month intervals until no residual lesion was detected. Patients re-entered a standard surveillance program after a first negative endoscopy.

The EMR scar was carefully inspected using white light, narrow-band imaging and magnification. Recurrence was defined as the histological confirmation of a detected residual lesion at the site of the scar. Any suspected recurrence was treated with forceps or a hot/cold snare, depending on its size. Biopsies of the scar were routinely carried out, even in the absence of a suspected recurrence. However, biopsies were not taken if no scar was visible and the patient was considered to be free of recurrence.

Statistical analysis

A dedicated software program (Medcalc 15.6.1, www.medcalc.be) was used for the statistical analysis. The distribution of continuous variables was presented as median and range. Subgroups were compared using the Mann-Whitney *U* test for continuous variables, whereas Fisher's exact test or the chi-squared test were used for non-continuous variables. Statistical significance was indicated by a P-value <0.05. Survival curves were compared by means of the log-rank test. The Cox regression model was used to identify a possible correlation between patient/lesion features and recurrence.

Results

A total of 406 EMRs for colorectal polyps ≥20 mm were performed at our institution between 2012 and 2020. After excluding *en bloc* resections, resections of non-flat lesions, and patients missing follow up, 155 pEMR were included in the analysis: 51 WF-EMR and 104 EMR-c.

Patient and lesion features are detailed in Table 1. The median lesion size was 30 (range: 20-80) mm, with the majority of lesions observed in the right colon (66.4%).

Based on the EMR technique, the 2 subgroups of lesions were homogeneous in terms of site, morphology and classifications. Incomplete submucosal lifting was more frequently displayed in the EMR-c group (P=0.001), which also included 15 LSTs initially treated with WF-EMR, and then switched to the cap-assisted technique during the same session to complete the resection.

Primary endpoints: recurrence rates and recurrence risk factors

Overall, the median endoscopic follow up was 15 (range: 3-76) months, with disease recurrence occurring in 29.0% of cases (Table 2). Endoscopy (1-3 treatments with forceps or snare) was always used to treat recurrence, and no surgical procedure was needed. Thermal avulsion with argon plasma coagulation was only applied to 4 patients, and one patient had an endoscopic full-thickness resection for a 12-mm non-lifting recurrence in the cecum.

In terms of risk factor analysis (Table 3), we investigated the variables suggested by the literature as predictive for disease recurrence [5,19,20]. By univariate analysis, the significant variables were lesion size, dentate line involvement and previous EMR attempts. However, by multivariate analysis, only lesion size was confirmed as an independent risk factor for recurrence.

Secondary endpoint: comparison between EMR-c and WF-EMR

Recurrence rates for the EMR technique were comparable between WF-EMR and EMR-c at SC1 (P=0.31) and SC2 (P=0.29) (Table 2). The survival curves confirmed these results (Supplementary Fig. 1).

In terms of procedure-related outcomes (Table 4), the 2 techniques performed similarly in terms of complete endoscopic resection and margin status (R0). Procedure time was significantly longer for EMR-c (123 vs. 104 min for WF-EMR; P=0.007) and involved the resection of more pieces (8 vs. 5, respectively; P<0.001).

Two patients diagnosed with adenocarcinoma were only offered endoscopic follow up: one in the WF-EMR group, who had a high surgical risk due to advanced age and comorbidities, and one in the EMR-c group, who had favorable histologic prognostic factors for superficial invasion. These patients did not develop any endoscopic recurrence during observation.

Hospitalization for clinical observation following the procedure was more frequently required by patients who underwent EMR-c (P<0.001); however, the median duration of hospitalization was similar in both groups.

Endoscopists used prophylactic clips and thermal ablation of resection margins (P=0.005) more frequently in WF-EMR. Conversely, the intraprocedural bleeding rate was higher for EMR-c than WF-EMR (P=0.02); however, endoscopy was routinely used during the same procedure to manage intraprocedural bleeding. Mural injuries were also consistently detected during EMR. These were treated with clip closure

Table 1 Characteristics of patients with laterally spreading tumors (LST) according to the endoscopic mucosal resection (EMR) technique

Features	All EMRs (n=155)	WF-EMR (n=51)	EMR-c (n=104)	P-value
Sex [female; *n* (%)]	67 (43.2)	20 (39.2)	47 (45.2)	0.50
Age [years; median (range)]	68 (42-87)	69 (50-87)	67.5 (42-84)	0.52
Use of antiplatelet drugs, *n* (%)	41 (26.4)	15 (29.4)	26 (25.0)	0.56
Use of anticoagulants, *n* (%)	9 (5.8)	4 (7.8)	5 (4.8)	0.48
Lesion size [mm; median (range)]	30 (20-80)	25 (20-60)	30 (20-80)	0.13
Lesion site				0.13
Right colon, *n* (%)	103 (66.4)	30 (58.8)	73 (70.2)	
Transverse colon, *n* (%)	19 (12.3)	8 (15.7)	11 (10.6)	
Left colon, *n* (%)	19 (12.3)	10 (19.6)	9 (8.6)	
Rectum, *n* (%)	14 (9.0)	3 (5.9)	11 (10.6)	
Difficult site	20 (12.9)	3 (5.9)	17 (16.3)	0.08
Ileocecal valve rim, *n* (%)	10 (6.5)	3 (5.9)	7 (6.7)	
Appendiceal orifice, *n* (%)	5 (3.2)	0 (0)	5 (4.8)	
Dentate line, *n* (%)	5 (3.2)	0 (0)	5 (4.8)	
Absent/scarce lifting, *n* (%)	27 (17.4)	2 (3.9)	25 (24.0)	0.001
Paris classification				0.32
0-IIa, *n* (%)	77 (49.7)	20 (39.2)	57 (54.9)	
0-IIb, *n* (%)	29 (18.7)	12 (23.5)	17 (16.3)	
0-IIc, *n* (%)	2 (1.3)	1 (2.0)	1 (0.9)	
Mixed type, *n* (%) [a]	47 (30.3)	18 (35.3)	29 (27.9)	
LST classification				0.21
LST-G-H, *n* (%)	62 (40.0)	16 (31.4)	46 (44.2)	
LST-G-M, *n* (%)	33 (21.3)	13 (25.5)	20 (19.2)	
LST-NG-F, *n* (%)	42 (27.1)	18 (35.3)	24 (23.1)	
LST-NG-PD, *n* (%)	13 (8.4)	2 (3.9)	11 (10.6)	
Mixed type, *n* (%)	5 (3.2)	2 (3.9)	3 (2.9)	
Kudo classification				0.52
II, *n* (%)	14 (9.0)	6 (11.7)	8 (7.8)	
III s, *n* (%)	27 (17.4)	7 (13.7)	20 (19.2)	
III L, *n* (%)	73 (47.1)	21 (41.2)	52 (50.0)	
IV, *n* (%)	39 (25.2)	16 (31.4)	23 (22.1)	
V, *n* (%)	2 (1.3)	1 (2.0)	1 (0.9)	
JNET classification				0.27
1, *n* (%)	14 (9.0)	7 (13.7)	7 (6.7)	
2A, *n* (%)	69 (44.5)	25 (49.0)	44 (42.4)	
2B, *n* (%)	71 (45.8)	19 (37.3)	52 (50.0)	
3, *n* (%)	1 (0.7)	0 (0)	1 (0.9)	
Previous EMR attempts, *n* (%)	6 (3.9)	1 (2.0)	5 (4.8)	0.66
Switch after WF-EMR failure, *n* (%)	15 (9.7)	0 (0)	15 (14.4)	-

[a]Including 0-IIa+Is, 0-IIa+IIc, 0-IIb+Is, IIb+IIc

EMR, endoscopic mucosal resection; WF-EMR, wide-field EMR; EMR-c, cap-assisted EMR; LST, laterally spreading tumor; G-H, granular homogeneous; G-M, granular mixed; NG-F, non-granular flat; NG-PD, non-granular pseudo-depressed

(Grade II and Grade III), along with conservative treatment with antibiotics.

Discussion

This study demonstrated that recurrence occurs in 29.0% of cases following pEMR of large colorectal LSTs and that these lesions can be safely treated by endoscopic removal. The risk of recurrence is influenced by the size of the lesion, but not by the use of EMR-c. In contrast to the literature, our results reveal a higher incidence of recurrence following pEMR for the removal of large colorectal LSTs [4-6]. A prospective, large population study by Moss *et al* [5], involving 799 successful EMRs, had a recurrence rate of 20.0%. However, the series was heterogeneous and also included sessile polyps and *en bloc* resections. In comparison, our study population was smaller but chosen more

Table 2 Recurrence rates according to the endoscopic mucosal resection (EMR) technique

Features	All EMRs (n=155)	WF-EMR (n=51)	EMR-c (n=104)	P-value
Follow-up time [months; median (range)]	15 (3-76)	10 (3-76)	21 (3-75)	<0.001
Recurrence (overall), *n* (%)	45 (29.0)	12 (23.5)	33 (31.7)	0.28
Recurrence at SC1, *n* (%)[a]	40 (28.6)	9 (21.4)	31 (31.6)	0.31
Recurrence at SC2, *n* (%)[b]	11 (10.4)	5 (16.1)	6 (8.0)	0.29
Number of retreatments, median (range)	1 (1-3)	1 (1-3)	1 (1-3)	0.44

[a]Performed in 140 patients

[b]Performed in 106 patients

EMR, endoscopic mucosal resection; WF-EMR, wide-field EMR; EMR-c, cap-assisted EMR; SC1, surveillance colonoscopy 1; SC2, surveillance colonoscopy 2

Table 3 Risk factors for disease recurrence after endoscopic mucosal resection (EMR)

Univariate analysis			
Variables	HR	95%CI	P-value
Lesion size, mm	1.03	1.01-1.06	0.002
EMR-c vs WF-EMR	1.40	0.72-2.72	0.32
Intraprocedural bleeding	0.87	0.39-1.96	0.74
Ileocecal valve rim involvement	0.35	0.05-2.54	0.30
Appendiceal orifice involvement	0.67	0.09-4.85	0.69
Dentate line involvement	4.81	1.69-13.68	0.003
High-grade dysplasia	0.87	0.48-1.57	0.65
Previous EMR attempts	3.80	1.43-10.76	0.01
Thermal ablation of margins	1.00	0.44-2.25	0.99
Multivariate analysis			
Variables	HR	95%CI	P-value
Lesion size, mm	1.03	1.00-1.06	0.02
Dentate line involvement	3.19	0.95-10.65	0.06
Previous EMR attempts	1.36	0.31-5.96	0.69

HR, hazard ratio; CI, confidence interval; EMR-c, cap-assisted endoscopic mucosal resection; WF-EMR, wide-field EMR

selectively. It consisted exclusively of pEMRs of large colorectal LSTs, a prospectively collected database with several years of follow up, and scar biopsies taken at surveillance colonoscopies. Based on these observations, previous publications may have underestimated the real recurrence risk because of their shorter follow-up periods and a lack of histological assessment of post-EMR scarring [21]. Furthermore, routine snare-tip coagulation of mucosal defect margins was only recently introduced into endoscopic practice, after high-quality evidence demonstrated its efficacy in reducing recurrences [22,23]. In consequence, it was only used in a minority of patients in our study: that is, the most recent cases.

In terms of EMR-c, Moss *et al* [5] stated that some of their population's lesions had been resected using the cap, but they omitted to report the results for this subgroup. In contrast, our study included a subanalysis based on the EMR technique, and, to our knowledge, no study has previously directly compared WF-EMR with EMR-c in terms of recurrence-free survival (RFS) rates.

The results for WF-EMR and EMR-c of large LSTs in our series were comparable in terms of RFS rates and complete resection. However, EMR-c was widely used in the case of challenging LSTs and after failed WF-EMR. This observation may help to explain the greater hospitalization requirement, the longer follow-up period, and the high rate of intraprocedural bleeding that we observed when a cap was used (23.1% vs. 3.9-9.0% reported in literature [10,24]). A higher rate of intraprocedural bleeding associated with EMR-c when compared to standard EMR was reported in a previous study investigating rectal neuroendocrine tumors [7]. We hypothesize that this may be due to vessels of a large diameter encountered in the deep submucosa when using the suction-and-cut technique. However, during the same endoscopic procedure, bleeding was always successfully treated with endoscopic hemostasis and probably also with the aid of a distal cap to manage the damaged vessels, as previously reported for upper gastrointestinal bleeding [25,26].

In terms of risk analysis, as previously discussed [5,27], lesion size was the independent risk factor for recurrence following pEMR in our series. Other risk factors reported in the literature (i.e., a lesion in a difficult location and previous EMR attempts) were not significant in our analysis. A possible explanation is that the majority of our cases represented challenging lesions treated at our institution by means of EMR-c, and that this may have introduced a potential bias to our analysis.

The low rate of invasive carcinoma observed in our series, even after the switch to EMR-c for difficult resections, confirmed that surgery would have been an overtreatment in these cases. As previously discussed, the outcome of the invasive lesions was favorable, since the pathological evaluation of the surgical specimen did not result in any residual disease or lymph node involvement, and there was no endoscopic recurrence in any of the patients who did not undergo surgery [16].

Table 4 Outcomes according to the endoscopic mucosal resection (EMR) technique

Features	All lesions (n=155)	WF-EMR (n=51)	EMR-c (n=104)	P-value
Complete endoscopic resection, *n* (%)	151 (97.4)	50 (98.0)	101 (97.1)	>0.99
Margin status (R0), *n* (%)[a]	128 (96.2)	35 (97.2)	93 (95.9)	>0.99
Histopathology				0.79
Tubular adenoma, *n* (%)	53 (34.2)	18 (35.3)	35 (33.6)	
Villous adenoma, *n* (%)	84 (54.2)	26 (51.0)	58 (55.8)	
Serrated, *n* (%)	18 (11.6)	7 (13.7)	11 (10.6)	
Presence of dysplasia/carcinoma				0.61
High-grade dysplasia, *n* (%)[b]	93 (60.0)	28 (54.9)	65 (62.5)	0.16
Invasive adenocarcinoma, *n* (%)	2 (1.3)	1 (1.9)	1 (0.9)	0.75
Procedure time [min; median (range)]	120 (48-306)	104 (48-230)	123 (60-306)	0.007
Number of pieces, *n* (%)	7 (2-37)	5 (2-30)	8 (2-37)	<0.001
Need for hospitalization, *n* (%)	42 (27.1)	4 (7.8)	38 (36.5)	<0.001
Hospital stay [days; median (range)]	3 (1-7)	2.5 (1-7)	3 (1-7)	0.39
Prophylactic clip placement, *n* (%)	54 (34.8)	31 (60.8)	23 (22.1)	<0.001
Thermal treatment of resection, *n* (%)	26 (16.8)	15 (29.4)	11 (10.6)	0.005
Adverse events				
Intraprocedural bleeding, *n* (%)	28 (18.1)	4 (7.8)	24 (23.1)	0.02
Delayed bleeding, *n* (%)	12 (7.7)	4 (7.8)	8 (7.7)	>0.99
Deep mural injury, *n* (%)	25 (14.0)	4 (6.3)	21 (20.2)	0.06
Grade I/II, *n* (%)	11 (8.1)	1 (1.6)	10 (9.6)	
Grade III, *n* (%)	13 (8.4)	2 (4.8)	11 (10.6)	
Post-polypectomy syndrome, *n* (%)	1 (0.6)	0 (0)	1 (0.9)	>0.99

[a]Not evaluable in 22 cases

[b]Including intramucosal carcinoma

EMR, endoscopic mucosal resection; WF-EMR, wide-field EMR; EMR-c, cap-assisted EMR

This study had some limitations, the main one being its retrospective design. However, this limitation may be offset by the prospectively collected database, the single-center design, and the selectively chosen population.

The risk of preselection bias surrounding the decision on whether to perform WF-EMR or EMR-c is also worth discussing, even though other authors have previously stated that the decision to perform large EMR-c for LSTs should be left to the endoscopist's discretion. Since a cap can aid in the resection of lesions not suited to standard pEMR, the frequent use of a cap in our series (104 EMR-c vs. 51 WF-EMR) is justified by the high referral rate of "challenging" LSTs in our second-level Endoscopy Unit. The risk of preselection bias in our series may also be mitigated by the observation that the 2 subsets of cases (based on the EMR technique) were homogeneous with respect to almost all features, except for the scarce submucosal lifting (Table 1).

Another potential limitation of our study is the omission of any cases treated with endoscopic submucosal dissection (ESD), despite the fact that some experts view this technique as being the gold standard for the removal of high-risk LSTs [28]. However, several drawbacks may outweigh ESD's curative potential: the time-consuming procedure with higher risks (particularly perforation), the steep learning curve, higher costs for post-procedural hospitalization, and poor reimbursement. ESD may have been riskier for our population, as in the majority of cases (66.4%) the tumors were located in the right colon. Furthermore, the extensive use of this technique beyond the rectum is currently not acceptable practice, particularly in western countries [29].

In conclusion, recurrence following the pEMR of large colorectal LSTs occurs in almost 30% of cases, is mainly dependent on lesion size, and can be easily removed with the use of forceps or *en bloc* hot/cold snare resection. With the same risk of recurrence, EMR-c may be an effective and safe alternative to WF-EMR in the case of challenging lesions. However, this technique must be performed by expert endoscopists in high-volume referral centers, in view of the increased risk of intraprocedural complications. Prospective studies are needed to confirm these results.

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Summary Box

What is already known:

- Laterally spreading tumors (LSTs) are challenging to remove because of their flat shape and large size, with a higher risk of submucosal invasive cancer for lesions ≥20 mm
- Piecemeal endoscopic mucosal resection (pEMR) has been successfully employed for LSTs up to 120 mm in diameter, but with initial major concerns regarding the high recurrence rate
- Cap-assisted EMR (EMR-c) has been extensively adopted as a backup technique in the case of flat colorectal lesions not suited to standard pEMR

What the new findings are:

- Recurrence following the pEMR of large colorectal LSTs occurred in almost 30% of cases
- The rate of recurrence was mainly dependent on lesion size, with no statistically significant difference between WF-EMR and EMR-c
- EMR-c may represent an effective and safe alternative to WF-EMR in the case of challenging colorectal LSTs, with the same risk of recurrence; however, this technique must be performed by expert endoscopists in high-volume referral centers

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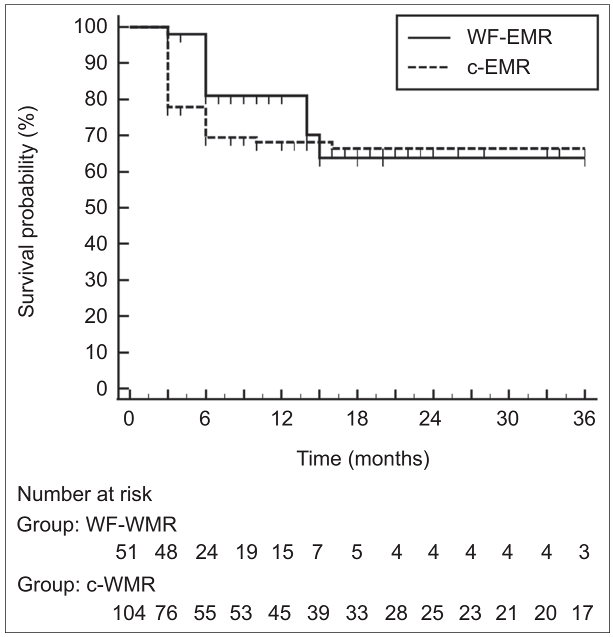
Supplementary material



Supplementary Figure 1 Recurrence-free survival (RFS) based on the endoscopic mucosal resection (EMR) technique. The median RFS was not reached both for WF-EMR and for EMR-c subgroups. At 12 months, the recurrence-free rate was 81.0% for WF-EMR and 68.2% for EMR-c; at 24 months, the recurrence-free rate stood at 63.8% and 66.4%, respectively (P=0.28)