

Adenoma recurrence after endoscopic mucosal resection: propensity score analysis of old and new colonoscopes and Sydney recurrence tool implementation



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ABSTRACT

Background and study aims Risk factors for colorectal adenoma recurrence after endoscopic mucosal resection (EMR) have been well documented. We assessed the effica-

cy of the newer 190 colonoscope versus the standard 180 colonoscope for complete resection of lateral spreading lesions.

Patients and methods A single-center, retrospective study of patients who underwent EMR with Olympus 180 or 190 colonoscopes from January 1, 2010 to September 30, 2016. We included patients with lesions ≥ 20 mm and surveillance colonoscopy (SC1) after index EMR. A propensity score approach with inverse probability weighting was used to control for potential confounders. A secondary aim was to identify risk factors for recurrence and assess the applicability of the Sydney EMR recurrence tool (SERT) by grading each lesion of our cohort and analyzing associations with recurrence.

Results Two hundred ninety-one lesions met inclusion criteria for the study. Odds ratio (OR) for recurrence with the 190 colonoscope was 1.06 ($P=.85$). Adenoma size ($P=.02$) and use of argon plasma coagulation (APC; $P<.001$) were risk factors for recurrence. Lesions with SERT scores > 0 had a higher recurrence risk during follow-up (32% vs 21%; OR 1.71; $P=.05$). Lesions with SERT scores = 0 reached a plateau for recurrence at 12 and 18 months in Kaplan-Meier curves.

Conclusions The use of 190 colonoscopes did not measurably affect adenoma recurrence at SC1. Recurrence was associated with adenoma size, complementary APC for resection, and SERT scores > 0 . Lesions with SERT scores = 0 that remain negative for recurrence at 18 months may return to routine surveillance.

Introduction

The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee defined the quality of endoscopic visualization as a function of video resolution and magnification [1]. High definition (HD), high power of magnification, and chromoendoscopy have been implemented as potential imaging enhancers during colonoscopy with the purpose of increasing the detection, pit pattern characterization, and target-

ted treatment of colonic lesions while decreasing the miss rate and unnecessary pathologic evaluation of non-neoplastic polyps. When large (> 1 cm), laterally spreading lesions (LSL) are detected; endoscopic mucosal resection (EMR) can be performed as a minimally invasive technique with high success rates and lower morbidity, mortality, and cost when compared to surgery [2].

At the beginning of every EMR procedure a detailed visualization to establish the margins, particularly of flat lesions, is

crucial to ensure a complete resection and minimize the risk of residual or recurrent adenoma (RRA). A recent study by Desomer et al [3] demonstrated that HD narrow-band imaging (HD-NBI) detects RRA with improved accuracy compared to white light. The newly available second generation 190 colonoscopes (190-NBI; see description below) provides at least 2-fold brighter HD images, with increased contrast and decreased halation compared to the previous version of colonoscopes [4]. The 190 colonoscope further allows polyp examination in standard and near-focus modes granting a true optical in-focus zoom [5]. Additionally, it has twice the viewable distance of 180 colonoscopes. An important question raised in a recent editorial to the Desomer paper by Cohen [6] is whether this advanced optical system reduces RRA by improving the initial visualization of affected tissue and subsequently improves complete endoscopic resection of LSLs. This question was the impetus for our study.

Intralesional and extralesional risk factors for adenoma recurrence after EMR have been well described in multiple studies [2, 7–11]. A more recent prospective multicenter study by Tate et al [12] proposed a scoring model for stratification of recurrence risk after EMR. The Sydney EMR recurrence tool (SERT) is a 0 to 4 point scale that grades a lesion based on a size of 40 mm or larger (2 points), presence of intraprocedural bleeding (IPB; 1 point), and high-grade dysplasia (HGD) in histopathology (1 point) [12]. The authors concluded that a score of 0 entails a low risk for recurrence at 6 months; therefore, these patients could safely undergo first surveillance colonoscopy (SC1) at 18 months. If clinically applicable, stratification of recurrence risk may considerably reduce the costs of colon cancer surveillance and bypass unnecessary histopathologic evaluation.

Patients and methods

The Mayo Clinic Institutional Review Board approved the study. The primary aim of this study was to assess the efficacy of the newer CF-HQ190L/I colonoscopes versus the standard CF-H180AL/I colonoscopes in the complete resection of LSL 20 mm or larger as demonstrated by a reduction in the rate of RRA at the EMR site during SC1. A secondary aim was to identify risk factors for RRA in our study population and assess the clinical applicability of the SERT score for further surveillance recommendations.

Patients

Consecutive patients who underwent EMR of colorectal polyps from January 1, 2010 to September 30, 2016 were extracted from the Mayo Clinic, Jacksonville, Florida, ProVation MD system and their electronic medical records were retrospectively reviewed. Of 836 resected lesions, we included 291 in patients who met the inclusion criteria for the study: LSL 20 mm or larger and at least 1 surveillance colonoscopy (SC) after index EMR for evaluation of RRA. If the patient had more than 1 LSL 20 mm or larger treated with EMR, every lesion was included in the study. Other inclusion and exclusion criteria are described in **Box**.

INCLUSION AND EXCLUSION CRITERIA FOR STUDY ELIGIBILITY

Inclusion criteria

- Age \geq 18 years
- Colonoscopy done with either Olympus 180 or 190 series colonoscopes
- Lateral spreading lesions \geq 20 mm
- Lesions adequately/partially lifted prior to EMR
- Lesions completely resected and retrieved according to endoscopist's assessment
- Polyps with or without prior therapy

Exclusion criteria

- Patients who failed to have a surveillance colonoscopy after index EMR done in our facility
- Lesions resected en bloc (excluded only for IPW analysis)

EMR, endoscopic mucosal resection; IPW, inverse probability weighting

Patients who failed to come back to our facility for SC after index EMR were excluded from the study. All collected data were filtered for inclusion criteria as shown in ► **Fig. 1**.

Procedures and endoscopy equipment

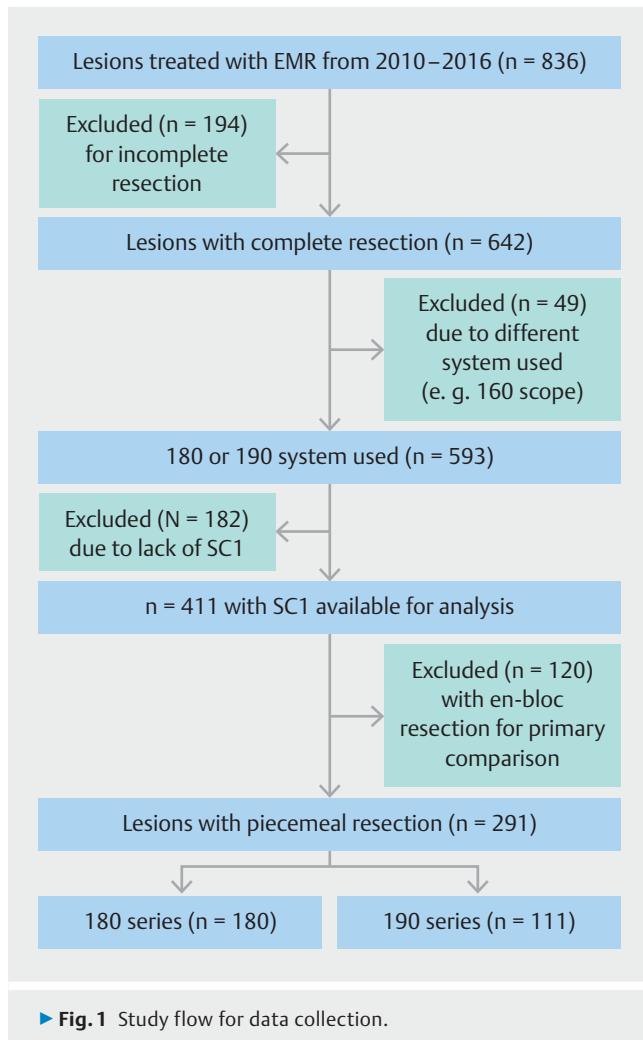
The procedure was performed by 1 of the 5 EMR specialists in our gastroenterology department. HD endoscopy with Olympus CF-H180AL/I and Olympus CF-HQ190L/I colonoscopes (Olympus America, Center Valley, Pennsylvania), and with EVIS EXERA II CV-180 and EVIS EXERA III CV-190 (Olympus Medical Systems, Tokyo, Japan) video processors were performed to characterize all lesions.

Olympus 190 colonoscopes were introduced in our practice at the end of 2013. From 2010 to early 2013, every patient included in our study underwent EMR with the 180 series. Starting in 2014, patients underwent EMR with either the 180 or 190 systems depending on the colonoscope availability at the time of the procedure. This assignment was therefore not a result of operator preference or patient characteristics.

White light imaging and HD-NBI were performed to inspect the mucosa. If the 190 scope was employed, zoom magnification (near focus or NF) of the lesion was used at the discretion of the endoscopist. Polyp size, anatomic site, and macroscopic morphology using the Paris classification were recorded [13]. Polyps were removed using the inject, lift, and cut method [14]. If removal was incomplete, snare tip soft coagulation, argon plasma coagulation (APC), or hot forceps avulsion were used to achieve complete removal of lesions. All polyps were sent for histopathologic analysis, and specialized gastrointestinal pathologists performed histologic examination.

Surveillance colonoscopy: defining recurrence

Repeat colonoscopy in 6 months was recommended for surveillance. SC and EMR scar assessment were done by an EMR specialist, and biopsy or snare resection of the scar were per-



formed if there was any suspicion of recurrence. The post-EMR scar was assessed with HD-NBI of the lesion with either 180 or 190 colonoscopes depending on availability. If there was high confidence of no residual/recurrent neoplasia, it was assumed to be negative. We have previously confirmed that such inspection has a high negative predictive value in a recent study by Kandel et al in our center. In all other cases biopsy samples were taken and histology served as the reference standard for recurrence.

Statistical analysis

Categorical variables were reported as numbers and percentages with group differences compared using the χ^2 test. Continuous variables were reported as the mean (SD) and interquartile range (IQR; first and third quartiles), and differences between 2 groups were evaluated using a *t* test. Due to substantial confounding between the colonoscope used and the type of resection (piecemeal vs en bloc), every procedure with en bloc resection was excluded from the comparative analysis. Logistic regression was used to estimate the odds ratio (OR) and CIs for risk factors and associations with recurrence.

A propensity score was developed using logistic regression to model the likelihood of the scope used based on patient and procedural characteristics. The variables used to construct the propensity score were age, sex, prior treatment of the lesion, polyp size, EMR location, Paris classification, endoscopist, lesion adequately lifted, IPB, use of APC, and initial pathology. Additionally, interactions between age and sex and initial pathology and prior treatment were included to improve covariate balance. Inverse probability weights (IPWs) were assigned to each patient according to the reciprocal of the estimated probability of being in their observed group. Weights were then normalized so that the weights within each group totaled the group sample size. On the weighted data, standardized differences were calculated to assess imbalance for continuous variables, differences in proportions were used for binary variables. A difference greater than 0.10 was considered a sign of imbalance.

The SERT score was calculated in all patients with piecemeal resection and a score above 0 was considered high-risk for recurrence. Sensitivity and specificity measures for the association between a SERT score above 0 and the incidence of any recurrence were calculated. ORs for recurrence at any point in follow-up were calculated using logistic regression. A multiple logistic regression model was used to estimate adjusted ORs for the 3 components of the SERT score. Recurrence was also estimated using Kaplan-Meier method, recognizing that this approach has limitations, given that the time of recurrence is not continuously monitored and is dependent on the timing of the follow-up colonoscopy.

Analyses were 2-tailed, and the threshold for statistical significance was $P < .05$. Analyses were conducted using R Software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient population and 180 versus 190 colonoscopes

A total of 378 patients with 411 resected lesions met the initial inclusion criteria (en bloc and piecemeal resections). The 180 colonoscope was used in 72% of resections ($n = 296$) and the 190 colonoscope was used in 28% ($n = 115$). Mean age was 67 years (± 10) with a median polyp size of 30 mm (20–140 mm). Median time to SC1 was 5 months (IQR 15–30 weeks). Some differences in baseline characteristics between the 2 groups included age, prior treatment of polyp, initial histopathology, use of APC, resection type, year of procedure, and endoscopist performing EMR, which were adjusted with IPW before final analysis. The prevalence of adenoma recurrence at SC1 in the whole cohort was 19.7% ($n = 81$).

En bloc resection of polyps historically decreases adenoma recurrence risk on follow-up compared to piecemeal EMR [15]. In our cohort, there was a large difference in the rate of en bloc resection between the 2 groups (39.2% [$n = 116$] with the 180 colonoscope versus 3.5% [$n = 4$] with the 190 colonoscope; $P < .001$). To avoid a bias in the results interpretation, en bloc resection cases were subsequently excluded ($n = 120$) from the final analysis.

The baseline characteristics of the final study cohort are reported in ► **Table 1**. Our final cohort consisting of piecemeal only resections included 291 lesions; 61.9% (n=180) were resected with the 180 colonoscope and 38.1% (n=111) with the 190 colonoscope. Mean age was 67 years±10 (57–77 y/o), median lesion size was 30 mm (20–140 mm), and median time to SC1 was 5 months (IQR 15–29 weeks; ► **Fig. 2**). The prevalence of adenoma recurrence at SC1 after piecemeal EMR was 24.1% (n=70). There was no difference in the rate of RRA between the 180 and 190 scopes (23.3% vs 25.2%, respectively; *P*=.82). Except for age, prior treatment of polyp, initial histopathology, year of procedure, and use of APC, baseline characteristics were similar in both groups (► **Table 2**). During SC1, 59.1% (n=172) of the EMR scars were assessed with the 180 colonoscope and 40.5% (n=118) were assessed with the 190 colonoscope (n=290). The remaining EMR scar was assessed by surgical resection secondary to RRA suspicious for malignancy. There was no evidence that the type of colonoscope used for surveillance had an impact in the rate of RRA (*P*=.44).

IPW was applied to control for confounders, resulting in groups with balanced covariates (► **Table 3**). The OR estimate for effect of the 190 colonoscope on recurrence was 1.11 (95% CI 0.64–1.92; *P*=.71) before adjustment and 1.06 (95% CI 0.60–1.86; *P*=.85) after IPW, suggesting no difference in adenoma recurrence based on the type of scope used for EMR (► **Table 4**).

Risk factors for recurrence

Adenoma size was documented as larger than 40 mm in 33% of the lesions (n=96). The majority of the lesions were located in the right colon (n=202, 69.3%), with the ascending colon (n=97, 33.3%) and cecum (n=63, 21.6%) being the most common locations. HGD occurred in 6.9% of the lesions (n=20) and IPB was reported in 10.7% of cases (n=31).

Concomitant use of APC was documented in 26.1% of procedures (n=76) and the frequency of lesions previously treated was 8.3% (n=24). On univariate logistic regression for all 411 lesions, risk factors for adenoma recurrence at SC1 were lesion size (OR 1.32 per 10 mm; 95% CI 1.11–1.56; *P*=.002) and complementary APC use (OR 3.31; 95% CI 1.93–5.67; *P*<.001). On univariate logistic regression for piecemeal only EMR (n=291), APC use and a SERT score 1–4 were found as significant risk factors for adenoma recurrence (► **Table 5**).

Upon multivariate logistic regression with the 3 SERT variables for recurrence prediction (IPB, adenoma size, and HGD), none of the 3 were found as significant independent predictors for RRA at SC1 in our cohort (► **Table 6**).

SERT score analysis

From the cohort of 291 lesions with piecemeal resection, 59.8% (n=174) were classified as SERT score 0 and 40.2% (n=117) had SERT scores of 1 to 4. The overall recurrence at SC1 was 24.1% (n=70) and the recurrence at any follow-up colonoscopy was 25.4% (n=74). The mean time to recurrence or last follow-up was 63.5 weeks (IQR 19–81 weeks). The rates of recurrence for SERT scores 0 to 4 at SC1 were 20.1%, 27.3%, 27.1%, 39.1%, and 50%, respectively (► **Table 7**). Lesions with SERT

scores greater than 0 had a higher risk of recurrence when compared to those with a SERT score of 0 (OR 1.71; 95% CI 1.00–2.92; *P*=.04).

Of 174 lesions classified as SERT score 0, 79.9% (n=139) had no recurrence at SC1 and 20.1% (n=35) had recurrence at SC1. The accuracy of the SERT score (0 versus >0) for predicting recurrence was modest with a sensitivity of 50%, a specificity of 63.1%, a positive predictive value of 31.6%, and a negative predictive value of 78.7%. Thus, we estimate that 79% of lesions with SERT score 0 were correctly classified as low-risk and did not recur.

For the display of time to recurrence according to SERT score of the lesion, Kaplan-Meier survival plots were generated (► **Fig. 3** and ► **Fig. 4**). For lesions with SERT score 0, there was a 16.4% (n=26) recurrence at 6 months. The cumulative incidence of recurrence escalated to 23.3% (n=34) at 12 months and remained at 23.3% at 18 months. After 18 months, there was a minimal incidence of event rate at 24 (25.4%, n=35) and 36 months (27.5%, n=36).

The cumulative incidence of lesions with SERT scores 1 to 4 was 21.9% (n=21) at 6 months, and consistently escalated at 12, 18, 24, and 36 months (37.6%, 43.6%, 47.1%, and 51.5%, respectively, log-rank test; *P*=.009; ► **Table 8**, ► **Fig. 5**).

Discussion

In our study, the use of second generation HD-NBI with Near-Focus (190 colonoscopes) for EMR of large LSL did not affect the rate of adenoma recurrence at follow-up colonoscopy when compared to first generation HD-NBI series (180 colonoscopes). A SERT score of 0 was associated with lower recurrence rates, but was of modest accuracy at identifying patients who do not need intensive surveillance. A strength of this study was a large sample size of lesions resected throughout 6 years by a highly experienced group of endoscopists on a steady learning curve. The potential for outcomes to be affected by confounding variables as a consequence of the retrospective nature of the study was mitigated by the use of IPW. Nonetheless, as a tertiary referral center, we frequently treat complicated or previously manipulated lesions, potentially increasing the risk for adenoma recurrence and referral bias. Our recent implementation of snare tip soft coagulation for prevention of recurrence after EMR, might overestimate the benefits of 190 colonoscopes in reducing RRA rates. Results from a multicenter study have shown that thermal ablation (snare tip soft coagulation of margins) significantly reduced adenoma recurrence after EMR in SC1 [16]. Additionally, due to the retrospective nature of the study, it is uncertain if the endoscopists were indeed using the Near-Focus feature of 190 colonoscopes for every EMR.

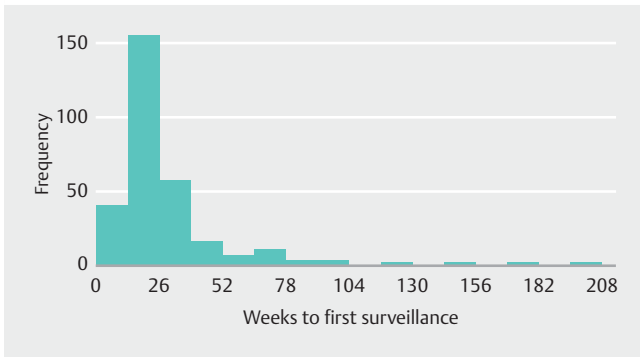
Variable rates of RRA continue to challenge the effectiveness of colorectal EMR. Several studies have been conducted to find potential clinical and endoscopic predictors for recurrence [2, 3, 7–10, 19, 20]. A recent metaanalysis of 30 articles and 3404 patients undergoing EMR reported an overall rate of recurrence of 13.1% [17]. Other studies found that the probability of clearance at first endoscopic resection attempt was affected by the

► **Table 1** Characteristics for 291 patients with piecemeal resections

Characteristic	Patients, No. (%) ¹
Age	
▪ Mean (SD)	67 (10.1)
▪ Q1, Q3	60, 75
▪ Range	36–89
Sex	
▪ Men	132 (45.4)
▪ Women	159 (54.6)
Prior treatment	
▪ No	267 (91.8)
▪ Yes	24 (8.2)
Polyp size, mm	
▪ 20–39	195 (67.0)
▪ 40+	96 (33.0)
EMR site	
▪ Cecum	63 (21.6)
▪ Ileocecal valve	16 (5.5)
▪ Ascending	97 (33.3)
▪ Hepatic flexure	26 (8.9)
▪ Transverse	32 (11.0)
▪ Descending	13 (4.5)
▪ Sigmoid	16 (5.5)
▪ Anorectal	20 (6.9)
▪ Others	8 (2.8)
Initial pathology	
▪ HGD	20 (6.9)
▪ TVA	80 (27.5)
▪ SSA	53 (18.2)
▪ TA	122 (41.9)
▪ Adenocarcinoma	8 (2.7)
▪ HP	8 (2.7)
HGD pathology	
▪ Not HGD	271 (93.1)
▪ HGD	20 (6.9)
SERT score	
▪ N-Miss	0
▪ 0	174 (59.8)
▪ 1	22 (7.6)
▪ 2	70 (24.1)
▪ 3	23 (7.9)
▪ 4	2 (0.7)
▪ 0	117 (40.2)

► **Table 1** (Continuation)

Characteristic	Patients, No. (%) ¹
Endoscopist	
▪ 1	96 (33.0)
▪ 2	60 (20.6)
▪ 3	96 (33.0)
▪ 4	9 (3.1)
▪ 5	28 (9.6)
▪ 6 (Other)	2 (0.7)
Lifted lesion	
▪ Adequate	279 (95.9)
▪ Partial	12 (4.1)
Intraprocedural bleeding	
▪ No	260 (89.3)
▪ Yes	31 (10.7)
Prophylactic APC	
▪ No	215 (73.9)
▪ Yes	76 (26.1)
Type of resection	
▪ Piecemeal	291 (100)
▪ En bloc	0 (0)
Scope used at SC1	
▪ 180	172 (59.1)
▪ 190	118 (40.5)
▪ Surgical specimen	1 (0.4)
Recurrence at first follow-up	
▪ No	221 (75.9)
▪ Yes	70 (24.1)
Recurrence at any follow-up	
▪ No	217 (74.6)
▪ Yes	74 (25.4)
Weeks to first follow-up	
▪ Mean (SD)	27.4 (23.3)
▪ Q1, Q3	15, 29.1
▪ Range	0–201
Weeks to recurrence or last follow-up	
Mean (SD)	63.5 (66.6)
Q1, Q3	18.9, 80.8
Range	0–325
APC, argon plasma coagulation; EMR, endoscopic mucosal resection; HGD, high-grade dysplasia; HP, hyperplastic; N-Miss, number missing; Q1, first quartile; Q3, third quartile; SC1: first surveillance colonoscopy; SERT: Sydney EMR recurrence tool; SSA: sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma	
¹ Unless otherwise indicated	



► **Fig. 2** Histogram showing the distribution of time to first surveillance colonoscopy.

► **Table 2** Summary of piecemeal resections stratified by type of colonoscope used for EMR (n = 291).

Variable	Colonoscope		P value
	180 (n = 180) ¹	190 (n = 111) ¹	
Age			.03
▪ Mean (SD)	68 (10.1)	65.3 (9.85)	
▪ Q1, Q3	62, 75	59, 72	
▪ Range	40–88	36–89	
Sex			.84
▪ Male	83 (46.1)	49 (44.1)	
▪ Female	97 (53.9)	62 (55.9)	
Prior treatment			.01
▪ No	159 (88.3)	108 (97.3)	
▪ Yes	21 (11.7)	3 (2.7)	
Polyp size, mm			.40
▪ N-Miss	0	0	
▪ 20–29	70 (38.9)	47 (42.3)	
▪ 30–39	46 (25.6)	32 (28.8)	
▪ 40–49	34 (18.9)	15 (13.5)	
▪ 50–59	16 (8.9)	11 (9.9)	
▪ 60–69	7 (3.9)	2 (1.8)	
▪ 70–99	4 (2.2)	2 (1.8)	
▪ 100+	3 (1.7)	2 (1.8)	
EMR site			.53
▪ Cecum	43 (23.9)	20 (18.0)	
▪ Ileocecal valve	11 (6.1)	5 (4.5)	
▪ Ascending	51 (28.3)	46 (41.4)	
▪ Splenic flexure	3 (1.7)	1 (0.9)	
▪ Hepatic flexure	15 (8.3)	11 (9.9)	
▪ Transverse	21 (11.7)	11 (9.9)	

► **Table 2** (Continuation)

Variable	Colonoscope		P value
	180 (n = 180) ¹	190 (n = 111) ¹	
▪ Descending	8 (4.4)	5 (4.5)	
▪ Sigmoid	11 (6.1)	5 (4.5)	
▪ Anorectal	15 (8.3)	5 (4.5)	
▪ Appendiceal orifice	1 (0.6)	2 (1.8)	
▪ Colon multiple	1 (0.6)	0 (0.0)	
Initial pathology			<.001
▪ TA with HGD	4 (2.2)	3 (2.7)	
▪ TVA	51 (28.3)	29 (26.1)	
▪ SSA	23 (12.8)	38 (34.2)	
▪ TA	90 (50.0)	32 (28.8)	
▪ TVA with HGD	8 (4.4)	5 (4.5)	
▪ Adenocarcinoma	4 (2.2)	4 (3.6)	
Paris Classification			.22
▪ Ip	3 (1.7)	0 (0.0)	
▪ Is	8 (4.4)	5 (4.5)	
▪ 0-IIa	40 (22.2)	28 (25.2)	
▪ 0-IIb	5 (2.8)	8 (7.2)	
▪ 0-IIc	2 (1.1)	0 (0.0)	
▪ IIc + IIa	0 (0.0)	1 (0.9)	
▪ Unknown	122 (67.8)	69 (62.2)	
Endoscopist			.08
▪ 1	57 (31.7)	39 (35.1)	
▪ 2	40 (22.2)	20 (18.0)	
▪ 3	64 (35.6)	32 (28.8)	
▪ 4	2 (1.1)	7 (6.3)	
▪ 5	15 (8.3)	13 (11.7)	
▪ 6	2 (1.1)	0 (0.0)	
Year of procedure			<.001
▪ 2010	53 (29.4)	0 (0.0)	
▪ 2011	41 (22.8)	0 (0.0)	
▪ 2012	42 (23.3)	0 (0.0)	
▪ 2013	15 (8.3)	6 (5.4)	
▪ 2014	14 (7.8)	32 (28.8)	
▪ 2015	9 (5.0)	50 (45.0)	
▪ 2016	6 (3.3)	23 (20.7)	
Lifted lesion			.58
▪ Adequate	174 (96.7)	105 (94.6)	
▪ Partial	6 (3.3)	6 (5.4)	
Intraprocedural bleeding			.90

► **Table 2** (Continuation)

Variable	Colonoscope		P value
	180 (n = 180) ¹	190 (n = 111) ¹	
▪ No	160 (88.9)	100 (90.1)	
▪ Yes	20 (11.1)	11 (9.9)	
Prophylactic APC			.04
▪ No	141 (78.3)	74 (66.7)	
▪ Yes	39 (21.7)	37 (33.3)	
Recurrence in EMR Scar			.98
▪ No	138 (76.7)	83 (74.8)	
▪ Yes	42 (23.3)	28 (25.2)	
Pathology of recurrence			.96
▪ No recurrence	138 (76.7)	83 (74.8)	
▪ TVA	11 (6.1)	6 (5.4)	
▪ SSA	5 (2.8)	7 (6.3)	
▪ TA	26 (14.4)	15 (13.5)	
Weeks to follow-up			.82
▪ N-Miss	1	0	
▪ Mean (SD)	27.9 (27.6)	27.2 (14.4)	
▪ Q1, Q3	14.1, 27.6	16.5, 30.3	
▪ Range	6–201	3.57–77.4	

APC, argon plasma coagulation; EMR, endoscopic mucosal resection; HGD, high-grade dysplasia; N-Miss, number missing; Q1, first quartile; Q3, third quartile; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma

► **Table 3** Summary of controls weighted to match cases (en bloc resection excluded; n = 291).

Variable	Colonoscope	
	180 (n = 180) ¹	190 (n = 111) ¹
Age		
▪ Mean (SD)	66.7 (9.95)	66.3 (10.4)
▪ Q1, Q3	60, 75	59.5, 75
▪ Range	40–88	36–89
Sex		
▪ Men	78.7 (43.7)	47 (42.4)
▪ Women	101 (56.3)	64 (57.6)
Prior treatment		
▪ No	166 (92.5)	109 (97.8)
▪ Yes	13.5 (7.5)	2.45 (2.2)
Polyp size, mm		
▪ N-Miss	0	0
▪ 20–29	74.9 (41.6)	46.1 (41.5)

► **Table 3** (Continuation)

Variable	Colonoscope	
	180 (n = 180) ¹	190 (n = 111) ¹
▪ 30–39	49.7 (27.6)	31.8 (28.6)
▪ 40–49	28.9 (16.1)	16.4 (14.7)
▪ 50–59	15.5 (8.6)	9.53 (8.6)
▪ 60–69	5.33 (2.96)	4.42 (3.98)
▪ 70–99	3.09 (1.8)	1.52 (1.4)
▪ 100+	2.58 (1.4)	1.34 (1.2)
EMR site		
▪ Cecum	36.3 (20.2)	23.2 (20.9)
▪ Ileocecal valve	10.6 (5.9)	4.69 (4.2)
▪ Ascending	65.9 (36.6)	37.6 (33.9)
▪ Splenic flexure	2.05 (1.1)	0.651 (0.6)
▪ Hepatic flexure	15.6 (8.7)	10.8 (9.8)
▪ Transverse	18.8 (10.5)	13 (11.8)
▪ Descending	7.71 (4.3)	5.77 (5.2)
▪ Sigmoid	9.48 (5.3)	7.83 (7.1)
▪ Anorectal	11.6 (6.4)	6.15 (5.5)
▪ Appendiceal orifice	1.18 (0.7)	1.18 (1.1)
▪ Colon multiple	0.603 (0.3)	0 (0)
Initial pathology		
▪ TA with HGD	4.62 (2.6)	4.27 (3.9)
▪ TVA	48.6 (27)	34.3 (30.9)
▪ SSA	37.1 (20.6)	25 (22.5)
▪ TA	79.9 (44.4)	41.8 (37.6)
▪ TVA with HGD	6.5 (3.6)	3.39 (3.1)
▪ Adenocarcinoma	3.24 (1.8)	2.29 (2.1)
Paris classification		
▪ Ip	1.81 (1.0)	0 (0)
▪ Is	9.93 (5.5)	6.29 (5.7)
▪ 0-IIa	37.8 (21)	23.3 (21)
▪ 0-IIb	6.4 (3.6)	5.32 (4.8)
▪ 0-IIc	1.21 (0.7)	0 (0)
▪ IIc + IIa	0 (0)	0.427 (0.4)
▪ Unknown	123 (68.2)	75.7 (68.2)
Endoscopist		
▪ 1	60.8 (33.8)	35.7 (32.1)
▪ 2	34.7 (19.3)	21 (18.9)
▪ 3	56.9 (31.6)	39.1 (35.3)
▪ 4	9.51 (5.3)	4 (3.6)
▪ 5	16.9 (9.4)	11.2 (10.1)
▪ 6	1.21 (0.7)	0 (0)

► **Table 3** (Continuation)

Variable	Colonoscope	
	180 (n = 180) ¹	190 (n = 111) ¹
Year of procedure		
▪ 2010	47.4 (26.3)	0 (0)
▪ 2011	34.6 (19.2)	0 (0)
▪ 2012	39.5 (22)	0 (0)
▪ 2013	17.6 (9.8)	8.85 (7.97)
▪ 2014	16.5 (9.2)	33.9 (30.5)
▪ 2015	9.96 (5.5)	47.2 (42.6)
▪ 2016	14.4 (7.99)	21 (18.9)
Lifted lesion		
▪ Adequate	173 (96)	106 (95.4)
▪ Partial	7.12 (3.95)	5.06 (4.6)
Intraprocedural bleeding		
▪ No	161 (89.4)	100 (90.5)
▪ Yes	19.1 (10.6)	10.6 (9.5)
Prophylactic APC		
▪ No	133 (73.8)	78.5 (70.7)
▪ Yes	47.1 (26.2)	32.5 (29.3)
Recurrence in EMR scar		
▪ No	140 (78)	85.4 (77)
▪ Yes	39.7 (22)	25.6 (23)
Pathology of recurrence		
▪ No recurrence	140 (78)	84.2 (75.8)
▪ TVA	9.78 (5.4)	5.73 (5.2)
▪ SSA	7.51 (5.7)	4.34 (3.9)
▪ TA	22.4 (12.4)	15.5 (14)
Weeks to follow-up		
▪ N-Miss	0.903	0
▪ Mean (SD)	27.5 (25.5)	27.4 (14.8)
▪ Q1, Q3	14.6, 28.9	16.5, 30.7
▪ Range	6–201	3.57–77.4
APC, argon plasma coagulation; EMR, endoscopic mucosal resection; HGD, high-grade dysplasia; N-Miss, number missing; Q1, first quartile; Q3, third quartile; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma		
¹ No. (%) unless otherwise indicated		

lesion complexity and there was a significant drop in complete cure rate at first attempt for lesions larger than 60 mm and for very complex or defiant adenomas with difficult access [18, 19]. Similarly, we found in our study a clear association between the rate of RRA and polyp size, supporting what literature has consistently shown [10, 11, 19, 20]. A retrospective study identified polyp size, piecemeal resection, concomitant use of APC, ex-

tension to lateral margins, and presence of HGD in histopathology as risk factors for RRA [19].

Large LSL (>20 mm) are generally resected with a piecemeal method. A systematic review and meta-analysis demonstrated that local recurrence after EMR occurs in 3% of cases in which the lesion is removed en bloc and in 20% of cases in which the lesion is removed with a piecemeal technique [17, 21]. Current ASGE guidelines recommend that if a piecemeal resection is performed on a large adenoma (>15 mm), the patient should have a subsequent colonoscopy in 6 to 12 months to evaluate for local recurrence [22], which entails a financial impact in the healthcare system and may be distressing for the patient.

In a retrospective study by Woodward et al [20], additional procedures were needed to achieve complete resection in more than 1 of 10 colonic EMRs and residual neoplasia occurred more often if the lesion was resected in pieces. Furthermore, the use of complementary APC for complete resection has consistently shown higher rates of RRA (47% [19] and 33% [10]). Our study corroborates these findings showing a substantial increase of recurrence in patients who received APC as part of the therapy. Typically, the APC settings used in our center included 0.8 liters/minute; Erbe, Tubingen, Germany, with 20 watts current flow and mostly used at the right colon. Interestingly, a recent study by Holmes et al [23] reported that avulsion is superior to APC for the treatment of residual visible neoplasia, decreasing the recurrence rate without increasing the procedure risks. Since we started using hot avulsion and snare tip soft coagulation in our EMR practice only after later 2016; there were only few cases that were not included in the final analysis to avoid bias.

Resections of fibrotic and scarred polyps are technically difficult as it possess the risk of perforation [24]. However, APC and cold avulsion technique can be used as a salvage approach to achieve complete removal of partially resected, non-lifting, and fibrotic polyps after piecemeal EMR [25]. There are few novel techniques for complete removal of large laterally spreading colorectal lesions such as hybrid techniques in which lateral margins are freed with circumferential SM incision and facilitated by submucosal elevation followed by snare resection [26]. In addition, Hybrid-knife is a novel device in which submucosal dissection is combined with injection of fluid concurrently [27]. This device has increased the efficiency of ESD on western endoscopists.

The ASGE recommends against EMR for non-lifting lesions or lesions classified as Paris II-c/III. However, non-lifting lesions that were manipulated (biopsy or attempted EMR) before referral for resection are usually amenable to EMR [22]. Our institution is a tertiary referral center and a large number of LSL have been previously manipulated, creating fibrosis and tissue scarring and making a complete resection theoretically more challenging. However, we did not find a strong association between prior treatment of the lesion and a higher rate of RRA in our cohort. A study limitation is that prior biopsy or treatment of the lesion in another facility could have been unreported. Moreover, these lesions are often treated with supplemental APC, which limits the interpretation of the results.

► **Table 4** Effect of the Olympus 190 colonoscope on adenoma recurrence at different stages of adjustment.

Model	Odds ratio	Lower 95 % CI	Upper 95 % CI	P value
Unadjusted-all patients (en bloc and piecemeal)	1.58	0.94	2.65	.08
Unadjusted-piecemeal resection only	1.11	0.64	1.92	.71
IPW adjustment-piecemeal resection	1.06	0.60	1.86	.85

CI, confidence interval; IPW, inverse probability weighting

► **Table 5** Unadjusted measures of association of different variables with probability of recurrence

Variable	OR	Lower 95 % CI	Upper 95 % CI	P Value	Concordance
SERT 1	1.39	0.471	3.64	.52	0.575
SERT 2	1.59	0.839	2.96	.15	.
SERT 3	2.38	0.927	5.87	.06	.
SERT 4	3.7	0.144	95.1	.36	.
SERT>0	1.71	1	2.92	.05	0.566
Size 40 mm +	1.69	0.973	2.91	.06	0.56
Pathology HGD	0.976	0.308	2.62	.96	0.501
IPB	1.72	0.759	3.73	.18	0.528
Age	0.835	0.641	1.08	.18	0.554
Sex: female	0.969	0.571	1.65	.91	0.504
Prior treatment	0.394	0.091	1.19	.14	0.528
Ileocecal valve	0.678	0.142	2.44	.58	0.568
Ascending colon	0.812	0.386	1.73	.58	.
Hepatic flexure	1.08	0.367	2.98	.88	.
Transverse colon	0.979	0.354	2.57	.97	.
Descending colon	1.31	0.319	4.63	.69	.
Sigmoid colon	0.979	0.247	3.28	.97	.
Anorectal	1.26	0.392	3.74	.69	.
Others	4.9	1.08	26.1	.04	.
Complementary APC	2.53	1.43	4.47	.001	0.597
SC1 with 190 scope	1.25	0.71	2.18	.44	-

APC, argon plasma coagulation; HGD, high-grade dysplasia; IPB, intraprocedural bleeding; OR, odds ratio; TA, tubular adenoma; SC1, first surveillance colonoscopy; SERT, Sydney endoscopic mucosal resection recurrence tool; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma.

► **Table 6** Multivariate model based on SERT variables.

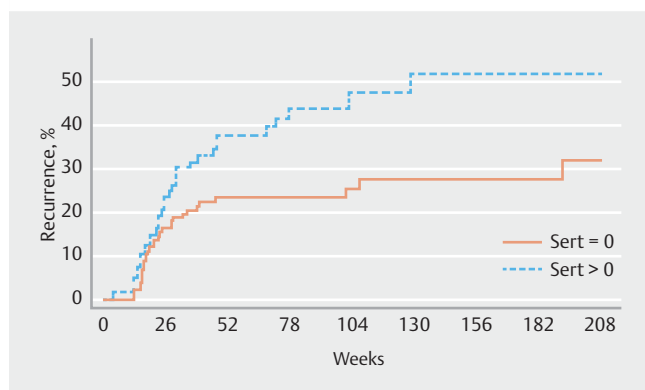
Variable	SE	OR	Lower 95 % CI	Upper 95 % CI	P value
Size 40 mm +	0.288	1.695	0.963	2.983	.07
HGD	0.555	0.771	0.260	2.287	.64
IPB	0.407	1.607	0.724	3.566	.24

HGD, high-grade dysplasia; IPB: intraprocedural bleeding; OR, odds ratio; SE, standard error; SERT, Sydney endoscopic mucosal resection recurrence tool

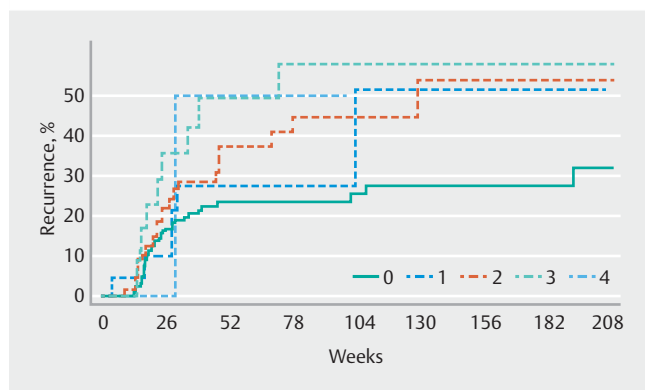
► **Table 7** Recurrence rates By SERT score (0–4).

Event	0 (n = 174) ¹	1 (n = 22) ¹	2 (n = 70) ¹	3 (n = 23) ¹	4 (n = 2) ¹	P value
Recurrence at any follow-up						.26
▪ No	137 (78.7)	16 (72.7)	49 (70)	14 (60.9)	1 (50)	
▪ Yes	37 (21.3)	6 (27.3)	21 (30)	9 (39.1)	1 (50)	
Recurrence at first follow-up						.23
▪ No	139 (79.9)	16 (72.7)	51 (72.9)	14 (60.9)	1 (50)	
▪ Yes	35 (20.1)	6 (27.3)	19 (27.1)	9 (39.1)	1 (50)	

SERT, Sydney endoscopic mucosal resection recurrence tool
¹ No. (%)



► **Fig. 3** Kaplan-Meier plot for time to recurrence of lesions with SERT score 0 (continuous line) and >0 (dashed line).



► **Fig. 4** Kaplan-Meier plot for time to recurrence of lesions with SERT score 0 (green continuous line) and 1, 2, 3, and 4 (dashed lines).

IPB rates during EMR of colorectal lesions larger than 20 mm are reported to be between 11% and 22%. IPB obscures the endoscopic view and shifts the endoscopist's focus away from the resection, compromising its efficacy [28, 29].

We speculated that improved imaging capabilities may lead to better index EMR visualization and effectiveness. This was based on recent studies regarding the 190, second generation HD-NBI colonoscopes. A prospective study by Szura et al [30]

found that using a 2-stage optical system (DF and HD-NBI) increased diagnostic accuracy for differentiating colorectal polyps with neoplastic potential (Kudo III to V). On the other hand, our own prospective study found “no difference in the accuracy of polyp histology prediction, adenoma detection, or surveillance interval prediction when comparing the 180 series with the dual focus 190 series colonoscopes” [5]. It remains possible that there are small incremental improvements with each generation of endoscopes, but these are too small to demonstrate statistically significant differences. We were unable to compare EMR done with prior, standard definition colonoscopes (Olympus 160 series or earlier) due to the small number of patients who underwent colonoscopy with this series and potential learning curve variations prior to 2010.

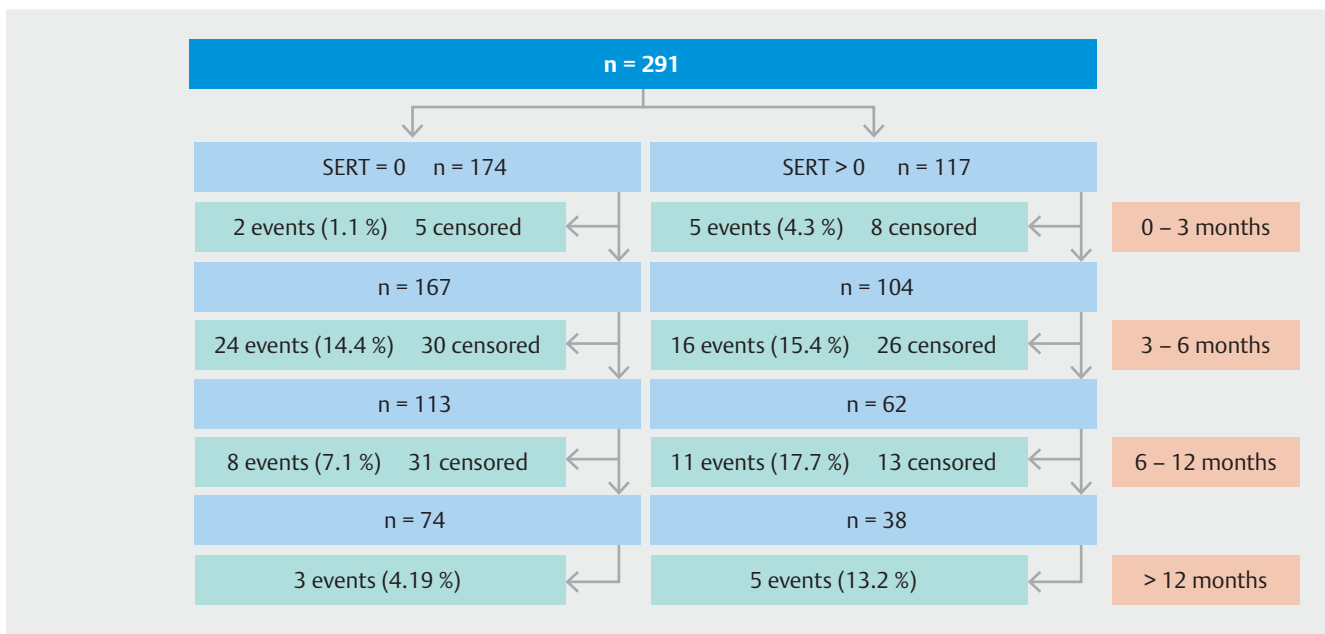
Preliminary data from an ongoing, prospective, double-blind trial by Kandel et al [31], have indicated a high diagnostic accuracy with HD-NBI near-focus system for optical detection of residual neoplasia in both real-time and offline evaluation. One hundred seven patients with 111 scar sites have been evaluated; sensitivity and negative predictive value are both 100% for HD-NBI near-focus with high confidence in real-time. Therefore, these advanced imaging modalities may improve real-time decision making for surveillance after colorectal EMR, particularly biopsy avoidance.

The recent development of SERT has demonstrated that RRA after EMR is predictable and stratifiable. In our cohort, SERT was capable of separating lesions with low risk for recurrence (SERT score 0) from lesions with higher recurrence rates (SERT score > 0). Cumulative incidence for each group of lesions demonstrated that lesions with SERT score 0 still need to be surveilled at 6 and 18 months after index EMR as RRA were found in 6.9% (n = 8) of cases in this time frame. Lesions with SERT score 0 that were negative at 18 months remained negative on subsequent surveillance, displaying a plateau in Kaplan-Meier curves. Our data suggests that lesions with SERT score 0 that are negative for recurrence at second SC could potentially undergo routine SC. Conversely, Lesions with SERT scores 1 to 4 exhibited a higher cumulative incidence of histologically determined recurrence over time, suggesting a need for continued surveillance protocol for these patients. It is important to acknowledge that in multivariate analysis, none of the SERT model variables were significantly associated with recurrence. This could be

► **Table 8** Cumulative incidence of recurrence at SC1 by SERT score in 291 Lesions.

Months	No. events [SERT=0]	Event rate, % [SERT=0]	No. events [SERT>0]	Event rate, % [SERT>0]
6	26	16.4	21	21.9
12	34	23.3	32	37.6
18	34	23.3	35	43.6
24	35	25.4	36	47.1
30	36	27.5	37	51.5
36	36	27.5	37	51.5

SC1, first surveillance colonoscopy; SERT, Sydney endoscopic mucosal resection recurrence tool



► **Fig. 5** Flowchart showing SERT 0 and SERT>0 recurrences in different time windows.

secondary to a smaller sample size and wider CIs compared to the study by Tate et al [12]. Interpretation of Kaplan-Meier curves was limited by the time at which the patients presented for SC. While the median time to SC1 was 5 months (► **Fig. 2**), there were some outliers who presented later, in whom recurrence could have been previously found if surveilled between 4 to 6 months. Further validation in a prospective study is required for clinical application of the SERT model in our patient population.

Conclusion

This is a retrospective study and results show that the 190, second generation colonoscopes with HD-NBI imaging and near focus magnification don't have an impact in the rate of adenoma recurrence at follow-up colonoscopy. These results need to be further substantiated with prospective studies, ideally randomizing the participants to EMR with either HD-NBI and DF magnification or HD-NBI alone. A key aspect for accuracy in

the interpretation of the results is the endoscopist's continuous education for better implementation of novel technologies in their practice. Evidence suggests that adenoma recurrence might be associated with adenoma size, HGD, prior treatment of the lesion, IPB, complementary APC, and endoscopist's expertise [32].

Competing interests

Dr. Wallace reports consulting income from Olympus and grant support from Boston Scientific, Olympus, Medtronic and Cosmo pharmaceuticals.

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