Endoscopic submucosal dissection for colorectal neoplasia: outcomes and predictors of recurrence

OPEN ACCESS

Authors

Roberta Maselli*,[1,2], Marco Spadaccini*,[1,2], Paul J. Belletrutti[2], Piera Alessia Galtieri[1], Simona Attardo[3], Silvia Carrara[1], Andrea Anderloni[1], Alessandro Fugazza[1], Elisa Chiara Ferrara[1], Gaia Pellegatta[1], Andrea Iannone[4], Cesare Hassan[5], Alessandro Repici[1,2]

Institutions

1 Humanitas University, Department of Biomedical Science, Pieve Emanuele (Milan), Italy
2 Digestive Endoscopy Unit, Division of Gastroenterology, Humanitas Research Hospital, Humanitas University, Rozzano (Milan), Italy
3 Gastroenterology Unit, Ospedale Maggiore della Carità, Novara, Italy
4 Section of Gastroenterology, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy
5 Digestive Endoscopy Unit, Nuovo Regina Margherita Hospital, Rome, Italy

submitted 23.1.2021
accepted after revision 9.7.2021

Bibliography
Endosc Int Open 2022; 10: E127–E134
DOI 10.1055/a-1551-3058
ISSN 2364-3722

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Corresponding author
Marco Spadaccini, MD, Digestive Endoscopy Unit, Humanitas Research Hospital, Via Manzoni 56, 20089 Rozzano (Milano), Italy
Fax: +390282242579
marcospadaccini9@gmail.com

Supplementary material is available under https://doi.org/10.1055/a-1551-3058

ABSTRACT

Background and study aims The role of endoscopic submucosal dissection (ESD) for colorectal lesions in Western communities is unclear and its adoption is still limited. The aim of this study is to assess the long-term outcomes of a large cohort of patients treated with colorectal ESD in a tertiary Western center.

Patients and methods A retrospective analysis was conducted on patients treated by ESD for superficial colorectal lesions between February 2011 and November 2019. The primary outcome was the recurrence rate. Secondary outcomes were en-bloc and R0 resection rates, procedural time, adverse events (AEs), and need for surgery. The curative resection rate was assessed for submucosal invasive lesions.

Results A total of 327 consecutive patients, median age 69 years (IQR 60–76); 201 men (61.5%) were included in the analysis. Of the lesions, 90.8% were resected in an en-bloc fashion. The rate of R0 resection was 83.1% (217/261) and 44.0% (29/66) for standard and hybrid ESD techniques, respectively. Submucosal invasion and piecemeal resection independently predicted R1 resections. A total of 18(5.5%) intra-procedural AEs (perforation:11, bleeding:7) and 12 (3.7%) post-procedural AEs occurred (perforation:2, bleeding: 10). Eighteen adenoma recurrences per 1,000 person-years (15cases, 5.6%) were detected after a median follow-up time of 36 months. All recurrences were detected within 12 months. No carcinoma recurrences were observed. R1 resection status and intra-procedural AEs independently predicted recurrences with seven vs 150 recurrences per 1,000 person-years in the R0 vs R1 group, respectively.

Conclusions Colorectal ESD is a safe and effective option for managing superficial colorectal neoplasia in a Western setting, with short and long-terms outcomes comparable to Eastern studies. En-bloc R0 resection and absence of intra-procedural AEs are associated with reduced risk of recurrence.

* These authors contributed equally.

Introduction

Colorectal cancer (CRC) is a major cause of cancer-related death in the Western world [1]. Most colorectal polyps are now amenable to endoscopic resection, altering the natural history of the disease and eliminating any malignant potential [2]. Nonetheless, large premalignant lesions cannot be treated by traditional polypectomy techniques, requiring more complex approaches such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) [3]. The main advantages of an ESD approach are a higher rate of en-bloc resection and a lower rate of tumor recurrence as compared to EMR [4]. However, ESD has been considered overly time-consuming, technically demanding and associated with a higher risk of adverse events (AEs) [5].

In Asian countries, the safety and efficacy of endoscopic submucosal dissection (ESD) is well-established for the minimally invasive treatment for early gastrointestinal cancer. Large retrospective studies on colorectal ESD have shown favorable long-term outcomes with endoscopic recurrence rates of 2.9 % at 3 years and 3.8 % at 5 years [6]. On the other hand, the role of ESD for colorectal lesions in Western countries is unclear. This may be attributed to the limited adoption of ESD in Western centers and disappointing technical outcomes in preliminary studies [5]. In addition, even considering the recent publication of several European and American studies [7–12], the lack of long-term data for Western-based colorectal ESD generates uncertainty as to the clinical relevance of such a procedure.

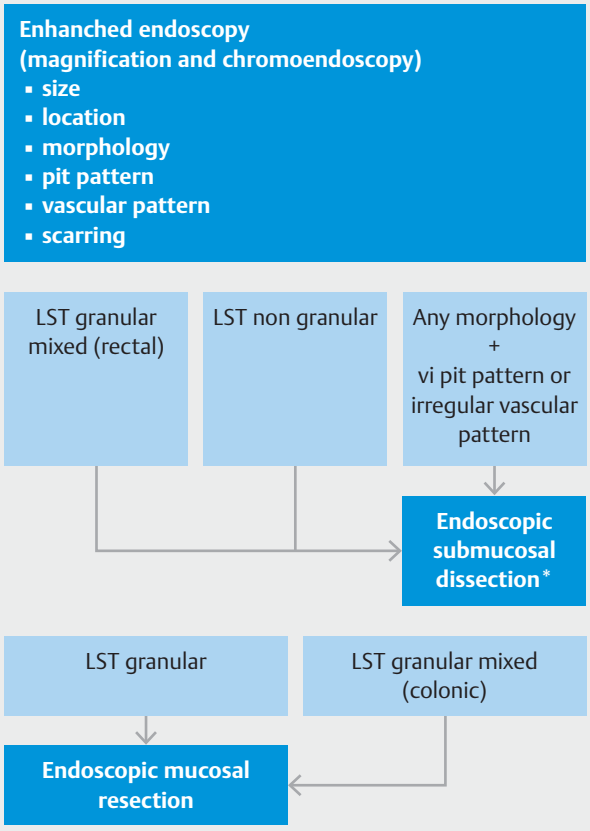
The primary aim of this study was to assess long-term follow-up data in a large cohort of Western patients treated with colorectal ESD.

Patients and methods

Study design

The methods of our study were based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [13]. Institutional review board approval was obtained (ENDO-OPER-REGISTRO/01; n° 2248).

From January 2011 to November 2019, consecutive patients treated by ESD for colorectal lesions ≥ 20 mm at a single European tertiary academic center were considered for analysis. The exclusion criteria were the coexistence of other cancers, ulcerative/Crohn colitis and/or familial adenomatous polyposis, histology other than adenoma or adenocarcinoma. All potential lesions were identified and characterized at a previous colonoscopy by an accredited consultant endoscopist. Lesions with endoscopic features of deep submucosal or frankly invasive cancer were referred for surgery as per standard guidelines [14]. On the other hand, lesions with low-risk features for superficial submucosal invasion were managed by EMR approach [14]. ▶ **Fig. 1** shows the decision-making process for selecting the resection technique appropriate to the lesion. A detailed consultation and written informed consent were obtained from all patients prior to the ESD procedure.



▶ **Fig. 1** Decision-making process for selecting the resection technique. *Excessive scarring/fibrosis may lead to hybrid-ESD technique.

ESD procedure

All procedures were performed under deep sedation administered by a dedicated anesthesiologist and carried out with CO_2 insufflation. ESD was performed using one of the following monopolar ESD knives: HybridKnife (ERBE Elektromedizin, GmbH); DualKnife, IT knife (Olympus Medical, Tokyo, Japan). Saline with dilute adrenaline and dyed with methylene blue was used for submucosal injection. Different ESD strategies, including the pocket creation method, tunneling technique and underwater ESD, were used depending on lesion location, size and morphology. Even if the initial intent of the procedure was completing the resection by ESD, in selected cases, because of technical challenges and/or unanticipated submucosal fibrosis, an initially planned conventional ESD was converted to a hybrid procedure by using a snare with monopolar current to complete the resection (Hybrid ESD). Specimens were finally collected, pinned and sent in formalin for histopathological examination.

Follow-up

Patients with complete endoscopic excision and no indication for surgery based on final histology were advised to undergo endoscopic surveillance at intervals of 6 and 12 months [14], then at subsequent intervals according to the endoscopic find-

ings. If any follow-up endoscopy detected an adenoma/tumor recurrence, it was resected endoscopically and sent for histology; in the case of suspicious invasive neoplasia, biopsies were taken.

Cross-sectional imaging follow-up with contrast enhanced computed tomography scan was performed along with endoscopic follow-up for patients included in the follow-up group with curative resection of early adenocarcinomas.

Variables and measurements

The following data were collected for each patient: age, gender, lesion location (rectum, left colon, transverse colon, right colon) and endoscopic aspects of the lesion: 1) morphology (including Paris classification [15]) and 2) surface glandular pattern (Kudo classification [16]). For flat lesions, termed laterally spreading tumors (LSTs), the surface morphology was also described as granular, granular mixed-type, and nongranular according to ESGE guidelines [17]. We also collected data on the size of the resected specimen (mm), total procedure time (minutes, defined as time from submucosal injection to complete removal of the lesion), type of treatment (pure ESD or Hybrid ESD) and histopathology evaluation [18, 19]. Irrespective of the dysplastic/neoplastic nature of the lesion on histopathology, the post-resection status was assessed. Complete resection was defined according to current guidelines [14]. The resection was considered complete and defined as R0 when the neoplastic/dysplastic tissue was removed en bloc with free lateral and vertical margins. The endoscopic resection was considered incomplete in two cases: 1) when the lateral or vertical margins were positive for neoplastic/dysplastic invasion (R1); and 2) when the margins were not evaluable because of artefact from burn effects (Rx). In the case of submucosal invasive neoplasia, the following parameters were also recorded: grade of tumor differentiation, extent of submucosal infiltration, lympho-vascular invasion (Y/N), tumor budding, vertical margin status, horizontal margin status, en-bloc resection (Y/N) and need for post-ESD surgery (Y/N). Surgery was recommended in the presence of lymphovascular invasion, infiltration deeper than 1000 µm (sm1), positive/non-evaluable vertical or lateral margins (R1/Rx), presence of tumor budding, and/or poorly-differentiated tumor grade with any submucosal invasion.

AEs analyzed were bleeding and perforation. Immediate bleeding was defined as persistent bleeding requiring a pause in the resection to apply dedicated endoscopic hemostasis with a device other than the ESD knife. Delayed bleeding was defined as clinical evidence of bleeding (melena or hematochezia) with a drop of hemoglobin ≥ 2 g/dL up to 14 days after the procedure [20]. Immediate perforation was defined as observation of a deep muscle layer defect and/or mesenteric fat, intraperitoneal organs or muscle splaying during the ESD procedure. Delayed perforation was considered in the case of clinical suspicion associated with radiological evidence of extramural air or an abdominopelvic fluid collection up to 28 days after the procedure [21].

Recurrence at follow-up was determined by histology and classified as either adenoma recurrence or carcinoma recurrence.

Statistical analysis

Continuous variable distribution was assessed using the Shapiro-Wilk test of normality and reported as a mean with standard deviation (SD) or a median with interquartile range (IQR). Categorical variables were expressed as counts and percentages.

The Kaplan-Meier method was used to investigate the predictors of recurrence after ESD. Time to events was defined as the time from the ESD procedure to the event or censoring. Patients were censored if they were event-free through the end of the study observation. The log-rank test was applied to assess the association between each possible predictive variable and post-ESD recurrence. Univariate Cox proportional hazards models were fitted to estimate crude hazard ratios (HRs) with their associated 95 % confidence intervals (95 %CIs). Only variables with $P < 0.05$ were included in the multivariable model and potential collinearity issues were investigated by fitting a linear regression model to the data. Significant predictors of recurrence were identified using the backward method and their association with the outcome was expressed using adjusted HRs with 95 %CIs.

Predictive models for R0 and ESD-related complications were also explored. The univariable analysis for each potential explanatory variable was performed using the χ^2 test or Fisher's exact test, as appropriate. Univariable logistic regression models were created to calculate unadjusted odds ratios (ORs) with 95 %CIs. The backward multiple logistic regression analysis was performed to identify significant predictors. The entry criterion of $P < 0.05$ was considered to build the predictive model. Adjusted ORs with 95 %CIs were estimated for the association between explanatory variables and the outcome.

Sensitivity, specificity and area under the curve of the predictive models were estimated, selecting the cut-off points that maximize the Youden's J index.

All statistical analyses were performed using the Statistical Analysis Software (SAS Institute Inc., Cary, North Carolina, United States).

Results

Clinicopathological characteristics of patients

From February 2011 and November 2019, 3324 consecutive patients underwent an advanced colorectal endoscopic resection (ie EMR, ESD) at our center. A total of 374 of them were treated with ESD. Forty-seven patients met the exclusion criteria. Thus, 327 patients (median age 69 years; IQR: 60–76; 201 [61.5 %]) male were included in the final analysis. The baseline patient and lesion characteristics are detailed in ▶ **Table 1**.

Procedural outcomes

Most of the lesions (261/327, 79.8 %) were treated with conventional ESD and the remaining 66 procedures (20.2 %) were completed through a hybrid approach. The median procedural time was 72 minutes (IQR: 54–103).

In total, 90.8 % of lesions were resected in an en-bloc fashion (Standard ESD: 260/261, 99.6 %; Hybrid ESD: 37/66, 56.0 %),

▶ **Table 1** Clinical, and endoscopic characteristics of included patients.

Parameter	Value (n = 327)
Age – mean±SD, years	69 (60–76)
Male sex – no. (%)	201 (61.5)
Hospital stay – median (IQR), days	1 (1–2)
Endoscopy – variable, no. (%)	
Procedure	
▪ ESD	261 (79.8)
▪ Hybrid-ESD	66 (20.2)
▪ Procedural time – median (IQR), minutes	72 (54–103)
Lesion location	
▪ Right colon	52 (15.9)
▪ Transverse	25 (7.7)
▪ Left colon	37 (11.3)
▪ Rectum	213 (65.1)
▪ Size – median (IQR), mm	40 (30–50)
Morphology classification	
▪ Paris Is	69 (21.1)
▪ LST-granular	66 (20.2)
▪ LST-granular mixed	102 (31.2)
▪ LST-non granular	90 (27.5)
Kudo classification	
▪ II	1 (0.3)
▪ IIIS	23 (7.0)
▪ IIIL	75 (23.0)
▪ IV	171 (52.3)
▪ V	57 (17.4)

IQR, interquartile range; ESD, endoscopic submucosal dissection; LST, laterally spreading tumor.

with an overall R0 resection rate of 75.2 % (246/327). In particular, the rate of R0 resection was 83.1 % (217/261) and 44.0 % (29/66) for standard and hybrid techniques, respectively. Submucosal invasion and piecemeal resection independently predicted R1 resections (**Supplementary Table 1**). Histopathological characteristics are reported in ▶ **Table 2**.

Seventy-five of 327 lesions (23.0 %) resulted in colorectal neoplasia with submucosal invasion. In 57 of these, final histology showed high-risk features of potential nodal involvement (ie. non-curative resection) and were excluded from the follow-up analysis. Forty of these patients had undergone surgical resection by the end of the follow-up period. Histopathological features of both endoscopic and surgical resection of patients with invasive cancer are reported in **Supplementary Table 2**.

▶ **Table 2** Histologic characteristics of included patients.

Parameter	Value (n = 327)
Histology – variable, no. (%)	
Grade of dysplasia	
▪ Low grade	110 (33.6)
▪ High grade	142 (43.4)
▪ Cancer	75 (23.0)
▪ En-bloc resection	297 (90.8)
▪ R0	246 (75.2)

Adverse events

A total of 18 (5.5 %) intra-procedural AEs occurred: 11 perforations (3.4 %) and 7 bleeding events (2.1 %). All intra-procedural AEs were managed endoscopically and the resection continued to completion. We also experienced 10 cases of delayed bleeding (3.1 %), that were managed either conservatively (n = 5) or by endoscopic hemostasis (n = 5). Two post procedural perforations (0.6 %) occurred, both requiring surgical intervention (these two patients were excluded from the follow-up analysis). There were no predictors of AEs on univariate or multivariate analysis (**Supplementary Table 3**).

Long-term follow up and recurrence

The endoscopic surveillance analysis included 268 patients with a median follow-up of 3.0 years (range 1.0–8.0), including 116 patients with ≥ 5 years of follow-up. No cancers were detected after curative endoscopic resection of an invasive adenocarcinoma. Adenoma recurrence was detected in 15 patients (5.6 %), or at a rate of 18 cases per 1,000 person-years. All recurrences were detected within 12 months and were managed endoscopically. R1 resection status (RR: 11.43, CI: 3.89–33.62) and intra-procedural adverse events (RR: 7.58, CI: 2.57–22.34) independently predicted recurrences (▶ **Table 3**, **Supplementary Fig. 1**). Seven vs 150 recurrences per 1,000 person-years were reported in the R0 vs R1 groups, respectively. When including R0 and complications during endoscopy the predictive model showed a sensitivity of 80 % and a specificity of 85 % for predicting recurrence. The area under the curve was 0.84 indicating excellent discrimination (▶ **Fig. 2**). Endoscopic and histologic characteristic of the 15 recurrent lesions are provided in **Supplementary Table 4**.

Discussion

According to this study, favorable colorectal ESD early and long-term outcomes can be achieved in a Western setting, with recurrence rates of around 5 % for adenomas and 0 % for cancers. In addition, we identified incomplete resections and intraprocedural adverse events as independent predictors of

▶ **Table 3** Association between each single predictive variable and recurrence after ESD.

Variable	Recurrence after ESD		Univariate analysis		Multivariate analysis	
	Yes (n = 15)	No (n = 253)	Crude hazard ratio (95 %CI)	*P* value	Adjusted hazard ratio[1] (95 %CI)	*P* value
Endoscopy – variable, no. (%)						
Procedure				< 0.0001		0.46
▪ ESD	6 (40.0)	213 (84.2)	1.00[2]		1.00[2]	
▪ Hybrid-ESD	9 (60.0)	40 (15.8)	6.88 (2.45–19.35)		1.66 (0.43–6.33)	
▪ Procedural time – median (IQR), min	98 (40–170)	71 (54–103)	1.01 (0.99–1.01)	0.15		
Lesion location				0.35		
▪ Rectum	8 (53.3)	165 (65.2)	1.00[2]			
▪ Other sites	7 (46.7)	88 (34.8)	1.60 (0.58–4.42)			
Size				0.09		
▪ < 40 mm	3 (20.0)	107 (42.3)	1.00[2]			
▪ ≥ 40 mm	12 (80.0)	146 (57.7)	2.80 (0.79–9.93)			
Morphology classification				0.70		
▪ Paris Is	4 (26.7)	46 (18.2)	1.00[2]			
▪ LST-granular/granular mixed	7 (46.6)	139 (54.9)	0.60 (0.17–2.04)			
▪ LST-non granular	4 (26.7)	68 (26.9)	0.70 (0.17–2.77)			
Kudo classification				0.86		
▪ II/IIIS/IIIL	5 (33.3)	84 (33.2)	1.00[2]			
▪ IV	9 (60.0)	141 (55.7)	1.07 (0.36–3.20)			
▪ V	1 (6.7)	28 (11.1)	0.61 (0.07–5.25)			
Histology – variable, no. (%)						
Grade of dysplasia				0.38		
Low grade	5 (33.3)	105 (41.5)	1.00[2]			
High grade	10 (66.7)	130 (51.4)	1.58 (0.54–4.62)			
Cancer	0 (0)	18 (7.1)	n.e.			
En-bloc resection				< 0.0001		0.54
Yes	9 (60.0)	237 (93.7)	1.00[2]		1.00[2]	
No	6 (40.0)	17 (6.3)	7.70 (2.74–21.66)		0.64 (0.15–2.67)	
R0				< 0.0001		< 0.0001
Yes	5 (33.3)	224 (88.5)	1.00[2]		1.00[2]	
No	10 (66.7)	29 (11.5)	12.27 (4.19–35.92)		11.43 (3.89–33.62)	
Procedural complications – variable, no. (%)						
During endoscopy				< 0.0001		0.002
No	10 (66.7)	243 (96.0)	1.00[2]		1.00[2]	
Yes	5 (33.3)	10 (4.0)	8.75 (2.99–25.61)		7.58 (2.57–22.34)	
Total[3]				0.0002		
No	10 (66.7)	236 (93.3)	1.00[2]			
Yes	5 (33.3)	17 (6.7)	5.71 (1.95–16.72)			

▶ **Table 3** (Continuation)

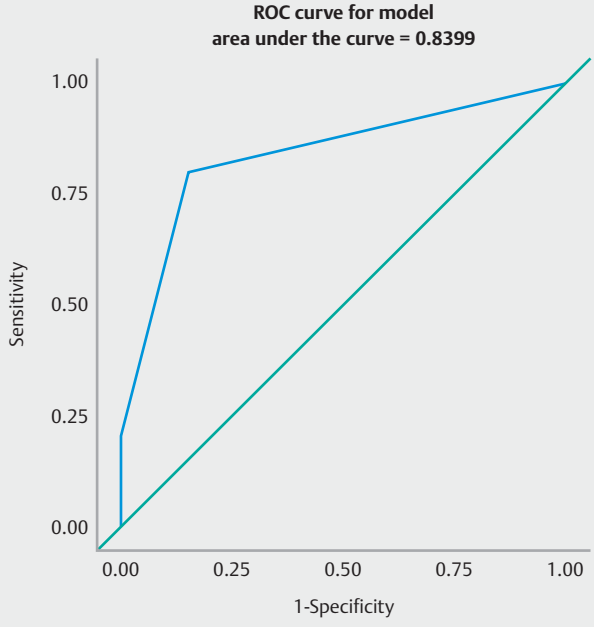
ESD, endoscopic submucosal dissection; IQR, interquartile range; LST, laterally spreading tumor; n.e., not estimable since there were no recurrence events in the cancer category.
[1] Adjusted for R0 and complications during endoscopy.
[2] Reference group.
[3] Excluded from the baseline multivariate model for collinearity issues with complications during endoscopy.

adenoma recurrence, indicating that a more intensive surveillance protocol may be required in these cases.

Our findings are highly relevant for the following reasons. First of all, our recurrence rates are similar to those previously reported in large Asian series, showing that Western patients can benefit from such a procedure, irrespective of the difference in technique and devices between Asian and European endoscopists, respectively. In detail, our 5.6 % overall adenoma recurrence rate corresponds to the 4.7 % rate reported in previous Asian studies on long-term outcomes [22], and appears to be significantly lower than EMR data on adenoma recurrence [23]. Notably, ESD appeared also to be an effective treatment in patients with early invasive cancer without high-risk histopathological features of nodal involvement, as neither cancer persistence nor recurrence was detected during subsequent surveillance, avoiding more invasive surgery.

Second, our study demonstrates a high rate of technical success for colorectal ESD in a Western setting. In our series, an R0 resection was achieved in 83.1 % of patients treated with standard ESD, as compared with 85.6 % and 71.3 % reported in a recent meta-analysis of Asian and early Western data, respectively [5]. More recent evidence from European and American centers [7, 10, 24] showed technical outcomes comparable to those from Asia and we are glad to corroborate these data in a large series. Furthermore, we confirmed the previous meta-analytical comparison between ESD and hybrid ESD [5, 25], underscoring the superiority of complete ESD in terms of both en-bloc and R0 resection rates. As a matter of fact, completing all the resections with a full ESD approach would be the ideal strategy to minimize the recurrence risk. However, in the real-world setting, certain lesions may present technical features, mainly related to high-grade fibrosis, preventing a safe submucosal dissection. This may result particularly relevant when treating older and fragile patients with increased surgical risk. Notably, in our series, the mean size of those lesions treated by hybrid ESD was around 40 mm, and the reported 56 % en-bloc resection rate among them, appears to be higher than what we would have expected if an EMR strategy had been chosen [23]. Hence, in our opinion, hybrid-ESD may still be considered as a viable option when facing large scarred lesions, in order to aim for an en-bloc resection, without compromising patient safety.

Third, we confirmed the unfavorable effect of an incomplete (R1) resection [6, 22, 26, 27], and here first report the impact of intraprocedural AEs on adenoma recurrence risk after ESD. Moss et al [28] previously highlighted the negative impact of intraprocedural bleeding on adenoma recurrence after widefield EMR. We confirm for the first time this finding being relevant for ESD as well. When such an AE occurs, endoscopists likely tend to be most concerned about controlling the complication, shifting the primary focus away from achieving a complete resection. Moreover, blood staining and subsequent charring of the submucosal space after endoscopic hemostasis may hinder visualization of tissue planes and may contribute to an unsuccessful resection. Speculating on the reason why this aspect has never been described in Eastern series, we hypothesize that Asian endoscopists, more inclined to opt for an ESD approach (for both upper and lower gastrointestinal lesions) are more accustomed to facing such events, and handle them without any influence on the intended resection plan. This attitude will probably grow among Western endoscopists as ESD becomes a more regular part of our endoscopic armamentarium. As a matter of fact, despite the potential advantages of ESD compared to EMR in terms of efficacy, safety remains the main limitation for ESD uptake in the West as a primary therapeutic option. Nevertheless, both our data and previous Eastern experience have clearly demonstrated ESD to be a full oncologic treatment and, from this perspective, the 4 % risk of perforation and the 5.2 % rate of bleeding need to be balanced with the evident gain in terms of spared surgery. In fact, if surgical complications are expected to be substantially higher [29], several large EMR series reported AE rates similar to both previous Eastern series and our study [28, 30].



▶ **Fig. 2** Receiver operating characteristic curve of the logistic model to predict recurrence.

Customizing the right treatment (EMR vs ESD vs surgery) to the right lesion in the right patient remains, of course, an incompletely addressed issue in need of further investigation. Some have argued that ESD of colorectal lesions may be considered either an undertreatment compared to surgery in case of most of the sm-invasive malignant lesions or an overtreatment compared to EMR for adenomatous lesions. However, there is mounting evidence that the safety profile of ESD is now comparable to EMR and thus may preclude considering ESD as an overtreatment. On the other hand, the low risk of nodal/residual disease (6/40) among patients with an R1/Rx resection referred for subsequent surgery in our series suggests that, from a practical perspective, most of these technically non-curative resections were in fact adequate treatments for these patients. Thus, ESD should not necessarily be considered undertreatment in these cases. Of course, this aspect should be further investigated in larger multicenter studies, in order to better counsel patients with multiple comorbidities and/or older age.

Despite its strengths, this study has several limitations. First of all, the retrospective design does not guarantee unbiased conclusions, mainly due to the risk of selection bias. In addition, the single-center setting does not allow us to reliably generalize our findings. However, we may have limited these risks by maintaining the same ESD indications over the entire study period. Despite supporting this approach, we have not given in to the temptation of opting for an indiscriminate use of ESD for all colorectal lesions before the accumulation of convincing data on its efficacy and safety. Thus, we have been managing all lesions without any endoscopic features of increased risk for submucosal invasion by EMR, as shown by the relatively high number of invasive cancers and the lesser number of low-grade adenomas in our series. On the other hand, this behavior led to mainly treat rectal lesions (213/327, 65.1 %) (**Supplementary Table 5**) because of their higher risk of submucosal invasion [31]. Indeed, our results may be best applied to such a decision-making process. It may be argued that rectal lesions are more easily resected through ESD compared to colonic ones; however, similar encouraging technical outcomes were recently reported in a large France ESD series [10] enrolling a greater proportion of colonic (and even proximal) lesions; long-term data are expected in the coming years.

Second, the median follow-up time of 3 years arguably is still not comparable to the largest Eastern series reporting long-term data [6, 22, 26, 27]. However, a relevant proportion of patients (n = 116) have been followed up for at least 5 years, providing the most accurate long-term Western perspective to date. Furthermore, we excluded from the analysis all patients without the 12-month follow-up endoscopy. This is relevant considering that the first year after ESD is the "hottest" period in terms of recurrence risk [6, 22], as confirmed by our results.

Conclusions

In conclusion, colorectal ESD in a Western setting is associated with short- and long-term outcomes comparable to Eastern series, with a low risk of adenoma recurrence, and a favorable safety profile. Moreover, ESD may be considered as an effective approach for managing superficially invasive colorectal neoplasia, and should prevent an indiscriminate referral for surgery.

Competing interests

The authors declare that they have no conflict of interest.

References

[1] Ferlay J, Autier P, Boniol M et al. Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol 2007; 18: 581–592

[2] Zauber AG, Winawer SJ, O'Brien MJ et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 2012; 366: 687–696

[3] Moss A, Bourke MJ, Williams SJ et al. Endoscopic mucosal resection outcomes and prediction of submucosal cancer from advanced colonic mucosal neoplasia. Gastroenterology 2011; 140: 1909–1918

[4] Fujiya M, Tanaka K, Dokoshi T et al. Efficacy and adverse events of EMR and endoscopic submucosal dissection for the treatment of colon neoplasms: a meta-analysis of studies comparing EMR and endoscopic submucosal dissection. Gastrointest Endosc 2015; 81: 583–595

[5] Fuccio L, Hassan C, Ponchon T et al. Clinical outcomes after endoscopic submucosal dissection for colorectal neoplasia: a systematic review and meta-analysis. Gastrointest Endosc 2017; 86: 74–86.e17

[6] Yamada M, Saito Y, Takamaru H et al. Long-term clinical outcomes of endoscopic submucosal dissection for colorectal neoplasms in 423 cases: a retrospective study. Endoscopy 2017; 49: 233–242

[7] Gupta N, Rodríguez-Ruiz G, Siddiqui UD et al. Endoscopic submucosal dissection for colorectal lesions: outcomes from a United States experience. Surg Endosc 2021: doi:10.1007/s00464-020-08262-4

[8] Ge PS, Jirapinyo P, Ohya TR et al. Predicting outcomes in colorectal endoscopic submucosal dissection: a United States experience. Surg Endosc 2019; 33: 4016–4025

[9] Draganov PV, Aihara H, Karasik MS et al. Endoscopic submucosal dissection in North America: A large prospective multicenter study. Gastroenterology 2021: doi:10.1053/j.gastro.2021.02.036

[10] Bordillon P, Pioche M, Wallenhorst T et al. Double-clip traction for colonic endoscopic submucosal dissection: a multicenter study of 599 consecutive cases (with video). Gastrointest Endosc 2021: doi:10.1016/j.gie.2021.01.036

[11] Roland D, Rahmi G, Pérez-Cuadrado-Robles E et al. Endoscopic submucosal dissection in rectal tumors extending or not to the dentate line: A comparative analysis. Dig Liver Dis 2020; 52: 296–300

[12] Taşkın OC, Aslan F, Kulaç I et al. Pathologic evaluation of large colorectal endoscopic submucosal dissections: an analysis of 279 cases with emphasis on the importance of multidisciplinary work and establishing examination protocols. Int J Surg Pathol 2020; 28: 600–608

[13] Vandenbroucke JP, von Elm E, Altman DG et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PLoS Med 2007; 4: e297

[14] Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015; 47: 829–854

[15] The Paris endoscopic classification of superficial neoplastic lesions. esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58: S3–S43

[16] Kudo S, Tamura S, Nakajima T et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996; 44: 8–14

[17] Ferlitsch M, Moss A, Hassan C et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2017; 49: 270–297

[18] Schlemper RJ, Riddell RH, Kato Y et al. The Vienna classification of gastrointestinal epithelial neoplasia. Gut 2000; 47: 251–255

[19] Kikuchi R, Takano M, Takagi K et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. Dis Colon Rectum 1995; 38: 1286–1295

[20] Tanaka S, Kashida H, Saito Y et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2015; 27: 417–434

[21] Saito Y, Uraoka T, Yamaguchi Y et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010; 72: 1217–1225

[22] Shigita K, Oka S, Tanaka S et al. Long-term outcomes after endoscopic submucosal dissection for superficial colorectal tumors. Gastrointest Endosc 2017; 85: 546–553

[23] Hassan C, Repici A, Sharma P et al. Efficacy and safety of endoscopic resection of large colorectal polyps: a systematic review and meta-analysis. Gut 2016; 65: 806–820

[24] Andrisani G, Fukuchi T, Hassan C et al. Rectal neoplasia extending to the dentate line: clinical outcomes of endoscopic submucosal dissection. Scand J Gastroenterol 2020; 55: 1363–1368

[25] McCarty TR, Bazarbashi AN, Thompson CC et al. Hybrid endoscopic submucosal dissection (ESD) compared with conventional ESD for colorectal lesions: a systematic review and meta-analysis. Endoscopy 2020: doi:10.1055/a-1266-1855

[26] Cong ZJ, Hu LH, Ji JT et al. A long-term follow-up study on the prognosis of endoscopic submucosal dissection for colorectal laterally spreading tumors. Gastrointest Endosc 2016; 83: 800–807

[27] Niimi K, Fujishiro M, Kodashima S et al. Long-term outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 2010; 42: 723–729

[28] Moss A, Williams SJ, Hourigan LF et al. Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. Gut 2015; 64: 57–65

[29] de Neree Tot Babberich MPM, Bronzwaer MES, Andriessen JO et al. Outcomes of surgical resections for benign colon polyps: a systematic review. Endoscopy 2019; 51: 961–972

[30] van Hattem WA, Shahidi N, Vosko S et al. Piecemeal cold snare polypectomy versus conventional endoscopic mucosal resection for large sessile serrated lesions: a retrospective comparison across two successive periods. Gut 2021; 70: 1691–1697

[31] D'Amico F, Amato A, Iannone A et al. Risk of covert submucosal cancer in patients with granular mixed laterally spreading tumors. Clin Gastroenterol Hepatol 2021; 19: 1395–1401