Switching from endoscopic submucosal dissection to salvage piecemeal knife-assisted snare resection to remove a lesion: a preoperative risk score from the beginning

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Received: 20/03/2018 · **Accepted:** 21/05/2018

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ABSTRACT

Background and aims: endoscopic submucosal dissection (ESD) in the Western setting remains a challenge. Therefore, other simplified techniques such as knife-assisted snare resection (KAR) have been reported to overcome this issue.

Methods: patients who underwent an ESD for the treatment of gastrointestinal neoplasms were included in a retrospective cross-sectional observational study. Factors associated with the end of ESD as a salvage p-KAR were identified and a logistic regression model was developed.

Results: a total of 136 lesions in 133 patients were analyzed. Operator experience of under 50 cases and the combination of lesion size > 30 mm and colorectal location were independent predictive factors for switching to a salvage p-KAR according to the multivariate logistic regression analysis. We developed a risk scoring system based on these four variables (experience, size, location and the combination of size and location) with a receiver operating characteristic curve of 0.81 (95% CI: 0.74-0.89). The diagnostic accuracy of the score for a cut-off point ≥ 5 had a sensitivity of 0.79 (95% CI: 0.66-0.93) and a specificity of 0.71 (95% CI: 0.61-0.80).

Conclusion: a simple predictive score system that includes four preoperative factors accurately predicts ESD to finish as a p-KAR. A careful selection of cases considering these variables could be useful to achieve better outcomes in the Western setting.

Key words: Endoscopic submucosal dissection. Endoscopic mucosal resection. Predictive value. Sensitivity and specificity. ROC curve. Area under curve.

INTRODUCTION

In recent years, endoscopic submucosal dissection (ESD) has been endorsed as an effective technique for the *en bloc* resection of certain subgroups of neoplasms (1). ESD has yielded excellent outcomes in large Asian series in terms of *en bloc* and R0 resection rates, for both colorectal (CR) (2) and gastric lesions (3). However, these results may not be replicable in Western series (4,5).

When standard ESD is difficult to complete, a circumferential mucosal incision around the tumor is performed and subsequently, a knife-assisted snare resection (KAR) is performed (6). The latter procedure has been previously defined as "hybrid ESD" by Japanese experts (1).

The aim of this study was to examine the outcome of ESD in the clinical practice at a Western European tertiary referral center. This reflects the real circumstances of the initial procedures that include gastric and colorectal tumors, in a case-mixed fashion. We also aimed to assess factors that were associated with switching the initially planned ESD to a piecemeal KAR (p-KAR) and to develop a risk prediction model to anticipate the end of the surgery via a piecemeal resection.

Marín-Gabriel JC, Lora-Pablos D, Díaz-Tasende J, Cancelas-Navia P, Rodríguez-Muñoz S, Del-Pozo-García AJ, Alonso-Riaño M, Rodríguez-Gil Y, Ibarrola-Andrés C, Castellano-Tortajada G. Switching from endoscopic submucosal dissection to salvage piecemeal knife-assisted snare resection to remove a lesion: a preoperative risk score from the beginning. Rev Esp Enferm Dig 2018;110(11):699-705.

DOI: 10.17235/reed.2018.5608/2018

METHODS

Study subjects

Consecutive patients referred to the Hospital Universitario 12 de Octubre, a tertiary referral center in Madrid, who underwent ESD for the treatment of esophageal, gastric or CR neoplasms between September 2008 and December 2015 were recruited into the study. Data were analyzed retrospectively using a prospectively collected database from the first lesion removed via ESD.

Written informed consent was obtained from all patients. The study was approved by the Institutional Review Board of the Hospital Universitario 12 de Octubre (CEI 14/384; 29/9/2015). The study was performed in accordance with the Declaration of Helsinki and was conducted following the STROBE statement for reporting cross-sectional studies.

Endoscopic examination

All lesions were assessed before the ESD procedure using a magnifying endoscope (EG 590 ZW for upper gastrointestinal lesions and EC 590 ZW or EC 600 ZW for CR lesions; Fujifilm, Tokyo, Japan). With regard to CR ESD, the proposed indications by the Japanese Colon ESD Standardization Implementation Working Group were considered (1). Curative resections in early gastric cancer were considered when the guideline or expanded criteria were met (7).

ESD procedure

ESD procedures were performed by two teams with two therapeutic endoscopists in each team (team 1: JCMG and JDT; and team 2: SRM and AJdPG). The lateral margins were marked using a Flush knife or Flush knife BT (Fujifilm, Tokyo, Japan) after targeted chromoendoscopy for esophageal and gastric lesions. ICC® 200 or VIO® 300D (ERBE, Tübingen, Germany) electrosurgical generators were used. Carbon dioxide insufflation was used in all cases (Olympus UCR, Olympus, Tokyo, Japan). The following electrosurgical knives were used for the dissection at the discretion of the endoscopist: Flush knife or Flush knife BT (Fujifilm, Tokyo, Japan) and IT knife 2™ or IT nano™ (Olympus, Tokyo, Japan). When unresolved technical difficulties occurred (poor maneuverability or a perpendicular approach to the muscle layer with a high risk of perforation) or when the ESD procedure was excessively long (usually over 180 minutes), a salvage knife-assisted snare resection (KAR) was performed. There was never a planned KAR in any case. Although the original intention was to achieve an *en bloc* resection, even for KARs, this could not be achieved in some circumstances.

Histopathological evaluation

The endoscopic morphology of the lesion was classified according to the Paris classification (8) and the proposed classification by Kudo et al. (9) was followed for laterally spreading tumors (LSTs). Tumor size was measured with a scaled ruler in the case of *en bloc* resections after being stretched with pins on a piece of foam. With regard to piecemeal resections, tumor size was estimated during colonoscopy by reference to an open 20 mm polypectomy snare. The histopathological diagnosis was based on the Vienna classification (10).

Outcome parameters

An *en bloc* resection was defined as a resection in a single piece. When a resection in more than one fragment was achieved, the technique was considered as a piecemeal resection. KAR was considered when the submucosal layer was partially dissected, although a snare was finally used to complete the resection. Curative resection was considered as an *en bloc* resection in a well or moderately differentiated carcinoma when the lateral and vertical margins were free of neoplasia, without lymphovascular involvement as well as the absence of submucosal invasion deeper than sm1 (11) (< 200 microns for esophageal squamous cell carcinoma, < 500 microns for gastric carcinoma and < 1,000 microns for colorectal carcinoma). The expanded criteria were used to assess curability for gastric neoplasms (7,12,13). Scarred lesions were defined as local recurrences after prior endoscopic resections.

Statistical analysis

Data collection was performed using MS-Access (Microsoft Corp., Redmond, WA, USA). The IBM SPSS Statistics software version 21.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous patient variables were described with mean (SD) values when they followed a normal distribution. Otherwise, median and range were obtained. Categorical variables were presented as absolute and relative frequencies. Data were stratified for *en bloc* resections and p-KARs and their distributions were compared with the Student's t test, Wilcoxon test or Chi-square statistics. Some potential risk factors related to the need for p-KAR were analyzed: the number of procedures performed, the team that performed the resection, any previous electrosurgery applied to the tumor, evidence of a non-curative submucosal invasion, tumor location, a depressed morphology of the tumor, the time it took to perform the procedure and the lesion size. Experience was categorized as ≤ 50 and > 50 procedures according to Saito et al. (2). Furthermore, the maximum diameter of the tumor was categorized as ≤ 30 mm and > 30 mm, as the recommended size for beginners is under 3 cm (14). A p value less than 0.05 was considered as statistically significant. The meaningful variables with a p value < 0.1 according to the univariate analysis were included in the multivariate binary logistic model. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. The model developed to predict the risk of p-KAR was simplified as an easy-to-use risk scoring system. In order to establish the clinical risk score for predicting a piecemeal resection, weighted points proportional to β regression coefficient values were assigned for the factors determined in the multivariate analysis (15). The β coefficients were divided by the smallest absolute value of the regression coefficient and rounded to the nearest integer. The performance of the predictive model and risk score were evaluated using receiver operating characteristic (ROC) curve analysis. The optimal cut-off point was calculated as the maximum value of the sum of sensitivity

and specificity. Sensitivity, specificity, predictive values, likelihood ratios and diagnostic accuracy were calculated for an optimal cutoff point using a 2 x 2 table analysis.

RESULTS

A total of 139 patients with 142 lesions were included in the study. The procedure was aborted in six cases (4.2%) due to technical difficulties: two cases were gastric lesions and four were CR neoplasms. Therefore, 136 lesions in 133 patients were finally analyzed (Fig. 1). Baseline characteristics of the patients and tumors are shown in table 1.

Procedural outcomes of ESD

The outcome of the ESD procedures are presented in table 2. The procedure had to be changed to KAR in 64 cases (47%). The specimen was resected in a piecemeal fashion in 44 KARs (32.3%). Thus, *en bloc* resections were achieved in 72 ESDs (53%) and 20 KARs (14.7%).

Risk factors for the need for p-KAR

Experience with the technique of ≤ 50 ESD procedures, lesion size > 30 mm, CR location and a depressed morphology were all significantly associated with a higher frequency of piecemeal resections, whereas the team that performed the procedure, a scarred lesion and the presence of deep submucosal invasion were not associated with piecemeal resections (Table 3).

Statistically significant differences with regard to lesion size of gastric and colorectal locations (stomach *vs* rectum: 29.3 ± 13.2 *vs* 38.6 ± 18.3, p = 0.009; colon *vs* rectum: 28.9 ± 13.7 *vs* 38.6 ± 18.3, p = 0.02) were found. An interaction between a colorectal location and a diameter of the tumor of > 30 mm was observed when their association with p-KAR was assessed (overall OR = 3.33 [95% CI: 1.6-7.1], CR location OR = 5.53 [95% CI: 2.1-14.6] and non-CR location OR = 0.26 [0.03-2.4]). There were no statistically significant differences with regard to the percentage of colorectal cases by year (p = 0.45). There were also no statistically significant differences with regard to the maximum diameter of the lesions by the year of recruitment (Fig. 2).

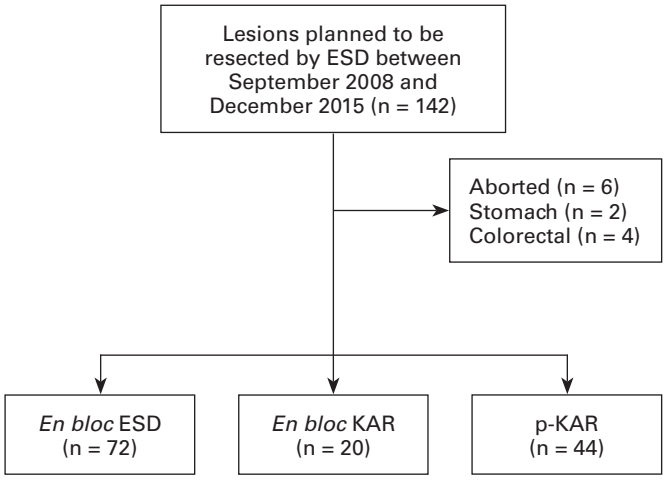

Fig. 1. *Flowchart of the lesions included in the study (ESD: endoscopic submucosal dissection; KAR: knife-assisted snare resection; p-KAR: piecemeal knife-assisted snare resection).*

Although the overall perforation rate was higher in the p-KAR group (22.7% *vs* 12%), the difference was not statistically significant (p = 0.11). In fact, there were no statistically significant differences in the intra-procedural perforation rate between both groups (n = 8: 8.7% in the en bloc group *vs* n = 8: 18.2% in the p-KAR group; p = 0.11).

According to the multivariate logistic regression analysis, experience with the technique of ≤ 50 procedures and the combination of CR location and lesion size (measured in cm) were significant factors for predicting a piecemeal resection during the procedure (Table 4). Although the simple variables of the interaction term (CR location and size > 30 mm) were not statistically significant according to the multivariate analysis, both were retained in the model as recommended.

Predictive model for p-KAR

The model to predict the end of the procedure with a piecemeal resection was as follows (Table 4): logit (p) = -2.56-0.8 (size > 30 mm) + 1.70 x (≤ 50 procedures) + 0.43 (CR location) + 2.82 x (CR location and size > 30 mm). This model calibrated well with the Hosmer-Lemeshow goodness-of-fit test (χ^2 = 1.25, df = 5, p = 0.94). The value of the area under the ROC curve for the predictive model was 0.82 (95% CI: 0.74-0.89), with a good discrimination ability.

The final predictive score system for a p-KAR was as follows: 1 x (colorectal location [0 = no; 1 = yes]) – 2 x (size > 30 mm [0 = no; 1 = yes]) + 4 x (number of the procedure < 50 [0 = no; 1 = yes]) + 6 x (size > 30 mm and colorectal location [0 = no; 1 = yes]). The score ranged from -2 (best prognosis to achieve an *en bloc* resection) to 9 (worst prognosis). For example, a patient with a colorectal tumor size smaller than 30 mm and an operator experience of under 50 cases would have an estimated risk of 39% of a p-KAR and would receive a score of five points. The value of the area under the ROC curve for the score (Fig. 3) was 0.81 (95% CI: 0.74-0.89). The diagnostic accuracy of the score for a cut-off point ≥ 5 had a sensitivity of 0.79 (95% CI: 0.66-0.93), a specificity of 0.71 (95% CI: 0.61-0.80), a positive predictive value of 0.56 (95% CI: 0.43-0.70) and a negative predictive value of 0.88 (95% CI: 0.80-0.96).

DISCUSSION

ESD training is a major issue in the European setting. Thus, suboptimal *en bloc* resection rates have been reported from the outset (16). Nevertheless, performing ESD in Western countries is challenging. It is recommended to start the learning curve of this procedure in the context of early gastric cancer. However, this condition is less prevalent in Europe. This is not a minor matter due to the fact that before moving to the CR area, Japanese experts recommended a minimum experience of 20 ESD procedures in

Table 1. *Baseline characteristics of the patients and lesions (133 patients; 136 lesions)*

	Total n = 136	*En bloc** (n = 92)	p-KAR (n = 44)	p
Age, year (mean ± SD)	71 ± 11.8	70.5 ± 11.8	72 ± 11.9	0.5
Sex, n (%)				
Male	77 (56.6)	52 (56.5)	25 (56.8)	0.9
Female	59 (43.4)	40 (43.5)	19 (46.2)	
Size of the tumor, mm, (mean ± SD)	32.9 ± 16.1	29.8 ± 13.4	39.1 ± 19.2	0.001
Size and morphology split by location, n (%)				
Esophagus	1 (0.7)	1 (1.1)	0 (0)	1.0
Size of the tumor, mm, median (range)	20 (0)	20 (0)	0 (0)	1.0
0-IIb	1 (0.7)	1 (1.1)	0 (0)	1.0
Stomach	50 (36.8)	43 (46.7)	7 (15.9)	0.0005
Size of the tumor, mm, mean (SD)	29.3 (13.2)	30.5 (13.6)	22.4 (8.4)	0.1
Upper third	5 (3.7)	4 (4.3)	1 (2.3)	1.0
Middle third	14 (10.3)	11 (11.9)	3 (6.8)	0.5
Lower third	31 (22.8)	28 (30.4)	3 (6.8)	0.002
0-Is	11 (8.0)	9 (9.8)	2 (4.5)	0.5
0-IIa	9 (6.6)	8 (8.6)	1 (2.3)	0.3
0-IIc/0-III	28 (20.7)	24 (26.1)	4 (9.1)	0.02
Scarred lesions	2 (1.5)	2 (2.2)	0 (0)	1.0
Rectum	53 (39)	28 (30.4)	25 (56.8)	0.005
Size of the tumor, mm, mean (SD)	38.6 (18.3)	33.0 (13.9)	44.9 (20.8)	0.02
0-Is	13 (9.5)	7 (7.6)	6 (13.6)	0.3
0-IIc/0-IIa+IIc	4 (2.9)	3 (3.3)	1 (2.3)	1.0
0-IIa (LST-G homogeneous type)	19 (14.0)	9 (9.8)	10 (22.7)	0.07
0-Is + IIa / 0-IIa + Is (LST-G mixed type)	13 (9.6)	7 (7.6)	6 (13.6)	0.2
0-IIa / 0-IIa+ IIc (LST-NG)	1 (0.7)	0 (0)	1 (2.3)	1.0
Scarred lesions	3 (2.2)	2 (2.2)	1 (2.3)	1.0
Colon	32 (23.5)	20 (21.7)	12 (27.3)	0.5
Size of the tumor, mm, mean (SD)	28.9 (13.7)	24.1 (11.4)	36.9 (14.0)	0.008
0-Is	5 (3.7)	4 (4.3)	1 (2.3)	1.0
LST-G homogeneous type	3 (2.2)	1 (1.1)	2 (4.5)	0.2
LST-G mixed type	4 (2.9)	3 (3.3)	1 (2.3)	1.0
LST-NG	17 (12.5)	10 (10.9)	7 (15.9)	0.4
Scarred lesions	3 (2.2)	2 (2.2)	1 (2.3)	1.0

SD: standard deviation; KAR: knife-assisted snare resection; LST: laterally spreading tumor; G: granular; NG: non-granular; p-KAR: piecemeal knife-assisted snare resection.
**En bloc* resections include ESD as well as KARs in which a single specimen was obtained.

gastric locations (17). After gaining experience with gastric cases, LST-Gs of 2-3 cm in size that are in the rectum are considered to be the most appropriate lesions for CR ESD beginners (14). Furthermore, in order to obtain a successful R0 resection rate of colonic lesions with few complications, some professionals believe that experience in up to 80-100 procedures is required (18).

We acknowledge that our case-mixed series (although mainly gastric and colorectal) could reduce the ability to compare our data with other published studies that focus on a specific organ. However, we provide data of the ESD procedure that is performed in a real-life scenario with Western endoscopists. In this setting, technically easy gastric lesions are difficult to find and cases are selected when trying to avoid surgery, even for difficult colorectal tumors. Therefore, our results can be generalized to patient populations in other tertiary referral centers that are performing their first procedures in a Western European setting. In our study, an *en bloc* resection could not be achieved in almost one third of the cases during the early learning curve. We were forced to conclude the procedure by changing to the KAR technique in some cases in order to successfully complete the resection.

DOI: 10.17235/reed.2018.5608/2018

Table 2. *Procedure outcomes of the initially planned endoscopic submucosal dissections (ESD)*

	Total (n = 136)	*En bloc** (n = 92)	p-KAR (n = 44)	p
Procedure time, min (mean ± SD)	193.5 ± 83.6	176.7 ± 76.1	228.5 ± 88.2	0.001
Histopathology, n (%)				
Mucosal low-grade neoplasia	36 (26.5)	23 (25)	13 (29.5)	0.7
Mucosal high-grade neoplasia	84 (61.8)	58 (63)	26 (59.1)	0.8
Curative submucosal invasion	3 (2.2)	3 (1.1)	0 (0)	0.5
Non-curative submucosal invasion	8 (5.8)	3 (1.1)	5 (11.4)	0.1
Other (subepithelial tumors, carcinoids)	5 (3.7)	5 (5.4)	0 (0)	0.2
Adverse events, n (%)				
Delayed bleeding	12 (8.8)	8 (8.7)	4 (9.1)	0.94
Patients receiving transfusion	7 (5.1)	5 (5.4)	2 (2.2)	1.0
Endoscopic treatment/surgery	8 (5.9) / 0 (0)	6 (6.5)/0 (0)	2 (4.5)/0 (0)	1.0/1.0
Perforation	21 (15.4)	11 (12)	10 (22.7)	0.1
Need for surgery	3 (2.2)	2 (2.2)	1 (2.3)	1.0
Increased length of hospital stay, median (range)	0 (0-54)	0 (0-36)	0 (0-54)	1.0
Procedure related deaths	1 (0.7)	1 (1.1)	0 (0)	0.38

SD: standard deviation; ESD: endoscopic submucosal dissection; p-KAR: piecemeal knife-assisted snare resection. *En bloc resections include ESD as well as KARs in which a single specimen was obtained.

Table 3. *Risk factors related to the need for a p-KAR procedure (univariate analysis)*

	ESD n = 92	p-KAR n = 44	p value
Number of procedures, n (%)			
≤ 50	25 (27.2)	25 (56.8)	0.001
> 50	67 (72.8)	19 (43.2)	
Team			
#1	63 (68.5)	25 (56.8)	0.25
#2	29 (31.5)	19 (43.2)	
Size, mm			
≤ 30	56 (60.9)	14 (31.8)	0.003
> 30	36 (39.6)	30 (68.2)	
Location			
Esophageal/gastric	44 (47.8)	7 (15.9)	0.0003
Colorectal	48 (52.2)	37 (84.1)	
Scarred lesion			
No	86 (93.5)	42 (95.5)	1.0
Yes	6 (6.5)	2 (4.5)	
Depressed lesion			
No	65 (70.7)	39 (88.6)	0.03
Yes	27 (29.3)	5 (11.4)	
Deep submucosal invasion			
No	89 (96.7)	39 (88.6)	0.11
Yes	3 (3.3)	5 (11.4)	

ESD: endoscopic submucosal dissection; p-KAR: piecemeal knife-assisted snare resection.

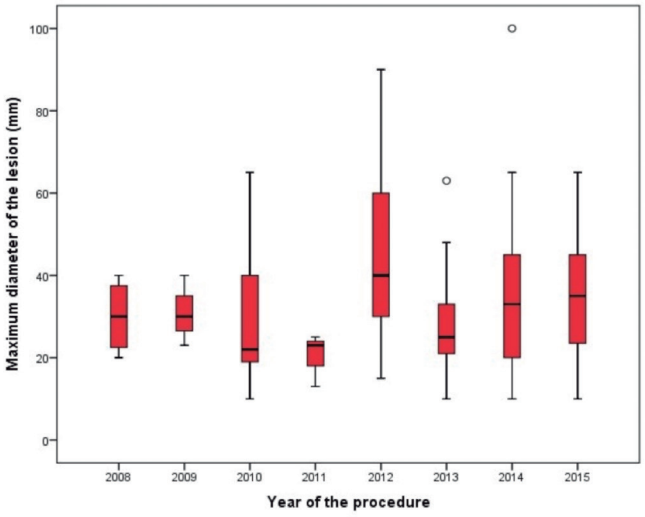

Fig. 2. *Maximum diameter of the lesions according to the year of recruitment.*

Our study demonstrates the association between some preoperative modifiable factors and the possibility to complete the procedure as a salvage piecemeal resection in a European setting. Experience with human ESD cases, as well as size and location of the tumor, are all predictive factors that can be easily determined preoperatively. This is undoubtedly the main strength of our study. Since this model has been conducted by a group of European endoscopists who were ESD beginners, our results may have special significance for other non-expert endoscopists when they encounter their first human cases. This study has demonstrated the good performance of the predictive model.

Table 4. *Multivariate logistic regression model and independent predictors for a piecemeal KAR*

Variable	OR (95% CI)	p value	β regression coefficient	Points
CR location and size > 30 mm	16.8 (1.4-202.4)	0.02	2.82	6
Experience (case number ≤ 50)	5.5 (2.1-14.3)	< 0.0001	1.70	4
CR location	1.5 (0.4-5.4)	0.5	0.43	1
Size > 30 mm	0.45 (0.05-4.4)	0.5	-0.78	-2

OR: odds ratio; CI: confidence interval; CR: colorectal; KAR: knife-assisted snare resection. The assignment of points to risk factors was based on a linear transformation of the corresponding β regression coefficient. The coefficient of each variable was divided by 0.43 (the lowest positive β value, corresponding to CR location) and rounded to the nearest integer.

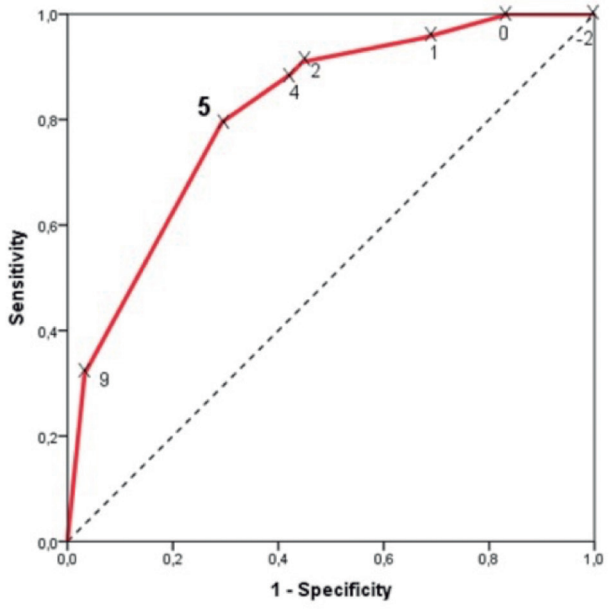

Fig. 3. *ROC curve of the predictive score system for a piecemeal knife-assisted snare resection (KAR) and cut-off points.*

The need to detect factors that predict technically difficult ESD has been addressed in the recent literature, mainly for CR lesions. Isomoto et al. (19) indicated that right-sided tumors with fibrosis have a high risk of an incomplete resection. Furthermore, they demonstrated that only fibrosis was significantly associated with the need for a piecemeal resection by multivariate analysis. However, the presence of submucosal fibrosis cannot be easily assessed preoperatively. With regard to failure of *en bloc* resection, Takeuchi et al. (20) noted that a low case-load, snare use and poor lifting after submucosal injection were associated with technical difficulties. Poor endoscopic maneuverability and deep submucosal invasion were identified as risk factors for an incomplete CR ESD in the study conducted by Hayashi et al. (21). Hori et al. (22) observed that scarring or a locally recurrent tumor and a tumor located at a flexure were all risk factors for a piecemeal resection. Finally, Imai et al. (23) have identified some independent predictors of *en bloc* resection failure in a large series of CR ESD procedures: fold convergence, a protruding morphology, poor endoscope operability, colonic location *vs* rectal lesions, an underlying semilunar fold and a less-experienced endoscopist (< 40 cases of CR ESD).

Our study has several limitations. First, there was a relatively small sample size. However, only four variables were used to predict more than 40 events in order to avoid the risk of overfitting the logistic regression model. Future studies with a pre-determined sample size will be needed in order to confirm our results. Second, a statistically significant difference with regard to size between the ESD and the p-KAR group was observed. The lesions that were finally removed via p-KAR were larger. However, we believe that a small difference in the mean size between both groups (only 1 cm) does not explain a selection bias. Third, although the four endoscopists who performed the procedures were not experts in the ESD technique, all of them had extensive experience with EMR with large colonic lesions. Therefore, our results may not be generalized to the general practice endoscopists. Fourth, a selection bias may not be fully excluded due to the lack of experience of the endoscopists. They could potentially bias the results by selecting the type of lesions with a greater chance of a successful *en bloc* resection *a priori.* However, the relatively high percentage of piecemeal resections, the percentage of lesions over 30 mm in size and the prevalence of scarred lesions in the study (approximately 6%) makes this scenario rather unlikely. Fifth, aborted procedures were not included in the final analysis. This decision might add a selection bias. However, only six of 142 procedures (4%) were aborted. Thus, the impact of removing them from the analysis should be negligible.

Finally, the main weakness of this study is the absence of internal and external validation groups. Further prospective multicenter studies are needed to confirm our results and to develop a more complete model.

CONCLUSIONS

In this retrospective study of ESD performed by less-experienced Western endoscopists, four simple preoperative variables were associated with completing a resection with a p-KAR. We developed a predictive model and a risk scoring system to estimate the risk for a piecemeal resection to complete the procedure that could be useful for selecting the most appropriate lesions at the beginning. Large-scale prospective trials are required for external validation of this predictive model.

ACKNOWLEDGMENTS

We thank Dr. Hernán-Ocaña (Department of Gastroenterology, Endoscopy Unit, Hospital Universitario 12 de Octubre, Madrid) and Dr. González-Blanco (Department of Gastroenterology, Hospital Universitario Rey Juan Carlos, Madrid) for assistance with the data collection. We also thank Mr. Kenneth McCreath for his valuable collaboration editing the English version.

REFERENCES

1. Tanaka S, Kashida H, Saito Y, et al. JGES guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2015;27(4):417-34. DOI: 10.1111/den.12456

2. Saito Y, Uraoka T, Yamaguchi Y, et al. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010;72(6):1217-25. DOI: 10.1016/j.gie.2010.08.004

3. Goto O, Fujishiro M, Kodashima S, et al. Outcomes of endoscopic submucosal dissection for early gastric cancer with special reference to validation for curability criteria. Endoscopy 2009;41(2):118-22. DOI: 10.1055/s-0028-1119452

4. Farhat S, Chaussade S, Ponchon T, et al. Endoscopic submucosal dissection in a European setting. A multi-institutional report of a technique in development. Endoscopy 2011;43(8):664-70. DOI: 10.1055/s-0030-1256413

5. Probst A, Pommer B, Golger D, et al. Endoscopic submucosal dissection in gastric neoplasia - Experience from a European center. Endoscopy 2010;42(12):1037-44. DOI: 10.1055/s-0030-1255668

6. Bhattacharyya R, Chedgy FJ, Kandiah K, et al. Knife-assisted snare resection (KAR) of large and refractory colonic polyps at a Western centre: feasibility, safety and efficacy study to guide future practice. United European Gastroenterol J 2016;4(3):466-73. DOI: 10.1177/2050640615615301

7. Gotoda T. Endoscopic resection of early gastric cancer. Gastric Cancer 2007;10(1):1-11. DOI: 10.1007/s10120-006-0408-1

8. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003;58(6 Suppl):S3-43.

9. Kudo S, Lambert R, Allen JI, et al. Nonpolypoid neoplastic lesions of the colorectal mucosa. Gastrointest Endosc 2008;68(4 Suppl):S3-47. DOI: 10.1016/j.gie.2008.07.052

10. Schlemper RJ, Riddell RH, Kato Y, et al. The Vienna classification of gastrointestinal epithelial neoplasia. Gut 2000;47(2):251-5. DOI: 10.1136/gut.47.2.251

11. Neuhaus H. ESD around the world: Europe. Gastrointest Endosc Clin N Am 2014;24(2):295-311. DOI: 10.1016/j.giec.2013.11.002

12. Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. Dig Endosc 2016;28(1):3-15. DOI: 10.1111/den.12518

13. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47(9):829-54. DOI: 10.1055/s-0034-1392882

14. Uraoka T, Parra-Blanco A, Yahagi N. Colorectal endoscopic submucosal dissection: is it suitable in western countries? J Gastroenterol Hepatol 2013;28(3):406-14. DOI: 10.1111/jgh.12099

15. Mehta HB, Mehta V, Girman CJ, et al. Regression coefficient-based scoring system should be used to assign weights to the risk index. J Clin Epidemiol 2016;79:22-8. DOI: 10.1016/j.jclinepi.2016.03.031

16. Hulagu S, Senturk O, Aygun C, et al. Endoscopic submucosal dissection for premalignant lesions and noninvasive early gastrointestinal cancers. World J Gastroenterol 2011;17(13):1701-9. DOI: 10.3748/wjg.v17.i13.1701

17. Uraoka T, Kawahara Y, Kato J, et al. Endoscopic submucosal dissection in the colorectum: present status and future prospects. Dig Endosc 2009;21(Suppl 1):S13-6. DOI: 10.1111/j.1443-1661.2009.00863.x

18. Hotta K, Oyama T, Shinohara T, et al. Learning curve for endoscopic submucosal dissection of large colorectal tumors. Dig Endosc 2010;22(4):302-6. DOI: 10.1111/j.1443-1661.2010.01005.x

19. Isomoto H, Nishiyama H, Yamaguchi N, et al. Clinicopathological factors associated with clinical outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. Endoscopy 2009;41(8):679-83. DOI: 10.1055/s-0029-1214979

20. Takeuchi Y, Iishi H, Tanaka S, et al. Factors associated with technical difficulties and adverse events of colorectal endoscopic submucosal dissection: retrospective exploratory factor analysis of a multicenter prospective cohort. Int J Colorectal Dis 2014;29(10):1275-84. DOI: 10.1007/s00384-014-1947-2

21. Hayashi N, Tanaka S, Nishiyama S, et al. Predictors of incomplete resection and perforation associated with endoscopic submucosal dissection for colorectal tumors. Gastrointest Endosc 2014;79(3):427-35. DOI: 10.1016/j.gie.2013.09.014

22. Hori K, Uraoka T, Harada K, et al. Predictive factors for technically difficult endoscopic submucosal dissection in the colorectum. Endoscopy 2014;46(10):862-70. DOI: 10.1055/s-0034-1377205

23. Imai K, Hotta K, Yamaguchi Y, et al. Preoperative indicators of failure of en bloc resection or perforation in colorectal endoscopic submucosal dissection: implications for lesion stratification by technical difficulties during stepwise training. Gastrointest Endosc 2016;83(5):954-62. DOI: 10.1016/j.gie.2015.08.024