

Endoscopic submucosal dissection for the treatment of gastrointestinal neoplasia in a tertiary-care center in Mexico

Disección endoscópica submucosa para el tratamiento de neoplasias gastrointestinales en un centro de tercer nivel en México

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Abstract

Objective: The aim of this study was to evaluate the experience of using endoscopic submucosal dissection (ESD), a technique considered as first-line of treatment, for the management of early neoplastic lesions (ENL), and subepithelial lesions (SEL) < 4 cms in size, in a tertiary-care, high-volume medical center in Mexico. **Method:** Patients > 18 years-old, candidates to ESD with ENL and SMT, between January 2008 and October 2022 were included. **Results:** ESD was performed in 246 patients (137 ENL and 109 SMT), 52.2% gastric, 23.1% colonic, 19.5% esophageal and 5.2% in duodenum. Benign/premalignant were 74.4%, and 25.6% malignant, being the SMT the most frequent (44.3%) and gastrointestinal stromal tumor. En-bloc resection, R0, and curative resection rates were 97.2%, 94.5%, and 85.8%, respectively. The most common adverse event was trans-procedural bleeding (18.3%) followed by perforation (6.9%), both endoscopically treated without mortality. Recurrence was presented in 9.44% at 177 months of follow-up. **Conclusions:** ESD is a safe and effective endoscopic surgical option of treatment for ENL and SMT in Mexican population when performed in experienced centers.

Keywords: Endoscopic submucosal dissection. Early neoplastic lesions. Subepithelial tumors. Safety. Efficacy.

Resumen

Objetivo: El objetivo del presente trabajo fue evaluar la experiencia en el uso de la disección endoscópica submucosa (DES), la cual es considerada una técnica de primera línea, para el tratamiento de lesiones neoplásicas tempranas (LNT) y lesiones subepiteliales (LSE) menores a 4 cms de tamaño, en un centro de tercer nivel de atención y alto volumen en México. **Método:** Se incluyeron, entre enero de 2008 y octubre de 2022, pacientes mayores de 18 años candidatos a DES por LNT y LSE en el tubo digestivo. **Resultados:** Se realizaron 246 intervenciones (137 LNT y 109 LSE), el 52.2% gástricas, el 23.1% colónicas, el 19.5% esofágicas y el 5.2% duodenales. El 74.4% fueron lesiones benignas/premalignas y el 25.6% fueron malignas, siendo las LSE las más frecuentes (44.3%) y dentro de estas el tumor del estroma gastrointestinal. La resección en bloque, R0 y curativas fueron el 97.2%, el 94.5% y el 85.8%, respectivamente. El evento adverso más común fue la hemorragia transprocedimiento (18.3%), seguida de la perforación (6.9%), ambas manejadas endoscópicamente, sin mortalidad. La recurrencia a 177 meses se presentó en el 9.44% de los pacientes. **Conclusiones:** La DES es una opción de tratamiento quirúrgico endoscópico segura y efectiva para LNT y LSE en nuestra población cuando se realiza en centros con alta experiencia.

Palabras clave: Disección endoscópica submucosa. Lesión neoplásica temprana. Lesión subepitelial. Eficacia. Seguridad.

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Introduction

Gastrointestinal cancer accounts for up to 35% of cancer-related deaths¹⁻⁴. It has a high morbidity and mortality rate, primarily due to late detection, which is more pronounced in Latin America⁵⁻⁹, despite best efforts for early detection¹⁰⁻¹².

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are key components in the management of premalignant or early GI malignancies and subepithelial lesions (SEL)^{13,14}. EMR is used for lesions <1.5 cm¹⁵, while ESD is used for larger lesions¹⁶, with the latter showing higher complete resection rates compared to EMR (92-98% vs 78-81%; $p < 0.001$)^{17,18}, and lower morbidity and mortality compared to conventional surgical treatments^{19,20}.

ESD is a safe and effective technique²¹, representing the reference method for treating early neoplastic lesions (ENL) and SELs ranging from 2 to 4 cm, specifically gastrointestinal stromal tumors (GISTs)^{22,23}. The recurrence rate is lower with ESD vs EMR (1-2% vs 6-10%; $p < 0.05$)^{1,2,12}. Its adoption in Mexico and Latin America is lower than in Asia^{24,25}, with contributing factors related to the procedure (difficulty, potentially severe adverse events, and prolonged procedure times) and to the physician (limited experience, extensive knowledge of the team and materials, lack of training centers, and low prevalence and incidence which limits the learning curve)²⁶⁻²⁸.

Given the advantages of ESD in treating ENL and SEL, its incorporation into clinical practice is necessary in our country. Therefore, our objective is to describe our experience with ESD for treating ENL and SEL in a tertiary care center in Mexico.

Method

We conducted a retrospective study from January 2008 through October 2022. Patients older than 18 years with suspected ENL or SEL in the digestive tract were included. For ENL, patients with poorly differentiated histology, endoscopic findings suggestive of deep invasion or advanced lesions were excluded, while for SEL, patients with poor prognosis factors (necrosis, ulceration, lymph node metastasis) were excluded. Informed consent was obtained from all cases.

Demographic characteristics of the patients, procedures, and histological analyses were documented. The procedures were performed by the authors, both

experienced endoscopists with previous experience in ESD (>200 procedures each).

Preoperative evaluation and equipment

Endoscopic evaluation for all cases was carried out with Olympus equipment models GIF-H-180 and GIF-H180 J (Olympus, Tokyo, Japan) or Fujinon models EG-450WR5 H, EG-590WR, EG-600 WR, and EG-760R (Fujinon, Tokyo, Japan), and for colonoscopy, Olympus models CF-Q180 and CF-H190L (Olympus, Tokyo, Japan) or Fujinon models EC-450WR5, EC-590WR, EC-600 WR, EC-760R, and EC-760R-VL (Fujinon, Tokyo, Japan).

ENL

Lesions were characterized using vital or digital chromoendoscopy with NBI (Narrow Band Imaging, Olympus, Tokyo, Japan) or BLI (Blue Light Imaging, Fujinon, Tokyo, Japan), depending on the equipment used. The classifications of the Japanese Esophageal Society, the international NBI group classification for Barrett's esophagus (BING), the simplified endoscopic algorithm for gastric cancer (MESDA-G), and the Kudo and NICE classifications for squamous esophageal cancer, early gastric cancer, and colon lesions, respectively, were used. To define the morphology of all gastrointestinal lesions found, the Paris classification was used²⁹⁻³⁵ (Fig. 1).

SEL

Endoscopic ultrasound (EUS) was performed for characterization, and histological confirmation was obtained. The treatment algorithm is shown in Fig. 2.

Endoscopic Submucosal Dissection

ESD for ENL

CO₂ was used in all cases, with an ENDOstratus insufflation pump (Medivators, Minneapolis, Minnesota, USA), an ERBE electrosurgical unit (ERBE, VIO-200D, 300-D, or VIO-3, Tübingen, Germany), type I, O, or T knives coupled to the ERBEJET unit (ERBE, Tübingen, Germany), BT-knife 2.0 or 2.5 mm (Fujifilm, Tokyo, Japan), and Coagrasper (Olympus, Tokyo, Japan) for hemostasis of vessels. Submucosal

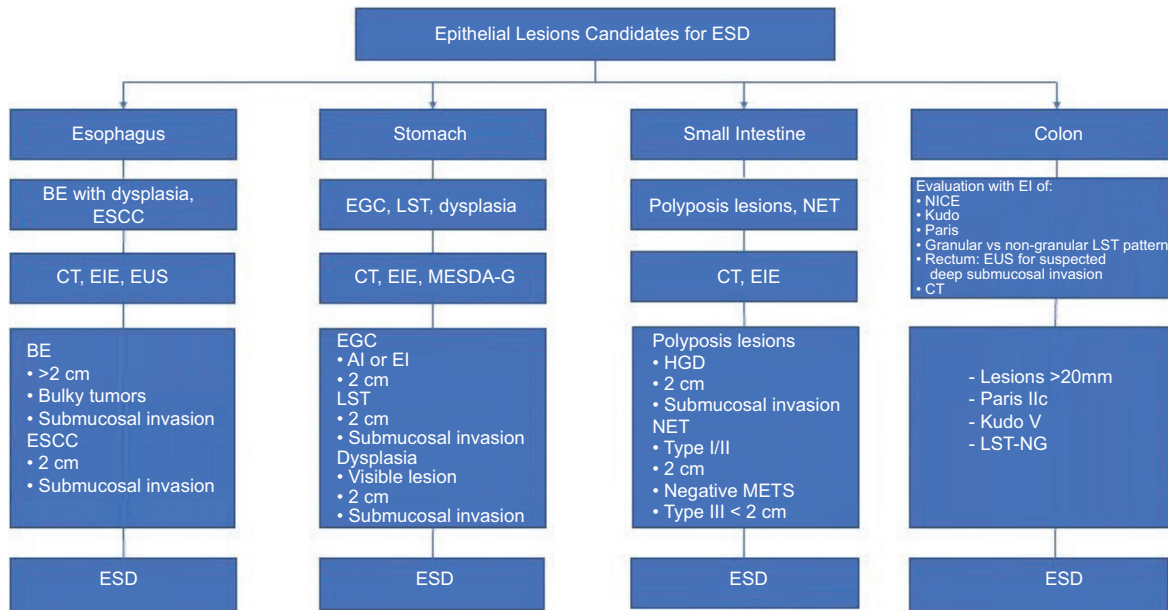


Figure 1. Diagnostic algorithm for epithelial lesions eligible for endoscopic submucosal dissection.

ESCC: Esophageal squamous cell carcinoma; EGC: Early gastric cancer; ESD: Endoscopic submucosal dissection; BE: Barrett's esophagus; HGD: High-grade dysplasia; EIE: Enhanced imaging endoscopy; NET: Neuroendocrine tumor; CT: Computed tomography; EUS: Endoscopic ultrasound; LST: lateral spreading tumor

+ Enhanced imaging endoscopy: use of digital chromoendoscopy and vital dye as well as magnification.

^aEUS use is restricted to cases of suspected deep submucosal invasion despite a thorough endoscopic evaluation.

AI = Absolute indications; EI = Extended treatment indications for EGC: AI = Well/moderately differentiated cancer, non-ulcerated, ≤ 2 cm. EI = Well/moderately differentiated cancer > 2 cm, ulcerated lesions ≤ 3 cm, poorly differentiated cancer and non-ulcerated ≤ 2 cm, cancer with submucosal invasion < 500 microns, well-differentiated and ≤ 3 cm.

elevation was performed with 0.9% saline solution or hydroxypropyl methylcellulose (Lagricel, Laboratorios Sophia, Mexico), combined with 0.5% methylene blue or 0.1-0.3% indigo carmine. The 5 steps of the original technique were performed:

1. Marking: Points made with monopolar coagulation 5 mm outside the lesion (soft coagulation, effect 4 at 80 W).
2. Submucosal injection: Elevation with 0.5% methylene blue plus saline solution.
3. Circular incision: Dissection with endocut mode I (interval 3, duration 3, effect 3) 5 mm outside the marking.
4. Submucosal dissection: Complete resection of the lesion in the submucosal plane; in the case of hemostasis, soft coagulation was performed at 80 W, effect 4.
5. Specimen extraction: Fixation and review of the treated area in search of muscle injury, and if necessary, endoscopic management using hemoclips (Boston Scientific, Natick, Massachusetts, USA) or OTS clip (Over-The-Scope clip, Tübingen, Germany), at the physician's discretion (Fig. 3).

ESD for SEL

According to the size, location, and characteristics of the lesion, the same ESD technique as for epithelial lesions was used, or a modification combining tunneling or EMR was performed (Fig. 4).

HISTOLOGICAL ANALYSIS

Histological analysis of the specimens was performed on epithelial lesions (EL), confirming the presence of marking points, and on SEL to assess the integrity of the capsule. Fixation was performed with formalin, and cuts were made every 2 mm. The specimens were classified as R0 (complete resection with negative lateral and deep margins), R1 (positivity in one of the margins), R2 (macroscopic presence of residual tumor), and RX (unable to assess complete resection).

Adverse events

Both in EL and SEL, adverse events before, during, and after the procedure were documented, as well as

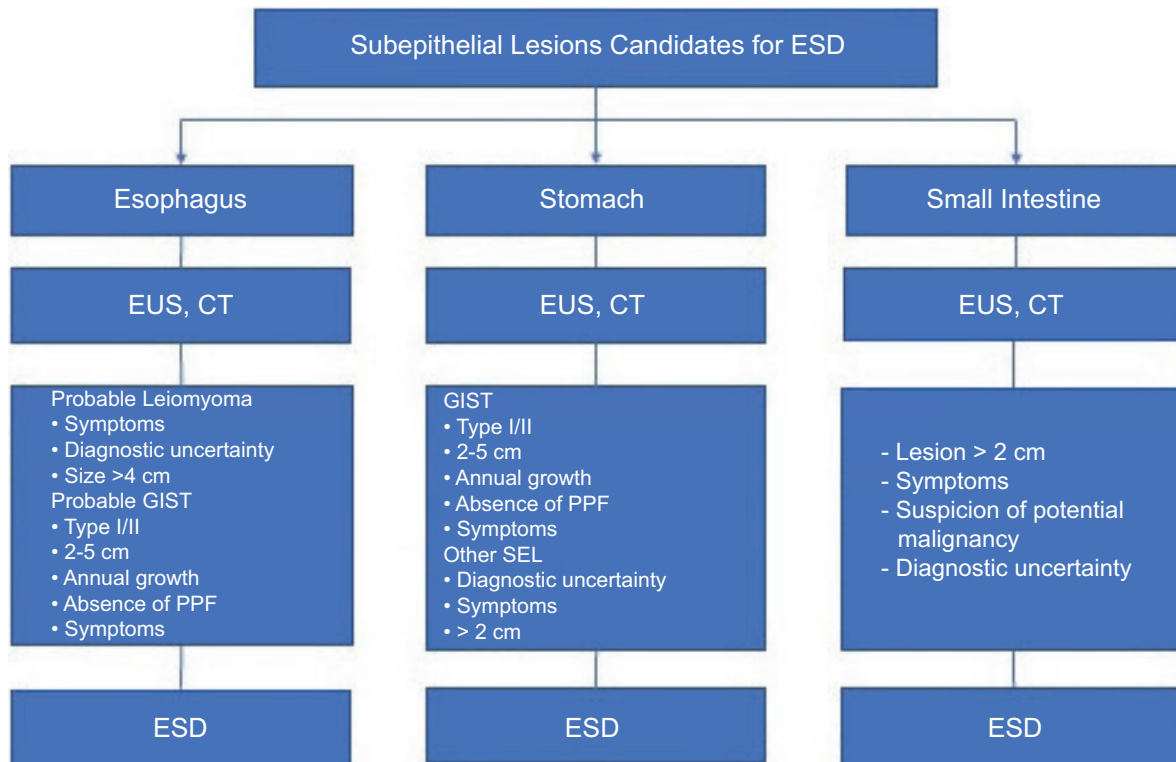


Figure 2. Diagnostic algorithm for subepithelial lesions eligible for endoscopic submucosal dissection.

GIST: Gastrointestinal stromal tumor; ESD: Endoscopic submucosal dissection; PPF: Poor prognosis factors; SEL: Subepithelial lesions; CT: Computed tomography; EUS: Endoscopic ultrasound.

PPF in GIST: Ulcerated lesions and/or presence of irregular borders, hypoechoic foci (necrosis), hyperechoic foci (bleeding), heterogeneous enhancement, presence of METS at distance or lymph nodes via EUS/CT.

the type of management (endoscopic, conservative, or surgical). In cases of clinically significant pneumoperitoneum (alteration in ventilatory or circulatory mechanics), abdominal or thoracic decompression was performed as needed, using a Veress needle. In the case of perforation or muscle damage, appropriate management was given at the discretion of the endoscopist.

Objectives

The objective of this study was to document the safety, efficacy, operative time, adverse events, clinical success, and tumor recurrence in patients undergoing ESD for the treatment of both neoplastic lesions (ENL) and subepithelial lesions (SEL) in the gastrointestinal tract.

Statistical analysis

The sample size calculation was based on the efficacy of ESD in the treatment of neoplastic lesions

(ENL) and subepithelial lesions (SEL), which according to previous studies^{12,16,23,25} is greater than 90%. With an alpha error of 5% and assuming a 95% confidence interval, a minimum of 138 patients was required, using a validated statistical program (Epi-Info, USA). The general characteristics of the patients and the procedures were documented. The results were expressed as mean and standard deviation, or as median and interquartile ranges, depending on their distribution, for quantitative variables, and as frequencies and percentages for qualitative variables. Bivariate comparison was performed with the Kruskal-Wallis test, and linear association with linear-by-linear association. A $p < 0.05$ was considered statistically significant. The SPSS 27 program (IBM, Chicago, IL, USA) was used.

Ethical considerations

Informed consent was obtained from each patient, and due to the retrospective nature of the study, approval from the ethics committee was not required.

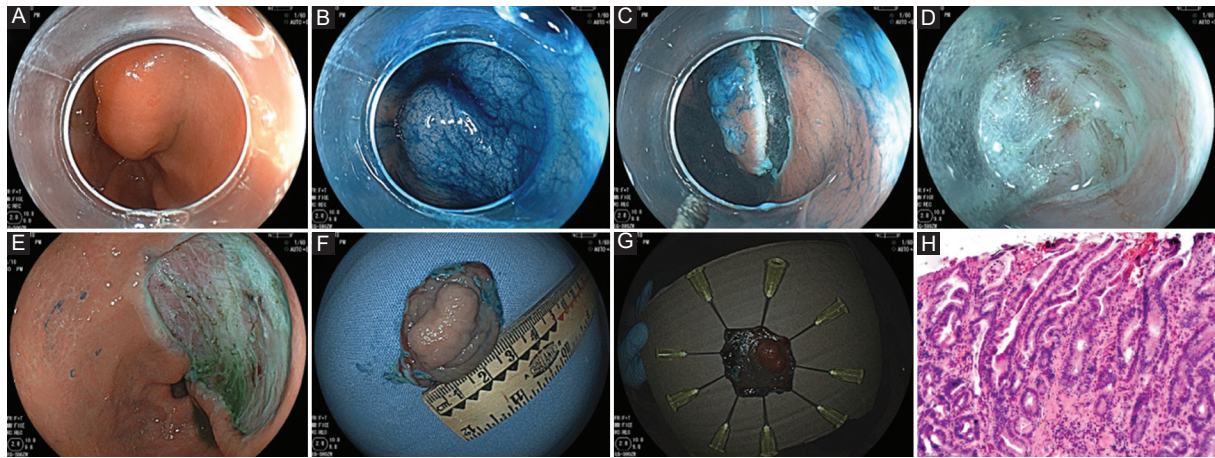


Figure 3. Endoscopic submucosal dissection performed on a gastric adenoma. **A:** lesion located in the pre-pyloric region. **B:** chromoendoscopy with methylene blue. **C:** circumferential incision. **D:** submucosal dissection. **E:** post-dissection surgical bed. **F and G:** specimen obtained. **H:** histology showing low-grade dysplasia.

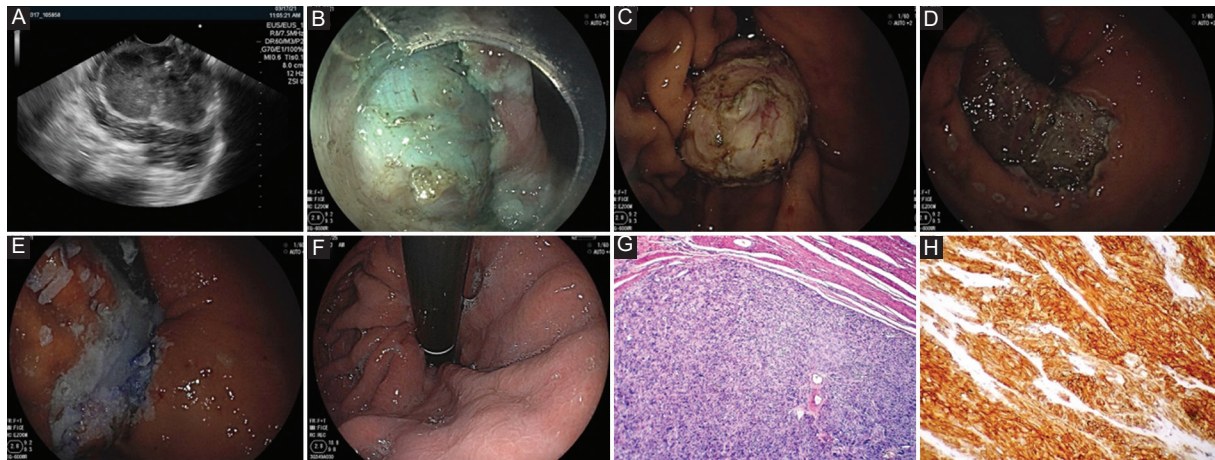


Figure 4. Combined endoscopic dissection with tunneling for resection of a subepithelial tumor. **A:** subepithelial lesion dependent on the 4th echolayer with cystic degeneration and calcifications, measuring 65 × 43 mm in diameter. **B:** exposed submucosal lesion. **C:** dissected lesion. **D:** resection bed. **E:** closure of the surgical bed with OVESCO clips and cyanoacrylate. **F:** follow-up 5 months after endoscopic submucosal dissection. **G:** histology with hematoxylin and eosin staining. **H:** immunohistochemistry with CD-117 positive.

Results

General characteristics of the patients and procedures

Between January 2008 and October 2022, 246 procedures were performed (137 ENL and 109 SEL). There were no differences in sex or age between the two groups. Insulin-independent diabetes was the most common comorbidity (ENL 54.7% and SEL 58.7%). A difference was found in the histology before ESD between the two groups due to the inherent nature of the epithelial or subepithelial pathology

($p = 0.01$). The stomach was the most common location for ESD, with 128 lesions (52%). The median size for ENL and SEL was 22.1 and 25.7 mm, respectively ($p = 0.22$). The classical technique was the most widely used in both groups, and en block resection was similar between ENL and SEL (97.1% vs 96.3%; $p = 0.53$). The length of stay was similar in both groups, with a median of 2 days (Table 1).

Adverse events

Pneumoperitoneum occurred in 74 patients (33 ENL and 41 SEL), 12 of whom (16.2%) required

Table 1. General Characteristics of Patients and Procedures According to the Type of Lesion

Characteristics	ENL (n = 137)	SEL (n = 109)	p
Male Sex, n (%)	74 (54)	61 (55.9)	0.21 ^a
Age (years), Median, IQR	55 (16-93)	52 (22-78)	0.35 ^b
Comorbidity, n (%)			
Diabetes	75 (54.7)	64 (58.7)	0.88 ^c
Hypertension	64 (46.7)	55 (50.4)	
Chronic kidney disease	42 (30.6)	21 (19.2)	
Ischemic Heart Disease	31 (22.6)	32 (29.3)	
Autoimmune Disease	18 (13.3)	12 (11)	
Other	4 (2.9)	5 (4.6)	
Anticoagulation, n (%)	26 (18.9)	18 (16.5)	0.35 ^a
ASA Use, n (%)	46 (33.5)	35 (32.1)	0.12 ^a
Alcohol, n (%)	28 (20.4)	22 (20.1)	0.45 ^a
Smoking, n (%)	65 (47.4)	33 (30.2)	0.51 ^a
Pre-ESD Histology, n (%)			0.01 ^c
IM with LGD	8 (3.3)	16 (14.6)	
IM with HGD	25 (10.2)	93 (85.4)	
GAC	16 (6.5)		
CA	12 (4.9)		
LST-G	29 (11.8)		
LST-NG	12 (4.9)		
Barrett with LGD	8 (3.3)		
Barrett with HGD	8 (3.3)		
EC	6 (2.4)		
NET	13 (5.3)		
Pb Leiomyoma	-		
Pb (GIST)	-		
Location, n (%)			0.02 ^c
Esophagus	28 (20.4)	20 (18.4)	
Stomach	73 (53.4)	55 (50.4)	
Duodenum	8 (5.8)	5 (4.6)	
Colon	28 (20.4)	29 (26.6)	
Size (mm), Median (IQR)	22.1 (6.5-81.2)	25.7 (14.5-65.5)	0.22 ^b
Technique, n (%)			0.37 ^c
Classic ESD	82 (59.8)	55 (50.4)	
ESD + Tunneling	44 (32.1)	41 (37.6)	
ESD + EMR	11 (8.1)	13 (12)	
Operative Time (min), Median (IQR)	71.5 (27.8-348.1)	78.5 (35.5-188.9)	0.91 ^b
EN Block Resection, n (%)	133 (97.1)	105 (96.3)	0.53 ^a
Length of stay (days), Median (IQR)	2 (1-4)	2 (1-6)	0.15 ^b

CA: Colon adenoma; GAC: Gastric adenocarcinoma; ASA: Aspirin; EC: Esophageal carcinoma; HGD: High-grade dysplasia; LGD: Low-grade dysplasia; ESD: Endoscopic submucosal dissection; GIST: Gastrointestinal stromal tumor; LNT: Early neoplastic lesion; SEL: Subepithelial lesion; LST-G: Lateral spreading tumor, granular variety; LST-NG: Lateral spreading tumor, non-granular variety; IM: Intestinal metaplasia; Pb: Probable; EMR: Endoscopic mucosal resection; IQR: Interquartile range; NET: Neuroendocrine tumor.

^aMann-Whitney U test.

^bChi-square test.

^cLinear by linear association.

decompression with a Veress needle. Transoperative bleeding occurred in 45 cases (18.3%), being more frequent in SEL (23.8% vs 13.8%; $p = 0.04$);

endoscopic management achieved control in all cases. In 17 patients (6.9%), bleeding occurred after 24 hours (10 ENL and 7 SEL; $p = 0.55$), and endoscopic review

Table 2. Adverse Events of Endoscopic Submucosal Dissection According to Lesion Type

Adverse Event	ENL (n = 137)	SEL (n = 109)	p
Post-polypectomy Syndrome, n (%)	2 (1.4)	2 (1.8)	0.21 ^a
Pneumoperitoneum, n (%)	33 (24.1)	41 (37.6)	0.26 ^a
None, n (%)	25 (18.2)	31 (28.4)	0.09 ^a
Pneumomediastinum, n (%)	15 (10.9)	13 (11.9)	0.11 ^a
Hemorrhage During Procedure, n (%)	19 (13.8)	26 (23.8)	0.04 ^a
Perforation, n (%)	8 (5.8)	9 (8.3)	0.34 ^a
Hemorrhage>24 hours, n (%)	10 (7.3)	7 (6.4)	0.55 ^a
Abdominal Pain, n (%)	8 (5.8)	15 (13.7)	0.19 ^a
Mortality, n (%)	0 (0)	0 (0)	0.08 ^a
Need for Surgery, n (%)	3 (2.1)	2 (1.8)	0.71 ^a

^aChi-square test.

was performed on all of them, with 7 patients requiring endoscopic management (3 hemoclips, 2 monopolar coagulation, and 2 combined treatment), achieving total control in all. Perforation occurred in 17 patients (6.9%) (8 ENL and 9 SEL; $p = 0.34$) and was treated endoscopically in 14 (6 hemoclips, 3 OTS clips, 2 cyanoacrylate, and 3 combined treatment) and surgically in 3. Five patients required surgical exploration 24 hours after ESD due to suggestive signs of perforation (1 in the duodenum, 2 in the colon, and 2 in the stomach), and perforation was confirmed in one case. There were no cases of mortality during or after the procedure (Table 2).

Histology

Benign/premalignant lesions were found in 74.4% and malignant lesions in 25.6%. Low-risk GIST was the most common lesion, with 60/183 (24.5%) patients, and well-differentiated gastric adenocarcinoma in malignant lesions, with 22 patients (8.8%). ENL occurred in 137/246 cases (55.7%), most of which were at SM1 level, in 120/137 (87.6%) patients. En block resection was performed in 239/246 (97.2%), with complete resection (R0) in 233/246 (94.7%; 130 ENL [94.8%] and 103 SEL [94.5%]), R1 in 12/246 (4.9%; 7 ENL and 5 SEL), and R2 in 1/246 (0.4%; 1 ENL). Finally, curative resection was achieved in 211/246 (85.8%; 117 ENL [85.4%] and 96 SEL [86.2%]). The correlation between pre- and

Table 3. Final Histological Findings

Characteristics	(n = 246)
Benign or Premalignant Lesions, n (%)	183 (74.4)
Barrett with LGD	5 (2)
Barrett with HGD	13 (5.3)
Intestinal Metaplasia with LGD	10 (4)
Intestinal Metaplasia with HGD	14 (5.7)
Tubulovillous Adenoma with LGD	15 (6.1)
Tubulovillous Adenoma with HGD	24 (9.7)
Villous Adenoma with LGD	4 (1.6)
Villous Adenoma with HGD	4 (1.6)
GI Stromal Tumor (GIST) Very Low, Low, or Intermediate Risk	60 (24.5)
Leiomyoma	30 (12.3)
Granular Cell Tumor	2 (0.8)
Lipoma	2 (0.8)
Malignant Lesions, n (%)	63 (25.6)
Well-Differentiated EC	2 (0.8)
Poorly Differentiated EC	2 (0.8)
Well-Differentiated GAC	22 (8.8)
Poorly Differentiated GAC	3 (1.2)
Well-Differentiated CA	4 (1.6)
Poorly Differentiated CA	2 (0.8)
GIST with High-Risk Features	16 (6.5)
NET	12 (4.9)
Depth of Invasion in ENL, n (%)	137 (100)
Mucosa and Superficial Submucosa (SM1)	120 (87.6)
Deep Submucosa (SM2)	17 (12.4)
Complete Resection (R0), n (%)	233 (94.7)
ENL	130/137 (94.8)
SEL	103/109 (94.5)
Final Curative Resection, n (%)	211 (85.8)
ENL	117/137 (85.4)
SEL	96/109 (86.2)
Histological Correlation Pre- vs Post-DES, n (%)	224/246 (91)
ENL	126/137 (91.6)
SEL	99/109 (90.8)

CA: Colorectal Adenoma; GAC: Gastric Adenocarcinoma; EC: Esophageal Carcinoma; HGD: High-Grade Dysplasia; LGD: Low-Grade Dysplasia; DES: Endoscopic Submucosal Dissection; GIST: Gastrointestinal Stromal Tumor; LNT: Early Neoplastic Lesion; SEL: Subepithelial Lesion; IM: Intestinal Metaplasia; SM1: Superficial Submucosa; SM2: Deep Submucosa.

post-ESD histology was found in 91% of cases (126 ENL [91.6%] and 99 SEL [90.8%]) (Table 3).

Lesion distribution

The region with the highest frequency of procedures was the stomach (128/246; 52%). In the esophagus, leiomyoma was the most common lesion, with 21 cases (43.8%); in the stomach, low-grade GIST was the most frequent, with 52 cases (40.6%); in the colon, the lateral growth lesion of the non-granular variety with high-grade dysplasia, with 24 cases (42.1%); and in the duodenum, neuroendocrine tumors, with 8 cases (61.5%) (Fig. 5).

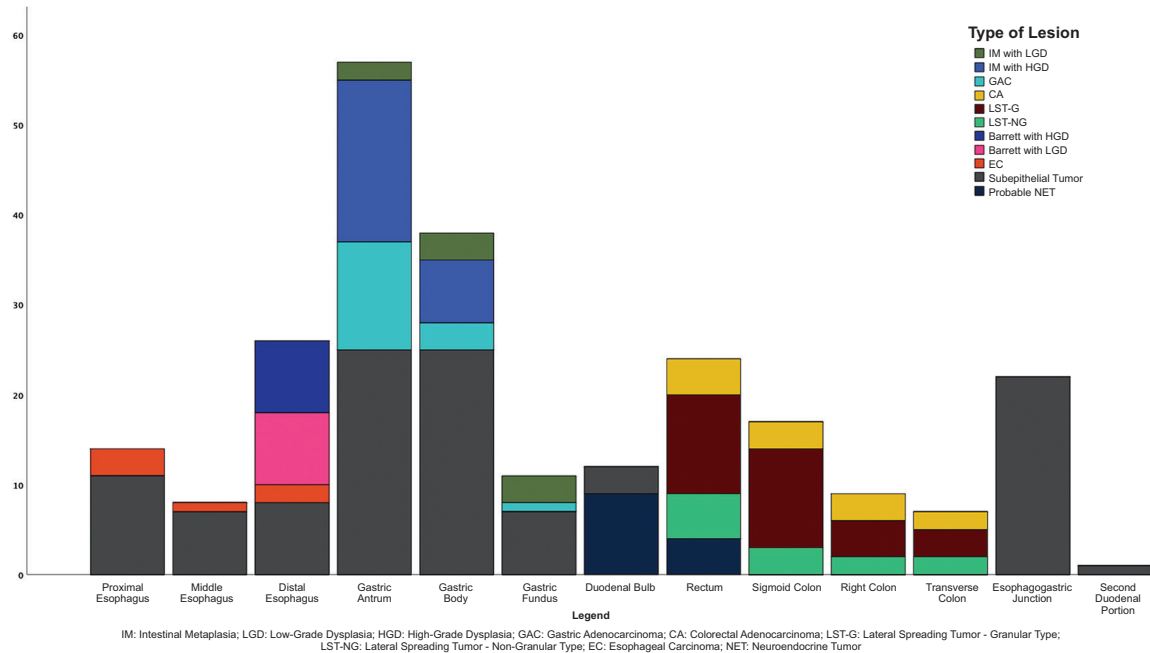


Figure 5. Distribution of resected lesions based on their location.

Table 4. Recurrence during Follow-up

Characteristics	Accumulated Recurrence (n = 233)
3 months, n (%)	1 (0.42) ENL 1/SEL 0
6 months, n (%)	2 (0.85) ENL 1/SEL 1
12 months, n (%)	3 (1.28) ENL 2/SEL 1
24 months, n (%)	6 (2.57) ENL 3/SEL 3
36 months, n (%)	9 (3.86) ENL 5/SEL 4
48 months, n (%)	12 (5.15) ENL 7/SEL 5
60 months, n (%)	17 (7.29) ENL 11/SEL 6
177 months (last cutoff), n (%)	22 (9.44) ENL 12/SEL 10

12 patients (7.29%), and by October 2022 (177 months post-ESD), a total of 22 (9.44%) recurrences were observed, 12 of which were ENL and 10, SEL. Treatment offered was endoscopic in 8 (successful in 6), while the other 14 recurrences required surgery and neoadjuvant therapy in all cases. Curative resection was achieved in 211/246 (85.8%; ENL 85.4% and SEL 86.2%; $p = 0.45$). No advanced lesions were found at follow-up, and mortality rate was 8.1% at 177 months, but without any association with tumor recurrence (Table 4 and Fig. 6).

Organ-related endoscopic submucosal dissection

The largest lesion sizes resected were in the colon vs the duodenum (26.5 vs 10.3 mm; $p < 0.001$), also showing the longest resection times (95.4 vs 55.6 min; $p < 0.001$). There were no differences in the length of hospital stay, en block resection rate, R0 rate, or type of lesion (ENL vs SEL). Bleeding was more common in the stomach, with 11 patients (8.6%), and perforation was more frequent in the colon, with 5 patients (8.8%) (Table 5).

Recurrence at Follow-up

Of the 239/246 patients who underwent en block resection (97.2%), 233/246 (94.7%) had R0 resection. Most recurrences occurred within the first 5 years in

Discussion

The aim of this study was to evaluate the experience of ESD for the treatment of ENL and SEL. We confirmed that it is a safe, effective, and reproducible technique in

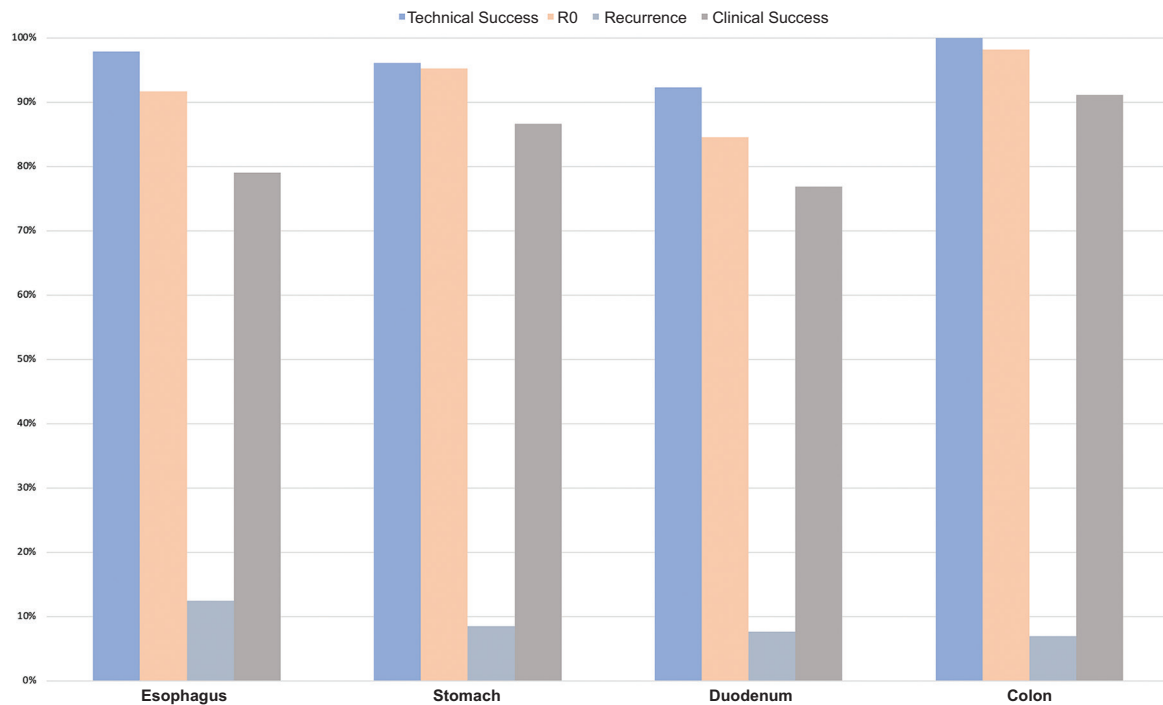


Figure 6. Technical success, R0, recurrence, and clinical success of endoscopic submucosal dissection by region.

Table 5. Characteristics of Endoscopic Submucosal Dissection by Regions of the Digestive Tract

Characteristics	Esophagus (n = 48)	Stomach (n = 128)	Duodenum (n = 13)	Colon (n = 57)	p
Size (mm), median, IQR	17.5 (8.1-40)	24.1 (10.1-65.1)	10.3 (6.5-15)	26.5 (8.4-81.2)	< 0.001 ^a
Time (min), median, IQR	62 (34.5-96)	78.1 (33.1-278)	55.6 (27.8-88)	95.4 (28.1-348)	< 0.001 ^a
Length of stay (days), median, IQR	1 (1-5)	3 (2-7)	3 (2-6)	2 (1-8)	0.22 ^a
En block resection, n (%)	47 (97.9)	123 (96.1)	12 (92.3)	57 (100)	0.25 ^b
Severe adverse events, n (%)					
Severe hemorrhage	3 (6.3)	11 (8.6)	1 (7.7)	2 (3.5)	0.04 ^b
Perforation	1 (2.1)	10 (7.8)	1 (7.7)	5 (8.8)	0.04 ^b
R0, n (%)	44 (91.7)	122 (95.3)	11 (84.6)	56 (98.2)	0.94 ^b

^aKruskal-Wallis.

^bLinear-by-linear association.

our setting. It has become established as a safe and effective technique^{12,13,36-39}, although its introduction in Latin America and Mexico has been slow^{14,16,40}. Despite this, countries such as Brazil, Chile, Peru, and Colombia have published good results for ESD in the treatment of ENL and SEL, similar to those documented in the East^{9,24,27,40-45}. In our country, the group of Carames et al.⁴⁶ reported the use of ESD in 32 patients with intestinal metaplasia, obtaining good results.

In the present study, we included 246 lesions (137 ENL and 109 SEL), with male sex being more

predominant (54% and 55.9%, respectively) in both groups, similar to what has been reported by various Latin American authors (52-66%), such as Emura et al.⁴³ and others^{27,41,44}. Age and other demographic factors were also similar to those reported by other authors, such as Medina et al.⁴⁷, who used this technique to treat ENL and SEL.

The largest lesions required longer ESD times and were more common in the colon (26.5 mm and 94.5 min), which is similar to what has been reported by other authors, such as Arantes et al.⁹ and Palacios

et al.²⁷, and also similar to what was found in Eastern centers by Su et al.⁴⁸ and Jiao et al.⁴⁹. These findings are clear for ENL, where the lesions are epithelial, and delays in dissection are associated with the presence of transoperative bleeding, location, and fibrosis, unlike SEL, where resection times are also highly variable but similar to other ESD studies in ENL and SEL^{41,44,48,49}.

Perforation occurred in 17 cases (ENL 5.8% and SEL 8.3%), and transoperative bleeding was slightly more frequent in SEL (23.8% vs 13.8% in ENL), probably related to the location and greater vascularization of SEL vs ENL. However, adverse events were controlled endoscopically, similar to what has been reported in other Asian and Latin American centers where endoscopic resolution demonstrated an efficacy higher than 80%^{1,9,10,13,16,49,50}, as observed in our cohort (82.5%).

Our case series represents the largest documented in Latin America, with an en block resection rate of 97.2% (97.1% for ENL vs 96.3% for SEL; $p = 0.53$), similar to results reported by other authors, such as Arantes et al.⁹ and Palacios et al.²⁷, with R0 for gastric ENL at 96.3% and 99%, respectively. These findings are also consistent with those published by Saito et al.⁵⁰ in East Asia, who, in a multi-center study for the treatment of colorectal lesions, reported a lesion size of 34.2 mm, an operative time of 90 minutes, and a block resection rate of 95.4%, all comparable to our results (26.5 mm, 95.4 minutes, and 100%).

The main benefit of ESD is that it provides a mid- and long-term prognosis very similar to what is observed with conventional surgical treatments^{36,42,48}. In gastric cancer, a reduction in mortality of up to 63% has been confirmed⁵⁰. This is achieved with adequate en block resection and R0, which in our case was 94.7% overall, being lower in the duodenum, with 84.6%, but consistent with what Eastern experts recommend, suggesting it should be > 80% in this region⁵⁰, and variable depending on the region and histology of the resected lesions. Specifically, in the stomach, R0 has been documented in 94.7-95.1%, in the colon in 92-95.3%, and in the esophagus in 91.5-93.9%; results similar to those in our cohort (95.3, 98.2, and 91.7%, respectively) and higher than those reported by other authors in Latin America, such as Arantes et al.⁹, with an en block resection rate of 95.5%, R0 of 88.8%, and a curative resection rate of 76.1%.

The overall recurrence in our cohort was 9.44% at 177 months, of which 12 cases were ENL and 10 were SEL, with a clinical success rate of 85.8% (ENL 85.4% and SEL 86.2%), which, although different from other centers, can be explained by the heterogeneity of the resected lesions. However, in the subgroup analysis by region, we found that ESD for gastric and colorectal ENL in our cohort was 1.4% and 2.1%, respectively, and the highest recurrence was in GIST-type lesions, similar to findings by other authors^{27,37,39,42,44}.

The weaknesses of our study stem from the inherent bias of its retrospective nature, being single-center, conducted by 2 physicians, and its limited applicability in other centers; the latter is due to the fact that, although our results are comparable to those from large Eastern centers, this is because, as a reference center, the number of cases and experience are greater compared to other Mexican centers where this advantage is not available, meaning the results could be different. However, our strengths include being the largest cohort reported in Latin America, the inclusion of ENL and SEL, long-term evaluation and follow-up of patients, and the clear and specific documentation of procedures, adverse events, and histology.

Conclusions

In patients with ENL or SEL who meet appropriate clinical indications, ESD represents the first-line therapy, with excellent short-, mid-, and long-term results, provided it is performed in centers with the appropriate infrastructure and experience.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed their workplace protocols regarding the publication of patient data.

Right to privacy and informed consent. The authors obtained approval from the Ethics Committee for the analysis and publication of clinically obtained data. Informed consent from patients was not required as this is a retrospective observational study.

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