

PAPER DETAILS

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PAGES: 6-12

ORIGINAL PDF URL: <https://dergipark.org.tr/tr/download/article-file/3824406>



The role of endoscopic submucosal dissection in the treatment of large superficial duodenal epithelial neoplasia

Büyük yüzeyel duodenal epitelyal neoplazi tedavisinde endoskopik submukozal diseksiyonun rolü

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Background and Aims: Endoscopic submucosal dissection is one of the recommended treatment modality in terms of facilitating en-bloc resection in patients with superficial duodenal epithelial neoplasm larger than 2 cm. There is limited information in the literature about the applicability of endoscopic submucosal dissection in superficial duodenal epithelial neoplasm. In this single-center study, the results of eight patients with superficial duodenal epithelial neoplasm who underwent endoscopic submucosal dissection were retrospectively analyzed. **Materials and Methods:** Twelve patients who underwent duodenal endoscopic submucosal dissection between February 2019 and November 2023 were screened. Eight patients with superficial duodenal epithelial neoplasm larger than 2 cm were included in the study. **Results:** The median tumor diameter was 27.5 mm (20 - 80 mm). The most common localization was the duodenum second part (87.5%). En bloc and R0 resection rates were each 100%. The median procedure time was 37.5 min. Two patients (20%) with complications were treated with endoscopic clips. No recurrence was observed in all patients (mean 21 months). **Conclusion:** Endoscopic submucosal dissection is a technically challenging but successful method in the treatment of superficial duodenal epithelial neoplasm. Due to the high risk of complications, duodenal endoscopic submucosal dissection should be performed in experienced centers.

Key words: Duodenum, endoscopic submucosal dissection, neoplasia

Giriş ve Amaç: Endoskopik submukozal diseksiyon, 2 cm'den büyük yüzeyel duodenal epitelyal neoplazmi olan hastalarda en-blok rezeksiyonun kolaylaştırılması açısından önerilen tedavi yöntemlerinden biridir. Literatürde endoskopik submukozal diseksiyonun yüzeyel duodenal epitelyal neoplazmda uygulanabilirliği hakkında sınırlı bilgi bulunmaktadır. Bu çalışmada endoskopik submukozal diseksiyon uygulanan sekiz yüzeyel duodenal epitelyal neoplasm hastasının sonuçları retrospektif olarak analiz edildi. **Gereç ve Yöntem:** Şubat 2019 ile Kasım 2023 tarihleri arasında duodenal endoskopik submukozal diseksiyon uygulanan 12 hasta tarandı. Yüzeyel duodenal epitelyal neoplazmi 2 cm'den büyük olan 8 hasta çalışmaya dahil edildi. **Bulgular:** Medyan tümör çapı 27.5 mm (20 - 80 mm) idi. En sık lokalizasyon duodenumun ikinci kısmıydı (%87.5). En blok ve R0 rezeksiyon oranlarının her biri %100 idi. Ortalama işlem süresi 37.5 dakika idi. Komplikasyon gelişen iki hasta (%20) endoskopik kliplerle tedavi edildi. Hastaların tamamında (ortalama 21 ay) nüks görülmedi. **Sonuç:** Endoskopik submukozal diseksiyon, yüzeyel duodenal epitelyal neoplazm tedavisinde teknik açıdan zor ancak başarılı bir yöntemdir. Komplikasyon riskinin yüksek olması nedeniyle duodenal endoskopik submukozal diseksiyon deneyimli merkezlerde yapılmalıdır.

Anahtar kelimeler: Duodenum, endoskopik submukozal diseksiyon, neoplazi

INTRODUCTION

Superficial duodenal epithelial neoplasms (SDENs) are encountered more frequently and in a wider localization due to the increased use of screening endoscopy (1). Biopsies taken for histopathological

sampling have a limited role in the diagnosis (2). Endoscopic resection, surgery, or both methods as hybrid treatment (duodenal laparoscopic - endoscopic combined treatment) can be applied (3-7).

Duodenum is the most difficult localization for endoscopic resection (ER) due to its thin wall. Among the ER methods, endoscopic mucosal resection (EMR) is recommended primarily because of its shorter procedure time and lower risk of complications (3). However, it may be technically difficult to grasp the lesion with a snare after submucosal injection in EMR treatment, especially in SDENs larger than 2 cm (8). In these cases, endoscopic submucosal dissection (ESD) may be a salvage method. There is limited data on the applicability of ESD in the duodenum. Herein, we present our experience with eight cases those underwent duodenal ESD for SDENs.

MATERIALS and METHODS

Patient Selection

A total of twelve patients underwent duodenal ESD at between February 2019 and November 2023. Among these, eight patients with SDENs larger than 2 cm were included in the study. Patients who underwent ESD for indications other than SDEN (2 patients who underwent ESD due to duodenal lipoma and 2 patients who failed ESD due to duodenal angle) were not included in the study. Informed consent was obtained from all patients.

Pre-procedural Evaluation

The anatomical localization in the duodenum, size, and macroscopic appearance of all lesions were recorded according to the Paris classification (9).

ESD Procedure

All procedures were performed under general anesthesia by an endoscopist (XXX) experienced in ESD. Fujinon EG-760 R (Fujifilm Medical Co., Ltd., Tokyo, Japan) or Olympus GIF-HQ190 gastroscopy devices (Olympus Medical Systems, Tokyo, Japan) were used during the procedures. ESD was

performed using a Flush knife with a length of 3 mm (DK2620J-B15S; FTS, Tokyo, Japan) powered by an electrosurgical unit (ESG 400-Olympus Corp.). Pocket-creation method was used during ESD. A small caliber type transparent hood (DH-28GR; Fujifilm Medical Co., Ltd., Tokyo, Japan) was used in the procedures.

Based on the appearance of the submucosal layer, mild fibrosis was grouped as F0 (no fibrosis) or F1 (appears as a blue transparent layer) and severe fibrosis was grouped as F2 (appears as a white muscle layer) (10). In cases where adequate elevation could not be achieved due to dense submucosal fibrosis, traction was applied with the multi-loop method (11). After dissection, all ESD ulcers were closed with through-the-scope (TTS) clips. Procedure time was defined as the time between mucosal injection and final dissection.

Enteral nutrition was started at 24 hours after ESD. The patients were hospitalized for at least 24 - 48 hours and intravenous antibiotic treatment (ceftriaxone 2 × 1 g) was administered during this period.

Follow-up Evaluation

Endoscopic control was performed at 3 and 12 months after ESD. Routine biopsy of the ESD scar was avoided unless recurrence was suspected at follow-up.

Measured Outcomes

The primary endpoint was en bloc and R0 resection rates. The secondary endpoint was ESD-related complication rates.

En bloc resection was defined as excision of the lesion as a single piece. R0 resection was defined as excision of the lesion with negative surgical margins. Delayed bleeding and presence of perforation were evaluated as complications. Post-procedural delayed bleeding was defined as hematemesis and/

Table 1 Demographic, procedural and histopathological data of patients treated with endoscopic submucosal dissection for large (> 2 cm) superficial duodenal epithelial neoplasms

Patient	Age	M/F	Localization	Size (mm)	Paris	Pathology	Time (min)	Complication	Follow up (month)
1	35	M	D2	45 x 30	Ila + Ilc	TVA + HGD	95	Post-op bleeding	26
2	63	M	D2	80 x 64	Ila + Ilc	Tis	180	Per-op minor perforation	34
3	58	M	D2	35 x 30	Is + Ila	TVA + HGD	100	-	37
4	65	M	D2	23 x 15	Ila + Ilc	TA + HGD	40	-	14
5	70	M	D1	20 x 20	Ila	TA	30	-	24
6	54	M	D2	25 x 23	Ila	TVA	22	-	8
7	69	F	D2	30 x 25	Is	TA + HGD	28	-	5
8	55	M	D1	25 x 20	Ila	TVA + HGD	35	-	18

M: Male; F: Female; D1: First (superior) part of the duodenum; D2: Second part of the duodenum; TVA: Tubulovillous adenoma; LGD: Low grade dysplasia; HGD: High grade dysplasia; TA: Tubular adenoma; Tis: Carcinoma in situ.

or melena after ESD together with a decrease in hemoglobin value > 2 g/dL compared to the preoperative value. Perforation was defined as intraoperative perforation if it occurred during ESD and delayed perforation if it developed after ESD.

Ethics Committee

Ethics Committee approval was obtained from Ege University Medical Research Ethics Committee (08.02.2024 with decision number 24-2T/38).

RESULTS

The median tumor diameter was 27.5 mm (range, 20 - 80 mm). The most common localization was the second segment of the duodenum (Table 1). Three of the lesions had a history of biopsy before ESD. On macroscopic examination, three lesions had a depressed appearance at their center (Figure 1). Non-lifting sign was positive in 3 out of 8 (37.5%) of the lesions. Traction method was applied in three patients (37.5%) due to severe submucosal fibrosis. En bloc and R0 resection rates were 100%. The median procedure time was 37.5 min (range, 30 - 180 min) (Table 2). Six clips (range, 3 - 15 clips) were

used on an average to close the ESD ulcer. ESD-related complications were observed in two patients (40%) (Table 2). Pre-op minor perforation was ob-

Table 2 Endoscopic submucosal dissection outcomes

Variables	N = 8
Submucosal fibrosis	
Mild (F0/F1)	5
Severe (F2)	3
Procedure time (min), median (range)	37.5 (30 - 180)
Dissection speed (mm ² /min) *	21.5
En bloc resection†	8 (100)
R0 resection ‡	8 (100)
Curative resection	8 (100)
Complication	2 (25)
Postoperative bleeding	1 (12.5)
Intraoperative perforation	1 (12.5)
Delayed perforation	0

* Dissection speed (mm²/min) was defined as the calculated ratio of the resected specimen area (mm²) divided by the procedure time (minutes). The resected specimen area was calculated using the formula for ellipse area (mm²) = longest length (mm) / 2 × shortest length (mm) / 2 × 3.14.

† Pathologically identified en bloc resection with negative horizontal and vertical margins.

‡ R0 resection of low grade dysplasia, high grade dysplasia, and T1 carcinoma satisfying all of the following: well/moderately differentiated or papillary carcinoma, no vascular invasion, submucosal invasion depth.

served in one patient and was treated by clipping. In the other patient, delayed bleeding developed post-op at 24th hour. Endoscopic examination revealed gushing hemorrhage from the ESD lumen although the clips were in place. Bleeding was stopped by applying an additional 10 TTS clips. There were no complications requiring surgical intervention. The mean duration of hospitalization was 2.5 days (range, 1 - 5 days). Histopathological examination revealed low-grade dysplasia in two

patients, high-grade dysplasia in five patients, and intramucosal carcinoma in another patient. No recurrence was observed at a mean follow-up of 21 months (range, 5 - 37 months).

DISCUSSION

In this retrospective case series, we aimed to investigate the efficacy and safety of the ESD method in the endoscopic treatment of SDENs larger

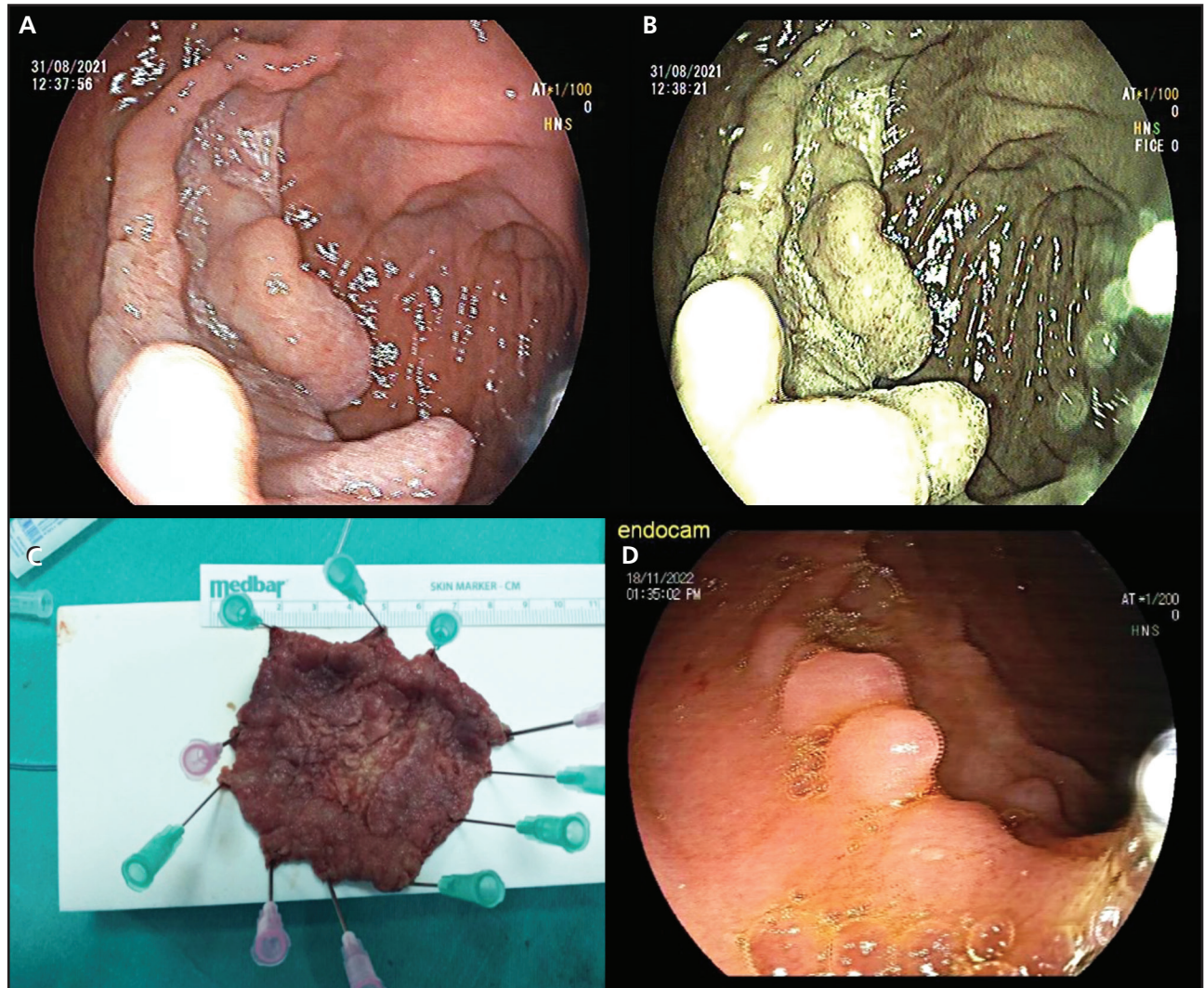


Figure 1 Large superficial epithelial neoplasia occupying more than more than half of the lumen and the lesion had a depressed appearance (A), in chromoendoscopic examination with FICE, lesion borders are more clear (B), en bloc resection of the lesion was achieved with ESD method (C), no recurrence was observed in the 3rd month follow-up (D).

than 2 cm. En bloc and R0 resection was achieved with ESD method in all of our limited number of patients. Complications were observed in two patients. Therefore, the results obtained in our series showed that duodenal ESD is effective in the treatment of SDEN, but it is a high-risk procedure in terms of complications.

Superficial epithelial tumors are less common in the duodenum compared to other gastrointestinal areas. For treatment, ER methods are usually sufficient. But duodenum is the most difficult localization for ER (7). This difficulty could be attributed to the narrow lumen of the duodenum, difficulty of endoscopic stability due to the sharp angle, submucosal Brunner's glands stiffening the duodenal mucosa and making elevation difficult after submucosal injection, the presence of dense vascular structure in the submucosal layer, and also the relatively thin muscle layer (7,12).

Various methods can be applied in the endoscopic treatment [EMR, under water EMR (U-EMR), ESD, endoscopic full thickness resection] of SDEN (3-7). Among these methods, EMR is the ER method primarily recommended by European Society of Gastrointestinal Endoscopy compared to other methods due to its lower risk of complications (3). U-EMR has become more popular in recent years due to its higher technical success compared to conventional EMR. However, EMR or U-EMR methods got more success particularly in SDENs smaller than 2 cm (4,8,13). EMR may also be a treatment option for larger lesions. In this regard, Binmoeller et al. reported in a limited case series that no recurrence was observed in a 16-month follow-up after piecemeal U-EMR in the treatment of SDENs larger than 2 cm. However, lack of a control group and limited follow-up period were the most important shortcomings of their study (4).

Data on the ESD method in the treatment of SDENs are very limited. In a retrospective study

conducted by Pérez et al. comparing EMR with ESD in the treatment of SDENs, en bloc, complete resection, and local recurrence rates were similar. In the ESD arm of this study, the en bloc resection rate was quite low (29.7%), and most of the patients (78.4%) in the ESD arm underwent hybrid ESD (14). However, Kato et al. analyzed 10-year data of 18 centers from Japan, and reported that the rate of R0 resection in large SDENs was below 50% in both conventional EMR and U-EMR, compared to 75% in the ESD arm (6). In our case series, R0 resection was achieved in all patients with the ESD method and no recurrence was observed in any of our patients. Our high treatment success rate is attributed to the following: ESD was performed by an experienced endoscopist, no hybrid treatment was needed in any procedure, and the low number of patients.

The difficulty with ESD in the treatment of SDEN has been associated with prolonged procedure time > 100 minutes or the presence of intraprocedural perforation (15). Accordingly, one third of ESDs in the duodenum were reported in the difficult category. According to these criteria, the rate of difficult ESD in our series was 25%. Localization in the flexure, lesion diameter > 4 cm, and lesions occupying more than half of the lumen are defined as risk factors for difficult ESD. It has been reported that applying Kocher's maneuver before ESD for SDENs located in the flexure may facilitate the procedure (16). In our series, Kocher maneuver was not used, but traction method was used in two patients due to submucosal fibrosis.

On the other hand, the high risk of ER-related complications in the treatment of SDEN (complications requiring surgery: 1.1% - 36.4%) may raise questions about the necessity of treatment in these patients. In this regard, Ikenoyama et al. reported that progression occurred in one third of patients with low-grade dysplasia SDEN who were followed up for an average of 45 months. In this

patient group, the risk of progression was low in lesions smaller than 5 mm (< 5%), while the risk of progression was $\geq 50\%$ in SDENs larger than 20 mm, which are in the high-risk group. Therefore, the authors recommended that SDENs larger than 2 cm should be treated (12).

Biopsy is usually the first-line diagnostic method in the diagnosis of SDEN. However, the diagnostic role of biopsy is limited (sensitivity 37.5%, specificity 83.1%, accuracy 71.6%) (2). In our case series, histopathological correlation was 50%. In addition, biopsies taken before treatment may cause submucosal fibrosis, making ER difficult. In our case series, severe fibrosis was observed in 37.5% of the patients. Classifications based on magnified narrow-band imaging to distinguish SDEN and non-neoplastic lesions or low-grade dysplasia vs. high-grade dysplasia/adenocarcinoma within SDEN may help the endoscopist in the diagnosis without biopsy. However, data on these classifications are limited (17). More widespread use of these classifications in the future may prevent the development of pre-ER fibrosis by eliminating the need for biopsy in the diagnosis and classification of SDEN. This may reduce the complication rate and improve success of treatment.

Prophylactic repair after duodenal ESD may reduce the risk of complications (7). Particularly in defects involving the papilla Vateri, repair may not

be possible. In this regard, it has been reported that catheterization for external bile and pancreatic fluid drainage may be a protective method in terms of adverse events (18). In our case series, all SDENs were nonampullary, and all ESD ulcers were successfully closed by TTS clipping. Despite this, delayed bleeding was observed in a patient. Hence, complications may be observed in the delayed period after duodenal ESD despite clip repair.

The important limitations of the present study are that it was retrospective, conducted in a single center, and included a limited number of patients. The fact that ESD procedures were performed by an experienced endoscopist makes it difficult to generalize the results of the present study. Due to these limitations, our results should be interpreted with caution.

In conclusion, this study demonstrated that ESD is an effective method in the treatment of large SDENs. Due to the high risk of complications, it is appropriate to perform duodenal ESD in centers which has experienced endoscopists.

Ethics Committee: *This study was approved by the Ege University Faculty of Medicine ethics committee on 08.02.2024 with decision number 24-2T/38.*

Conflict of Interest: *There is no conflict of interest with any institution or person. No financial support was received.*

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