Surgical Endoscopy (2022) 36:6601–6608
https://doi.org/10.1007/s00464-022-09068-2

Endoscopic submucosal dissection for proximal duodenal subepithelial lesions: a retrospective cohort study

Yan-rong Zhang[1] · Chang Sun[1] · Chun-li Cheng[2] · Jie Gao[1] · Jing Zhang[3] · Jie Chen[1] · Luo-wei Wang[1] · Ying Chen[1] · Xiao-hua Man[1] · Xin-Gang Shi[1] · Wei An[1]

Received: 23 August 2021 / Accepted: 12 January 2022 / Published online: 3 February 2022

Abstract

Background and aim Endoscopic submucosal dissection (ESD) has been used to remove subepithelial lesions (SELs) in recent years; however, duodenal ESD is associated with high rates of immediate or delayed bleeding and perforation. Whether ESD can be recommended for the treatment of duodenal SELs remains controversial. Therefore, we evaluated the efficacy and safety of ESD for duodenal SELs.

Methods We conducted a retrospective cohort study in 62 patients (62 lesions) who underwent ESD for duodenal SELs between January 2012 and December 2020. The therapeutic outcomes from ESD for duodenal SELs and procedure-related complications were analyzed.

Results En bloc resection and complete resection rates associated with duodenal ESD were 90.3% and 100%, respectively; four patients had a positive microscopic margin on pathologic examination. The median procedure time was 45 min (range 20–106 min). During the procedure, two patients received emergency surgery for uncontrolled bleeding and perforation, respectively. After the procedure, delayed bleeding occurred in three patients (4.8%), which was successfully managed by clipping, and delayed perforation occurred in two patients (3.2%) and needed emergency surgery. Risk factors related to complications were analyzed. Lesion size was found to be significantly associated with the complications ($P = 0.028$). No recurrences were detected, and no distant metastasis was observed in any patient during a median follow-up period of 45.5 months (range, 6–103 months).

Conclusion Duodenal ESD is relatively safe and feasible for duodenal SELs, especially for lesions no more than 2 cm in size.

Keywords Endoscopic submucosal dissection · Duodenal subepithelial lesions

Subepithelial lesions (SELs) include many lesions that originate from the muscularis mucosa, muscularis submucosa, and muscularis propria (MP) of the gastrointestinal (GI) tract. Most SELs are benign; however, some tumors are malignant or potentially malignant such as gastrointestinal stromal tumors (GISTs) and neuroendocrine tumors (NETs). Endoscopic ultrasound (EUS) is the most accurate imaging test for the evaluation of SELs of the GI tract [1, 2], because of its ability to delineate the layer of origin, echogenicity, homogeneity, and margins. However, the diagnostic accuracy associated with EUS for SELs was unsatisfactory [3, 4]. The accuracy of EUS for SELs < 20 mm and SELs ≥ 20 mm in size was 73.3% and 53.3%, respectively [5]. Because the effectiveness of EUS surveillance in the management of SELs has not been validated [6], the American Society for Gastrointestinal Endoscopy (ASGE) guidelines for the management of SELs of the upper GI tract [7] suggested that lipomas, vascular lesions, or cysts can be diagnosed only by using EUS and other types of lesions should be evaluated histologically. Furthermore, if the size of hypoechoic lesions

Yan-rong Zhang, Chang Sun, and Chun-li Cheng have contributed equally to this work.

✉ Xin-Gang Shi
dr_shixg@sina.com

✉ Wei An
anweisusan@163.com

[1] Department of Gastroenterology, Changhai Hospital of Second Military Medical University, 168 Changhai Road, Shanghai 200433, China

[2] Information Centre, Linfen Central Hospital, Shanxi, China

[3] Department of Pathology, Changhai Hospital of Second Military Medical University, Shanghai, China

is ≥ 2 cm and the lesions are symptomatic or increase in size, removal is recommended. In addition, a recent study suggested that regular follow-up with serial endoscopy may be sufficient for small SELs (< 2 cm), because the size of most incidentally detected small SELs did not change during follow-up. Nevertheless, the long-term follow-up strategy could be bothersome and stressful for patients, increases the risks associated with repeated endoscopic procedures, and delays the diagnosis of malignancy [8]. Therefore, many guidelines and research recommend resection for obtaining a histological diagnosis even if the lesion size is < 2 cm [9–12].

Endoscopic submucosal dissection (ESD), an endoscopic technique for the treatment of early gastrointestinal cancer, has been used to remove SELs in recent years. It is effective and reasonably safe for treating/removing upper GI SELs [13, 14]. However, thus far, research has been mainly limited to the stomach and esophagus [15, 16], and there have been few studies of the duodenum. Compared to other parts of the upper GI tract, the duodenum is the most challenging site for ESD: the duodenal wall is thin, the intestinal space is narrow, peripheral blood flow is rich, and the duodenum is close to the vital organs and exposed to gastric acid, bile, and pancreatic juice. Thus, duodenal ESD is associated with high rates of immediate and delayed bleeding, as well as perforation [17]. Although complete closure of the mucosal defect after duodenal ESD significantly decreased the number of delayed adverse events [18], ESD for duodenal SELs remains controversial, Thus, we conducted this retrospective cohort study to investigate the efficacy and safety of ESD for duodenal SELs and determination of possible complication-related factors.

Materials and methods

Patients

The case records of all patients who underwent duodenal endoscopic resection (ER) at ChangHai Hospital, Shanghai, China, between January 2012 and December 2020 were reviewed. During that time, 129 ER procedures were performed in consecutive 129 patients with duodenal lesions at the Endoscopy Center of ChangHai Hospital, Shanghai, China. Thirty-seven patients were excluded for treatment by endoscopic mucosal resection (EMR), 30 patients were excluded because the histological diagnosis was duodenal epithelial lesions (11 duodenal polyps, 17 duodenal adenomas, and 2 duodenal adenocarcinomas). Finally, 62 patients with duodenal SELs treated by ESD were included in this study.

This study was approved by the Ethics Committee of the Changhai Hospital, Shanghai, China. Written informed consent was obtained from all patients before the ER procedure.

Procedures

Pre-procedure evaluation

All the patients underwent a routine upper GI endoscopy (GIF-Q260 or GIF-Q290; Olympus Optical Co., Tokyo, Japan). The assessment for each tumor included the location and appearance. EUS was performed with a radial-scanning 20- or 12-MHz echoendoscope (GF-UM3R, GF260, Olympus; EG-530UR, Fujinon, Japan) to assess tumor size (the largest tumor diameter), margin demarcation, echogenicity, and the layer of origin. SELs were classified as either originating from the muscularis mucosa or the submucosal layer or originating from the proper muscle layer. CT was performed to assess tumor size and growth pattern and exclude the possibility of metastasis. Furthermore, CT was performed if the tumor margin was unclear on EUS or the size of tumor was larger than 2 cm.

ESD procedure

The equipment used for ESD included a carbon dioxide (CO_2) insufflator (UCR; Olympus, Tokyo, Japan). A forward-viewing endoscope (GIFQ260J; Olympus) was used with a transparent distal cap attachment ((D-201–11,804; Olympus) and an injection needle (NM-200L-0423; Olympus). A mixed solution of 100 mL of normal saline solution, 2–3 mL of indigo carmine, and 1 mL of epinephrine was prepared for submucosal injection. A dual knife (KD-650L, Olympus), insulation-tipped-2 (IT-2) knife (KD-611L, Olympus), or a hybrid knife (ERBE, Tübingen, Germany) was used to dissect the submucosal layer and the tumors. A snare (SD-230U-20; Olympus ASJ-1-S; COOK) was used to remove the tumor in the last step. A coagulating forceps (FD-410LR; Olympus) was used to close larger vessels before dissection or for hemostasis. A VIO 200D electrogenerator (ERBE) was used for the operation. For the final closure of the surgical incision or gastric wall defect repair, clips (Micro-tech, Nanjing China; or AGS Medtech; Hangzhou China; or HX-610-090L, Olympus; or Resolution clip, M00522600; Boston Scientific, Boston USA) and an endoloop (MAJ-254; Olympus) were applied.

ESD procedure for duodenal SELs: The procedures were performed with the patients under general anesthesia. First, dots were marked around the lesion by using a dual knife or hybrid knife, and a mixture solution was injected into the submucosa. The mucosal and submucosal layers around the lesion were precut. Thereafter, the submucosal layer was dissected until the tumor was exposed. Then, the tumor was dissected carefully to ensure complete en bloc resection of the lesion (Fig. 1). If the tumor was located in the deep MP layer and closed to the serosa, tumor dissection from the serosal

layer was difficult, and endoscopic full-thickness resection (EFTR) procedure was performed (Fig. 2). A circumferential incision into the serous membrane around the tumor was performed with an IT-2 knife, and an "artificial" perforation was made. Lastly, metal clips were used to close the wound surface. If the duodenal wall defect (including perforation and EFTR) was too large, a purse-string suture [19] was used with an endoloop and clips via dual-channel gastroscopy (GIF-2TQ260M; Olympus). After tightening the endoloop, the wound surface was simultaneously closed from the rim to the center. If a pneumoperitoneum developed, a 20-gauge needle was inserted into the right lower quadrant to relieve the gas [20].

Three experienced endoscopists (X.G. Shi, L.W. Wang, and J. Chen with > 5 years of experience in ESDs and who had performed > 200 ESDs) performed the ESD [21]. All patients provided informed consent for the benefits and risks of ESD were communicated. They opted for the endoscopic treatment instead of simple follow-up or the surgical option. The study was approved by the Ethics Committee of the Changhai Hospital, Shanghai, China.

Postoperative management

The post-procedure observations included evaluations for abdominal pain or abdominal distention, body temperature, and signs of peritonitis or hemorrhage. Patients were told to fast for 24 h. Antibiotics, proton pump inhibitors, and hemostatic drugs were routinely used to prevent infection and postoperative hemorrhage. For patients who underwent EFTR, it was necessary to place a GI decompression drainage tube and ensure fasting for more days. After patients were discharged from the hospital, a proton pump inhibitor was administered orally for 8 weeks. Patients with mild or high-risk GIST or NET G3 should be accepted further therapies according to the NCCN guidelines.

Pathologic evaluation

The size and the horizontal and vertical margins of the tumor were assessed. In addition, if the lesion was diagnosed as a GI NET, the histopathologic type, tumor size, depth of invasion, and lymphovascular invasion were evaluated microscopically. To further diagnose NET and distinguish GIST from leiomyoma, immunohistochemical staining for Syn,

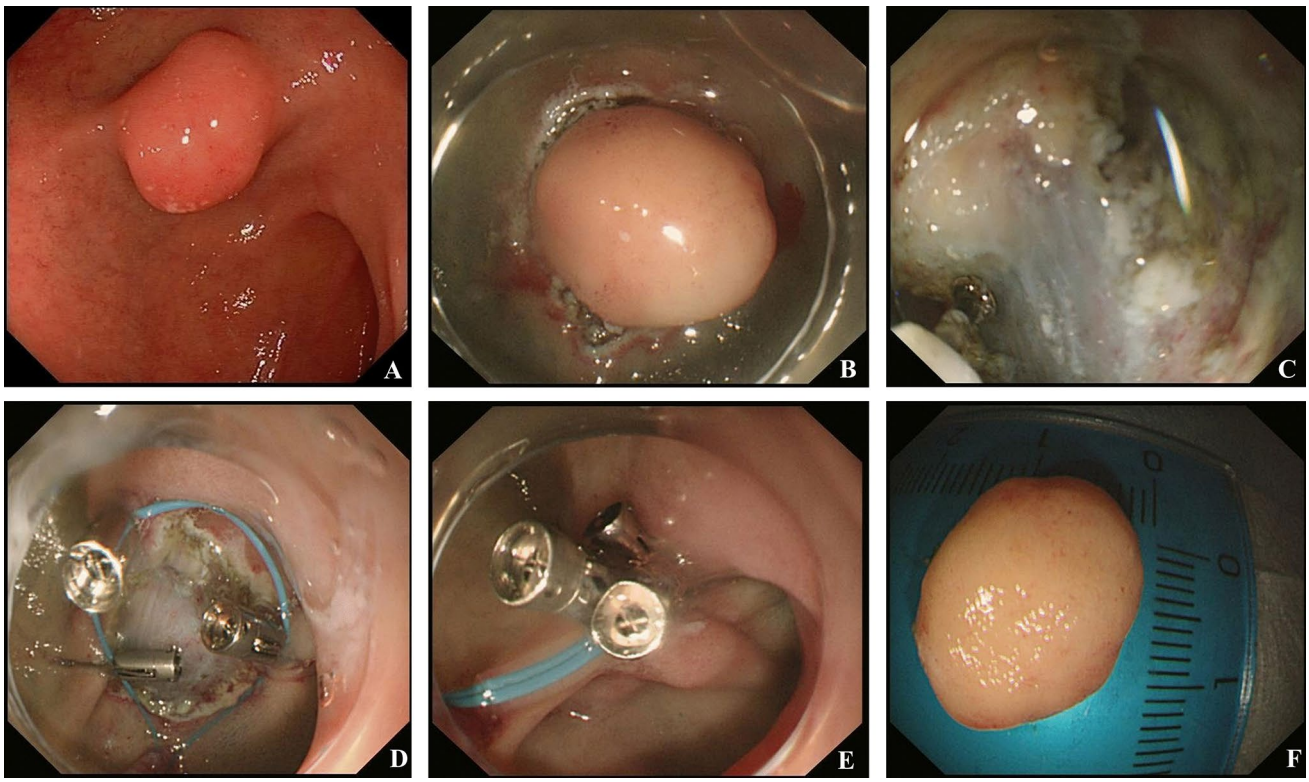

Fig. 1 Endoscopic submucosal dissection: **A** Endoscopic view of a lesion in the bulb of the duodenum; **B** a circular incision was made into the mucosa around the lesion; **C** the lesion was on the surface of the muscularis propria, and submucosal dissection was performed; **D** placement of a clip and endoloop at the proximal edge of the wound surface; **E** after tightening the endoloop and releasing the grasper, the mucosal defect was successfully closed; **F** view of the lesion after resection

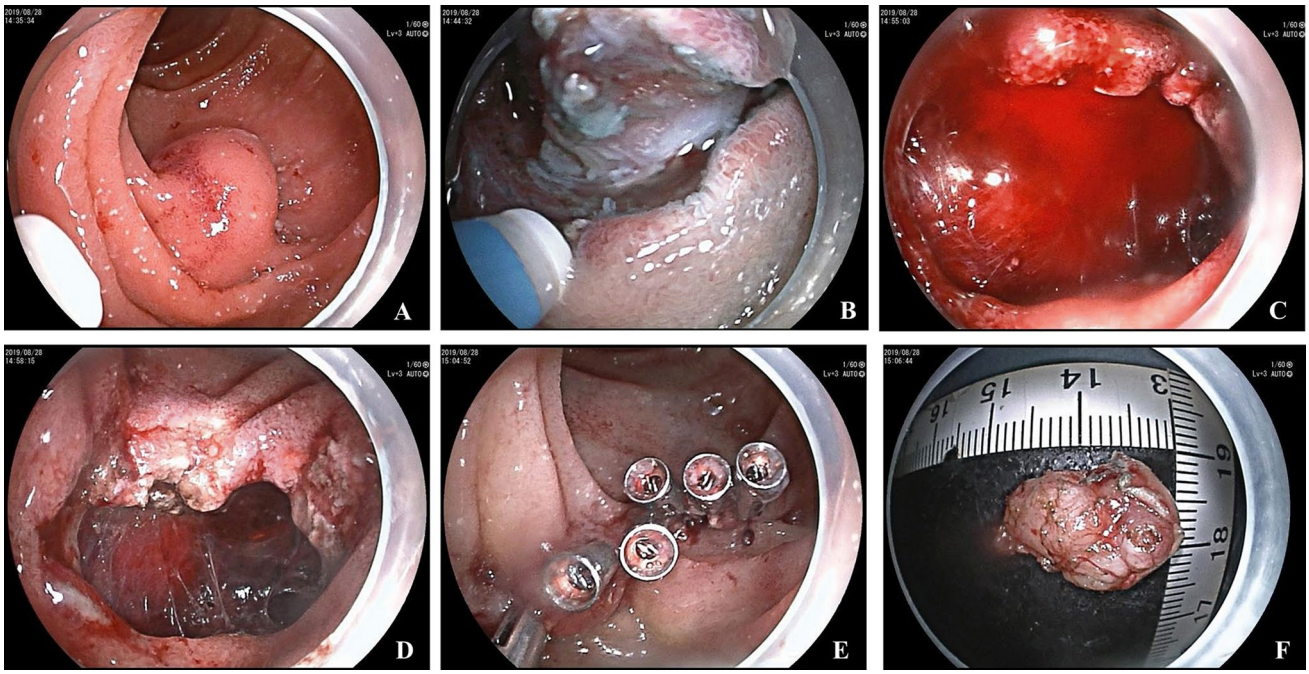

Fig. 2 Endoscopic full-thickness resection: **A** Endoscopic view of a lesion in the second portion of the duodenum; **B** the lesion was in the layer of the muscularis propria, and endoscopic full-thickness resection was performed; **C** a duodenal wall defect, which led to bleeding; **D** endoscopic bleeding was controlled; **E** the wound surface was closed by using slips; **F** view of the lesion after resection

NEC, CgA, KI-67%, CD117 (c-Kit), CD34, DOG-1, desmin, smooth muscle actin, S-100, and vimentin was performed. The mitotic rate per 50 high-power fields was determined, and these criteria were used for the risk assessment of NET and GIST [22–24]. The pathological diagnosis was confirmed by two experienced pathologists.

Follow-up

Patients underwent follow-up endoscopy at 6 and 12 months after ESD and annually thereafter to observe the healing of the wound and check for any residual tumor or recurrence for 5 years. For patients with potential malignant tumors, close follow-up by endoscopy, chest radiography, and contrast medium–enhanced CT was conducted to evaluate distant metastasis every year indefinitely.

Data collection and outcome parameters

Patients' clinical data (age and sex), tumor characteristics (size, location, original layer, resection margin status, and pathologic diagnosis), procedure-related variables (operation time, en bloc resection rate, duration of hospital stay, cost, and complications), and follow-up findings (recurrence and mortality) were collected from hospital records for a retrospective analysis.

The primary outcome parameter was the success of ESD, which included the rates of en bloc resection and complete pathologic resection. En bloc resection was defined as resection of the lesion as a single piece as opposed to piecemeal resection, in which the lesion was resected in multiple segments. Complete pathologic resection was defined on the basis of the following criteria: performance of an en bloc resection, no involvement of the lateral or vertical margins, and, in cases of NETs, tumor invasion limited to the submucosal layer with no additional lymphovascular invasion.

The secondary outcome parameters were the procedure time, procedure-related complications (bleeding and MP injury), and the local recurrence rate. The procedure time was defined as the time from the start of the injection of the saline solution to the completion of wound management. Intraoperative bleeding was evaluated on the basis of the degree of endoscopic resection bleeding (ERB) [25]. Grade ERB-0 represented no bleeding, characterized by the absence of obvious bleeding during the operation. Grade ERB-control (ERB-c) indicated controllable endoscopic bleeding, which was further divided into three sub-grades: ERB-c1, endoscopic bleeding that was easy to control, with the patients showing stable intraoperative vital signs and not requiring postoperative blood transfusion; ERB-c2, intraoperative bleeding between c1 and c3; ERB c3, controllable endoscopic bleeding that required blood transfusion during or after the operation. Grade ERB-uncontrol (ERB-unc) was

used to categorize intraoperative bleeding that could not be controlled under endoscopy, and required immediate surgery or vascular embolization. Delayed bleeding was defined as bleeding shown via endoscopic evaluation within 24 h, clinical evidence of melena or hematemesis, or massive bleeding requiring transfusion. MP injury (MPI) was graded on the basis of the severity of the injury [25]. Grade MPI-0 indicated no injury of the MP; Grade MPI-injury (MPI-i) indicated that the MP was damaged but not penetrated. Grade MPI-i was divided into two sub-grades: in MPI-ia, the MP was not completely penetrated, and the gas in the GI did not penetrate the outside of the GI after compression; in MPI-ib, the MP was not completely penetrated, but the gas in the GI penetrated outside the GI after compression. Grade MPI-perforation (MPI-p) indicated that the MP was completely broken. Grade MPI-p can be further divided into two subgrades: MPI-pa: MP perforation that could be successfully repaired under an endoscope; MPI-pb: MP perforation that could not be treated under an endoscope and required surgical treatment. Delayed perforation was defined by the presence of abdominal pain, abdominal signs, fever, and inflammation after the ESD procedure.

Statistical analysis

All statistical analyses were conducted using the PASW Statistics for Windows software, version 25.0 (SPSS, Inc., Chicago, IL, USA). Categorical data are presented as the number of cases and percentage. Continuous data are reported as mean (SD) or median (range). Statistical differences between groups were assessed using the χ^2 test, Fisher's exact test, Mann–Whitney U test, and the Kruskal–Wallis H test for categorical data. A two-sided P value of < 0.05 was considered statistically significant in all tests.

Results

Clinical characteristics of the patients with duodenal SELs

In this study, ESD was performed in 62 patients with duodenal SELs. The mean age of the patients was 51.4 ± 10.1 years, and the study population included 34 males (54.8%) and 28 females (45.2%). Among the SELs, 69.4% were located in the duodenal bulb, while 19 were in the second portion of the duodenum. The median lesion size was 1.2 cm (range, 0.5–5.5 cm). Fifty lesions originated from the submucosa, while 12 lesions originated from the MP layer. Based on the pathologic diagnosis, 23 lesions were diagnosed as ectopic pancreas, six lesions were diagnosed as GISTs (two very-low-risk lesions, three low-risk lesions, and one high-risk lesion), 15 lesions were NETs (G1 grade, 13 lesions; G2 grade, two lesions), three lesions were leiomyomas, six lesions were lipomas, four lesions were Brunner's gland hyperplasias, three lesions were cystadenomas, and two lesions were cysts (Table 1).

Therapeutic outcomes and complications

En bloc complete resection rate with ESD was 90.3%, of which three patients with NETs and one patient with ectopic pancreas showed a positive microscopic margin on pathologic examination. The median procedure time was 45 min (range, 20–106 min). During the procedure, 35 patients (56.5%) did not have MP injuries, 20 patients had MP injuries (MPI-ia, 18 patients; MPI-ib, 2 patients), and seven patients had a completely broken MP (MPI-pa, six patients; MPI-pb, 1 patient). The patient with MPI-pb received emergency surgery. No obvious bleeding occurred during the operations in 12 patients, 45 patients were categorized as grade ERB-c1, four patients were categorized as grade ERB-c2, and only one patient with ERB-unc was treated by emergency surgery. While 82.3% of the mucosal defects were closed with clips, eight defects were closed with a purse-string suture. During hospitalization, delayed bleeding occurred in three patients (4.8%) and was successfully treated by clips, while delayed perforation occurred in two patients (3.2%) and was treated by emergency surgery. The

Table 1 Characteristics of duodenal Subepithelial lesions in 62 patients who underwent with endoscopic submucosal dissection

Characteristic	
Age (years), Mean ± SD	51.4 ± 10.1
Gender, *n* (%)	
Male	34 (54.8)
Female	28 (45.2)
Lesion location, *n* (%)	
Bulb	43 (69.4)
Second portion	19 (30.6)
Lesion size (cm), median (range)	1.2 (0.5–5.5)
Layer of lesion origin, *n* (%)	
Submucosa	50 (80.6)
Muscularis propria	12 (19.4)
Pathologic diagnosis, *n* (%)	
Ectopic pancreas	23 (37.1)
Gastrointestinal stromal tumor	6 (9.7)
Leiomyoma	3 (4.8)
Lipoma	6 (9.7)
Neuroendocrine tumor	15 (24.2)
Brunner's gland hyperplasia	4 (6.5)
Cystadenoma	3 (4.8)
Cyst	2 (3.2)

median hospital stay after the operation was 4 days (range, 2–29 days) (Table 2).

Risk factors in relation to complications of ESD for duodenal SELs

Complications occurred in seven patients. The analysis results showed no statistically significant relationship between complications and age, sex, lesion location, or layer of lesion origin. Lesion size was significantly associated with the complications ($P=0.028$) (Table 3), and the odds ratio of the risk of complications for lesions larger than 3 cm compared to that for lesions less than 2 cm was 20.8 (95% CI: 1.592–271.740, $P=0.021$).

Follow-up

The median follow-up period after the procedure was 45.5 months (range, 6–103 months). No residual or recurrent tumor was detected, and no distant metastasis occurred in any patient during the follow-up period (Table 2).

Table 2 Therapeutic outcome and complications of endoscopic submucosal dissection for duodenal subepithelial lesions

Therapeutic outcome/complication	*N* (%)
En bloc resection	56 (90.3)
Positive microscopic margin	4 (6.5)
Duration of procedure (minutes), median (range)	45 (20–106)
Grade of muscularis propria injury(MPI)	
MPI-0	35 (56.5)
MPI-ia	18 (29.0)
MPI-ib	2 (3.2)
MPI-pa	6 (9.7)
MPI-pb	1 (1.6)
Grade of endoscopic resection bleeding (ERB)	
ERB-0	12 (19.4)
ERB-c1	45 (72.6)
ERB-c2	4 (6.5)
ERB-unc	1 (1.6)
Closure mucosal defect	
No	1 (1.6)
Closure with clips	51 (82.3)
Closure with purse-string suture	8 (12.9)
Postoperative complication	
Delayed bleeding	3 (4.8)
Delayed perforation	2 (3.2)
Emergency surgery	4 (6.5)
Postoperative hospital stays (days), Median (range)	4 (2–29)
Hospital cost (dollars), Median (range)	3602.6 (2004.4–19,647.0)
Duration of follow-up (months), Median (range)	45.5 (6–103)
Local recurrence or distant metastasis	0 (0)

Table 3 Risk factors in relation to Complications* of endoscopic submucosal dissection for duodenal subepithelial lesions

Factors	Complications		*P* value
	No ($n=55$)	Yes ($n=7$)	
Age, *n* (%)			
≤60 years	45 (81.8)	7 (100.0)	0.493
>60 years	10 (18.2)	0 (0.0)	
Gender, *n* (%)			
Male	31 (56.4)	3 (57.1)	0.785
Female	24 (43.6)	4 (42.9)	
Lesion location, *n* (%)			
Bulb	39 (70.9)	4 (57.1)	0.757
Second portion	16 (29.1)	3 (42.9)	
Layer of lesion origin, *n* (%)			
Submucosa	45 (81.8)	5 (71.4)	0.883
Proper muscle	10 (18.2)	2 (28.6)	
Lesion size, *n* (%)			
≤2 cm	52 (94.5)	5 (71.4)	0.028
2.1–3 cm	2 (3.6)	0 (0.0)	
>3 cm	1 (1.8)	2 (28.6)	

Complications* include delayed bleeding, delayed perforation, or emergency surgery

Discussion

A previous study suggested that ESD for duodenal epithelial tumors was associated with a high rate of adverse events [26], so the use of ESD for duodenal SELs is debatable because of its higher rate of perforation. In this retrospective cohort study, we investigated the efficacy and safety of ESD for duodenal SELs and determined the possible factors related to this complication.

In the present study, the en bloc and the complete resection rates for duodenal SELs were 90.3% and 100%, respectively. The lesions that were not treated with en bloc resection included four ectopic pancreas and two NETs, because these two kinds of lesions had no obvious capsule and an unclear boundary with the surrounding tissue. A positive microscopic margin was also noted in one ectopic pancreas and three NETs. When an en bloc resection was achieved, if the normal tissue covering the tumor was damaged to some extent, the microscopic margin was considered to be positive. However, there were no local recurrences during the median follow-up period of 45.5 months (range, 6–103 months) after ESD was performed. EMR is the other ER method used for the treatment of duodenal SELs, and a

previous study showed that the complete pathologic resection rate of EMR was 82.1% [17], lower than that of ESD. Thus, ESD is a more effective ER method to treat duodenal SELs.

Although ectopic pancreas constituted the highest proportion of duodenal SELs in the present study, NETs and GISTs were potentially malignant lesions. The complete pathologic resection rates of NETs and GISTs were 80% (12/15) and 100% (6/6), respectively. During the follow-up period, none of the patients developed recurrence. However, other studies suggested that duodenal ER for NETs was associated with a lower curative rate because most of the cases were treated by EMR or EMR-L [27, 28].

Based on experience, although ESD has a higher en bloc resection rate than EMR, the procedure is prolonged and associated with a higher surgical risk. However, in the present study, the rate of delayed perforation was 3.2%, lower than the previously reported perforation rate of approximately 20% for ESD of duodenal epithelial tumors [29] and 37.5% for ESD of duodenal SELs [17]. This can be attributed to the improvement of operation skills and the application of the closure of the mucosal defect. Kato et al. suggested that complete closure of the mucosal defect after duodenal ESD significantly decreased the number of delayed adverse events and improved other outcomes [18]. In the present study, 95.2% of the cases showed complete closure of the mucosal defect after duodenal ESD; among them, six cases underwent closure of the duodenal wall defect by purse-string suture for EFTR. Only two patient required an emergency operation, and no deaths occurred in relation to this procedure. The duodenum has a dual blood supply system with abundant blood vessels in the submucosal layer. The exposure of post-procedural artificial ulcers to gastric acid may increase the risk of delayed bleeding. In the present study, the frequency of delayed bleeding was 4.8%, which is consistent with the results from previous studies on duodenal ER [17, 29, 30]. Furthermore, we tried to identify the risk factors in relation to the complications of ESD for duodenal SELs. The result showed that lesion size was related to the occurrence of complications, especially when the lesion was larger than 3 cm. Therefore, ESD for duodenal SELs is a relatively safe operation, especially for lesions less than 3 cm in size.

The present study involved a relatively larger number of patients to date, demonstrated a favorable long-term prognosis associated with duodenal ESD, and provided evidence that ESD is effective and safe. However, the study also had several limitations. First, this was a retrospective study, and it may have had selection or information biases. The indications for duodenal SELs were not clearly defined, and the patients were selected to undergo ESD or surgery on the basis of patients' needs and doctors' experience. Second, only 12 SELs originated from the proper muscle layer, so it is unclear whether the lesion origin layer is related to the occurrence of complications. Third, lesion size in most of the patients was not more than 2 cm, and this may have reduced the complication rate. Fourth, given the high malignant potential of duodenal GISTs in comparison with gastric GISTs, surgery is the better treatment choice for duodenal GISTs, so the GIST cases in our study were limited. Finally, we did not compare ESD with other surgical, laparoscopic, or other ER techniques. In fact, ESD is less invasive than surgical procedures and is more effective than other endoscopic therapies for removing small SELs in many reports.

In conclusion, duodenal ESD is relatively safe and feasible for duodenal SELs, especially if the lesion size is not more than 2 cm. Further prospective multicenter studies with more cases of SELs are needed to generate more useful information in relation to ESD of duodenal SELs.

Acknowledgements This study is partly supported by Shanghai "New-Star" Youth Doctor Program [Grant No. HWRS2020087 (WA)], Scientific Research Program of Shanghai Municipal Science and Technology Commission [Grant No. 18411966300 (WA)], and 234 Subject Climbing peak Program of Changhai Hospital award to WA.

Funding Shanghai "New-Star" Youth Doctor Program, HWRS2020087, Wei An, Scientific Research Program of Shanghai Municipal Science and Technology Commission, 18411966300, Wei An, 234 Subject Climbing peak Program of Changhai Hospital, 2020, Wei An.

Declarations

Disclosures Yan-rong Zhang, Chang Sun, Chun-li Cheng, Jie Gao, Jing Zhang, Jie Chen, Luo-wei Wang, Yin Chen, Xiao-hua Man, Xin-Gang Shi, and Wei An have no conflicts of interest or financial ties to disclose.

References

1. Papanikolaou IS, Triantafyllou K, Kourikou A, Rosch T (2011) Endoscopic ultrasonography for gastric submucosal lesions. World J Gastrointest Endosc 3:86–94
2. Humphris JL, Jones DB (2008) Subepithelial mass lesions in the upper gastrointestinal tract. J Gastroenterol Hepatol 23:556–566
3. Hwang JH, Saunders MD, Rulyak SJ, Shaw S, Nietsch H, Kimmey MB (2005) A prospective study comparing endoscopy and EUS in the evaluation of GI subepithelial masses. Gastrointest Endosc 62:202–208
4. Karaca C, Turner BG, Cizginer S, Forcione D, Brugge W (2010) Accuracy of EUS in the evaluation of small gastric subepithelial lesions. Gastrointest Endosc 71:722–727
5. Zhang MM, Zhong N, Gu X, Wang X, Zuo XL, Ji R, Li CQ, Li LX, Li Z, Yu YB, Li YQ (2020) In vivo real-time diagnosis of endoscopic ultrasound-guided needle-based confocal laser endomicroscopy in gastric subepithelial lesions. J Gastroenterol Hepatol 35:446–452
6. Reddymasu SC, Oropeza-Vail M, Pakseresht K, Moloney B, Esfandyari T, Grisolano S, Buckles D, Olyaee M (2012) Are

endoscopic ultrasonography imaging characteristics reliable for the diagnosis of small upper gastrointestinal subepithelial lesions? J Clin Gastroenterol 46:42–45
7. Faulx AL, Kothari S, Acosta RD, Agrawal D, Bruining DH, Chandrasekhara V, Eloubeidi MA, Fanelli RD, Gurudu SR, Khashab MA, Lightdale JR, Muthusamy VR, Shaukat A, Qumseya BJ, Wang A, Wani SB, Yang J, DeWitt JM (2017) The role of endoscopy in subepithelial lesions of the GI tract. Gastrointest Endosc 85:1117–1132
8. Demetri GD, von Mehren M, Antonescu CR, DeMatteo RP, Ganjoo KN, Maki RG, Pisters PW, Raut CP, Riedel RF, Schuetze S, Sundar HM, Trent JC, Wayne JD (2010) NCCN Task Force report: update on the management of patients with gastrointestinal stromal tumors. J Natl Compr Canc Netw 8(Suppl 2):S1–S41
9. Khashab MA, Pasricha PJ (2013) Conquering the third space: challenges and opportunities for diagnostic and therapeutic endoscopy. Gastrointest Endosc 77:146–148
10. Casali PG, Blay JY, Experts ECECP (2010) Gastrointestinal stromal tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 21(Suppl 5):v98–v102
11. Nishida T, Hirota S, Yanagisawa A, Sugino Y, Minami M, Yamamura Y, Otani Y, Shimada Y, Takahashi F, Kubota T, Subcommittee GG (2008) Clinical practice guidelines for gastrointestinal stromal tumor (GIST) in Japan: English version. Int J Clin Oncol 13:416–430
12. Zhou PZY, Li Q (2018) Chinese consensus on endoscopic diagnosis and management of gastrointestinal submucosal tumor (version 2018). Chin J Gastrointes Surg 21:841–852
13. Ye LP, Zhang Y, Luo DH, Mao XL, Zheng HH, Zhou XB, Zhu LH (2016) Safety of endoscopic resection for upper gastrointestinal subepithelial tumors originating from the muscularis propria layer: an analysis of 733 tumors. Am J Gastroenterol 111:788–796
14. Chen H, Li B, Li L, Vachaparambil CT, Lamm V, Chu Y, Xu M, Cai Q (2019) Current status of endoscopic resection of gastric subepithelial tumors. Am J Gastroenterol 114:718–725
15. Inoue H, Ikeda H, Hosoya T, Onimaru M, Yoshida A, Eleftheriadis N, Maselli R, Kudo S (2012) Submucosal endoscopic tumor resection for subepithelial tumors in the esophagus and cardia. Endoscopy 44:225–230
16. Lee CK, Lee SH, Chung IK, Lee TH, Park SH, Kim EO, Chung MS, Cho HD, Kim SJ (2012) Endoscopic full-thickness resection of a gastric subepithelial tumor by using the submucosal tunnel technique with the patient under conscious sedation (with video). Gastrointest Endosc 75:457–459
17. Kim TW, Kim GH, Park DY, Ahn S, Lim W, Lee BE, Song GA (2017) Endoscopic resection for duodenal subepithelial tumors: a single-center experience. Surg Endosc 31:1936–1946
18. Kato M, Ochiai Y, Fukuhara S, Maehata T, Sasaki M, Kiguchi Y, Akimoto T, Fujimoto A, Nakayama A, Kanai T, Yahagi N (2019) Clinical impact of closure of the mucosal defect after duodenal endoscopic submucosal dissection. Gastrointest Endosc 89:87–93
19. Zhang Y, Wang X, Xiong G, Qian Y, Wang H, Liu L, Miao L, Fan Z (2014) Complete defect closure of gastric submucosal tumors with purse-string sutures. Surg Endosc 28:1844–1851
20. Xu MD, Cai MY, Zhou PH, Qin XY, Zhong YS, Chen WF, Hu JW, Zhang YQ, Ma LL, Qin WZ, Yao LQ (2012) Submucosal tunneling endoscopic resection: a new technique for treating upper GI submucosal tumors originating from the muscularis propria layer (with videos). Gastrointest Endosc 75:195–199
21. Kim SH, Kim BG, Choi HS, Hong D, Jang SH, Hong K, Choi JW, Kim SH, Lee JM, Kim ES, Keum B, Jeen YT, Lee HS, Chun HJ (2021) Endoscopic submucosal dissection using a detachable assistant robot: a comparative in vivo feasibility study (with video). Surg Endosc 35:5836–5841
22. Miettinen M, Lasota J (2006) Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol 23:70–83
23. Joensuu H (2008) Risk stratification of patients diagnosed with gastrointestinal stromal tumor. Hum Pathol 39:1411–1419
24. Anlauf M, Gerlach P, Raffel A, Schott M, Baum R, Pavel M, Klöppel G (2011) Neuroendokrine Neoplasien des gastroenteropankreatischen Systems. Onkologe 17:572–582
25. Experts (2018) Endoscopic resection for early gastric cancer (2018, Beijing). Chin J Gastrointest Endosc (Electronic Edition) 5:49–60
26. Fukuhara S, Kato M, Iwasaki E, Sasaki M, Tsutsumi K, Kiguchi Y, Akimoto T, Takatori Y, Nakayama A, Maehata T, Minami K, Ogata H, Kanai T, Yahagi N (2020) Management of perforation related to endoscopic submucosal dissection for superficial duodenal epithelial tumors. Gastrointest Endosc 91:1129–1137
27. Gincul R, Ponchon T, Napoleon B, Scoazec JY, Guillaud O, Saurin JC, Ciocirlan M, Lepilliez V, Pioche M, Lefort C, Adham M, Pialat J, Chayvialle JA, Walter T (2016) Endoscopic treatment of sporadic small duodenal and ampullary neuroendocrine tumors. Endoscopy 48:979–986
28. Kobara H, Miyaoka Y, Ikeda Y, Yamada T, Takata M, Fujihara S, Nishiyama N, Fujita K, Tani J, Kobayashi N, Chiyo T, Yachida T, Okano K, Suzuki Y, Mori H, Masaki T (2020) Outcomes of endoscopic submucosal dissection for subepithelial lesions localized within the submucosa, including neuroendocrine tumors: a multicenter prospective study. JGLD 29:41–49
29. Nonaka S, Oda I, Tada K, Mori G, Sato Y, Abe S, Suzuki H, Yoshinaga S, Nakajima T, Matsuda T, Taniguchi H, Saito Y, Maetani I (2015) Clinical outcome of endoscopic resection for nonampullary duodenal tumors. Endoscopy 47:129–135
30. Gaspar JP, Stelow EB, Wang AY (2016) Approach to the endoscopic resection of duodenal lesions. World J Gastroenterol 22:600–617