Surgical Endoscopy (2024) 38:6485–6492
https://doi.org/10.1007/s00464-024-11244-5

Conventional versus rubber band traction-assisted endoscopic submucosal dissection for rectal neuroendocrine tumors: a single-center retrospective study (with video)

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Received: 13 May 2024 / Accepted: 29 August 2024 / Published online: 13 September 2024

Abstract

Background Endoscopic submucosal dissection (ESD) is a safe and effective technique for the treatment of gastrointestinal tumors, including rectal neuroendocrine tumors (r-NETs). However, the relative advantages of traction-assisted ESD for the treatment of small rectal lesions are still debated.

Aims We conducted a study to compare the efficacy and safety of rubber band traction-assisted ESD (RBT-ESD) to conventional ESD (C-ESD).

Methods This study retrospectively analyzed consecutive patients with r-NET treated with ESD between October 2021 and October 2023. Our study assessed differences between the groups in the complete resection rate of lesions, muscular layer injury, surgical complications, operation time, resection speed, time to liquid diet, postoperative hospital stay, hospital cost, and recurrence rate.

Results A total of 119 patients with r-NETs participated in this study (RBT-ESD group, $n=27$; C-ESD group, $n=92$). The operation time in RBT-ESD group was shorter than in C-ESD group, but the difference was not statistically significant (16.0 min [9.0–22.0 min] vs. 18.0 min [13.3–27.0 min], $P=0.056$). However, the resection speed was significantly faster in the RBT-ESD group (6.7 vs. 4.1 mm^2/min, $P=0.005$). Furthermore, the RBT-ESD group showed significantly less muscular layer injury ($P=0.047$) and faster diet recovery ($P=0.035$). No significant differences were observed in the complete resection rate, surgical complications, postoperative hospital stay, hospital cost, or recurrence rate between the two groups.

Conclusion For r-NETs of < 2 cm in size, the RBT method did not significantly shorten the operation time but resulted in faster resection speed, less muscular layer injury, and earlier postoperative recovery to a liquid diet.

Keywords Rubber band traction · Endoscopic submucosal dissection · Rectal neuroendocrine tumors · Muscular layer injury · Resection speed

Neuroendocrine tumors (NETs) are a rare type of tumor that originate from peptidergic neurons and neuroendocrine

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cells, with neuroendocrine differentiation and the expression of neuroendocrine markers. They can occur in all parts of the body, with the gastrointestinal tract and pancreas being the most common locations [1]. The incidence rate of rectal neuroendocrine tumors (r-NETs) is 0.17%, accounting for 12–27% of all NETs. Although r-NETs are uncommon tumors, their incidence has increased over the past few years, possibly due to the improved detection rate from advanced endoscopic examinations and increased participation in screening colonoscopy programs [2]. r-NETs often present as submucosal elevation, often incidentally detected during colonoscopy. Approximately 80–90% of r-NETs have a maximum diameter of < 1 cm, with only 5% having a maximum diameter of > 2 cm [3, 4]. Most r-NETs are localized at the time of the diagnosis, and distant metastasis is rare (2–8%) [5]. Treatment of r-NETs depends on the tumor size. According to the guidelines of the European Neuroendocrine Tumor Society (ENETS), tumors of < 1 cm, well-differentiated tumors, and tumors of 1–2 cm, with no muscularis or lymphatic invasion, can be removed by local resection [6].

Endoscopic submucosal dissection (ESD) is considered a safe and effective technique for the treatment of gastrointestinal tumors including r-NETs [2]. However, to safely and effectively perform colorectal ESD, clear visualization of the submucosal layer is crucial. Various traction methods have been developed to improve the visibility of the submucosal layer, including rubber bandclip traction, the clip and snare method, and magnetic methods [7–10]. However, the relative advantages of traction-assisted ESD for the treatment of small rectal lesions are still debated. Many previous studies have shown that a traction-assisted strategy shortened the colorectal ESD operation time and reduced operative complications [11, 12]. However, the results of a recent multicenter randomized controlled study showed that the traction method neither reduced rectal ESD operation time nor increased the speed of rectal ESD resection [13]. A propensity-matched study by Liu et al. showed that for lesions with a diameter of > 2 cm, rubber band traction can significantly improve speed, but there was no advantage to rubber band traction for colorectal lesions of < 2 cm in diameter [14]. Therefore, by comparing the outcomes of conventional ESD (C-ESD) and rubber band traction-assisted ESD (RBT-ESD) for the treatment of r-NETs with a diameter of < 2 cm, the present study aimed to explore the efficacy and safety of the traction method for small rectal lesions.

Materials and methods

Patients

This retrospective study was approved by the ethics committee of Taizhou Hospital of Zhejiang Province, Wenzhou Medical University (KL20240442). All r-NET ESD procedures performed between October 2021 and October 2023 were included in this study. The inclusion criteria were as follows: (1) age > 18 years, (2) surgical method of RBT-ESD or C-ESD, and (3) pathologically confirmed r-NET. The exclusion criteria were as follows: (1) cessation of anticoagulant or antiplatelet medications was impossible; (2) active infection; and (3) prior endoscopic resection with incomplete resection.

Patient demographic and clinicopathological data

Data were collected on the patient's general condition (age, sex), tumor size, pathological characteristics, operation data (operation method, operation time, resected area, resection speed, muscular layer injury, presence of en bloc resection, complete resection, cutting edge, surgical complications [e.g., infection, bleeding, and perforation]), postoperative recovery (time to liquid diet, postoperative hospital stay), hospital cost, postoperative follow-up [follow-up time, survival, recurrence, metastasis], and operators. Operators were divided into experts with < 5 years of ESD experience, experts with 5–10 years of ESD experience, and experts with > 10 years of ESD experience.

The tumor size was defined as the maximum diameter of the tumor. Operative time was defined as the time between the initial mucosal incision and the completion of resection. The resected area was calculated as follows: long-axis diameter (mm)/2 × short axis diameter (mm)/2 × 3.14. Resection speed was calculated according to the following formula: resected area (mm^2)/operation time(min). Bleeding included intraoperative bleeding (detected during ESD) or delayed bleeding (detected after ESD), with the former referring to intraoperative active oozing or jet bleeding requiring endoscopic hemostasis and the latter referring to active bleeding confirmed by emergent endoscopy, which was performed due to hematemesis, melena, or progression of anemia (> 2 g/dL decrease in hemoglobin) within 28 days of ESD [15, 16]. Muscular layer injury was defined as exposure and partial tearing of the muscularis propria without perforation during ESD [17] (Fig. 1A). Two independent endoscopists assessed whether there is muscular layer injury or not. Perforation was defined as other organs, extraluminal fat, or extraluminal space outside the muscle layer that could be observed through endoscopy during ESD [18]. En bloc resection was defined as the resection of the tumor in a single piece, whereas complete resection was defined as the en bloc resection of the tumor with negative margins on pathologic examination.

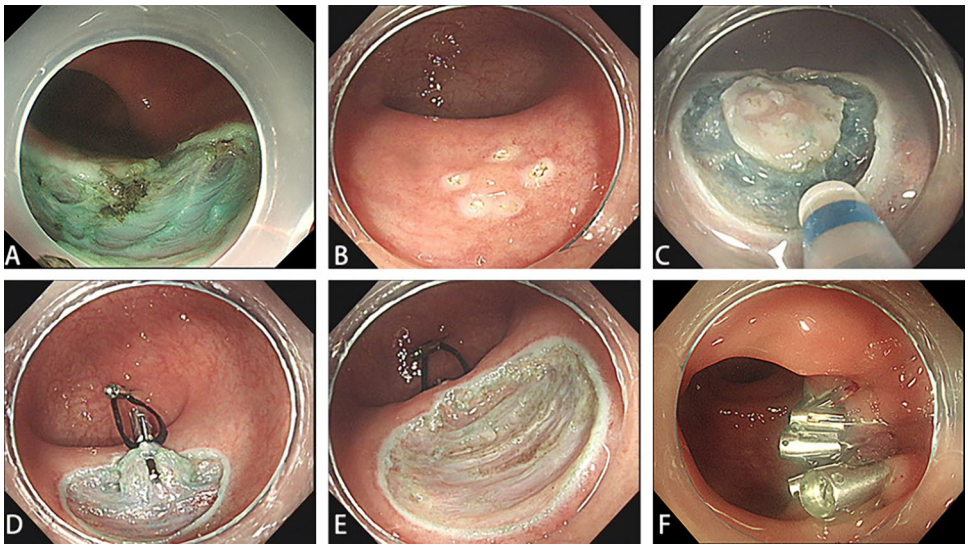

Fig. 1 RBT-ESD procedure of a rectal neuroendocrine tumor. **A** Muscular layer injury during ESD. **B** Spot electrocoagulation marking. **C** Incision of the mucosa around the lesion along the lateral aspect of the marked point. **D** The lesion is completely dissected using rubber band traction. **E** The lesion is completely dissected by using rubber band traction. **F** The wound surface is closed by titanium clips. *RBT-ESD* rubber band traction-assisted endoscopic submucosal dissection

The ESD procedure

All ESD procedures were performed using a single-channel endoscope (CF-H290I; Olympus, Tokyo, Japan) with a transparent hood (D-201-13404; Olympus Co., Tokyo, Japan) and electrosurgical generator (VIO-200D; ERBE Elektromedizin GmbH, Tubingen, Germany). Submucosal injection of sodium hyaluronate mixed with 1:100,000 adrenaline and methylene blue was performed using an injection needle (NM-400L-0425; Olympus Co., Tokyo, Japan). A dual knife (KD-650; Olympus) was used as the cutting device. Visible vessels were heated using a heat biopsy forceps (2.3 × 1600; Micro-Tech, Nanjing, China). Titanium clips (HX-610-135R; Micro-Tech, Nanjing, China) were used to close the wound and immobilize the rubber band.

(1) Marking: Spot electrocoagulation marks are made 3–5 mm from the lesion edge. (2) Submucosal injection: Sodium hyaluronate is injected underneath the lesion to elevate it and separate it from the muscularis propria. (3) Incision: Incision of the mucosa around the lesion along the lateral aspect of the marked point and deep into the submucosa.

C-ESD group

The mucosa is gradually completely separated from the muscular layer and the lesion was completely excised at one time.

RBT-ESD group

(1) Partial submucosal dissection: Part of the submucosal layer on the anal side is dissected with a dual knife. (2) Rubber band traction: A rubber band is fixed to the anal edge of the resected lesion and to the opposite rectal wall using clips to provide traction. (3) Submucosa dissection: Through traction, the submucosal space is exposed, and the lesion is completely dissected along the submucosal layer close to the muscular layer. If the traction effect is weakened or overpowered during dissection, the strength of traction can be adjusted with insufflation and deflation of carbon dioxide. (4) The clip fixed on the bowel wall is removed with another new titanium clip. (Fig. 1B–F, Video 1).

Wound treatment: Blood vessels exposed on the wound surface are treated by electrocoagulation, and the wound surface is closed by titanium clips. Specimen Processing: The ESD specimen is pinned on a foam plate and fixed with 10% formalin.

Histopathological evaluation

The resected specimens were evaluated histologically using light microscopy to determine the histological type, depth of invasion, involvement of margins, and lymphovascular invasion. To support this diagnosis, immunohistochemical staining for neuron-specific enolase and synaptophysin was performed. The mitotic count and Ki-67 index were evaluated to determine the tumor grade. The pathologists were blinded to the method of lesion excision, whether C-ESD or RBT-ESD.

Follow-up

Initial CT scans were performed at the time of the diagnosis in order to assess lymph node and distant metastases. After endoscopic resection, patients were followed up with an abdominopelvic CT scan and colonoscopy for an initial period of 6–12 months and then annually thereafter. Patients with incomplete resection and refusal of salvage treatment, such as additional endoscopic resection or surgery, were

recommended to undergo additional colonoscopy examination 1 month after the initial endoscopic resection. If no recurrence or residual lesions were detected on follow-up endoscopy, the next endoscopy and CT scan were performed 6 months later.

Statistical analysis

Quantitative data with a skewed distribution were expressed as medians with interquartile range, and the Mann–Whitney *U* test was used for comparisons. Qualitative data were expressed as the frequency (%), and characteristics were compared between groups using the χ^2 test or Fisher's exact test. Statistical significance was set at $P<0.05$. All statistical analyses were performed using SPSS (version 26.0; IBM, New York, NY, USA).

Results

Patient characteristics

A total of 119 r-NET patients who were managed at the Department of Gastroenterology in Taizhou Hospital of Zhejiang Province between October 2021 and October 2023 were enrolled. Among these, 92 patients were classified into the C-ESD group and 27 patients were classified into RBT-ESD group. The median age of the patients in the RBT-ESD and C-ESD groups was 50 (47–58) years and 53 (46–60) years, respectively. There were 12 males (44.4%) and 15 females (55.6%) in the RBT-ESD group and 54 males (58.7%) and 38 females (41.3%) in the C-ESD group. The median tumor size was 0.6 cm (0.5–0.7 cm) in the RBT-ESD group and 0.6 cm (0.5–0.8 cm) in the C-ESD group. There were no significant differences between the two groups in terms of age, sex, tumor size, or operator experience (Table 1).

Outcomes of the RBT-ESD and C-ESD groups

The median operation time was 16.0 (9.0–22.0) min in RBT-ESD group and 18.0 (13.3–27.0) min in C-ESD group (P = 0.056). The resection area in the RBT-ESD group was larger than that in the C-ESD group, but the difference was not statistically significant ($P=0.259$). However, the resection speed was significantly faster in the RBT-ESD group (6.7 mm^2/min [4.7–7.8 mm^2/min] vs. 4.1 mm^2/min [2.4–6.5 mm^2/min], $P=0.005$). No significant differences were observed in postoperative hospital stay and hospital costs between the two groups (both $P>0.05$). The median time to liquid diet was significantly shorter in the RBT-ESD group than in the ESD group (0.80 [0.65–1.07] days vs. 0.94 [0.81–1.70] days, $P=0.035$). In terms of muscular layer injury, there were 4 cases (14.8%) in the RBT-ESD group and 32 cases (34.8%) in the C-ESD group, and the rate of muscular layer injury was significantly lower in the former than in the latter ($P=0.047$) (Table 2).

The complications in the two groups are summarized in Table 2. In our study, complications among all 119 r-NET patients included intraoperative bleeding, intraoperative perforation, delayed bleeding, and postoperative infections. The incidence of complications in the RBT-ESD and C-ESD groups was 22.2% and 18.5%, respectively; the difference was not statistically significant ($P=0.665$). Complications occurred in 6 patients in the RBT-ESD group (intraoperative bleeding, $n=2$; intraoperative perforation, $n=2$; and postoperative infection, $n=2$). In the C-ESD group, 18 patients had complications (intraoperative bleeding, $n=2$; intraoperative perforation, $n=4$; delayed postoperative hemorrhage, n = 2; postoperative infection, $n=10$). Among them, 4 patients with intraoperative bleeding and 1 patient with delayed postoperative bleeding successfully achieved hemostasis under endoscopy; 6 patients with intraoperative perforation were closed with a combination of nylon rope and titanium clips under

Table 1 Baseline characteristics of the RBT-ESD and C-ESD groups

	Total $n=119$	RBT-ESD $N=27$	C-ESD $n=92$	*P*
Age (years)	51.0 (47.0–59.0)	50.0 (47.0–58.0)	53.0 (46.0–60.0)	0.513
Sex				0.190
Male	66 (55.5)	12 (44.4)	54 (58.7)	
Female	53 (44.5)	15 (55.6)	38 (41.3)	
Tumor size (cm)	0.6 (0.5–0.8)	0.6 (0.5–0.7)	0.6 (0.5–0.8)	0.357
Operator				0.256
> 10 years	41 (34.5)	7 (25.9)	34 (37.0)	
5–10 years	63 (52.9)	18 (66.7)	45 (48.9)	
< 5 years	15 (12.6)	2 (7.4)	13 (14.1)	

RBT-ESD rubber band traction-assisted endoscopic submucosal dissection, *C-ESD* conventional endoscopic submucosal dissection; Quantitative data expressed as medians with interquartile range; Qualitative data expressed as the frequency (%)

Table 2 Treatment outcomes of the RBT-ESD and C-ESD groups

	Total $n=119$	RBT-ESD $n=27$	C-ESD $n=92$	*P*
Operation time (min)	18.0 (13.0–26.0)	16.0 (9.0–22.0)	18.0 (13.3–27.0)	0.056
Resected area (mm^2)	7.9 (5.7–13.2)	9.4 (6.3–13.3)	7.7 (4.8–12.4)	0.259
Resection speed (mm^2/min)	4.9 (2.6–7.3)	6.7 (4.7–7.8)	4.1 (2.4–6.5)	0.005
Time to liquid diet (d)	0.92 (0.78–1.56)	0.80 (0.65–1.07)	0.94 (0.81–1.70)	0.035
Postoperative hospital stay (d)	3.0 (3.0–4.0)	3.0 (3.0–4.0)	3.0 (3.0–4.0)	0.517
Hospital cost (RMB)	11,382.8 (9861.8–12,872.9)	11,827.5 (10,832.9–13,236.7)	10,983.2 (9778.2–12,495.1)	0.129
Muscular layer injury				0.047
Yes	36 (30.3)	4 (14.8)	32 (34.8)	
No	83 (69.7)	23 (85.2)	60 (65.2)	
Complications				0.762
Yes	23 (19.3)	6 (22.2)	18 (19.6)	
No	96 (80.7)	21 (77.8)	74 (80.4)	
Intraoperative bleeding				0.221
Yes	4 (3.4)	2 (7.4)	2 (2.2)	
No	115 (96.6)	25 (92.6)	90 (97.8)	
Intraoperative perforation				0.890
Yes	6(5.0)	2 (7.4)	4 (4.3)	
No	113 (95.0)	25 (92.6)	88 (95.7)	
Delayed bleeding				> 0.999
Yes	2 (1.7)	0 (0.0)	2 (2.2)	
No	117 (98.3)	27 (100.0)	90 (97.8)	
Postoperative infection				0.871
Yes	12 (10.1)	2 (7.4)	10 (10.9)	
No	107 (89.9)	25 (92.6)	82 (89.1)	
Complete resection				0.404
Yes	2 (1.7)	1 (3.7)	1 (1.1)	
No	117 (98.3)	26 (96.3)	91 (98.9)	

RBT-ESD rubber band traction-assisted endoscopic submucosal dissection, *C-ESD* conventional endoscopic submucosal dissection; Quantitative data expressed as medians with interquartile range; Qualitative data expressed as the frequency (%)

endoscopy, and 12 patients with postoperative infections recovered after antibiotic treatment. En bloc resection was achieved in all 119 patients. One patient each in the RBT-ESD and C-ESD groups had positive horizontal margins, and all patients had negative vertical margins. The two patients with positive horizontal margins were followed for more than 2 years, and no tumor recurrence or lymph node metastasis was observed in that time. There was no significant difference between the two groups in terms of intraoperative bleeding, intraoperative perforation, delayed bleeding, postoperative infection, or complete resection (All $P > 0.05$). In terms of histopathological grading, with the exception of one case (G2), all other cases were classified as G1.

As of April 30, 2024, with a median follow-up period of 19.1 months, no patients developed recurrence or metastasis in either of the two groups during the follow-up period, and there were no r-NET-related deaths.

Discussion

Traction is also known as the "third hand of endoscopic therapy." It effectively pulls the mucosal layer apart, enabling faster visualization of the submucosal dissection plane. With these characteristics, traction can speed up ESD procedures and reduce the risk of perforation [8]. r-NETs involve the deep and submucosal layers of the mucosa, and endoscopic treatment requires sufficient tumor-free vertical margins to achieve complete resection [19]. r-NETs have an abundant blood supply, and stripping blindly can easily cause bleeding. The rubber band traction-assisted ESD method has good reported outcomes [20, 21]. However, the advantages of rubber band traction-assisted ESD in the treatment of small r-NETs are controversial.

Previous studies have generally suggested that traction-assisted ESD can speed up the operation and shorten the operation time [11, 12]. A prospective randomized study

showed a traction-assisted colorectal ESD time of 40 (11–86) min, while C-ESD had a time of 70 (30–180) min, demonstrating that traction significantly reduced the ESD procedure time [22]. Ritsuno et al. also reported that the mean operation time for the traction-assisted ESD group was significantly shorter than that for the C-ESD group (37.4 ± 32.6 vs. 67.1 ± 44.1 min) [23]. A recent prospective, multicenter, randomized controlled trial showed that the traction method increased the speed of total colon (except rectum) ESD resection. However, the speed of rectal ESD resection was not increased and the colorectal ESD operation time was not significantly shortened [13]. In our study, the RBT method did not significantly shorten the operative time. We believe that this can be explained by the fact that the resected area was slightly larger in the RBT-ESD group than in the C-ESD group, although the difference was not significant. In addition, the small lesions (< 2 cm) may explain the non-significant tendency toward shorter ESD operation times. Lastly, the operation time in the RBT group included the time for securing the rubber band, which could not be removed in this retrospective study design. A study has indicated that the larger the lesion, the more time is saved (specifically, for every 1-mm increase in lesion size, approximately 0.7 min of time is saved) [11]. Similar results were obtained in other studies, with no significant differences in the operating time for lesions of < 20 mm in size [24]. In terms of resection speed, Liu et al. reported that for colorectal lesions of < 2 cm in diameter, rubber band traction did not improve the speed of resection [14]. However, in this study, for r-NETs of < 2 cm in diameter, RBT-ESD also significantly increased the resection speed, which was consistent with the majority of previously published studies [11, 12].

In addition, in our study, the RBT-ESD group had fewer muscular layer injuries. Xie et al. showed that traction ESD is beneficial for preventing muscular layer injuries [25]. This finding confirms our results. With traction, the submucosal plane can be clearly visualized and efficient submucosal dissection can be performed under direct vision, thus avoiding inadvertent injury to the muscle layers [12]. However, if excessive traction is applied, it can also lead to muscular layer injury. In this study, the above phenomenon occurred in two cases in the RBT-ESD group. The RBT-ESD group resumed a liquid diet earlier after surgery than the C-ESD group, which might be associated with less muscle damage in the RBT-ESD group. However, the liquid diet time in both groups was less than 1 day, which could also be due to changes in recovery protocol or temporal bias. Additionally, the RBT-ESD group showed no advantage in terms of the postoperative hospital stay or hospital costs.

The en bloc and complete resection rates of both groups were satisfactory and similar to those of other studies in Asia [26, 27]. There were no significant differences between the two groups in terms of complication data. This may be due to the fact that the procedures were performed by experienced operators using ESD techniques.

The ideal method for colorectal ESD traction should be simple, economical, convenient, effective, and easy to perform. Complex equipment and accessories are not required. Our rubber band combined with clipping method meets these requirements. First, rubber bands are inexpensive and easily accessible. Although two titanium clips need to be additionally used during the traction process, resulting in an increase in cost of $40, the traction leads to less muscular layer injury, reduced risk of perforation, and greater benefits for the patients. Second, the internal traction method does not require reinsertion of the endoscope, as it uses clips connected by a rubber band, which can pass through the instrument channel of the endoscope. This system is separate from the endoscope; therefore, it is not limited by endoscopic movement. Finally, the amount of traction can be adjusted by adjusting the insufflation and deflation of gas. However, it has been suggested that this is a disadvantage of RBT. With the progress of large lesion dissection, the traction gradually weakens, and excessive insufflation may lead to difficulties in colonoscopy, especially for right colonic lesions, resulting in premature fall off of the clip and even complications, such as abdominal distension and perforation [28]. However, for the small rectal lesions in our study, the aforementioned disadvantages were not obvious. Furthermore, RBT-ESD is easy for endoscopists to learn. According to cumulative sum (CUSUM) analysis, only about 6 cases are needed to master the skill proficiently (Supplementary Fig. 2).

The present study was associated with several limitations. First, it was a single-center retrospective study, which may have resulted in a selection bias. In this study, some endoscopists exclusively performed C-ESD procedures, while some others conducted C-ESD and RBT-ESD procedures (Supplementary Fig. 1), potentially influencing the results based on individual endoscopist skills. Moreover, there is no unified criterion for endoscopists when selecting cases, and some endoscopists stated that they would choose traction if the submucosal layer was not adequately exposed during the partial submucosal dissection, potentially introducing bias. Second, the sample size was relatively small. Third, there are various methods of traction, and only the outcomes of rubber band traction are discussed in this study. To date, there are currently no direct comparisons among traction techniques [20].

In conclusion, for r-NETs of < 2 cm in size, the RBT method did not significantly shorten the operation time, but resulted in faster resection speed, less muscular layer injury, and earlier postoperative recovery to a liquid diet. Therefore, RBT is an effective, safe, and economical traction technique for rectal ESD of small lesions.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00464-024-11244-5.

Acknowledgements No acknowledgments.

Funding This work was supported in part by the Medical Science and Technology Project of Zhejiang Province (2024KY1792, 2023KY1312), Health Science and Technology Program of Zhejiang Province (22PY101), Program of Taizhou Science and Technology Grant (22ywb08, 22ywb14), and the Scientific Research Fund Program of Enze Medical Center (22EZB12, 22EZC17).

Declarations

Disclosures Jinbang Peng, Jiajia Lin, Lina Fang, Jingjing Zhou, Yaqi Song, Chaoyu Yang, Yu Zhang, Binbin Gu, Ziwei Ji, Yandi Lu, Xinli Mao and Lingling Yan have no conflicts of interest or financial ties to disclose.

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