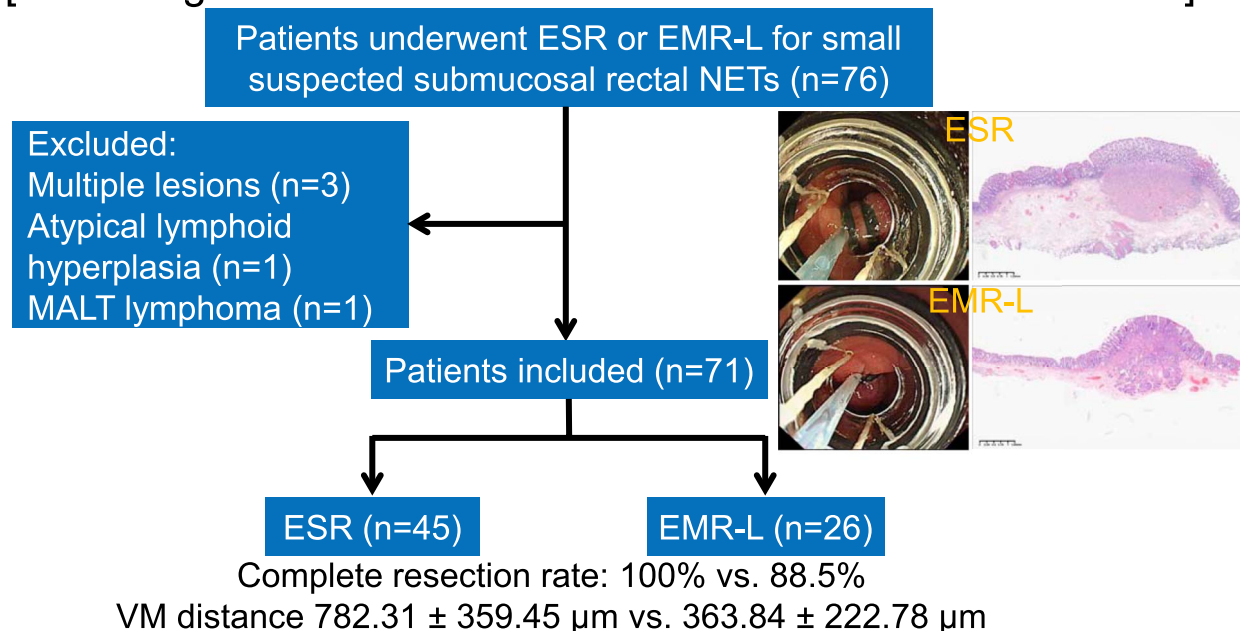


# Double Band Ligation-Assisted Endoscopic Submucosal Resection for Rectal Neuroendocrine Tumors: Comparison With Conventional Endoscopic Mucosal Resection With Ligation (With Video)

Yuan Gao, MD<sup>1</sup>, Liansong Ye, MD<sup>1</sup>, Xu Li, MM<sup>2</sup>, Long He, MD<sup>3</sup>, Bin Yu, PhD<sup>4</sup>, Wei Liu, MD<sup>1</sup>, Yuwan Cao, MA<sup>5</sup>, Liuxiang Chen, MD<sup>1</sup>, Yi Mou, MD<sup>1</sup>, Ou Chen, MD<sup>1</sup>, Jia Xie, NP<sup>1</sup>, Jiang Du, NP<sup>1</sup>, Qiongying Zhang, NP<sup>1</sup> and Bing Hu, MD<sup>1</sup>

**INTRODUCTION:** Based on endoscopic mucosal resection with ligation (EMR-L), we developed double band ligation-assisted endoscopic submucosal resection (ESR) for complete resection of small submucosal rectal neuroendocrine tumors (NETs). Both procedures use a multiband device to perform resection, with the only difference being that ESR adds an additional band to obtain deeper resection margin. The aim of this retrospective study was to validate its feasibility, safety, and effectiveness compared with EMR-L.

## [Double ligation-assisted ESR vs. EMR-L for small rectal NETs]



Gao et al. *Clin Trans Gastroenterol*. 2025. doi:10.14309/ctg.0000000000000830

Clinical and Translational  
GASTROENTEROLOGY

<sup>1</sup>Department of Gastroenterology and Hepatology, Digestive Endoscopy Medical Engineering Research Laboratory, Med-X Center for Materials, West China Hospital, Sichuan University, Chengdu, China; <sup>2</sup>Department of Clinical Research Management, Center of Biostatistics, Design, Measurement and Evaluation (CBDME), West China Hospital, Sichuan University, Chengdu, China; <sup>3</sup>Department of Pancreatic Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; <sup>4</sup>Institute for Disaster Management and Reconstruction, Sichuan University, Chengdu, China; <sup>5</sup>School of Philosophical, Historical, and Interdisciplinary, Curating, University of Essex, Colchester, UK. **Correspondence:** Bing Hu, MD. E-mail: hubing@wchscu.edu.cn. Received July 23, 2024; accepted January 31, 2025; published online February 19, 2025

© 2025 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology

- METHODS:** This retrospective study included consecutive patients with small ( $\leq 10$  mm) suspected submucosal rectal NETs who underwent ESR ( $n = 45$ ) or EMR-L ( $n = 26$ ) between June 2018 and October 2023 at West China Hospital. *En bloc* resection rate, complete resection rate, procedure time, margin distance, and adverse events were compared between 2 groups.
- RESULTS:** *En bloc* resections were achieved in all patients. The complete resection rate of ESR was higher than EMR-L (100% vs 88.5%,  $P = 0.045$ ). The vertical margin distance and lateral margin distance were significantly longer in ESR group than EMR-L group (vertical margin distance  $782.31 \pm 359.45$   $\mu\text{m}$  vs  $363.84 \pm 222.78$   $\mu\text{m}$ ,  $P < 0.001$ ; and lateral margin distance  $4,205.75 \pm 2,167.43$   $\mu\text{m}$  vs  $3,162.94 \pm 1,419.22$   $\mu\text{m}$ ,  $P = 0.008$ , respectively). There were no significant differences in procedure time, adverse events, postprocedural hospital stay, or medical cost between 2 groups. In addition, there was no evidence of recurrence or metastasis during the follow-up.
- DISCUSSION:** ESR seems to be safe and effective for complete resection of small submucosal rectal NETs. Larger, multicenter, prospective studies are needed to further assess this technique.

**KEYWORDS:** endoscopic mucosal resection; ligation; neuroendocrine tumor; rectum

**SUPPLEMENTARY MATERIAL** accompanies this paper at <http://links.lww.com/CTG/B285>

*Clinical and Translational Gastroenterology* 2025;16:e00830. <https://doi.org/10.14309/ctg.0000000000000830>

## INTRODUCTION

The rectum remains the second most common site of primary neuroendocrine tumors (NETs), accounting for 26.3% of all gastroenteropancreatic NETs (1). Rectal NETs  $> 20$  mm usually invade the muscularis propria, with a high risk of metastasis (30–80%) (2). However, approximately 80% of rectal NETs are small ( $\leq 10$  mm) and confined to the mucosa or submucosa, with a low risk of metastasis ( $< 3\%$ ) (3).

Currently, endoscopic resection is generally regarded as the first choice for the management of small rectal NETs owing to its relatively good prognosis (2–5). On this basis, complete histological resection is mandatory to avoid overtreatment or unnecessary follow-up (6,7). Endoscopic submucosal dissection (ESD) remains the first-line method for treating rectal NETs owing to the high rate of complete resection (93.5%–97.7%) (8,9). However, the technical difficulties and high medical costs suggest that this approach seems to be more appropriate for larger lesions (10–12). Hybrid endoscopic mucosal resection (EMR)-ESD has been proposed to simplify the procedure, but this technique carries the risk of incomplete resection (5.9%) (13). EMR and several modified techniques, including cap-assisted EMR (EMR-C) and EMR with ligation (EMR-L), have been applied for safe and fast resection of small rectal NETs (10,11,14,15), but incomplete resection can also be noted because the submucosal layer cannot be resected deeply using these techniques (9–11,14,16). Recently, endoscopic full-thickness resection (EFTR) with a full-thickness resection device (FTRD) has been reported for resection of small colorectal subepithelial tumors, without the risk of incomplete resection (17). However, the EFTR devices are expensive and not currently available in most settings.

There is still controversy concerning the best endoscopic method for small and deep rectal NETs. Based on EMR-L, we developed a new modified EMR technique, double band ligation-assisted endoscopic submucosal resection (ESR) without submucosal injection, during which snare resection below the second band was performed to secure a deeper resection margin (Figure 1). We had previously reported this method for treating 2

small submucosal rectal NETs (18,19). This retrospective study was designed to evaluate the feasibility, safety, and effectiveness of the ESR approach for removing small submucosal rectal NETs compared with conventional EMR-L.

## METHODS

### Study design

This is a single-center, retrospective study conducted at West China Hospital. Consecutive patients who underwent endoscopic resection for small suspected submucosal rectal NETs between June 2018 and October 2023 at the center were retrospectively evaluated. The study protocol was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Biomedical Research Ethics Committee of the West China Hospital of Sichuan University (HX2023.2130.V2.1).

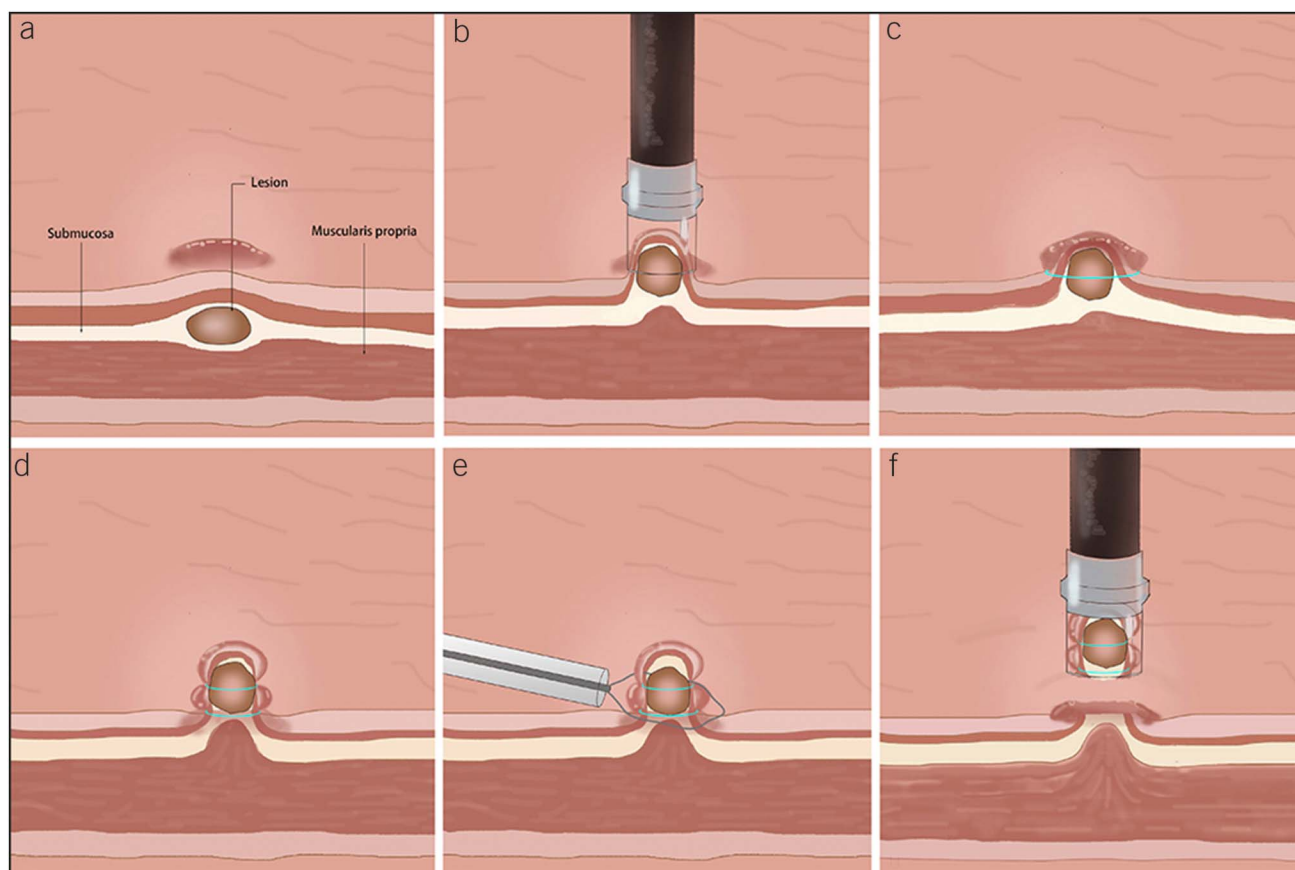
### Patients

Patients with small ( $\leq 10$  mm) suspected submucosal rectal NETs who underwent ESR or conventional EMR-L procedure during the study period were included in this study. The selection of the resection method by endoscopists was based on their evaluation of the lesion, combined with preoperative examination and intraoperative findings. The exclusion criteria were as follows: (i) patients with multiple lesions and (ii) patients with a diagnosis of non-neuroendocrine tumors according to postoperative histopathology.

### Endoscopic devices and procedures

All ligation procedures were performed using a single-channel endoscope (PCF-Q260JL/I, Olympus, Japan), crescent-type snare (SD-221 L-25, Olympus, Japan), and multiband mucosectomy (DT-6-5F, Cook, Ireland).

The ESR procedure involved the following steps (Figure 2, Video 1): (i) assessment of lesion size and invasion depth, (ii) marking for lesions without a clear boundary, (iii) suction of the lesion into the cap without submucosal injection, (iv) deployment of the first elastic band to trap the lesion, (v) deployment of the second elastic band below the first elastic band after continual



**Figure 1.** Illustration of double ligation-assisted endoscopic submucosal resection (ESR) for small submucosal rectal neuroendocrine tumors. (a) Assessment of lesion size and invasion depth; (b) suction of the lesion into the cap without submucosal injection; (c) deployment of the first elastic band to trap the lesion; (d) deployment of the second elastic band below the first elastic band after continual suction of the protuberance; (e) snare resection below the second elastic band; (f) the mucosal defect.

suction of the protuberance, (vi) snare resection below the second elastic band (ERBE; Effect 3, Cut duration 2, Cut interval 4), and (vii) wound management with or without closure.

The EMR-L procedure was similar to the ESR procedure except that only 1 elastic band was deployed, and snare resection was performed below the single elastic band (Supplementary Figure 1, <http://links.lww.com/CTG/B285>).

All endoscopic procedures were performed by 2 expert endoscopists (those with endoscopy experience > 20 years, performed more than 2,000 EMR procedures and 500 ESD procedures before the study) and 3 senior endoscopists (those with endoscopy experience > 5 years, each performed more than 500 EMR procedures and 100 ESD procedures before the study). The resected specimens were immediately sent to the pathology department for pathological analysis. Pathologists remained unaware of grouping when evaluating the specimens.

#### Data collection

Clinical data were collected from medical records, endoscopic images and videos, and telephone interviews.

Patient demographics, American Society of Anesthesiologists physical status scores, medical histories, antithrombotic utilization, and lesion characteristics were collected. Endoscopic morphology was classified as follows: I, protruded; II, flat or slightly elevated; and III, depressed or ulcerated on the surface (8). The

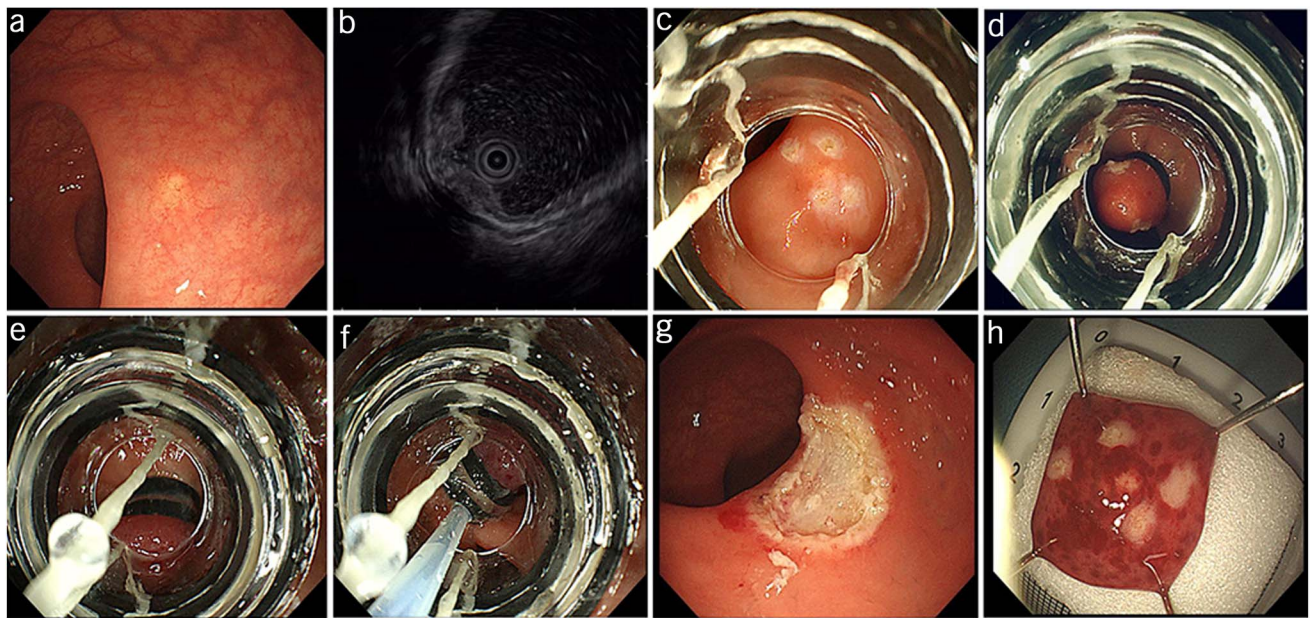
clinical outcomes of NETs, including *en bloc* resection, complete resection, adverse events, procedure time, postprocedural hospital stay, medical cost, and pathological diagnosis, were also collected. After resection, a follow-up protocol was recommended: short-term (1–3 months), colonoscopy for healing and residual tumor; medium-term (6 months–2 years), regular blood tests (CgA), colonoscopy every 6–12 months, and annual abdominal imaging; long-term (3–5 years+), blood tests and colonoscopy and imaging every 1–2 years. It can be individualized, and patients should stay healthy and report symptoms promptly. All patients were followed until March 2024. During the follow-up period, data on tumor recurrence or metastasis were collected.

#### Outcomes and definitions

The effectiveness was evaluated by assessing the rates of *en bloc* resection, complete resection, vertical and lateral margin (LM) distances, tumor recurrence, and metastasis. The safety was evaluated by assessing the adverse events. The feasibility of the procedure was evaluated by assessing the procedure time, postprocedural hospital stay, and medical cost.

*En bloc* resection was defined as the tumor being entirely endoscopically resected in 1 piece, and complete resection was defined as a single-piece (*en bloc*) resection of the lesion with a tumor-free margin in both the lateral margin (LM) and vertical





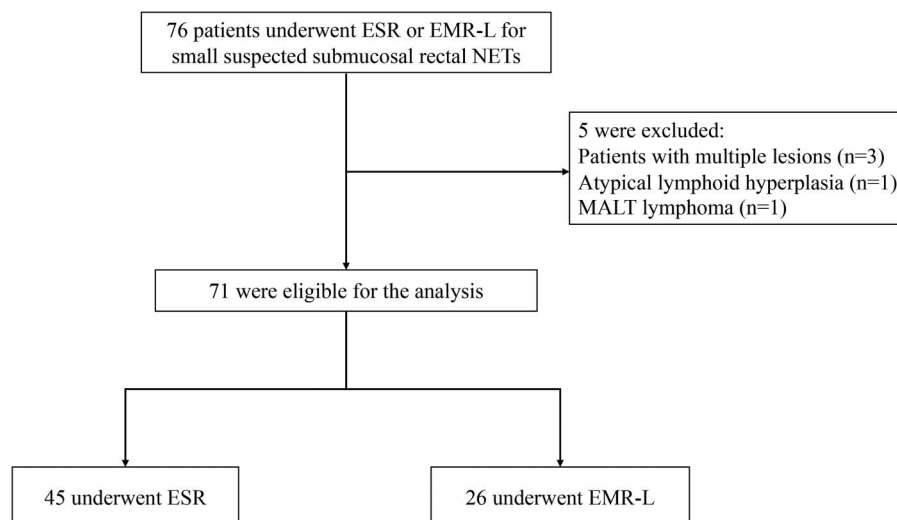
**Figure 2.** Endoscopic images of double ligation-assisted endoscopic submucosal resection (ESR) for small submucosal rectal neuroendocrine tumors. (a) The lesion shown in colonoscopy; (b) the lesion shown in endoscopic ultrasonography; (c) the lesion marking for lesions without clear boundary; (d) deployment of the first elastic band to trap the lesion; (e) deployment of the second elastic band below the first elastic band after continual suction of the protuberance; (f) snare resection below the second elastic band; (g) the mucosal defect; (h) the specimen.

margin (VM) (8,10). The adverse events mainly included bleeding and perforation, and were graded according to the American Society for Gastrointestinal Endoscopy lexicon (20). Bleeding was defined as hematochezia after the ESR procedure, requiring endoscopic hemostasis or further intervention (8). Perforation was defined as an actual hole within a white cautery ring with or without observed contamination corresponding to Sydney deep mural injury classification IV/V (21). The procedure time was measured from identification of the lesion to resection of the lesion. Medical cost was defined as all costs incurred during hospitalization. Tumor recurrence was defined as lesions recurring in the same location, whereas tumor metastasis was defined as lesions recurring in another organ. The VM distance was

defined as the distance from the lower edge of the NET to the vertical cutting edge, whereas the LM distance was defined as the distance from the edge of the NET to the horizontal cutting edge (Supplementary Figure 2, <http://links.lww.com/CTG/B285>) (11). The LM distance was recorded as the minimal LM of the specimen (between the lesion and the closest edge). In cases with horizontal margin or VM positivity, this distance was assumed to be zero.

#### Statistical analysis

Continuous variables are expressed as mean  $\pm$  SD or median (range) according to their distribution and were compared using the Student *t*-test or Whitney *U*-test, as appropriate. Categorical



**Figure 3.** Flowchart of patient selection into the groups of ESR and conventional EMR-L for small suspected submucosal rectal NETs. EMR-L, endoscopic mucosal resection with ligation; ESR, endoscopic submucosal resection; MALT, mucosa-associated lymphoid tissue; NETs, neuroendocrine tumors.

variables are expressed as proportions and were compared using the  $\chi^2$  test or Fisher exact test accordingly. Statistical significance was declared if 2-sided  $P < 0.05$ . Statistical analysis was performed with SPSS version 26.0 (IBM Corp., Armonk, NY).

## RESULTS

A total of 76 patients underwent ESR or EMR-L for small suspected submucosal rectal NETs during the study period (Figure 3). Among these patients, 5 patients were excluded from the analysis owing to multiple lesions ( $n = 3$ ), atypical lymphoid hyperplasia ( $n = 1$ ), or mucosa-associated lymphoid tissue lymphoma ( $n = 1$ ). Therefore, 71 patients with 71 submucosal rectal NETs were included in the analysis. Among these 71 patients, 45 and 26 patients underwent ESR and conventional EMR-L, respectively.

### Baseline characteristics

The characteristics of the patients and lesions in the 2 groups are presented in Table 1. The average ages of the patients in the ESR and EMR-L groups were comparable between the 2 groups ( $49.49 \pm 12.05$  vs  $43.96 \pm 11.44$ ,  $P = 0.062$ ). There were also no significant differences between the ESR and EMR-L groups regarding sex, body mass index, American Society of Anesthesiologists score, or comorbidities (all  $P > 0.05$ ). Both groups had small lesion sizes: 5 (3–10) mm vs 6 (3–10) mm;  $P = 0.083$ . Moreover, there was no significant difference in location (average distance from the anus) between the ESR and EMR-L groups (6 [2–15] cm vs 6 [3–15] cm;  $P = 0.932$ ).

### Clinical outcomes

The comparison of clinical outcomes between the 2 groups is summarized in Table 2. The rates of *en bloc* resection were similar between the 2 groups. Compared with that of EMR-L, the ESR of complete resection was longer (100% vs 88.5%,  $P = 0.045$ ). VM distance and LM distance were significantly longer in the ESR group than in the EMR-L group (VM distance  $782.31 \pm 359.45 \mu\text{m}$  vs  $363.84 \pm 222.78 \mu\text{m}$ ,  $P < 0.001$ ; LM distance  $4,205.75 \pm 2,167.43 \mu\text{m}$  vs  $3,162.94 \pm 1,419.22 \mu\text{m}$ ,  $P = 0.008$ , respectively). There were no significant differences in procedure time, postprocedural hospital stay, or medical cost between the ESR and EMR-L groups. Two days after EMR-L, one case of delayed perforation was noted in 1 patient. The patient was subsequently transferred for laparoscopic exploration and repair of the resection site. There were no adverse events in the ESR group. No patients in the ESR or EMR-L group presented evidence of tumor recurrence or metastasis at the follow-up examination.

## DISCUSSION

This retrospective study validated the innovative ESR technique for removing suspected submucosal small rectal NETs compared with EMR-L. This study suggested that the technique is feasible and efficient, with a 100% complete resection rate and no adverse events, in a quick procedure.

With the rapid development of endoscopic techniques, guidelines are increasingly recommending that endoscopic resection be used for small rectal NETs (3,4,22). These endoscopic modalities have showed their own advantages and disadvantages. The EMR-L was reported to be preferable for tumors  $\leq 10$  mm in diameter (2,3). EMR-L can also be called endoscopic submucosal resection with ligation (ESMR-L) in some studies, when the

**Table 1.** Baseline characteristics of the patients and lesions

Variables	Mean $\pm$ SD, median (IQR, range) or n (%)		P value
	ESR (n = 45)	EMR-L (n = 26)	
Age, yr	49.49 $\pm$ 12.05	43.96 $\pm$ 11.44	0.062 <sup>a</sup>
Sex			0.994 <sup>c</sup>
Male	26 (57.8%)	15 (57.7%)	
Female	19 (42.2%)	11 (42.3%)	
BMI, kg/m <sup>2</sup>	23.49 $\pm$ 2.88	23.38 $\pm$ 2.50	0.865 <sup>a</sup>
ASA score			0.999 <sup>c</sup>
I	6 (13.3%)	3 (11.5%)	
II	39 (86.7%)	23 (88.5%)	
III	0 (0%)	0 (0%)	
Comorbidity			
Hypertension	5 (11.1%)	2 (7.7%)	0.999 <sup>c</sup>
Coronary heart disease	2 (4.4%)	1 (3.8%)	0.999 <sup>c</sup>
Asthma	1 (2.2%)	0 (0%)	0.999 <sup>d</sup>
Hypothyroidism	2 (4.4%)	0 (0%)	0.529 <sup>d</sup>
Diabetes	1 (2.2%)	1 (3.8%)	0.999 <sup>c</sup>
Antithrombotics <sup>e</sup>	1 (2.2%)	0 (0%)	0.999 <sup>d</sup>
Distance from anus to lesion, cm	6 (2–15)	6 (3–15)	0.932 <sup>b</sup>
Lesion size (EUS), mm <sup>f</sup>	5 (3–10)	6 (3–10)	0.083 <sup>b</sup>
Endoscopic morphology			0.397 <sup>c</sup>
I	11 (24.4%)	10 (38.5%)	
II	33 (73.3%)	15 (57.7%)	
III	1 (2.2%)	1 (3.8%)	

ASA, American Society of Anesthesiologists; BMI, body mass index; EMR-L, endoscopic mucosal resection with ligation; ESR, endoscopic submucosal resection; EUS, endoscopic ultrasonography.

<sup>a</sup>T: Student *t*-test.

<sup>b</sup>U: Whitney *U*-test.

<sup>c</sup> $\chi^2$ : Chi-square test.

<sup>d</sup>F: Fisher exact test.

<sup>e</sup>One patient received aspirin regularly but discontinued for 5 d before the procedure.

<sup>f</sup>Lesion size was measured by endoscopic ultrasonography.

submucosal layer is resected. However, the R0 resection rate still requires further enhancement (8,23). When another band is added, the height of the lesion ascension increases significantly compared with 1 band, ESR 8 (6–12) mm vs EMR-L 6 (4–8) mm,  $P < 0.001$ , which helps the ESR achieve deeper vertical and wider horizontal resection margins (Figure 4 and Supplementary Figure 3, <http://links.lww.com/CTG/B285>). This was confirmed by the higher complete resection rate in our study (ESR 100% vs EMR-L 88.5%,  $P = 0.045$ ). It merits contemplation that there are differences in R0 resection rate of EMR-L between our research results and those of other studies, but they are still within a reasonable range. Previous studies reported higher R0 resection rates of EMR-L than this study did, with the rates ranging from 86.2% to 95.5% (8,11,16,23). This may be attributable to the circumstance that most studies included many tumors limited to

**Table 2.** Procedure details, histopathological analyses, and clinical outcomes

Variables	Mean ± SD, median (IQR, range) or n (%)		P value
	ESR (n = 45)	EMR-L (n = 26)	
Endoscopist			0.166 <sup>c</sup>
Expert	40	19	
Senior	5	7	
Lesion marking	25 (55.5%)	11 (42.3%)	0.342 <sup>c</sup>
Protuberance height, mm <sup>e</sup>	8 (6–12)	6 (4–8)	< 0.001 <sup>b</sup>
Endoscopic closure	4 (8.9%)	4 (15.4%)	0.657 <sup>c</sup>
Procedure time, min	9 (6–16)	9 (7–18)	0.483 <sup>b</sup>
En bloc resection	45 (100%)	26 (100%)	—
Complete resection	45 (100%)	23 (88.5%)	0.045 <sup>d</sup>
Bleeding	0 (0)	0 (0)	—
Perforation	0 (0)	1 (4.2%)	0.328 <sup>d</sup>
Histology			0.970 <sup>c</sup>
G1	43 (95.6%)	24 (92.3%)	
G2	2 (4.4%)	2 (7.7%)	
Lesion depth			0.970 <sup>c</sup>
Mucosal	43 (95.6)	24 (92.3)	
Submucosal	2 (4.4)	2 (7.7)	
VM distance, μm	782.31 ± 359.45	363.84 ± 222.78	< 0.001 <sup>a</sup>
LM distance, μm	4,205.75 ± 2,167.43	3,027.33 ± 1,447.54	0.008 <sup>a</sup>
Postprocedural hospital stays, d	2 (0–5)	3 (0–7)	0.510 <sup>b</sup>
Medical cost, USD	1,495.89 ± 683.45	1,765.42 ± 1,189.93	0.228 <sup>a</sup>
Follow-up duration, mo	23 (6–48)	22 (5–65)	0.929 <sup>b</sup>
Recurrence	0 (0%)	0 (0%)	—
Metastasis	0 (0%)	0 (0%)	—

EMR-L, endoscopic mucosal resection with ligation; ESR, endoscopic submucosal resection; LM, lateral margin; VM, vertical margins.

<sup>a</sup>T: Student *t*-test.

<sup>b</sup>U: Whitney *U*-test.

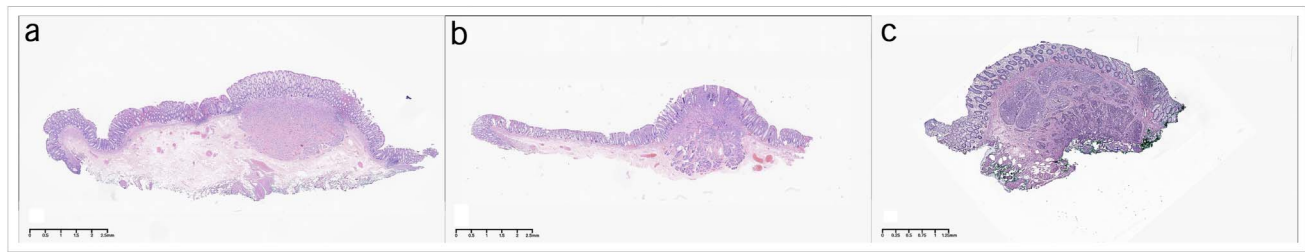
<sup>c</sup>χ<sup>2</sup>: Chi-square test.

<sup>d</sup>F: Fisher exact test.

<sup>e</sup>Protuberance height was measured by retrospective analysis of endoscopic videos and images using software Image J (National Institutes of Health), with elastic band width as the reference length (1 mm).

mucosal layer; thus, complete resection is easier for these shallower lesions. The specific therapeutic efficacy of EMR-L for NETs in the submucosa has rarely been studied specifically. Fujimoto et al evaluated the efficacy of ESMR-L for treating

duodenal submucosal NETs. In their study, 10 patients with 10 lesions achieved a 100% *en bloc* resection rate and a 70% histopathologically complete resection rate (24). The main purpose of this study was to compare the effectiveness of 2 endoscopic



**Figure 4.** Resection depth of double band ligation-assisted ESR and EMR-L for small submucosal rectal neuroendocrine tumors. (a) A specimen resected by ESR; (b) a specimen resected by EMR-L; (c) a specimen resected by EMR-L (vertical margin positivity). EMR-L, endoscopic mucosal resection with ligation; ESR, endoscopic submucosal resection.



resection methods for submucosal lesions that are difficult to completely resect. This study also revealed that the VM distance in the EMR-L group was essentially consistent with that reported in previous studies of EMR-L (the mean value varied from 277 to 672  $\mu\text{m}$ ) (9–11), and the LM distance was also consistent with that reported in previous study ( $1,661 \pm 849 \mu\text{m}$ ) (7). Based on this, we found that the VM distance and LM distance in the ESR group were significantly longer than those in the EMR-L group. In addition, ESR also exhibited safe resection. One delayed perforation was noted in 1 patient 2 days after EMR-L, whereas there were no adverse events in the ESR group. Given the limited sample size of this study, further investigations with larger and more diverse samples are warranted to comprehensively examine the safety profile of the ESR. Adverse events were reported to occur in 4.2%–4.8% of patients in the EMR-L cohort (10,16). We speculated that this difference may be related to the preoperative evaluation of the depth and size of the lesion and the operation of the endoscopist during ligation. Attention should be given to avoid injury to the muscularis propria during EMR-L, which is also important for the ESR. A sufficient preoperative assessment and accurate operation may also lead to our accomplishment to reduce adverse events. In addition, compared with EMR-L, ESR results in little increase in technical difficulty, procedure time, and medical cost.

Endoscopic procedures such as ESD, hybrid-ESD, and EFTR with FTRD are also alternative treatments of rectal NETs. Compared with ESD, ESR seems to be a simpler and less costly technique with sufficient resection. It is reported that the mean medical cost of ESD for rectal NETs varied from \$1,759 to \$2,987 (25,26), and the mean value of procedure time varied from 13.2 to 26.6 minutes (10,11,13,25,26). The complete resection rate of ESD varied from 93.5% to 97.7% (8,9), and the mean VM distance varied from 202 to 536  $\mu\text{m}$  (9–11). Another noteworthy problem with ESD is the procedure-related adverse events, which are reported to occur in 2.6%–14% of patients after ESD (8,10,13). A study conducted by Huang et al (27) contrasted the performance of EMR with double band ligation vs ESD and concluded that both approaches had similar curative effects, with EMR with double band ligation being more time efficient. Therefore, ESD seems to be more appropriate for rectal NETs >10 mm in size (2,10,28). On the other hand, hybrid-ESD with circumferential incision and snare resection, a variant derived from ESD technology, is considered to have a high complete resection rate profile as ESD with shorter procedure time (13). However, the advanced operational skills of ESD are still needed, and there is no difference in the incidence of adverse events between hybrid ESD and ESD when performed in colorectum (29). Another elegant technique, EFTR with FTRD, is a thorough endoscopic resection method not inferior to transanal endoscopic microsurgery. Considering invasive resection, procedure time, and the cost, EFTR is more recommended for rectal NETs >10 mm (17). Compared with other endoscopic modalities, including ESD (2–4) and EFTR (17), the ESR we presented is limited to small NETs as the diameter of the cap for lesion suction in mucosectomy or ligator is approximately 10 mm. Thus, the ESR technique is not suggested for NETs larger than 10 mm.

Currently, there are no clear recommendations for the selection of the technique for endoscopic resection. Summing up our data and the available evidence, we suggest to use ESR for small ( $\leq 10$  mm), submucosal NETs. ESD/EFTR is more recommended for these moderate-sized lesions (10–20 mm). For larger tumors,

more invasive operations, such as transanal endoscopic microsurgery, can be conducted.

There are several points to note when performing the ESR. First, we often mark flat and small lesions at the upper, lower, left, and right positions (accounting for 55.5% of all lesions) before ligation, making them easier to be recognized. Second, when placing the second elastic band, prolonged time applying suction appropriately and slightly rotate the endoscope to get more tissues suctioned in. Another point to note is that submucosal injection was not performed during the ESR procedure we presented. ESMR-L without submucosal injection could be used to treat these NETs safely and effectively with a short procedure time (30).

It is worth mentioning that snare resection of the ESR technique we presented was performed below the second elastic band. This can increase the risk of perforation, which is also the key to resecting more submucosal tissue and achieving complete resection for submucosal NETs. Theoretically, when the lesions and part of the muscularis propria layer are ligated by band ligation, considering the intestinal inflation, the muscularis propria layer can fall out of the band ligation over time because of the ductility of muscularis propria layer, leaving only the mucosal layer and submucosa, which may reduce the risk of perforation during resection. Although no perforation during ESR occurred in our study, ways to mitigate the risk of perforation remain necessary. During the endoscopic resection with a double ligation procedure by Moon et al (31), the snare resection was performed above the second elastic band, which may help reduce the risk of perforation. Regarding the risk of perforation, our experience suggests that snare resection close to the second elastic band helps reduce this risk. For lesions with deep ligation depth and a high risk of perforation, the application of prophylactic titanium clips could also prove beneficial.

Currently, the underwater endoscopic mucosal resection is considered to effectively avoid muscularis propria damage, but the problem of unclear complete resection remains (26). We envisage combining ESR and underwater endoscopic mucosal resection in the future, and further research is needed to evaluate the effect of the underwater ESR.

There were several limitations to the study. First, this was a retrospective and single-center study, and randomization could not be performed because the bias of selection may exist. Second, owing to the limited number of patients whose data could be collected, the relatively small sample size may have limited the statistical power of this study. Large, prospective, comparative, and multicenter studies are warranted to further assess the safety and effectiveness of ESR for small submucosal rectal NETs.

ESR is feasible, safe, and effective for the complete resection of small ( $\leq 10$  mm) submucosal rectal NETs. Further prospective studies are warranted to fully assess this method.

## CONFLICTS OF INTEREST

**Guarantor of the article:** Bing Hu, MD.

**Specific author contributions:** Y.G., L.Y. and L.H. collected the data, drafted the manuscript, and edited the video. X.L. and B.Y. contributed to the study design and data analysis. Y.C. and Y.G. draw the illustration of ESR procedure. W.L., L.C., Y.M., O.C., J.X., J.D., Q.Z., and B.H. performed the procedure and revised the manuscript. All authors reviewed and approved the final manuscript.

**Financial support:** This study was funded by the Med-X Innovation Programme of Med-X Center for Materials, Sichuan University

(Grant No: MCM202302), the Natural Science Foundation of China (Grant No: 82170675), the 1·3·5 Project for Disciplines of Excellence-Clinical Research Incubation Project, West China Hospital, Sichuan University (Grant No: 2020HXFH016), the China Postdoctoral Science Foundation (Grant No: 2022M712265), and the Sichuan Science and Technology Program (Grant No: 2023NSFSC1622).

**Potential competing interests:** None to report.

## ACKNOWLEDGEMENTS

We acknowledge the pathologists from the Department of Pathology, West China Hospital, Sichuan University, for their support in evaluating the specimens. We acknowledge all the participating colleagues for their contributions in conducting this study. We acknowledge all the funding for supporting this study.

## Study Highlights

### WHAT IS KNOWN

- ✓ Endoscopic resection is regarded as the first choice for small rectal neuroendocrine tumors.
- ✓ There is still controversy concerning the best endoscopic method for small and deep lesions.

### WHAT IS NEW HERE

- ✓ Endoscopic submucosal resection provides a new option for these lesions.
- ✓ Endoscopic submucosal resection is better recommended for small ( $\leq 10$  mm), submucosal rectal neuroendocrine tumors.
- ✓ For larger tumors, endoscopic submucosal dissection/endoscopic full-thickness resection/surgery can be conducted selectively.

## REFERENCES

- Cives M, Strosberg JR. Gastroenteropancreatic neuroendocrine tumors. *CA Cancer J Clin* 2018;68(6):471–87.
- de Mestier L, Lorenzo D, Fine C, et al. Endoscopic, transanal, laparoscopic, and transabdominal management of rectal neuroendocrine tumors. *Best Pract Res Clin Endocrinol Metab* 2019;33(5):101293.
- Maione F, Chini A, Milone M, et al. Diagnosis and management of rectal neuroendocrine tumors (NETs). *Diagnostics (Basel)* 2021;11(5):771.
- de Mestier L, Lepage C, Baudin E, et al. Digestive neuroendocrine neoplasms (NEN): French Intergroup clinical practice guidelines for diagnosis, treatment and follow-up (SNFGE, GTE, RENATEN, TENPATH, FFCU, GERCOR, UNICANCER, SFCD, SFED, SFRO, SFR). *Dig Liver Dis* 2020;52(5):473–92.
- Dąbkowski K, Szczepkowski M, Kos-Kudła B, et al. Endoscopic management of rectal neuroendocrine tumours. How to avoid a mistake and what to do when one is made? *Endokrynol Pol* 2020;71(4):343–9.
- Deprez PH, Moons LMG, O'Toole D, et al. Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* 2022;54(4):412–29.
- Gonzalez RS. Diagnosis and management of gastrointestinal neuroendocrine neoplasms. *Surg Pathol Clin* 2020;13(3):377–97.
- Wang XY, Chai NL, Linghu EQ, et al. The outcomes of modified endoscopic mucosal resection and endoscopic submucosal dissection for the treatment of rectal neuroendocrine tumors and the value of endoscopic morphology classification in endoscopic resection. *BMC Gastroenterol* 2020;20(1):200.
- Kim KM, Eo SJ, Shim SG, et al. Treatment outcomes according to endoscopic treatment modalities for rectal carcinoid tumors. *Clin Res Hepatol Gastroenterol* 2013;37(3):275–82.
- Kamigaichi Y, Yamashita K, Oka S, et al. Clinical outcomes of endoscopic resection for rectal neuroendocrine tumors: Advantages of endoscopic submucosal resection with a ligation device compared to conventional EMR and ESD. *DEN Open* 2022;2:e35–7.
- Lim HK, Lee SJ, Baek DH, et al. Resectability of rectal neuroendocrine tumors using endoscopic mucosal resection with a ligation band device and endoscopic submucosal dissection. *Gastroenterol Res Pract* 2019;2019:8425157.
- Hong SM, Baek DH. Endoscopic treatment for rectal neuroendocrine tumor: Which method is better? *Clin Endosc* 2022;55(4):496–506.
- Wang XY, Chai NL, Linghu EQ, et al. Efficacy and safety of hybrid endoscopic submucosal dissection compared with endoscopic submucosal dissection for rectal neuroendocrine tumors and risk factors associated with incomplete endoscopic resection. *Ann Transl Med* 2020;8(6):368.
- Yang DH, Park Y, Park SH, et al. Cap-assisted EMR for rectal neuroendocrine tumors: Comparisons with conventional EMR and endoscopic submucosal dissection (with videos). *Gastrointest Endosc* 2016;83(5):1015–22; quiz 1023–6.
- Niimi K, Goto O, Fujishiro M, et al. Endoscopic mucosal resection with a ligation device or endoscopic submucosal dissection for rectal carcinoid tumors: An analysis of 24 consecutive cases. *Dig Endosc* 2012;24(6):443–7.
- Lee J, Park YE, Choi JH, et al. Comparison between cap-assisted and ligation-assisted endoscopic mucosal resection for rectal neuroendocrine tumors. *Ann Gastroenterol* 2020;33(4):385–90.
- Meier B, Albrecht H, Wiedbrauck T, et al. Full-thickness resection of neuroendocrine tumors in the rectum. *Endoscopy* 2020;52(1):68–72.
- He L, Wen W, Ye L, et al. Endoscopic mucosal resection with double band ligation for small rectal neuroendocrine tumors. *Am J Gastroenterol* 2021;116(9):1827–8.
- Liu W, Yuan XL, Hu B. Double ligation-assisted endoscopic submucosal resection for rectal neuroendocrine tumors. *Endoscopy* 2022;54(3):E106–7.
- Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: Report of an ASGE workshop. *Gastrointest Endosc* 2010;71(3):446–54.
- Burgess NG, Bassan MS, McLeod D, et al. Deep mural injury and perforation after colonic endoscopic mucosal resection: A new classification and analysis of risk factors. *Gut* 2017;66(10):1779–89.
- Rinke A, Ambrosini V, Dromain C, et al. European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for colorectal neuroendocrine tumours. *J Neuroendocrinol* 2023;35(6):e13309.
- Inada Y, Yoshida N, Fukumoto K, et al. Risk of lymph node metastasis after endoscopic treatment for rectal NETs 10 mm or less. *Int J Colorectal Dis* 2021;36(3):559–67.
- Fujimoto A, Sasaki M, Goto O, et al. Treatment results of endoscopic mucosal resection with a ligation device for duodenal neuroendocrine tumors. *Intern Med* 2019;58(6):773–7.
- Gao X, Huang S, Wang Y, et al. Modified cap-assisted endoscopic mucosal resection versus endoscopic submucosal dissection for the treatment of rectal neuroendocrine tumors  $\leq 10$  mm: A randomized noninferiority trial. *Am J Gastroenterol* 2022;117(12):1982–9.
- Shi H, Wang C, Wu J, et al. Underwater endoscopic mucosal resection for rectal neuroendocrine tumors (with videos): A single center retrospective study. *BMC Gastroenterol* 2022;22(1):276.
- Huang JL, Gan RY, Chen ZH, et al. Endoscopic mucosal resection with double band ligation versus endoscopic submucosal dissection for small rectal neuroendocrine tumors. *World J Gastrointest Surg* 2023;15(3):440–9.
- Bang BW, Park JS, Kim HK, et al. Endoscopic resection for small rectal neuroendocrine tumors: Comparison of endoscopic submucosal resection with band ligation and endoscopic submucosal dissection. *Gastroenterol Res Pract* 2016;2016:6198927.
- Bae JH, Yang DH, Lee S, et al. Optimized hybrid endoscopic submucosal dissection for colorectal tumors: A randomized controlled trial. *Gastrointest Endosc* 2016;83(3):584–92.
- Oono Y, Shinmura K, Hori K, et al. Endoscopic submucosal resection using a ligation device without injection for duodenal neuroendocrine tumors. *Surg Endosc* 2019;33(6):2008–14.
- Moon JH, Kim JH, Park CH, et al. Endoscopic submucosal resection with double ligation technique for treatment of small rectal carcinoid tumors. *Endoscopy* 2006;38(5):511–4.

**Open Access** This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.