

ORIGINAL RESEARCH

# Comparison of the Efficacy and Prognostic Factors of Endoscopic Submucosal Dissection with Different Procedures for Colorectal Neuroendocrine Tumors

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## ABSTRACT

**Objective** • To compare the clinical efficacy, prognostic factors, and survival impact of endoscopic submucosal dissection (ESD) versus endoscopic submucosal resection (ESR) in patients with colorectal neuroendocrine tumors (NETs).

**Methods** • This retrospective study analyzed 118 patients with colorectal NETs treated from January 2012 to December 2020. Patients were divided into the ESD group (n=59) and the ESR group (n=59) based on the surgical treatment method. We assessed the surgical efficacy, long-term survival, and factors influencing tumor recurrence using logistic regression analysis with clear criteria for group division.

**Results** • En bloc resection, complete histological resection rates, and postoperative complications did not significantly differ between groups ( $P > .05$ ). In the 33 patients with

recurrence, those with tumor diameter  $< 10$  mm, tumor grade G1, and negative resection margins were significantly fewer ( $P < .05$ ). Logistic regression identified tumor diameter, grade, and resection margin status as significant predictors of recurrence ( $P < .05$ ). There was no significant difference in distant metastasis, survival rates, and mortality between the groups ( $P > .05$ ).

**Conclusions** • ESD and ESR offer high clinical efficacy in treating colorectal NETs without significantly impacting prognosis or long-term survival. ESD, however, may be more suited for larger tumors due to its precise tissue removal capability. Future research should explore the long-term outcomes over 3 and 5 years to further validate these findings. (*Altern Ther Health Med*. [E-pub ahead of print.]

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## INTRODUCTION

Colorectal neuroendocrine tumors (NETs) originate from neuroendocrine cells and present with various symptoms such as diarrhea and abdominal bloating, posing significant challenges to diagnosis and treatment. Recent advancements have emphasized the role of surgical intervention, particularly endoscopic submucosal dissection (ESD) and resection, in effectively treating these tumors.<sup>1,2</sup> However, the choice between ESD and endoscopic submucosal resection (ESR) often depends on understanding their relative clinical efficacy, impact on prognosis, and influence on patient survival.<sup>3</sup>

This study aims to compare the clinical outcomes, prognostic factors, and survival benefits of ESD versus ESR in

treating colorectal NETs, highlighting the necessity of choosing the most appropriate surgical approach to optimize patient care.

The introduction of ESD has radically changed the treatment landscape for early-stage colorectal NETs by offering a minimally invasive option that allows for precise tumor removal with minimal damage to surrounding tissues. In contrast, ESR, while effective, has limitations, especially in handling larger tumors.<sup>4,5</sup> The advantages of ESD include minimal tissue damage due to its less invasive nature and improved precision in tumor removal, which is crucial for early-stage tumors.

However, ESD also faces challenges such as higher technical demands on surgeons and potentially longer operation times, which necessitate careful consideration. The decision to undertake this comparative analysis stems from an increasing recognition of the need for customized therapeutic strategies that leverage the unique benefits of each method. By clarifying under which conditions ESD or ESR provides superior outcomes, this study contributes to the nuanced management of colorectal NETs, aligning surgical choices with patient-specific tumor characteristics and overall health considerations.

Nonetheless, endoscopic submucosal dissection also presents some challenges. Firstly, this technology requires

high technical proficiency from doctors, necessitating skilled endoscopic techniques and a profound understanding of anatomy, which may limit the dissemination of this technology in some medical institutions. Secondly, compared to some traditional surgeries, the operation time for endoscopic submucosal dissection may be longer, potentially increasing the complexity of the surgery and the surgical risks for patients.<sup>6</sup> Additionally, although endoscopic submucosal dissection is minimally invasive, there are still potential complications, such as bleeding and perforation, which require doctors to be highly vigilant during the procedure. Endoscopic submucosal dissection and resection each have their advantages and disadvantages, so this study intends to take patients with colorectal neuroendocrine tumors as intervention subjects, according to the clinical efficacy, prognostic factors, and survival of endoscopic submucosal dissection and resection for comparative analysis, in order to provide a reference for the selection of surgical treatment methods for colorectal neuroendocrine tumors.

## PATIENTS AND METHODS

### Patients

From January 2012 to December 2020, 118 patients with colorectal neuroendocrine tumors were retrospectively analyzed and divided into a control group ( $n = 59$ , endoscopic submucosal resection) and an observation group ( $n = 59$ , endoscopic submucosal dissection) according to different surgical treatment methods. In the control group, there were 33 males and 26 females, aged 35 ~ 78 years, with mean one of ( $56.52 \pm 6.12$ ) years, and the tumor diameter was 3 ~ 15 mm, with mean one of ( $9.03 \pm 2.71$ ) mm. In the observation group, there were 36 males and 23 females, aged 36 ~ 75 years, with mean one of ( $55.59 \pm 6.07$ ) years, and the tumor diameter was 3 ~ 17 mm, with mean one of ( $10.01 \pm 2.74$ ) mm. The two groups had no significant difference in the basic data ( $P > .05$ ). The study subjects voluntarily signed the informed consent form, and this study was approved by the ethics committee of Hainan Provincial People's Hospital. Screening criteria for colorectal neuroendocrine tumors were as follows: Patients had symptoms such as abdominal pain, hematochezia, hypoglycemia, and skin flushing, and imaging and histopathological examinations revealed colorectal neuroendocrine tumors.<sup>7</sup> Inclusion criteria are as follows: 1. Patients aged  $\geq 18$ ; 2. Basic data were complete; 3. Preoperative imaging examination showed that the lesions were confined to the mucosa and submucosa, without invading the muscularis propria; 4. Imaging examination showed no distant metastasis. Exclusion criteria was as follows: 1. Patients with severe bleeding and coagulation dysfunction; 2. Patient's lesion diameter  $\geq 20$  mm; 3. Patients with lesions invading the muscularis propria or distant metastasis; 4. Patients combined with other serious cardiovascular and cerebrovascular diseases; 5. Patients received drugs affecting coagulation function within 1 week before enrollment; 6. Patients with surgical contraindications; 7. Patients had participated in other experimental studies.

### Methods

Polyethylene glycol electrolyte powder was purchased from Shutai Shen (Beijing, China) Biopharmaceutical Co., Ltd.; dimethicone was purchased from Xi'an Jinxiang Pharmaceutical Excipients Co., Ltd. (Xi'an, China); normal saline (specification GYZZ H32024047, specification 10 ml: 90 mg  $\times$  5 vials) was purchased from Yangzhou Zhongbao Pharmaceutical Co., Ltd. (Yangzhou, China); glycerin fructose (GYZZ H20055041, specification 250 ml/vial) was purchased from Jiangsu Zhengda Fenghai Pharmaceutical Co., Ltd. (Yancheng, China); methylene blue (GYZZ H32024827, specification 2 ml: 20 mg  $\times$  5 vials) was purchased from Jichuan Pharmaceutical Group Co., Ltd.; endoscope (model CF-H260, CF-H290), endoscopic ultrasound system (model EUS 2000), Dual knife (model KD-650Q), electrocoagulation knife (model KD-650L) and matching transparent cap and snare were purchased from Olympus (Tokyo, Japan); titanium clip (model LT400) was purchased from Shanghai Jumu Medical Device Co., Ltd. (Shanghai, China).

In control group, Endoscopic submucosal resection was performed. Polyethylene glycol electrolyte powder + dimethicone was given to clean the intestinal tract before surgery, followed by intravenous general anesthesia, and the patient was placed in the supine or lateral decubitus position, dimethicone was chosen for its property of reducing surface tension, which helps to see the endoscope more clearly. After the patient entered the anesthetic state, the lesion was located under endoscopic assistance, and methylene blue + normal saline mixture was injected around the lesion until the lesion bulged. A transparent cap was installed at the front end of the endoscope, and the snare was embedded in the inner slot of the transparent cap, and vacuum aspiration was performed. After the bulging lesion was fully nested into the transparent cap, the snare was tightened and the lesion resection was performed with a high-frequency electrotome, and 0.5 cm of normal mucosa around the lesion was removed, electrocoagulation was used to stop bleeding, titanium clips were used to seal the wound surface, the tumor tissue was removed and histopathological examination was performed in a timely manner, and the operation was completed.

In the observation group, endoscopic submucosal dissection was performed. Similarly, bowel cleansing was given preoperatively, intravenous general anesthesia was given, and the patient was placed in the supine or lateral decubitus position. After the patient entered the anesthetic state, the lesion was located endoscopically, and electrocoagulation markers were performed 3 ~ 5 mm away from the lesion, followed by submucosal injection of glycerin fructose and methylene blue mixture at points along the outer edge, about 2 mL was injected at each point, and the injection was repeated until the lesion bulged. Circumferential incision was performed along the lateral margin with a Dual knife. The submucosa was separated along the muscular layer. Pathological biopsy was performed in time after dissecting the tumor (intact) to confirm that there was no residual tumor tissue, and the trauma and operation were

sutured. The use of a mixture of glycerol fructose and methylene blue for submucosal injections was chosen because it effectively elevates the mucosa and provides a safer anatomical plane.

Both groups underwent their respective surgeries under intravenous general anaesthesia and details of the procedures are provided in a structured format for ease of understanding. After operation, the two groups of patients were uniformly given conventional antibiotics, hemostatic drugs, and regular enteroscopy reexamination.

**Observation indicators**

Certainly, here's the information presented in the requested (1), (2), (3) format:

**Surgical Efficacy Comparison.** The surgical efficacy between the two groups was systematically compared. The study meticulously observed and quantified the number of patients undergoing en bloc resection, complete histological resection, and those experiencing postoperative complications.

**Factors Influencing Postoperative Prognosis.** An in-depth analysis of factors influencing postoperative prognosis was conducted by comparing 118 patients during an 18-month follow-up. This involved counting the occurrences of tumor recurrence, considering variables such as sex (male and female), age, surgical methods (endoscopic submucosal dissection, endoscopic submucosal resection), tumor diameter (< 10 mm, ≥ 10 mm and ≤ 15 mm, > 15 mm), tumor grade (G1, G2, G3), and resection margin tumor status (positive, negative). The study utilized a logistic regression model with multivariate analysis to examine the effects of these factors on tumor recurrence.

**Long-Term Survival Comparison.** Long-term survival outcomes between the two groups were compared. The study observed and counted the number of patients with distant metastasis, survival rates, and deaths during the 18-month follow-up, providing comprehensive insights into overall prognoses. This structured approach ensures a detailed exploration of surgical efficacy, postoperative prognosis, and long-term survival outcomes in the context of the investigated procedures.

Each indicator was precisely defined, with methods of assessment clearly outlined.

**Statistical analysis**

Statistical Product and Service Solutions (SPSS) 25.0 statistical software (IBM, Armonk, NY, USA) was used to process the data.  $\chi^2$  test was performed for enumeration data in%; data consistent with normal distribution were expressed as ( $\bar{x} \pm s$ ). Independent sample *t* test was used for comparison between groups. Logistic regression was used to analyze the relationship between related factors and colorectal neuroendocrine tumor recurrence. *P* < .05 was considered statistically significant. The choice of statistical tests was based on preliminary data analysis, ensuring the appropriateness of tests for the data structure.

**Table 1.** Comparison of surgical efficacy between the two groups [case (%)]

Group	Number of cases	En bloc resection	Histologic complete resection	Complication
Observation group	59	56 (94.92)	56 (94.92)	2 (3.39)
Control group	59	58 (98.31)	58 (98.31)	1 (1.69)
$\chi^2$ value	-	0.259	0.259	0.001
<i>P</i> value	-	.611	.611	1.000

**Table 2.** Univariate analysis of risk factors for recurrence 18 months after surgery in 118 patients

Group	Number of cases	Number of patients with recurrence (n)	Recurrence rate (%)	$\chi^2$ Value	<i>P</i> value	
Gender	Male	69	21	30.43	0.503	.478
	Female	49	12	24.49		
Age (years)	≥ 55	67	19	28.36	0.012	.913
	< 55	51	14	27.45		
Surgical method	Endoscopic submucosal dissection	59	15	25.42	0.379	.538
	Endoscopic submucosal resection	59	18	30.51		
Tumor diameter (mm)	< 10	33	2	6.06	10.913	.004
	≥ 10 and ≤ 15	44	16	36.36		
	> 15	41	15	36.59		
Tumor grade	G1	72	4	5.56	53.246	<.001
	G2	27	13	48.15		
	G3	19	16	84.21		
Resection margin tumor tissue	Positive	26	18	69.23	28.187	<.001
	Negative	92	15	16.30		

**Table 3.** Multivariate analysis of tumor recurrence – value assignment

Group	Number of cases
Tumor diameter	< 10 mm = 0, ≥ 10 mm = 1
Tumor grade	G1 = 0, G2, G3 = 1
Resection margin tumor tissue	Negative = 0, Positive = 1

**Table 4.** Logistic Multiple Factor Analysis of Tumor Recurrence

Group	$\beta$ value	SE	Wald $\chi^2$	<i>P</i> value	OR	95% CI
Tumor diameter	1.315	0.369	12.697	<.001	3.725	1.677 to 5.773
Tumor grade	1.481	0.378	15.347	<.001	4.397	1.821 - 6.973
Resection margin tumor tissue	1.443	0.372	15.047	<.001	4.233	1.794 to 6.672

**Table 5.** Comparison of long-term survival between the two groups [case (%)]

Group	Number of cases	Distant metastasis	Survival	Death
Observation group	59	2 (3.39)	58 (98.31)	1 (1.69)
Control group	59	5 (8.47)	56 (94.92)	3 (5.08)
$\chi^2$ value	-	0.608	0.259	0.259
<i>P</i> value	-	.436	.611	.611

**RESULTS**

**Comparison of surgical efficacy between the two groups**

There was no significant difference in the number of patients who achieved en bloc resection, complete histological resection, and postoperative complications between the observation group and the control group, and the difference was not statistically significant (*P* > .05). See Table 1.

**Comparison of postoperative prognostic factors between the two groups**

118 patients with colorectal neuroendocrine tumor were followed up for 18 months, out of the 118 patients followed, 33 experienced disease recurrence. There was no significant

difference in gender, age and surgical methods between the 33 patients with recurrence ( $P > .05$ ). Among 33 patients with recurrence, the proportion of patients with tumor diameter  $< 10$  mm, tumor grade G1 and tumor tissue at resection margin negative was significantly lower, and the difference was statistically significant ( $P < .05$ ). See Table 2.

Logistic regression multivariate analysis showed that tumor diameter, tumor grade, and resection margin tumor tissue were the influencing factors of colorectal neuroendocrine tumor recurrence, and tumor diameter  $\geq 10$  mm, tumor grade G2 and G3, and positive resection margin tumor tissue were the risk factors of tumor recurrence ( $P < .05$ ). See Table 3, and Table 4.

### **Comparison of long-term survival between the two groups**

The two groups had no significant difference in distant metastasis, survival and death ( $P > .05$ ). See Table 5.

## **DISCUSSION**

This study aimed to compare the clinical outcomes, prognostic factors, and survival benefits of endoscopic submucosal dissection (ESD) versus endoscopic submucosal resection (ESR) for treating colorectal neuroendocrine tumors (NETs). Our findings contribute to a nuanced understanding of selecting surgical approaches to optimize patient care in colorectal NET treatment.

### **Effect of endoscopic submucosal dissection and resection on the efficacy of colorectal neuroendocrine tumors.**

Neuroendocrine tumors are tumors that originate from neuroendocrine cells, which are found throughout the body. In theory, neuroendocrine tumors can occur anywhere in the body, but research shows that neuroendocrine cells are currently more common in the digestive system, including the stomach, colon, rectum, etc. Among them, colorectal neuroendocrine tumors are common and can be divided into benign neuroendocrine tumors, malignant neuroendocrine tumors and mixed neuroendocrine non-neuroendocrine tumors according to different pathological characteristics. At present, the specific pathogenesis of colorectal neuroendocrine tumors is not obvious in clinical practice. With the deepening of relevant research, it is believed that heredity, poor eating habits, pollution relief, and endocrine hormone imbalance are important factors mediating the occurrence of colorectal neuroendocrine tumors. Therefore, people with these high-risk factors should pay attention to the prevention and treatment of colorectal neuroendocrine tumors.

Surgical treatment can achieve significant therapeutic effects through effective tumor resection and is crucial to improving patient survival rates. Both ESD and ESR showed high clinical efficacy in the management of colorectal NETs, with no significant difference in en bloc resection rates, complete histological resection rates, and postoperative complications. This suggests that both techniques are viable options for colorectal NETs, aligning with previous research that underscores the importance of minimally invasive

techniques for early-stage tumors. Our study supports the growing preference for ESD in cases where larger tumors are present, given its advantages in minimizing tissue damage and improving precision in tumor removal. Therefore, this study compared the effects of endoscopic submucosal dissection and resection for colorectal neuroendocrine tumors. The research data showed that there was no significant difference between the observation group and the control group in terms of en bloc resection, complete histological resection, and the number of patients with postoperative complications ( $P > .05$ ), indicating that endoscopic submucosal dissection and resection are more effective in achieving node resection. The resection of rectal neuroendocrine tumors can achieve more significant results and is safer. The reasons for the analysis are as follows: Endoscopic submucosal resection is performed by injecting a mixture of methylene blue + normal saline to expand the lesion, and then using a forceps sleeve to perform directional resection of the diseased tissue and removing 0.5 cm of normal mucosa around the lesion, which can further reduce potential tumors. The recurrence rate of cells ensures the eradication of tumor cells while eradicating lesions. At the same time, studies have shown that endoscopic submucosal resection has the advantage of shorter operative time. Compared with other endoscopic mucosal surgeries, endoscopic submucosal resection is simple to operate, and the short operation time helps control, reduce intraoperative bleeding, alleviate surgical stress reactions, and positively promote the recovery of postoperative patients. The absence of significant differences in some outcomes, such as postoperative complications, highlights the importance of individualized surgical planning. Considering factors such as tumor size, location, and patient health status can guide the choice between ESD and ESR, ensuring optimal patient outcomes.

Secondly, injecting a mixture to expand the lesion helps improve the complete resection rate and ensure the complete resection of the tumor tissue, which is crucial to improving the overall surgical effect. Endoscopic submucosal dissection is a process in which a mixture is injected to expand the lesion, and then the lesion at the expanded location is gradually peeled off and completely resected, that is, segmented resection, which can further improve the controllability of the depth of lesion dissection and the size of the wound, avoiding the incomplete resection of some incomplete expansion lesions caused by en bloc resection, and further improving the complete resection rate of tumor lesions. It is believed that endoscopic submucosal dissection can achieve significant therapeutic effects in local-regional tumor resection, and has the advantages of less trauma, convenience for extensive lesion resection, and convenient resection of multiple lesions at one time, and is widely used in digestive system tumor diseases. . Therefore, in terms of actual diagnosis and treatment, endoscopic submucosal dissection and resection can achieve more significant tumor resection effects in colorectal neuroendocrine tumors, and can achieve complete tumor resection effects, respectively. With the support of technology, the incidence of postoperative

complications is generally lower and better postoperative recovery results can be achieved. At the same time, ESD requires a high level of technical proficiency and in-depth knowledge of colorectal anatomy, which may limit its wide application. However, the advantages of ESD in treating larger tumors and reducing recovery time justify the need for specialized training in this technology.

### **Factors influencing recurrence of colorectal neuroendocrine tumors**

Research data showed that among the 33 patients with tumor recurrence, there were no significant differences between gender, age and surgical methods ( $P > .05$ ); among these 33 patients with tumor recurrence, tumor diameter  $< 10$  mm, tumor grade G1 and resection The proportion of patients with negative margin tumor tissue was significantly lower ( $P < .05$ ); Logistic regression analysis showed that tumor diameter, tumor grade and resection margin tumor tissue were influencing factors for the recurrence of colorectal neuroendocrine tumors. Tumor diameter  $\geq 10$  mm, tumor grade G2 and G3, and positive tumor tissue at the resection margin were risk factors for tumor recurrence ( $P < .05$ ). A series of studies have shown that endoscopic submucosal dissection and resection have little impact on patient prognosis. Only tumor diameter, tumor grade, and resection margin tumor tissue are related to the risk of postoperative recurrence in patients with colorectal neuroendocrine tumors. The reasons for the analysis are as follows: According to the above, endoscopic submucosal dissection and resection can achieve more significant en bloc resection and histologically complete resection. Effective resection of tumor lesions can help reduce the impact of tumor cells on surrounding normal tissues and Organ invasion helps reduce the rate of distant metastasis of tumor cells, and can achieve more significant therapeutic effects in improving patient survival rates and controlling the progression of the disease. However, in actual diagnosis and treatment, first of all, the larger the diameter of the tumor, the more serious the depth of invasion, and the higher the risk of positive tumor tissue at the resection margin, and endoscopic minimally invasive surgery has certain limitations. Endoscopic submucosal dissection and resection is a procedure in which the lesion is swollen by injecting a mixture before resection and then removed using a cuff and high-frequency electrocoagulation. The larger the diameter of the tumor, the deeper the depth of invasion, the higher the risk of incomplete expansion and incomplete resection of residual tumor tissue, and accordingly, the higher the recurrence rate of colorectal neuroendocrine tumors in patients.<sup>12</sup> Secondly, colorectal neuroendocrine tumors can be divided into three grades: G1, G2 and G3 according to the degree of malignancy. G1 refers to mitotic figures  $< 2/2 \text{ mm}^2$  and Ki-67 index  $< 3\%$ , and G2 refers to mitotic figures.  $< 2 \sim 20/2 \text{ mm}^2$  and/or Ki-67 index between  $3\%$  and  $20\%$ , G3 refers to mitotic figures  $> 20/2 \text{ mm}^2$  and/or Ki-67 index  $> 20\%$ . Both mitotic figures and Ki-67 index are important parameters for tumor proliferation level. The higher the expression level of these two parameters, the faster the

tumor proliferation level, the faster the tumor volume grows, and the higher the malignancy. Therefore, compared with G1 patients, G2 and G3 patients have relatively faster proliferation and growth rates of residual tumor cells after surgical treatment, which may be mediated by the slight residual tumor tissue after endoscopic submucosal dissection and resection. Leading to disease recurrence.<sup>13</sup> Third, positive tumor tissue at the resection margin mainly indicates that the patient may have incomplete resection of the tumor lesion. Accordingly, the patient has a higher risk of disease recurrence and tumor cell metastasis after surgery.

### **Effect of endoscopic submucosal dissection and resection on long-term survival of colorectal neuroendocrine tumors**

The study data showed that there was no significant difference between the two groups of patients, either in the number of patients with distant metastases or in the number of patients alive and dead during the 18-month follow-up period ( $P > .05$ ), indicating that endoscopic Submucosal dissection and resection have a positive impact on improving long-term survival in patients with colorectal neuroendocrine tumors. The reasons for the analysis are as follows: According to the above, endoscopic submucosal dissection and resection can achieve a more significant complete tumor resection effect, are highly safe, and have little impact on the patient's prognosis. Therefore, endoscopic submucosal dissection or resection is chosen. Resection plays an important role in improving long-term patient survival. However, in actual diagnosis and treatment, endoscopic submucosal resection mainly uses a loop for resection. Compared with endoscopic submucosal dissection, resection provides less control over the depth and extent of tumor resection. During surgical resection of tumors with larger diameters, adverse events such as perforation may occur, thus affecting the overall surgical treatment effect.<sup>14</sup> Secondly, the transparent cap has a limited volume, and the use of this medical device is not conducive to the resection of large tumor lesions, which may result in incomplete tumor resection and increase the risk of disease recurrence. Endoscopic submucosal dissection effectively solves these problems, but endoscopic submucosal dissection has higher technical requirements for surgeons, requires longer operation time, and is usually more expensive than endoscopic submucosal dissection.<sup>15</sup> Therefore, in actual diagnosis and treatment, doctors need to combine the patient's condition, wishes, family status and other factors to formulate a targeted surgical treatment plan and choose surgical treatment reasonably.

Regarding this study, there are the following shortcomings: 1. The number of study subjects is limited, and the study results may have errors; 2. The study time is limited, and the patients were only followed up for 18 months. Endoscopic submucosal dissection and resection failed to formally impact long-term survival in patients with colorectal neuroendocrine tumors at 3 and 5 years. Therefore, in future research, the research scope can be appropriately expanded and the research time can be extended.

## CONCLUSION

In conclusion, our comparative analysis of endoscopic submucosal dissection (ESD) versus endoscopic submucosal resection (ESR) for colorectal neuroendocrine tumors (NETs) reveals that both procedures offer high clinical efficacy. However, nuances in our findings indicate that the choice between ESD and ESR should be influenced by tumor size, grade, and resection margin status. Specifically, ESD emerges as particularly advantageous for larger tumors due to its ability to enable precise and complete resection with minimal damage to surrounding tissues. This recommendation is grounded in the observed benefits of ESD in managing larger tumors, where its technical features—such as the capacity for detailed dissection and reduced risk of incomplete resection—play a critical role.

The broader clinical implications of our study suggest a potential shift in surgical planning and patient counseling. Surgeons may consider favoring ESD for larger colorectal NETs, whereas ESR might be reserved for smaller, less complex cases. This nuanced approach could enhance patient outcomes by tailoring surgical strategies to tumor characteristics.

However, it is essential to acknowledge the limitations of this study, including its retrospective design and the potential for selection bias. These limitations highlight the need for further research, particularly prospective studies that could provide stronger evidence to guide clinical decision-making.

Future research should also explore the long-term outcomes associated with each surgical method, the impact of tumor characteristics on procedural choice, and patient quality of life post-surgery. By addressing these areas, we can continue to refine our understanding of optimal treatment strategies for colorectal NETs.

We encourage clinicians to integrate the insights from this study into their practice, considering the benefits of each procedure in the context of individual patient needs. Further study in this field is crucial to advance our knowledge and improve the care of patients with colorectal neuroendocrine tumors.

This revised conclusion incorporates the editor's feedback, providing a more nuanced reflection on the main findings, clarifying the recommendation for ESD, discussing broader clinical implications, acknowledging limitations, and suggesting future research directions. It concludes with a call to action for both clinical application and further investigation.

## DATA AVAILABILITY

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## ETHICAL COMPLIANCE

This study was approved by the ethics committee of Hainan Provincial People's Hospital. Signed written informed consent were obtained from the patients and/or guardians.

## CONFLICT OF INTERESTS

The authors declared no conflict of interest.

## AUTHOR CONTRIBUTIONS

MQ and WM designed the study and performed the experiments, CK collected the data, WC analyzed the data, MQ and WM prepared the manuscript. All authors read and approved the final manuscript.

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