Original Article

Treatment outcomes of endoscopic resection for nonampullary duodenal neuroendocrine tumors

Wenyu Li, Yong Liu, Lizhou Dou, Shun He, Yueming Zhang, Yan Ke, Xudong Liu, Guiqi Wang

Department of Endoscopy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Contributions: (I) Conception and design: W Li; (II) Administrative support: G Wang; (III) Provision of study materials or patients: Y Liu, L Dou, S He, Y Zhang, Y Ke, X Liu; (IV) Collection and assembly of data: W Li; (V) Data analysis and interpretation: W Li, Y Liu, L Dou; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Guiqi Wang, MD. Department of Endoscopy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17 Panjiayuan Street, Chaoyang District, Beijing 100021, China. Email: wangguiq@126.com.

Background: The incidence rate of duodenal neuroendocrine tumors has been increasing in recent years. Endoscopic resection [ER; endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD)] is recommended for nonampullary duodenal neuroendocrine tumors (NAD-NETs) ≤10 mm in diameter that are confined to the submucosal layer and without lymph node or distant metastasis. However, the efficacy and safety of and indications for EMR/ESD remain unclear.

Methods: Between November 2011 and April 2021, 12 NAD-NETs in 12 patients who underwent either EMR or ESD were analyzed retrospectively. The rates of en bloc resection, complete resection, pathologic complete resection, margin involvement, lymphovascular invasion, perineural invasion, complications and prognosis were determined during follow-up (median observation period 53.0 months).

Results: EMR was performed for two tumors, and ESD was performed for ten tumors. En bloc resection was performed for both tumors (100%) in the EMR group, and complete resection was achieved in one case (50%). Pathological complete resection was achieved in one case (50%), while in the ESD group, these three rates were 90% (9/10), 80% (8/10), and 80% (8/10), respectively. Intraoperative perforation occurred in one patient (10%) during ESD treatment, with no intraoperative or delayed bleeding in either group. Recurrence and distant metastasis were not observed during the mean follow-up period of 53.0 months (range, 18–131 months).

Conclusions: For NAD-NETs that measure ≤10 mm in size, are confined to the submucosal layer and have neither suspicious lymph nodes nor distant metastasis, ER (EMR and ESD) may be a safe, effective, and feasible endoscopic technique for removing them.

Keywords: Nonampullary duodenal neuroendocrine tumors (NAD-NETs); endoscopic mucosal resection (EMR); endoscopic submucosal dissection (ESD)

Submitted Aug 18, 2023. Accepted for publication Apr 07, 2024. Published online Jun 27, 2024.
doi: 10.21037/jgo-23-692
View this article at: https://dx.doi.org/10.21037/jgo-23-692

Introduction

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms in terms of their anatomical location, clinical presentation and histological characteristics. Although duodenal neuroendocrine tumors (D-NETs) comprise only 2–3 % of all gastrointestinal (GI) NETs, their incidence has increased in the past few decades, possibly as a result of the increasing use of GI endoscopy (1-3).

According to their anatomical location, D-NETs are categorized into ampullary duodenal NETs (AD-NETs) and nonampullary duodenal NETs (NAD-NETs). Compared with AD-NETs, NAD-NETs are smaller in

volume, have a lower malignancy rate and are associated with a better prognosis at the time of diagnosis (4,5). Endoscopic resection (ER) techniques, such as endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), are currently recommended by European Neuroendocrine Tumor Society guidelines for removing NAD-NETs smaller than 10 mm that do not penetrate the muscularis propria and without lymph node or distant metastasis (6). As endoscopic treatment technology improves, the number of reports on ER for NAD-NETs has increased (7-12). These less invasive, less expensive, and less traumatic therapies also offer the patient a better postoperative quality of life than conventional surgery (13,14). Since there are only a few published studies on a very small number of patients, the aim of our study was to assess the efficacy, safety and long-term prognosis of ER for NAD-NETs. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-692/rc).

Methods

Patients and lesions

Between November 2011 and April 2021, EMR or ESD was performed on 12 lesions in 12 patients with NAD-NETs at the Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China. Patients were divided into two groups according to operation methods. Related data of the patients and lesions collected from our clinical and endoscopic databases were analyzed, as well as ongoing long-term follow-up. The exclusion criteria were as follows: (I) missing or incomplete patient information; (II) tumors removed using biopsy forceps and simple polypectomy; Because it is hard to accurately evaluate the margin, invasion depth, and lymphovascular or perineural invasion of specimens removed by these two techniques; (III) tumors removed by radical surgery; and (IV) muscularis propria invasion or lymph node or distant metastasis confirmed before the endoscopic procedure. Endoscopic ultrasonography (EUS), abdominopelvic computed tomography (CT) or somatostatin receptor scintigraphy (SRS) was used to exclude muscularis invasion as well as lymph node or distant metastasis before the procedure. The choice of technique was made at the discretion of the attending endoscopist. All patients were informed of the risks and benefits of the endoscopic treatment, and all provided written informed consent to undergo EMR or ESD. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by our institutional review board (No. 24/171-4451). Because of the retrospective nature of the study, the requirement for informed consent for the publication of details relating to the patients was waived.

Endoscopic procedures

All NAD-NETs were detected using GI endoscopy. A conventional single-channel endoscope (GIF-Q260J, Olympus, Tokyo, Japan) was used to visualize the lesion. Marking dots were made on the circumference of the lesion by using an electrocautery hook knife (Olympus, Tokyo, Japan). A solution (normal saline, mixed with a small amount of indigo carmine) was injected into the submucosal layer to make a mucosal bleb. For EMR, an additional submucosal injection was carried out beneath the tumor, the adequately lifted lesion was ensnared and resected by using an electrosurgical current (*Figures 1-4*). For ESD, following solution injection, the lesion was incised (precut) along the outer border of the marking dots and then dissected along the submucosal plane under direct vision (*Figures 5-8*). The specimens were carefully evaluated histopathologically by experienced pathologist in slices collected at two mm intervals.

Highlight box

Key findings

- Our study found that for nonampullary duodenal neuroendocrine tumors (NAD-NETs) that measure ≤10 mm in size, are confined to the submucosal layer and have neither suspicious lymph nodes nor distant metastasis, endoscopic resection [ER; endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD)] may be a safe, effective, and feasible endoscopic technique for removing them. This discovery can provide comprehensive guidance for clinical treatment decisions of NAT-NETs.

What is known and what is new?

- ER (ESD and EMR) is recommended for NAD-NETs ≤10 mm in diameter without lymphovascular invasion. However, the efficacy and safety of ER for NAD-NETs remains unclear.
- In NAD-NETs treated by ER, the rates of en bloc, complete and pathologic complete resection were sufficiently high. Intraoperative perforation occurred in one case, but no emergency surgery was needed. ER is an efficacious and safe treatment for NAD-NETs.

What is the implication, and what should change now?

- NAD-NET is a rare disease with malignant tendency and more exploration is needed.

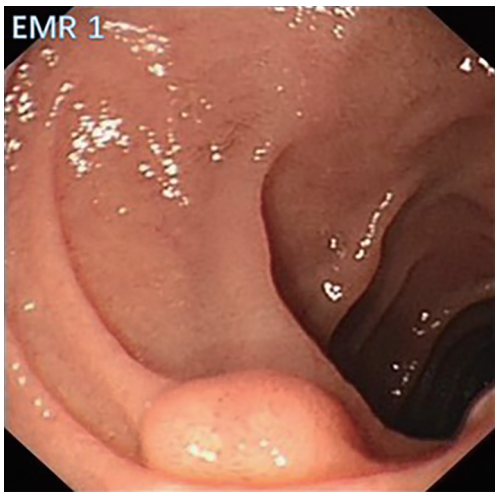

Figure 1 A 5 mm nodular lesion was located at descending duodenum. EMR, endoscopic mucosal resection.

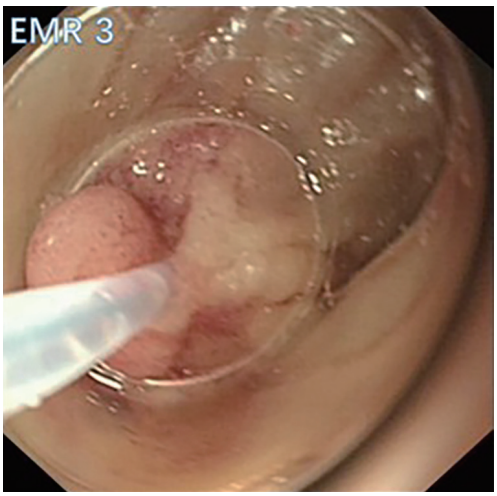

Figure 3 After submucosal injection, the lesion is sucked into the cap, as the snare is closed at the base of the lesion. EMR, endoscopic mucosal resection.

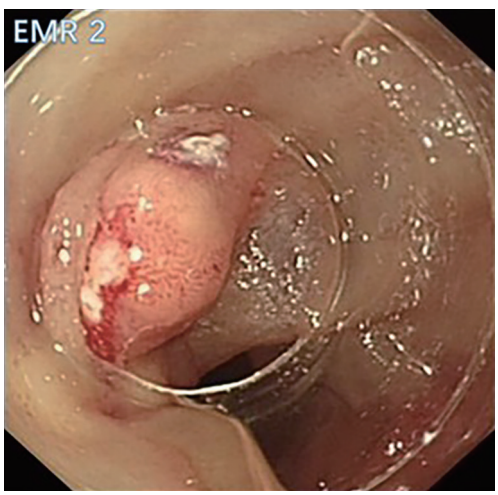

Figure 2 Endoscopic marking was performed and submucosal injection was performed from the oral side. EMR, endoscopic mucosal resection.

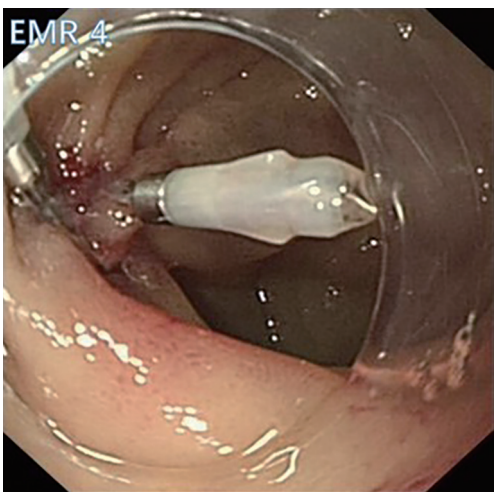

Figure 4 Use titanium clips to close the defect caused by endoscopic mucosal resection. EMR, endoscopic mucosal resection.

Histopathological evaluation and complications

Resected specimens, fixed with formalin, were serially sectioned at 2-mm intervals, and histopathologic type, depth of invasion, tumor involvement in the lateral and vertical margins, presence of lymphovascular invasion and perineural invasion was assessed. The classification of histological type was determined using the World Health Organization (WHO) 2019 classification of tumors of the digestive system (15). The Ki-67 index and mitotic rate was evaluated in all cases to classify tumors as G1, G2, or G3. En bloc resection was defined as the tumor being endoscopically resected entirely in one piece. Complete resection was defined as en bloc resection with no evidence of a tumor on both vertical and lateral margins upon histological examination. Pathological complete resection was defined as R0 resection with no lymphovascular invasion or perineural invasion. Complications related to

Figure 5 A 5 mm nodular lesion was located at duodenal bulb. Marking dots were made on the circumference of the lesion. ESD, endoscopic submucosal dissection.

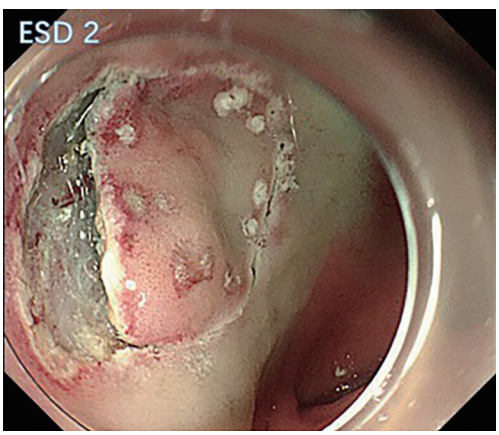

Figure 6 Submucosal injection was performed from the oral side. Mucosal incision was made using DualKnifeJ. ESD, endoscopic submucosal dissection.

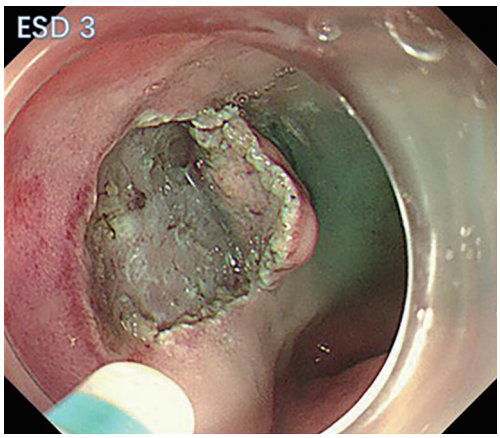

Figure 7 Partial circumferential incision can maintain higher elevation of the submucosa. It is easy to cut the residual mucosa. ESD, endoscopic submucosal dissection.

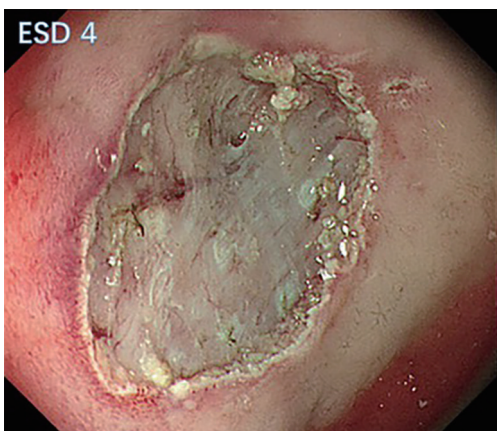

Figure 8 Endoscopic submucosal dissection (ESD) was completed without any complication. ESD, endoscopic submucosal dissection.

the procedure included intraoperative perforation, delayed perforation, intraoperative bleeding and delayed bleeding. Intraoperative perforation was defined as a defect of the whole duodenal wall; the surrounding tissues or organs could be seen through the hole during the procedure (Sydney score IV or V) (16). Delayed perforation was diagnosed when patients experienced a sudden onset of high fever accompanied by the presence of peritoneal or retroperitoneal free air on CT scans during a month after surgery. This diagnosis was made in cases where there was no evidence of intraoperative perforation and no signs of free air on CT scans immediately following tumor removal (17). Intraoperative bleeding was defined as bleeding that resulted in the patient needing a blood transfusion or bleeding that could not be controlled under endoscopy and resulted in the patient needing to undergo surgery or vascular embolization. Delayed bleeding was defined as clinical evidence of bleeding during the month following the resection leading to transfusion, new hospitalization, or a second-look endoscopy for hemostasis.

Follow up

All patients were followed-up by an EGD three and six

Table 1 Characteristics of patients and tumors

Characteristics	EMR (n=2)	ESD (n=10)
Age (years)	55.0±4.0	55.8±3.4
Sex		
Male	0 (0.0)	6 (60.0)
Female	2 (100.0)	4 (40.0)
Tumor location		
D1	1 (50.0)	9 (90.0)
D1–D2 junction	0 (0.0)	1 (10.0)
D2	1 (50.0)	0 (0.0)
Tumor size (mm)	6.0±1.0 [5–7]	6.4±0.7 [3–10]
≤10	2 (100.0)	10 (100.0)
>10	0 (0.0)	0 (0.0)
Invasion layer		
Mucosal	0 (0.0)	0 (0.0)
Submucosal	2 (100.0)	10 (100.0)
Pathological type		
G1	2 (100.0)	8 (80.0)
G2	0 (0.0)	2 (20.0)

Data are presented as n (%), mean ± SD or mean ± SD [range]. EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; SD, standard deviation; D1, duodenal bulb; D2, descending part of duodenum.

Table 2 Clinical outcomes of ER for NAD-NETs

Outcomes	EMR (n=2)	ESD (n=10)
Procedure time (min)		
Mean ± SD	44.0±10.0	66.8±14.1
Range	34–54	32–182
Specimen size, mean ± SD (mm)	8.5±1.5	15.7±1.1
En bloc resection, n (%)	2 (100.0)	9 (90.0)
Complete resection, n (%)	1 (50.0)	8 (80.0)
Pathologic complete resection, n (%)	1 (50.0)	8 (80.0)
Lateral margin involvement	0 (0.0)	0 (0.0)
Vertical margin involvement	1 (50.0)	2 (20.0)
Lymphovascular invasion	0 (0.0)	0 (0.0)
Perineural invasion	0 (0.0)	0 (0.0)
Complication, n (%)		
Intraoperative perforation	0 (0.0)	1 (10.0)
Delayed perforation	0 (0.0)	0 (0.0)
Intraoperative bleeding	0 (0.0)	0 (0.0)
Delayed bleeding	0 (0.0)	0 (0.0)
Follow-up duration (months)		
Median	127	46
Range	123–131	18–88
Local recurrence	0 (0.0)	0 (0.0)
Distant metastatic lesions	0 (0.0)	0 (0.0)

ER, endoscopic resection; NAD-NETs, nonampullary duodenal neuroendocrine tumors; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; SD, standard deviation.

months after surgery and an annual EGD or CT check for local recurrence, lymph node and distant metastases. Follow up was through outpatient or telephone visits. The starting point of follow-up was the end of surgical treatment for NAD-NETs patients, and the last follow-up was in October 2022.

Statistical analysis

Statistical analyses were performed using a statistical software package (SPSS version 27.0; SPSS Inc., Chicago, IL, USA). Continuous variables were presented as medians and ranges, and categorical variables are presented as percentages.

Results

During the study period, we treated 12 lesions using ER (EMR, 2; ESD, 10) and all of them were included in the study. The patients' and tumors' clinicopathological characteristics are summarized in *Table 1*. Ten of the twelve tumors (83.3%) were located in D1 (duodenal bulb), one was located in D2 (descending part of duodenum) (ESD group), and one was located in D1-D2 junction (EMR group). The sizes of the tumors were 6.0±1.0 mm (range, 5–7 mm) and 6.4±0.7 mm (range, 3–10 mm) in the two groups. All tumors were confined to the submucosal layer. Two of the 12 tumors (16.7%) were in the G2 stage (both in the ESD group).

Table 2 shows the clinical outcomes of ER for NAD-NETs. The procedure time in the two groups was 44.0±10.0 min (range, 34–54 min) and 66.8±14.1 min (range, 32–182 min) respectively. The en bloc, complete and pathologic

Table 3 Clinicopathological characteristics of patients with NAD-NETs who underwent ER

No. sex/ age (years)	Tumor location/ size (mm)	Treatment technique	Tumor depth/ pathological morphology	En bloc resection	Margin involvement	Lymphovascular invasion or perineural invasion	Complication	Remnant lesion, recurrence or distant metastasis	Additional treatment	Follow-up duration (months)
#1. F/59	D1/7	EMR	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	131
#2. F/51	D1–D2/5	EMR	SM/G1	Yes	LM(–)/VM(+)	(–)	No	No	No	123
#3. M/50	D1/3	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	88
#4. M/68	D1/4	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	74
#5. F/60	D1/7	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	62
#6. F/40	D1/5	ESD	SM/G2	Yes	LM(–)/VM(–)	(–)	No	No	No	56
#7. M/75	D1/10	ESD	SM/G2	Yes	LM(–)/VM(+)	(–)	Intraoperative perforation	No	No	50
#8. M/63	D1/8	ESD	SM/G1	No	LM(–)/VM(+)	(–)	No	No	No	42
#9. M/47	D1/9	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	34
#10. F/54	D1/7	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	22
#11. F/54	D2/5	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	20
#12. M/47	D1/6	ESD	SM/G1	Yes	LM(–)/VM(–)	(–)	No	No	No	18

NAD-NETs, nonampullary duodenal neuroendocrine tumors; ER, endoscopic resection; F, female; M, male; D1, duodenal bulb; D2, descending part of duodenum; D1–D2, D1–D2 junction; EMR, endoscopic mucosal resection; SM, submucosa; LM, lateral margin; VM, vertical margin; ESD, endoscopic submucosal dissection.

complete resection rates were 100.0%, 50.0%, and 50.0% in the EMR group and 90.0%, 80.0%, and 80.0% in the ESD group, respectively. Intraoperative perforation occurred in 1 patient during ESD treatment. Closure using endoscopic clips was performed immediately after removing the tumor, and emergency surgery was prevented. There was no intraoperative or delayed bleeding in either group.

Table 3 shows the details of patients with NAD-NETs who underwent ER. During the median follow-up period of 127.0 months (range, 123–131 months) in the EMR group and 46 months (range, 18–88 months) in the ESD group, no remnant lesion, local recurrence or distant metastasis was found.

Discussion

In the early stage, NAD-NETs develop mainly in the submucosal layer and are often diagnosed using endoscopic biopsy when they are small and may not be related to the patient's symptoms (18). Surgery has been the mainstream treatment of NAD-NETs for a long time. However, with continuous progress in endoscopic diagnosis and treatment technology, the endoscopic treatment of NAD-NETs has gradually gained increasing interest (1,19). Our research has indicated that ER for NAD-NETs can achieve significant therapeutic effects with low incidence of complications.

When choosing the optimal treatment for NAD-NETs, the presence of lymph node or distant metastasis is one of the most important considerations. Although no consensus has been reached, it has been reported that the risk factors for the metastasis of NAD-NETs are tumors >10 mm in diameter, muscular invasion, poorly differentiated neuroendocrine histology, and lymphovascular invasion (20,21). Nakao *et al.* found that a tumor size ≥10 mm, positive lymphovascular invasion, and 0–Is morphology were significant risk factors for lymph node metastasis (22). A recent study assessing risk factors for metastases in nonampullary lesions <20 mm in size revealed lymphovascular invasion, tumor size >11 mm and WHO G2 as risk factors for metastatic disease (23). Therefore, patients with NAD-NETs smaller than 10 mm that do not penetrate into the muscularis propria and without lymph node or distant metastasis are candidates for ER (6,10,24). In this study, all included tumors met this condition, and the pathologic complete resection rate reached 75%. Even when the three patients with positive margins were

included, no recurrence or metastasis was found during follow-up.

Complete resection is ideal for the ER of NAD-NETs. Different endoscopic treatment techniques, such as EMR and ESD, are used in the treatment of NAD-NETs, but there is no consensus on the treatment of choice. In the present study, we determined the efficacy of EMR and ESD for resecting NAD-NETs. Both groups achieved high rates of en bloc resection, with a success rate of 100% in the EMR group and 90% in the ESD group. However, the EMR group did not achieve perfect complete resection rate and pathological complete resection rate due to one case showing a positive vertical margin, whereas the ESD group had two such cases. Previous studies have also investigated similar topics. Lee *et al.* described 50 patients with 50 D-NETs treated using EMR-D (n=19), EMR-L (n=16), EMR-C (n=6), EMR-P (n=5), or ESD (n=4). In their study, the en bloc resection rates in the EMR-D, EMR-L, EMR-C, EMR-P and ESD groups were 73.7%, 100%, 100%, 100% and 75%, respectively, while the complete resection rates were 84.2%, 93.8%, 100%, 100% and 100% (13). A study in Korea in 2014 also showed that ESD was superior to EMR, EMR-L or EMR-P, as evidenced by the en bloc resection rate or the complete resection rate (9). Other studies that focused on the efficacy of ESD also showed its effectiveness in treating NAD-NETs (8,10,12). Surprisingly, these results were more favorable than the previously reported results for NETs in other locations, such as the stomach or rectum (25-27). The reasons were as follows: the NETs were mostly located in the submucosal layer. Although submucosal injection is performed during EMR, the submucosal part of the tumor is unable to be seen in the visual field. The depth of resection cannot be guaranteed during resection, and the size of the resectable lesion is limited by the use of a snare or ligation device for snare resection of the whole lesion, resulting in a positive margin. Furthermore, too much pursuit of resection depth will increase the risk of perforation. In contrast, ESD enables us to complete the dissection of the submucosal part of the lesion under direct vision with clear vision and an appropriate resection depth.

We also assessed the complications occurring during ER for NAD-NETs. Only one patient (8.3%) treated with ESD in our study developed intraoperative perforation. However, because of their thin and rich vascular duodenal wall and difficult access, ER for D-NETs is challenging (28). Gincul *et al.* reported 32 D-NETs treated using EMR (11). The overall complication rate was 38%; bleeding occurred in nine patients, perforation occurred in in two patients, and procedure-related death occurred in one patient. Suzuki *et al.* reported the outcomes of ESD in three D-NET patients (12). The R0 resection rate was 98%, but the perforation rate of duodenal ESDs was 66%. While the use of therapeutic scope can enhance surgeons' operating angles and provide clearer surgical perspectives to some extent, it is crucial to note that these procedures are primarily recommended for experienced endoscopists in high-volume centers with ample resources. Some relatively new devices or technologies are gradually playing an increasingly important role in the safe resection of duodenal tumors. A grasping forceps can be used in conjunction with a double-channel scope to provide counter traction during ESD. Another option is to utilize the outer sheath of an injection needle for counter traction. By pushing and lifting up the bottom of the dissected mucosal layer using the injection sheath, the submucosal layer is revealed and adequate counter traction of the cutting lines is ensured (29). The main advantage of the double-channel scope method is that it only requires a conventional grasping forceps or injection sheath. However, this method has a thicker size and longer radius of curvature, which can be considered as a disadvantage. Furthermore, it may sometimes be challenging to insert it into the submucosal layer, and its maneuverability is poorer compared to a thin therapeutic scope during ESD. Endoscopic full-thickness resection (EFTR) with a full-thickness resection devise for duodenal tumors has been successfully used in the resection of duodenal neoplasias. Although its effectiveness needs to be further confirmed, it seems to be an ideal resection tool for these tumors that originate deep within the submucosa, such as small NAD-NETs (30,31). The laparoscopic and endoscopic cooperative surgeries (LECS) concept has also been rapidly accepted for the treatment of GI tumors due to its effectiveness and safety (32,33), which have been indicated in several case reports (34-36). There is still room for improvement to lessen its technical difficulty. Advances in treatment techniques and skills can potentially reduce the complication rates in the future. However, a further understanding of these lesions and studies with a large cumulative number of patients are also required.

The final point to discuss is the prognostic value of ER for NAD-NETs. In the present study, there were three patients with positive vertical margins, one in whom we did not achieve en bloc resection. After explaining to the patient and their families the greater difficulty of the second endoscopic surgery, the higher risk of perforation, and the possible negative postoperative pathology, none of

the three patients chose to receive additional surgery, and no residual tumor, recurrence or distant metastasis were found in any of the 12 patients during the median follow-up period of 53.0 months. At present, the natural history and clinical ramifications of D-NETs are poorly understood. Some scholars believe that D-NETs have the characteristic of indolent growth, and their prognosis is much better than that of other small bowel NETs (37). Exarchou *et al.* also claimed that for localized, grade 1, nonfunctioning NAD-NETs ≤10 mm in diameter, the 'watch and wait' strategy may be a safe alternative management strategy (38). Therefore, considering the independent biological behavior of NETs, we believe that margin involvement does not directly imply the presence of a residual tumor, and the presence of lymphovascular invasion and perineural invasion does not imply the need for additional surgery (39). Of course, continuous follow-up and monitoring are still essential and useful.

The purpose of this study was to clarify the efficacy and safety of ER for NAD-NETs. As for the single-center study, to our knowledge, we included the largest number of patients who underwent ESD for NAD-NETs, which increases the validity of the research. The limitations of our study include the following. First, this was a single-center retrospective study that included patients who were treated more than 10 years ago. Second, the number of patients in each group was small (only two patients in the EMR group), which would cause bias. Third, this was an observational study. Due to the rarity of D-NETs, multicenter studies and larger population-based datasets are needed to further validate these guidelines.

Conclusions

In conclusion, the results of our study suggest that ER (EMR and ESD) may be a safe, effective, and feasible endoscopic technique for removing NAD-NETs measuring ≤10 mm in size confined to the submucosal layer. Lymph node metastasis and distant metastasis were not found on preoperative imaging examinations. ESD seems to have a higher complete resection rate and pathologic complete resection rate than EMR. Close follow-up can be selected depending on the situation rather than immediate radical secondary surgery when a lesion is not completely resected. Further large-scale, prospective, randomized, and well-designed studies with long-term clinical outcomes are needed to validate our findings.

Acknowledgments

Funding: The study was supported by the CAMS Innovation Fund for Medical Sciences (CIFMS) (grant Nos. 2021-I2M-1-061, 2021-I2M-1-013, 2021-I2M-1-015, and 2022-I2M-C&T-B-054), Sanming Project of Medicine in Shenzhen (No. SZSM201911008), Capital's Funds for Health Improvement and Research (grant No. CRF2020-2-4025), and Beijing Hope Run Special Fund of Cancer Foundation of China (grant No. LC2021A03).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-692/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-692/dss

Peer Review File: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-692/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-692/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective study was approved by our institutional review board (No. 24/171-4451). Because of the retrospective nature of the study, the requirement for informed consent for the publication of details relating to the patients was waived.

References

1. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer 2003;97:934-59.
2. Yao JC, Hassan M, Phan A, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol 2008;26:3063-72.
3. Fraenkel M, Kim MK, Faggiano A, et al. Epidemiology of gastroenteropancreatic neuroendocrine tumours. Best Pract Res Clin Gastroenterol 2012;26:691-703.
4. Randle RW, Ahmed S, Newman NA, et al. Clinical outcomes for neuroendocrine tumors of the duodenum and ampulla of Vater: a population-based study. J Gastrointest Surg 2014;18:354-62.
5. Dumitrascu T, Dima S, Herlea V, et al. Neuroendocrine tumours of the ampulla of Vater: clinico-pathological features, surgical approach and assessment of prognosis. Langenbecks Arch Surg 2012;397:933-43.
6. Delle Fave G, O'Toole D, Sundin A, et al. ENETS Consensus Guidelines Update for Gastroduodenal Neuroendocrine Neoplasms. Neuroendocrinology 2016;103:119-24.
7. Karagiannis S, Eshagzaiy K, Duecker C, et al. Endoscopic resection with the cap technique of a carcinoid tumor in the duodenal bulb. Endoscopy 2009;41 Suppl 2:E288-9.
8. Matsumoto S, Miyatani H, Yoshida Y, et al. Duodenal carcinoid tumors: 5 cases treated by endoscopic submucosal dissection. Gastrointest Endosc 2011;74:1152-6.
9. Kim GH, Kim JI, Jeon SW, et al. Endoscopic resection for duodenal carcinoid tumors: a multicenter, retrospective study. J Gastroenterol Hepatol 2014;29:318-24.
10. Nishio M, Hirasawa K, Ozeki Y, et al. Short- and long-term outcomes of endoscopic submucosal dissection for non-ampullary duodenal neuroendocrine tumors. Ann Gastroenterol 2020;33:265-71.
11. Gincul R, Ponchon T, Napoleon B, et al. Endoscopic treatment of sporadic small duodenal and ampullary neuroendocrine tumors. Endoscopy 2016;48:979-86.
12. Suzuki S, Ishii N, Uemura M, et al. Endoscopic submucosal dissection (ESD) for gastrointestinal carcinoid tumors. Surg Endosc 2012;26:759-63.
13. Lee SW, Sung JK, Cho YS, et al. Comparisons of therapeutic outcomes in patients with nonampullary duodenal neuroendocrine tumors (NADNETs): A multicenter retrospective study. Medicine (Baltimore) 2019;98:e16154.
14. Dasari BVM, Al-Shakhshir S, Pawlik TM, et al. Outcomes of Surgical and Endoscopic Resection of Duodenal Neuroendocrine Tumours (NETs): a Systematic Review of the Literature. J Gastrointest Surg 2018;22:1652-8.
15. Nagtegaal ID, Odze RD, Klimstra D, et al. The 2019 WHO classification of tumours of the digestive system. Histopathology 2020;76:182-8.
16. 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;66:1779-89.
17. Inoue T, Uedo N, Yamashina T, et al. Delayed perforation: a hazardous complication of endoscopic resection for non-ampullary duodenal neoplasm. Dig Endosc 2014;26:220-7.
18. Scherübl H, Jensen RT, Cadiot G, et al. Neuroendocrine tumors of the small bowels are on the rise: Early aspects and management. World J Gastrointest Endosc 2010;2:325-34.
19. Scherübl H, Cadiot G. Early Gastroenteropancreatic Neuroendocrine Tumors: Endoscopic Therapy and Surveillance. Visc Med 2017;33:332-8.
20. Hoffmann KM, Furukawa M, Jensen RT. Duodenal neuroendocrine tumors: Classification, functional syndromes, diagnosis and medical treatment. Best Pract Res Clin Gastroenterol 2005;19:675-97.
21. Soga J. Early-stage carcinoids of the gastrointestinal tract: an analysis of 1914 reported cases. Cancer 2005;103:1587-95.
22. Nakao E, Namikawa K, Hirasawa T, et al. Risk factors for lymph node metastasis and indication of local resection in duodenal neuroendocrine tumors. JGH Open 2022;6:189-95.
23. Hatta W, Koike T, Iijima K, et al. The Risk Factors for Metastasis in Non-Ampullary Duodenal Neuroendocrine Tumors Measuring 20 mm or Less in Diameter. Digestion 2017;95:201-9.
24. Valli PV, Mertens JC, Sonnenberg A, et al. Nonampullary Duodenal Adenomas Rarely Recur after Complete Endoscopic Resection: A Swiss Experience Including a Literature Review. Digestion 2017;96:149-57.
25. Kim HH, Kim GH, Kim JH, et al. The efficacy of endoscopic submucosal dissection of type I gastric carcinoid tumors compared with conventional endoscopic mucosal resection. Gastroenterol Res Pract 2014;2014:253860.
26. Lee DS, Jeon SW, Park SY, et al. The feasibility of endoscopic submucosal dissection for rectal carcinoid tumors: comparison with endoscopic mucosal resection.

Endoscopy 2010;42:647-51.
27. Zhang J, Liu M, Li H, et al. Comparison of endoscopic therapies for rectal carcinoid tumors: Endoscopic mucosal resection with circumferential incision versus endoscopic submucosal dissection. Clin Res Hepatol Gastroenterol 2018;42:24-30.
28. Basford P, Bhandari P. Endoscopic resection of sporadic duodenal neuroendocrine tumors: Why is this not so easy? Endoscopy 2016;48:965-6.
29. Oyama T. Counter traction makes endoscopic submucosal dissection easier. Clin Endosc 2012;45:375-8.
30. Bauder M, Schmidt A, Caca K. Endoscopic full-thickness resection of duodenal lesions-a retrospective analysis of 20 FTRD cases. United European Gastroenterol J 2018;6:1015-21.
31. Al-Bawardy B, Rajan E, Wong Kee Song LM. Over-the-scope clip-assisted endoscopic full-thickness resection of epithelial and subepithelial GI lesions. Gastrointest Endosc 2017;85:1087-92.
32. Hiki N, Yamamoto Y, Fukunaga T, et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. Surg Endosc 2008;22:1729-35.
33. Niimi K, Ishibashi R, Mitsui T, et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal tumor. Ann Transl Med 2017;5:187.
34. Yorimitsu N, Oyama T, Takahashi A, et al. Laparoscopy and endoscopy cooperative surgery is a safe and effective novel treatment for duodenal neuroendocrine tumor G1. Endoscopy 2020;52:E68-70.
35. Nagasawa Y, Okauchi H, Kojima M, et al. Laparoscopic-endoscopic cooperative surgery for a duodenal neuroendocrine tumor: A case report. Asian J Endosc Surg 2017;10:183-6.
36. Tsushimi T, Mori H, Harada T, et al. Laparoscopic and endoscopic cooperative surgery for duodenal neuroendocrine tumor (NET) G1: Report of a case. Int J Surg Case Rep 2014;5:1021-4.
37. Fitzgerald TL, Dennis SO, Kachare SD, et al. Increasing incidence of duodenal neuroendocrine tumors: Incidental discovery of indolent disease? Surgery 2015;158:466-71.
38. Exarchou K, Moore AR, Smart HL, et al. A "Watch and Wait" Strategy Involving Regular Endoscopic Surveillance Is Safe for Many Patients with Small, Sporadic, Grade 1, Non-Ampullary, Non-Functioning Duodenal Neuroendocrine Tumours. Neuroendocrinology 2021;111:764-74.
39. Cha B, Shin J, Ko WJ, et al. Prognosis of incompletely resected small rectal neuroendocrine tumor using endoscope without additional treatment. BMC Gastroenterol 2022;22:293.

Cite this article as: Li W, Liu Y, Dou L, He S, Zhang Y, Ke Y, Liu X, Wang G. Treatment outcomes of endoscopic resection for nonampullary duodenal neuroendocrine tumors. J Gastrointest Oncol 2024;15(3):1255-1264. doi: 10.21037/jgo-23-692

