


Low recurrence rate after endoscopic resection in non-ampullary duodenal lesions

A 16-year single-center retrospective study

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Abstract

Endoscopic resection (ER) for non-ampullary duodenal lesions (NADLs) is technically more difficult than lesions of the stomach. However, endoscopic treatment of duodenal lesions has been increasingly performed in recent years. This study aimed to evaluate the efficacy and safety of ER for NADLs.

Patients who underwent ER for NADLs between 2004 and 2019 were retrospectively reviewed. Clinical and pathologic features of the lesions including the clinical outcomes and adverse events were analyzed.

The study included 80 patients with NADLs. The mean age of patients was 59.3 years (22–80 years), the mean size of the lesion was 8.8 ± 7.0 mm, and the mean procedure time was 13.2 ± 11.2 min. Half (40/80) of the lesions were in the duodenal bulb including the superior duodenal angle. Final histological data showed 56 adenomas (70.5%), 13 Brunner gland tumors (16.2%), and 4 pyloric gland tumors (5.0%). The final diagnoses of 5 lesions after ER showed higher-grade dysplasia compared to pre-ER biopsy findings. The en bloc resection rate was 93.8% (75/80), and the complete resection rate with clear margins was 90.0% (72/80). Micro-perforation occurred in 2 of 80 patients and was successfully treated with conservative treatment. There were no cases of delayed bleeding. The mean follow-up period was 27.0 months (2–119 months) with no cases of recurrence.

ER may be an effective treatment for NADLs with favorable long-term outcomes. However, the possibility of perforation complications should always be considered during ER.

Abbreviations: EMR = endoscopic mucosal resection, ER = endoscopic resection, ESD = endoscopic submucosal dissection, EUS = endoscopic ultrasonography, FAP = familial adenomatous polyposis, NADL = non-ampullary duodenal lesion, SD = standard deviations, UEMR = underwater endoscopic mucosal resection.

Keywords: duodenal lesion, endoscopic resection, perforation

1. Introduction

The diagnosis of duodenal lesions has increased with the increasing number of esophagogastroduodenoscopy for screen-

ing. Based on previous reports, approximately 5% of duodenal polyps were identified during endoscopy, and only 7% of them were diagnosed as adenomas.^[1,2] In a previous study about endoscopic resection (ER) of non-ampullary duodenal lesions (NADLs), adenoma was diagnosed in 68%, Brunner gland hyperplasia in 21%, and adenocarcinoma in 1%.^[3] However, ER of NADLs remains complicated due to the following reasons: 1. the anatomical location is narrow and fixed. 2. the lesion is difficult to be seen in the front view. 3. mucosal lifting is more difficult because Brunner glands are in the submucosal layer. 4. the incidence of perforation and other complications such as delayed bleeding and delayed perforation is higher because the muscle layer is thin.^[4–6] Despite these difficulties, several institutions have performed ER on NADLs.^[7,8]

In previous studies, ER can be performed instead of surgery, but safety has been the main concern. In addition, there have been many studies comparing endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) concerning efficacy and safety. However, there have been few studies investigating recurrence rates after ER. This study was conducted to determine the success, recurrence, and safety rates of ER. This study tried to confirm the efficacy of ER of NADLs and efficacy was defined as the percentage of cases with no remaining lesions and no recurrence. In addition, we analyzed the cases that should be noted after ER: remaining tissue at the resected margin, the higher biopsy result than expected, and side effects.

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GMO and HSJ contributed equally to this work.

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2. Materials and methods

2.1. Patients

The medical records of all patients who underwent ER for NADLs at a single tertiary hospital (Kosin University Gospel Hospital) in South Korea during the period from January 2004 to June 2019 were reviewed. Patients with a history of familial adenomatous polyposis (FAP) and previous resection for duodenal neoplasm were excluded. Medical records of all persons who undergoing ER clinically were investigated. The characteristics of included patients such as age, sex, tumor location, tumor size, tumor morphology, pre-ER histology, final histology, procedure time, follow-up duration, and complications were collected. The study protocol was approved by the Institutional Review Board of the Kosin University Gospel Hospital (2019-10-015).

2.2. ER procedures

All ER procedures were performed with the patient under intravenous sedation using midazolam or propofol. Intravenous scopolamine (20 mg) was given for intestinal relaxation, and intravenous pethidine was given to control pain. All duodenal ER procedures were performed by 4 experienced endoscopists. Therapeutic gastroscopes (GIF-Q260, GIF-H260, GIF-H290, Olympus Tokyo, Japan), and an endoscopic knife (dual knife, Insulated Tip-2 knife, Olympus, Tokyo, Japan), and snare (Olympus, Tokyo, Japan) were used during the procedures.

The method of ER was decided based on the tumor size, macroscopic morphology, and the endoscopist's preference. Pre-resection endoscopic ultrasonography (EUS) was not performed routinely. When endoscopic findings (white light imaging, narrow-band imaging) were not found as the typical mucosal lesions by the endoscopist, EUS was performed to make sure this is a mucosal lesion. Duodenal EMR was performed by submucosal injection of saline with diluted epinephrine (1:10,000) and 1% indigo carmine, and subsequent resection with standard polypectomy snares. Duodenal ESD was performed by submucosal injection following a circumferential incision and dissection using knives and an electrosurgical unit (ERBE, Tubingen, Germany). Prophylactic clipping (EZ clip, Olympus, Japan, Resolution, Boston Scientific, Marlborough, MA, USA) was performed for post-procedure ulcers to reduce the risk of delayed bleeding and also for preventing delayed perforation depending on the location, size, and endoscope stability.

2.3. Histopathological evaluation and post-procedure care

The resected specimens were fixed in 10% buffered formalin and cut into 2 mm slices. The histopathologic type, size, vertical and horizontal margins, and depth of invasion were evaluated. All adenomas were classified into low- or high-grade dysplasia according to the highest-grade cell in the tumor. The classification was followed by WHO dysplasia classification in 2000.^[9]

After ER, patients were not permitted oral intake for at least 48 hours. They were closely monitored for bleeding or perforation which were procedure-related adverse events after ER. All patients underwent a second-look endoscopy to check for delayed bleeding or perforation on the second day following ER. ER-associated bleeding was defined as bleeding that required transfusions, endoscopic intervention, or surgical intervention and was categorized into intra-procedural bleeding and post-procedural bleeding (delayed bleeding). Perforation was classified

as frank perforation and micro-perforation. Frank perforation was defined as an intra-abdominal space or duodenal wall hole defect that can be directly observed during the procedure. Micro-perforation was defined as free air found on a plain chest or abdomen radiography after the procedure.

Following the procedures, all patients received proton pump inhibitors for 3 days intravenously and it was maintained for 4–8 weeks orally. Endoscopic follow-up was carried out in all patients 6–12 weeks after ER to confirm the healing of the post-procedural ulceration. Then, consecutive follow-up was conducted once a year. Biopsies were performed during follow-up endoscopy in case of suspected residual/recurrent adenoma.

2.4. Statistical analyses

Continuous variables were compared using Mann–Whitney *U* test. Categorical variables were compared using Fisher exact test because the number of cases was small and the continuous values were not normally distributed. Statistical significance was based on 95% confidence ($P < 0.05$). All analyses were performed using SPSS software (version 24; IBM, Armonk, NY). Continuous data are expressed as the means \pm standard deviations (SDs) or medians with ranges and categorical data are presented as proportions.

2.5. Definition of term

The efficacy of ER was defined as the ratio of no residual tumor and no recurrence. Pre-ER biopsy was defined as forceps biopsy performed when the NADL was first discovered. The final diagnosis was defined as the diagnosis confirmed by the pathologist after ER. En bloc resection was defined as the resection of NADL in a single piece. Piecemeal resection refers to a resection when the lesion could not be cut out at once so that it was cut into more than 2 pieces. Completed resection (R0 resection) was defined as en bloc resection with no residual tumor at the resection margin. Uncompleted resection (non-R0 resection) was defined when the lesions were removed through the piecemeal method or the remnant tumor at the resection margin was present.

3. Results

3.1. Patient characteristics

Eighty-three patients who received ER for NADLs were included. Three were excluded as FAP, and a total of 80 were enrolled in this study. The mean age of the included patients was 59.3 years (Table 1). The first portion of the duodenum was the most common location ($n = 40$, 50.0%) and the mean lesion size was 8.8 mm at the longest diameter. Regarding the morphologic classification based on Paris classification, type Is was the most common type ($n = 56$, 64.4%).^[10]

3.2. Discordance of pathology between forceps biopsy and ER specimen

Duodenal adenoma accounted for 68.7% of the pre-ER biopsies (Table 2). After ER, the portion of adenoma increased to 70.0% at the final diagnosis. Only 1 patient was diagnosed with Brunner gland tumor before ER, but 13 patients were diagnosed with Brunner gland tumor after ER. Nine patients were considered to have chronic duodenitis in the pre-ER biopsy test, but only 1 patient was diagnosed after the procedure.

Table 1
Baseline characteristics of patients with non-ampullary duodenal lesions.

Variables	
Patients, n	80
Age, years, mean ± SD* (range)	59.3 ± 10.9 (22 to 80)
Sex, n (%)	
Male	53 (66.3)
Female	27 (33.7)
Location in duodenum, n (%)	
First part	40 (50.0)
Second part	36 (45.0)
Third part	4 (5.0)
Tumor size, mm, mean ± SD	8.8 ± 7.0
Paris classification, n (%)	
Ip	10 (12.5)
Isp	7 (8.7)
Is	50 (62.5)
Ila	10 (12.5)
Ila + Ilc	3 (3.8)

*SD = standard deviation.

Five patients had higher-grade dysplasia at the final diagnosis. One patient was diagnosed with tubular adenoma with high-grade dysplasia in forceps biopsy, but was finally diagnosed with adenocarcinoma after resection; the other 4 patients were diagnosed with adenoma with low-grade dysplasia, but finally confirmed as high-grade dysplasia. None of the cases showed a better diagnosis after the ER than at the initial biopsy.

3.3. Clinical outcome and complication of ER

Duodenal EMR was performed on 72 of 80 patients (Table 3), and 1 patient underwent underwater EMR (UEMR). The average procedure time was 13.1 minutes, en bloc resection was performed in 75 cases (93.8%), and piecemeal resection was performed in 5 cases (6.2%). Additional coagulation was required in 7 cases, and prophylactic clipping was performed in 75 cases. Three cases had microscopic remnant tumor at the horizontal margin, but none of the cases had microscopic

Table 2
Histopathological results and discrepancy after endoscopic resection (n = 80).

	Pre-ER* biopsy diagnosis, n (%)	Final diagnosis, n (%)
Duodenal adenoma	55 (68.7)	56 (70.0)
Tubular	55	53
Tubulovillous	0	2
Villous	0	1
Brunner gland tumor	1 (1.3)	13 (16.2)
Hamartoma/adenoma	0	10
Hyperplasia	1	3
Pyloric gland adenoma	1 (1.3)	4 (5.0)
Papillary hyperplasia	1 (1.3)	0
Chronic duodenitis	9 (11.2)	1 (1.3)
Hyperplastic polyp	3 (3.7)	4 (5.0)
Adenocarcinoma	0	2 (2.5)
Not performed	10 (12.5)	0

*ER = endoscopic resection.

Table 3
Short-term outcomes and complications of endoscopic resection (n = 80).

Outcomes	
EMR* : ESD†	72 (90):8 (10.0)
En bloc resection, n (%)	75 (93.8)
RO resection, n (%)	72 (90.0)
Procedure time, minutes, mean ± SD	13.1 ± 11.2
Additional coagulation, n (%)	7 (8.8)
Prophylactic clipping, n (%)	75 (93.8)
Horizontal margin, n (%) (n = 80)	
Negative	77 (96.2)
Positive	3 (3.8)
Vertical margin, n (%) (n = 80)	
Negative	80 (100)
Positive	0
Complications	
Bleeding, n (%)	0 (0)
Intra-procedural bleeding	0
Delayed bleeding	0
Perforation, n (%)	2 (2.3)
Frank perforation	0
Micro-perforation	2

*EMR = endoscopic mucosal resection.

†ESD = endoscopic submucosal dissection, SD = standard deviation.

remnant tumor at the vertical margin. There were 2 cases of micro-perforations, but there was no bleeding.

The EMR and ESD groups were compared (Table 4). The ESD group had a longer procedure time than the EMR group (P = .001), and RO resection was higher in the EMR group (P = .030). En bloc resection in the EMR group had a numerically higher success rate than the ESD group (95.8% and 75.0%, respectively) (P = .076). The clinical features of the complete

Table 4
Comparisons of the therapeutic outcomes between endoscopic mucosal resection and endoscopic submucosal dissection groups.

	EMR* (n = 72)	ESD† (n = 8)	P
Age, years, mean ± SD‡ (range)	59.0 ± 10.9	62.4 ± 10.6	.516
Sex, n (%)			.548
Male	48 (66.7%)	5 (62.5%)	
Female	24 (33.3%)	3 (37.5%)	
Tumor location, n (%)			.405
1st portion	35 (48.6%)	5 (62.5%)	
2nd portion	33 (45.8%)	3 (37.5%)	
3rd portion	4 (5.6%)	0	
Tumor size, mm, mean ± SD	8.4 ± 6.6	13.0 ± 9.1	.209
Procedure time, minutes, mean (range)	11.9 (3–60)	26.6 (9–50)	.001
Histology, n (%)			.848
Low grade dysplasia	47 (65.3%)	5 (62.5%)	
High grade dysplasia	3 (4.2%)	1 (12.5%)	
Cancer	1 (1.4%)	1 (12.5%)	
Other benign tumors	21 (29.2%)	1 (12.5%)	
En bloc resection	69 (95.8%)	6 (75.0%)	.076
RO resection	67 (93.1%)	5 (62.5%)	.030
Bleeding, n	0	0	–
Perforation, n (%)	1 (1.3%)	1 (12.5%)	.191

*EMR = endoscopic mucosal resection.

†ESD = endoscopic submucosal dissection.

‡SD = standard deviation.

Table 5
Clinicopathological differences between the complete resection group and the uncompleted resection group.

	Complete resection (n=72)	Uncompleted resection (n=8)	P
Age, years, mean ± SD* (range)	59.0 ± 10.5	63.2 ± 13.4	.129
Sex, n (%)			.432
Male	49 (68.1%)	4 (50.0%)	
Female	23 (31.9%)	4 (50.0%)	
Tumor location, n (%)			.885
1st portion	36 (50%)	4 (50.0%)	
2nd portion	32 (44.4%)	4 (50.0%)	
3rd portion	4 (5.6%)	0	
Tumor size, mm, mean ± SD	7.8 ± 5.6	18.5 ± 10.2	<.001
Procedure time, mean (range)	10.9 (3–40)	38.7 (15–60)	.002
Procedure type, n (%)			.030
EMR [†]	67 (93.1%)	5 (62.5%)	
ESD [‡]	5 (6.9%)	3 (37.5%)	
En bloc resection, n (%)	72 (90.0%)	3 (37.5%)	<.001
Histology, n (%)			.633
Low grade dysplasia	47 (65.3%)	5 (62.5%)	
High grade dysplasia	2 (2.8%)	2 (25.0%)	
Cancer	1 (1.4%)	1 (12.5%)	
Other benign tumors	22 (30.5%)	0	
Bleeding, n	0	0	–
Perforation, n (%)	1 (1.4%)	1 (12.5%)	.191

* SD = standard deviation.

[†] EMR = endoscopic mucosal resection.

[‡] ESD = endoscopic submucosal dissection.

resection group and the uncompleted resection group were compared (Table 5). In the uncompleted group, the size was larger ($P < .001$), the treatment time was longer ($P = .002$), and the number of ESD cases was bigger than EMR cases ($P = .030$). There was no correlation with tumor location ($P = .405$) or histologic outcome ($P = .848$) in both groups.

In total, the biopsy results of 5 lesions had a higher final diagnosis than pre-ER biopsy (Table 6). The average size of the long axis was 22 mm which was larger than the overall average (8.8 mm), and erythema and nodularity were present. According to the medical records at the time of ER, if the endoscopists judged that dysplasia was present, en bloc resection was

attempted as much as possible. However, in Case 1, the tumor was removed with a piecemeal resection due to its large size. In Case 5, ESD was performed due to the presence of high-grade dysplasia in the pre-ER biopsy, but the tumor was removed with a piecemeal resection due to the risk of perforation.

The 3 cases with positive margins are presented in Table 7. In the first case, tumor size was smaller than those in the other 2 cases, but located in the second portion and was removed by EMR. In the second case, the tumor was in the first portion, larger than average, and removed through ESD. In the third case, the tumor was in the first portion, larger than average, and removed through EMR. All 3 cases were removed with en bloc resection.

3.4. Long-term outcomes

A total of 55 patients were followed up for an average of 27.0 months (2–119 months) (Table 8). Six cases of non-R0 resections were followed up for an average of 42.3 months. No local recurrence was observed in any of the cases.

4. Discussion and conclusions

In this study, a total of 80 patients were observed. Seventy-two underwent EMR (including 1 of UEMR) and 8 underwent ESD; 72 patients had a curative resection. Fifty-five patients were observed for an average of 27.0 months, and there was no local recurrence during the 123.8 patient-years observation period. Six cases of non-R0 resection were observed for mean 42.3 months with no recurrence.

Duodenal adenoma has malignant potential and deserves resection.^[11–13] Previous studies have shown that NADLs are rare (<0.5% of all endoscopy patients); however, the incidence is increasing due to the increased number of esophagogastroduodenoscopy.^[2,12,14] Although surgical resection has been considered for the first treatment of NADL previously, surgery can cause complications and be fatal. Recently, ER has been possible with advances in endoscopic technology and now many ERs have been done for NADLs. A recent study also revealed that ER is a safer method than operation and shows a high success rate.^[15]

There are 2 types of ER; EMR and ESD. The small bowel has a thin and narrow wall, so it is more technically difficult to remove tumors of the duodenum compared to the stomach. When

Table 6
Characteristics of upgraded lesions after endoscopic resection.

	Case 1	Case 2	Case 3	Case 4	Case 5
Pre-ER diagnosis*	Tubular adenoma with LGD [†]	Tubular adenoma with LGD [‡]	Tubular adenoma with LGD	Tubular adenoma with LGD	Tubular adenoma with HGD
Final diagnosis	Tubular adenoma with HGD	Tubular adenoma with HGD	Tubular adenoma with HGD	Tubular adenoma with HGD	Adenocarcinoma
Location	1st portion	1st portion	1st portion	3rd portion	1st portion
Size, mm	40 × 40	23 × 22	23 × 15	22 × 15	17 × 17
Macroscopic type	ls	ls	ls	ls	lsp
Sur-face					
Erythema	+	+	–	–	+
Unevenness (nodularity)	+	+	+	+	+
Erosion or ulcer	–	–	–	–	+
Procedure type	EMR [§]	ESD	EMR	EMR	ESD
En bloc/piecemeal	Piecemeal	En bloc	En bloc	En bloc	Piecemeal

* Pre-ER diagnosis = pre-endoscopic resection diagnosis.

[†] LGD = low-grade dysplasia.

[‡] HGD = high-grade dysplasia.

[§] EMR = endoscopic mucosal resection.

^{||} ESD = endoscopic submucosal dissection.

Table 7**Characteristics of cases that had a residual tumor at the horizontal margin.**

	Case 1	Case 2	Case 3
Location	Second part Lateral wall	First part (bulb) Lesser curvature	First part (bulb) Anterior wall
Size, mm	8 × 7	23 × 22	23 × 15
Macroscopic type	Ila	Is	Is
Procedure type	EMR	ESD	EMR
En bloc/piecemeal	En bloc	En bloc	En bloc

EMR=endoscopic mucosal resection, ESD=endoscopic submucosal dissection.

comparing EMR and ESD, EMR is generally easier than ESD and has fewer side effects, but is likely to leave remnant tumor at the resection margin. Conversely, ESD has a high probability of en bloc resection due to the characteristics of removing the submucosa, but requires a more challenging technique and is known to have a higher risk of perforation. There is no absolute superiority between EMR and ESD. The previous studies had different results and conclusions also. The operator determines the type of procedure according to the location and shape of the lesion as well as the preference of the endoscopic operator.^[16] In this current study, we observed no significant difference in en bloc resection, unlike previous studies.^[17] R0 resection was achieved more often in EMR. However, the statistical power of the current study is low due to the small number of ESD; we cannot say which one is better. It should be noted that 1 patient who had micro-perforation during ESD also showed a positive remnant tumor at the lateral margin. The patient was an 80-year-old woman who had a huge mass of 30 × 28 mm in the duodenal bulb and showed high-grade dysplasia. Even though performing ESD for the large mass, the remnant tumor was found at the margin and micro-perforation also occurred as a side effect of ESD. Previous studies have suggested that old age is a risk factor for perforation caused by endoscopy.^[18,19]

In general, it is more difficult to remove the distal lesion in the duodenum. There were 4 patients who had lesions in the third portion of the duodenum with an average size of 9 mm in this study. All lesions were removed through EMR and en bloc method, the average procedure time was 9 minutes. R0 resection was accomplished for all, and no recurrence was confirmed during the follow-up period (mean 29 months). The deeper the lesion was, the longer the procedure time and the higher probability of failure generally, but there was no significant

Table 8**Long-term outcomes of endoscopic resection for non-ampullary duodenal lesions.**

Surveillance	
Follow-up, n (%)	55 (68.8)
Follow-up loss, n (%)	25 (31.2)
Period, mean (range), months	27.0 (2–119)
Follow-up period of non-R0 resection, mean (range), months	42.3 (9–104)
Mortality	0
Recurrence	
R0 resection (n=49)	0
Piecemeal resection (n=3)	0
Resection margin positive (n=3)	0
Total (n=55)	0

difference in these 4 patients. However, the number of patients was small; it did not have a significant meaning.

According to a meta-analysis study of ER for NADLs,^[20] in a total of 14 studies by August 2017, 784 NADL patients underwent ER; 242 ESD and 542 EMR. A total of 626 cases were followed (210 of EMR and 416 of ESD) with a total of 38 local recurrences (10 of EMR and 28 of ESD). Delayed bleeding occurred in 57 (21 of EMR and 36 of ESD) of 772 cases (236 of EMR and 536 of ESD). There were 49 cases of perforation during the procedure (41 of EMR and 8 of ESD) and a total of 10 delayed perforations (8 of EMR and 2 of ESD). In the present study, only 2 patients had micro-perforation and it is judged that the perforation was few due to the high EMR ratio.^[15]

Bleeding and perforation were the main complications of ER. Complications may occur during endoscopic procedures but are sometimes delayed which may not be noticed until the second-look endoscopy. There was no delayed bleeding in this study. Severe delayed bleeding may show abrupt symptoms like hypotension or syncope rather than hematemesis. Endoscopic procedures of the duodenum (both ampullary and non-ampullary) generally have a high probability of bleeding within 24 hours after treatment and occur in 5.5% of EMR and 8.4% of ESD. Therefore, clinicians must observe the patient closely for up to 24 hours after the procedure.^[21] If bleeding occurs, endoscopic hemostasis is required, and angiography or surgical treatment should be considered for repeated bleeding. There was no delayed bleeding in this study which is the result of prophylactic clipping. Clipping is effective in preventing delayed bleeding in previous studies.^[15]

Delayed perforation is also a concern after endoscopic treatment for NADL and according to a study presented by Inoue et al^[22] delayed perforation may appear even after 84 hours. Since pancreatic enzymes can provoke delayed perforation at the resection site scar, preventive clip closure is usually performed. After the preventive clip ligation, even if a micro-perforation occurs, it can be treated with conservative care. In addition, using CO₂ gas can be reabsorbed quickly and can reduce the pain caused by micro-perforation.^[23] It is necessary to check the presence of air around the kidney in plain radiography in cases where the second and third portion of the duodenum in retroperitoneal space is endoscopically resected. In this study, there were 2 cases of micro-perforations, but they were improved by prophylactic clip closure and conservative treatment after ER without additional side effects or surgical treatment. Preventive clip closure can prevent micro-perforated lesions from becoming more severe and help to recover quickly.

The final diagnosis of NADLs after ER could be different from the pre-ER forceps biopsy results.^[24] Therefore, though no adenoma is observed in the pre-ER biopsy, once endoscopic findings show an adenomatous polyp, it is necessary to perform ER. Indeed, previous studies have indicated that some endoscopists think pre-resection biopsy was not important and prefer not to perform forceps biopsy before ER in NADL since forceps biopsy can cause fibrosis around the lesion and the result after ER can be higher by up to 40%; a pre-ER biopsy is unreliable. In this study, 4 cases showed low-grade dysplasia at forceps biopsy, but high-grade dysplasia after resection. In these patients, the lesions were erythematous and uneven and the size of these lesions was over 2 cm and the maximum size was 4 cm. Therefore, even if the forceps biopsy shows a good result, ER should be considered when the lesion is over 2 cm in size with an uneven appearance.

In cases where NADLs were removed endoscopically, patients showed good outcomes during the follow-up period, even if a remnant tumor existed at the horizontal margin. In this study, 3 patients had positive horizontal margins, but no local recurrence during follow-up. In all cases, the en bloc method was used for removal. The burning effect of the ablation surface is the reason why there was no local recurrence even though there was a remnant tumor at the horizontal margin.^[25,26] However, if the remnant tumor is present, constant surveillance is required: 3 patients in this study were followed for an average of 48.33 months. In the study presented by Yamamoto et al^[16] local recurrence was observed in 1 person who underwent EMR and the lesion was removed by the piecemeal method. The piecemeal method which can leave the NADL's floor increased the possibility of residual tumor, thereby increasing the possibility of local recurrence. That study concluded that piecemeal resection should be avoided and en bloc method should be performed. There were 4 piecemeal resection cases in the present study, but no local recurrence was observed.

We found that patients would have good prognosis once ER is performed for NADLs regardless of the procedure type (ESD or EMR) or the number of resection fragments (en bloc or piecemeal). In the previous study, If the lesion was a high-grade dysplasia or was more than 20mm in size, it is necessary to immediately treat it as a high risk of malignancy.^[27] Also, another previous study indicated that ER, especially ESD, is not recommended when the lesion is bigger than 20mm.^[16] From these previous 2 studies, doctors can think that surgery is an appropriate treatment for NADLs larger than 20 mm. However, in the current study, 5 patients had a tumor size of 20 mm or more and 2 patients had residual tumors at the resection margin. We followed 2 patients who had lesions larger than 20 mm and residual tumors at the resection margin for 103 and 33 months each, but no recurrence was observed. Therefore, even though there were residual tumors at the resection site, and the lesions had histologically dysplasia and were larger than 20 mm, the prognosis was good. However, the current study included a small number.

The strength of this study is that 55 cases were followed up for a long time. The limitation of this study is its retrospective nature. Furthermore, the results of endoscopic procedures performed in a single tertiary organ may not be generalizable. Since it was implemented by only 4 operators working in 1 single institution, there can be biases for this. To compensate for this limitation, we applied the same ER protocol for medication, second-look endoscopy, and subsequent outpatient follow-up. Third, the percentage of loss of follow-up cases was high (31%). Among these, there may be recurrences, adverse events, and even death. It can be a hasty conclusion to say that there are fewer recurrence rates in a population with a high rate of losses to follow-up.

In conclusion, duodenal ER for NADLs is a safe and effective treatment with no recurrence observed in the current study. Furthermore, even if the resection margin shows a microscopic residual tumor, it has a good prognosis. However, close observation of the patient is required after the procedure for early detection of postoperative complications.

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