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Contents

Contents

Contents

ABOUT COVER

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AIMS AND SCOPE

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ORIGINAL ARTICLE

Retrospective Study

Clinical outcomes of endoscopic resection of superficial nonampullary duodenal epithelial tumors: A 10-year retrospective, single-center study

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Abstract
BACKGROUND
Although premalignant duodenal lesions such as adenomas are uncommon, the incidences of these lesions have increased in recent times, and thus, the demand for minimally invasive treatments such as endoscopic resection (ER) has also increased. However, ER in the duodenum is more challenging than ER in other locations of the gastrointestinal tract.

AIM
To evaluate the safety and efficacy of ER for superficial nonampullary duodenal epithelial tumors (SNADETs)

METHODS
We performed a retrospective observational study on 56 consecutive patients (58 lesions) diagnosed with SNADETs that underwent ER from January 2011 to December 2020 at Yeungnam University Hospital. Patient demographics, lesion characteristics, and procedural and technical data were collected, and clinical outcomes, including procedure-related complications, completeness of resection, and recurrence were analyzed.

RESULTS
Median patient age was 57 years [range, 26–77, 30 (53.6%) men]. Endoscopic mucosal resection (EMR) was performed on 57 lesions (98.3%) and snare polypectomy on one (1.7%). Lesions consisted of 52 adenomas with low-grade dysplasia (89.7%), 3 adenomas with high-grade dysplasia (5.2%), and 3 intramucosal adenocarcinomas (5.2%). There were 16 cases of intraprocedural bleeding (27.6%) and 1 case of delayed bleeding (1.7%), and all these 17 cases were successfully managed endoscopically. No perforation or procedure-related death

occurred. Larger lesion size was associated with an increased risk of EMR-related bleeding (P = 0.033). During a median follow-up period of 23 mo (range 6–100 mo), no local recurrence occurred, despite the fact one-third of the patients (19 lesions, 32.8%) underwent piecemeal resection and 3 patients (3 lesions, 5.2%) that underwent *en bloc* resection had a pathologically determined positive lateral margin. No patient died from a primary duodenal neoplasm.

CONCLUSION
The majority of SNADETs can be safely and curatively resected by EMR, and thus, based on consideration of the high incidence of fatal complications attributable to ESD, we conclude EMR, including piecemeal resection, should be considered the treatment of first choice for SNADETs.

Key Words: Duodenum; Adenoma; Endoscopic mucosal resection; Endoscopic resection; Superficial nonampullary duodenal epithelial tumor

Core Tip: This long-term retrospective observational study shows that superficial nonampullary duodenal epithelial tumors (SNADETs) can be safely and curatively managed by endoscopic mucosal resection (EMR), even after piecemeal resection. Therefore, based on consideration of the high incidence of fatal complications attributable to endoscopic submucosal dissection in duodenum, we recommend that EMR, including piecemeal resection, be considered the treatment of first choice for SNADETs. However, we caution that because of its technical difficulty, EMR on duodenum should only be performed by highly skilled endoscopists. In addition, we emphasize that more attention is required during EMR of a large duodenal tumor because lesion size is positively associated with the risk of EMR-related bleeding.

INTRODUCTION

Superficial nonampullary duodenal epithelial tumors (SNADETs) such as primary duodenal adenomas and adenocarcinomas are rare compared with other gastrointestinal (GI) tract cancers. However, as the use of screening endoscopy continues to increase and endoscopic skills and technology improve, small early SNADETs are being diagnosed more frequently[1]. The adenoma-carcinoma sequence is also accepted for lesions in the small bowel[2,3], and reported malignant transformation rates of duodenal adenoma range from 30% to 85%[4,5]. Therefore, once diagnosed, surgical excision and endoscopic resection (ER) are the initial considerations, and ER is generally preferred over operative interventions because of its less invasive nature.

However, the duodenum is the most challenging location in the GI tract for ER. Several anatomic features of the duodenum contribute to these difficulties, such as a narrow lumen, a ''C-loop'' that reduces endoscope stability, the presence of Brunner's glands in the deep mucosal and submucosal layers that stiffen the wall and lead to poor mucosal lifting, a thin deep muscle layer that increases the risk of complications like perforation, and difficulties associated with accessing sites if emergency or salvage surgery becomes necessary[6-8].

Endoscopic submucosal dissection (ESD) is regularly performed at expert centers in South Korea for superficial lesions of the esophagus, stomach, or colorectum. ESD has a high *en bloc* resection rate, which enables accurate histopathological assessments. However, we refrain from aggressive duodenal ESD because the procedure is technically difficult and associated with a higher incidence of consequential perforation than at other sites in the GI tract[9-11]. Although endoscopic mucosal resection (EMR) is a safer, easier, and quicker procedure than ESD, EMR results in fewer *en bloc* resections[12-18]. Even though debate continues as to which ER method is preferable, EMR is currently recognized as the standard procedure for the endoscopic treatment of SNADETs.

Duodenal lesions that require ER are limited in number, and thus, although several reports have been published, little information is available on the long-term clinical outcomes of ER for SNADETs. In this study, we evaluated the safety and efficacy of ER for the treatment of SNADETs and associated factors using a 10-year follow-up.

MATERIALS AND METHODS

Patients

We retrospectively analyzed our institutional database for patients that underwent duodenal ER between January 2011 and December 2020. During this period, 56 consecutive patients with 58 lesions underwent ER for SNADETs. In all cases, these were primary tumors without a previous history. Patients with polyposis syndrome, an ampullary duodenal tumor, or a neuroendocrine tumor were excluded. Written informed consent was obtained from all patients before they underwent ER, and the study protocol was reviewed and approved beforehand by the Institutional Review Board of Yeungnam University Hospital (IRB No. 2021-10-045).

Patient demographics, lesion characteristics, and procedural descriptions were collected from the institutional database and electronic medical records. Data on the use of antiplatelet or anticoagulant medication or nonsteroidal anti-inflammatory drugs (NSAIDs) were also obtained for analysis. Follow-up was defined as time between ER and recurrence, death, or loss to follow-up. If none of these events was documented, the end of the follow-up period was defined as the time of last patient contact before June 30, 2021.

Endoscopic procedure and follow-up

Suitability for ER was determined based on endoscopic appearance as determined by high-definition white light endoscopy and narrow-band imaging in patients with histologically confirmed adenoma or adenocarcinoma confined to mucosa. Suspected invasive neoplasia was deemed unsuitable for endoscopic resection. Patients on antiplatelet and/or anticoagulant medications were instructed to consult with their prescribing physicians for permission to withhold medications before ER. EMR was carried out by highly skilled endoscopists. With patients under propofol and midazolam sedation and cardiorespiratory function monitoring, conventional EMR was performed using a snare-assisted technique with submucosal injection of methylene blue-tinted normal saline containing a small amount of epinephrine (0.01 mg/mL) using a single-use 21-gauge needle (Olympus, Japan). Two types of oval electrosurgical snares were used of diameter 15 or 25 mm (Olympus). In one case, standard snare polypectomy was performed without submucosal injection.

The EMR technique was individualized on a case-by-case basis. *En bloc* resection was attempted if a lesion had a largest diameter of < 2.0 cm and < 25% of the luminal circumference. Piecemeal resection was conducted for larger lesions and when there was endoscopic evidence of residual tumor after an *en bloc* resection attempt. Adjunctive coagulation using a hot-biopsy forceps (Boston Scientific, Natick, MA, USA) or an argon plasma coagulation (APC) unit (ERBE, Elektromedizin, Tuebingen, Germany) was sometimes used to reduce the risk posed by any residual tumor, based on endoscopist judgment when the residual portion was too small to remove using a snare. Prophylactic clip placement was performed to reduce the risk of delayed bleeding and perforation when technically possible, depending on lesion location and size, and endoscope stability[9,13,16,19]. EMR was performed only after hospital admission.

After endoscopic treatment, routine chest and abdominal radiography were performed to evaluate possible adverse events, such as perforation and aspiration pneumonia. Routine second-look endoscopy was performed 1 d after EMR. After discharge, follow-up endoscopy was performed at 6 and 12 mo post-EMR during the first year and annually thereafter. If recurrence was suspected, forceps tissue sampling was performed, and further endoscopic treatment such as EMR, and/or ablation were performed at the discretion of the endoscopist.

Clinical outcomes and adverse events

Outcomes were classified as short- or long-term. Short-term outcomes included ER success, which included *en bloc* resection and complete resection rates, and procedure-related complications, which included bleeding and perforation. *En bloc* resection was defined as lesion resection as a single piece, and piecemeal resection as resection resulting in multiple pieces. Complete resection was defined as resection with no endoscopic or histologic evidence of residual tumor tissue at resection sites, irrespective of whether *en bloc* resection was undertaken. EMR-related bleeding was categorized as intraprocedural or delayed bleeding requiring directed intervention. Intraprocedural bleeding was defined as persistent bleeding during the procedure that did not cease spontaneously and required endoscopic intervention involving the injection of diluted epinephrine solution (1:10000), snare-tip soft coagulation, coagulation forceps, or hemoclip placement. Delayed bleeding was defined as any bleeding that prompted medical intervention after the procedure. Perforation was diagnosed endoscopically during procedures or based on the presence of free air in post-procedural chest or abdomen radiographs.

Long-term outcomes included local recurrence and disease-specific survival rates of patients followed for > 6 mo. Incomplete follow-up data were retrieved in various ways, such as by telephone contact or correspondence with patients, families, or referring physicians. Local recurrence was defined as the presence of a tumor on or adjacent to a previous endoscopic resection scar.

Statistical analysis

Data were analyzed using SPSS version 20.0 for Windows (SPSS Inc, Chicago, IL, United States). All variables are presented as mean ± SD, medians and ranges, or absolute numbers and proportions. For univariate analyses, categorical variables were analyzed using the chi-square test or Fisher's exact test. A multivariable logistic regression model was used to identify independent predictors of outcomes and adverse events. Significant variables (P-values < 0.05) by univariate analysis and variables with clinical correlations were included in the multivariate model. Multivariate comparisons are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). All statistical tests were two-sided and statistical significance was accepted for P values < 0.05.

RESULTS

Patient characteristics

Over the ten-year study period, 56 patients underwent 57 EMR and 1 snare polypectomy procedures. Two patients had two duodenal adenomas, and all lesions were treated simultaneously. The baseline clinicopathologic characteristics of the study population are summarized in Table 1. The patients included 30 men (53.6%) and 26 women of median age 57 years (range 26-77 years). Six patients (10.7%) were on at least 1 antiplatelet medication, and no patient was taking an anticoagulant or NSAID. Nine lesions (15.5%) were located in the duodenal bulb, 47 (81.0%) in the 2nd portion, and 2 (3.4%) in the 3rd portion. Colonoscopy was performed in 69.6% of the patients with SNADETs, and colorectal adenomas were found in 46.2% of these patients. Macroscopic types were classified as Is in 24 patients (41.4%), IIa or IIb in 24 (41.4%), and Ip in 10 (17.2%). Based on the pathologies of biopsy specimens before EMR, there were 55 (94.8%) low-grade dysplasia (LGD) lesions, 2 (3.4%) high-grade dysplasia (HGD) lesions, and 1 (1.7%) adenocarcinoma.

EMR and complications

En bloc resection was achieved successfully for 39 lesions (67.2%), and 19 lesions (32.8%) were resected piecemeal, which resulted in two resected specimens in each case (Table 2). Lesion sizes was categorized into 4 groups for further analysis, that is, a < 10 mm group [n = 20 (34.5%)], a ≥ 10 to < 15 mm group [n = 26 (44.8%)], a ≥ 15 to < 20 mm group [n = 7 (12.1%)], and a ≥ 20 mm group [n = 5 lesions (8.6%)]. Twenty-nine lesions (50.0%, 10 lesions that underwent *en bloc* resection and all of 19 lesions treated by piecemeal resection) underwent adjunctive coagulation by hot biopsy or APC to eliminate residual tumor risk. Immediate closure after EMR was performed for 48 lesions (82.8%) by prophylactic clip placement.

Sixteen lesions (27.6%) developed EMR-related bleeding; 15 were intraprocedural and 1 was delayed. All intraprocedural bleedings were successfully controlled endoscopically. Ten of these patients underwent endoscopic hemostasis with hemoclips and electrocoagulation. Only electrocoagulation was needed for five patients with bleeding. Delayed bleeding occurred in 1 EMR case despite prophylactic clipping and was successfully managed endoscopically with hemoclips and electrocoagulation. No patient required further surgical or radiological treatment. Neither perforation nor procedure-related mortality occurred.

Histopathological results

The pathologic results of ER specimens are summarized in Table 3. Median tumor size as determined by histopathology was 12 mm (range 4-20 mm). There were 52 adenomas with LGD, 3 adenomas with HGD, and 3 intramucosal adenocarcinomas. Lateral margins were estimated pathologically to be negative for 36 (62.1%), positive for 3 (5.2%), and inconclusive for 19 (32.8%) lesions, and vertical margins were negative for 50 (86.2%), positive for 0 (0 %), and inconclusive for 8 (13.8%) lesions.

Factors associated with EMR-related bleeding

Increasing lesion size was significantly associated with a higher risk of EMR-related bleeding (P = 0.033) (Table 4), but antiplatelet use, piecemeal resection, tumor location, macroscopic type, and pathology were not found to be associated with bleeding risk. Multivariate logistic regression analysis to identify independent predictors of EMR-related bleeding could not preformed due to only 17 events.

Long-term outcomes

Six of the 56 patients followed for less than 6 mo were excluded from the analysis of long-term outcomes. All 22 patients (22 lesions) with a histopathologic result of an inconclusive or positive resection margin were followed for more than 6 mo (median follow-up duration 28 mo; range 12–101 mo). Clinicopathologic data and the outcomes of 3 cases of incomplete resection are summarized in Table 5, and long-term outcomes are summarized in Table 6. All 3 lesions of incomplete resection with a positive lateral margin were those that had undergone adjunctive coagulation. Of the 50 patients (52 lesions) followed for more than 6 mo, 2 died and 48 survived, but these deaths were not ascribed to a

Table 1 Baseline characteristics of the study subjects

Patients	56
Median age, yr (range)	57 (26-77)
Male, *n* (%)	30 (53.6)
Number of lesions, *n* (%)	
1	54 (96.4)
2	2 (3.6)
Medications, *n* (%)	
Aspirin	3 (5.3)
Clopidogrel	1 (1.8)
Dual antiplatelets	2 (3.6)
Anticoagulants	0
NSAIDs	0
Patients that underwent colonoscopy	39 (69.6)
Colonoscopy positive for adenoma	18 (46.2)
Lesions	**58**
Location, *n* (%)	
Bulb	9 (15.5)
Second portion	47 (81.0)
Third portion	2 (3.4)
Macroscopic type, *n* (%)	
Ip	10 (17.2)
Is	24 (41.4)
IIa or IIb	24 (41.4)
Biopsy diagnosis, *n* (%)	
Adenoma/LGD	55 (94.8)
Adenoma/HGD	2 (3.4)
Adenocarcinoma	1 (1.7)

NSAID: Nonsteroidal anti-inflammatory drug; LGD: Low-grade dysplasia; HGD: High-grade dysplasia.

primary duodenal tumor. One patient succumbed to aspiration pneumonia and the other patient to colon cancer with multiple liver metastases. In addition, none of the 50 patients experienced local recurrence during follow-up (median follow-up duration 23 mo; range 6–100 mo).

DISCUSSION

In this 10-year retrospective study, we investigated the safety and efficacy of EMR for SNADETs. The results obtained suggest that the prognoses of patients treated by EMR are excellent. In the present study, no death was attributable to a primary duodenal tumor. Furthermore, no local recurrence occurred, although one-third of the patients underwent piecemeal EMR, and no perforation or procedure-related mortality occurred. These findings affirm that EMR of SNADETs has excellent safety and efficacy profiles.

The oncologic long-term outcomes of patients with tumors that are not resected in an *en bloc* fashion are of considerable importance. In the present study, *en bloc* resection was achieved in 67.2%, piecemeal resection in 32.8%, and complete (R0) resection in 62.1%. Due to the risks associated with ESD, endoscopists at our institute chose EMR or polypectomy for all 58 lesions, even for lesions > 20 mm. Considering the effects of *en bloc* resection on oncologic outcomes, this low proportion is obviously unsatisfactory. However, it was largely the result of attempting to minimize mucosal defects due to

Table 2 Endoscopic treatment and complications for the 58 lesions

Treatment methods, *n* (%)	
EMR	57 (98.3)
Snare polypectomy	1 (1.7)
Lesion size, mm, *n* (%)	
Size < 10	20 (34.5)
10 ≤ size < 15	26 (44.8)
15 ≤ size < 20	7 (12.1)
20 ≤ size	5 (8.6)
Results of resection, *n* (%)	
En bloc	39 (67.2)
Piecemeal	19 (32.8)
Adjunctive coagulation, *n* (%)	29 (50.0)
Prophylactic clip placement, *n* (%)	48 (82.8)
Complication, *n* (%)	
Intraprocedural bleeding	16 (27.6)
Delayed bleeding	1 (1.7)
Perforation	0 (0)

EMR: Endoscopic mucosal resection.

Table 3 Histopathologic results for the 58 lesions

Tumor size, mm, median (range)	12 (4–20)
Final pathology, *n* (%)	57 (98.3)
Adenoma/LGD	52 (89.7)
Adenoma/HGD	3 (5.2)
Intramucosal adenocarcinoma	3 (5.2)
Lateral margin, *n* (%)	
Negative	36 (62.1)
Positive	3 (5.2)
Inconclusive	19 (32.8)
Vertical margin, *n* (%)	
Negative	50 (86.2)
Positive	0 (0)
Inconclusive	8 (13.8)
Complete (R0) resection	36 (62.1)

LGD: Low-grade dysplasia; HGD: High-grade dysplasia.

concerns about perforation and bleeding and to enable prophylactic clipping. Fortunately, no local recurrences or death attributable to primary duodenal tumors occurred even after a median follow-up of 23 mo.

Median tumor size (12 mm) in this study was smaller than the 22 to 25 mm sizes reported in Western studies, which also reported higher incidences of local recurrence (14.4%-30.8%) after EMR (*en bloc* rates varied from 23.5% to 31.0%)[20,21]. On the other hand, other studies on smaller lesions have reported local recurrence incidence rates between 5.8% and 8.3% and *en bloc* rates of 69.2%-82% (R0 30%-59%) for

Table 4 Factors associated with endoscopic mucosal resection -related bleeding

	Bleeding (+) (*n* = 17)	Bleeding (-) (*n* = 41)	*P* value
Antiplatelet use			0.661
Yes	1 (14.3)	6 (85.7)	
No	16 (31.4)	35 (68.6)	
Lesion size, mm, *n* (%)			**0.033**
Size < 10	1 (5.0)	19 (95.0)	
10 ≤ size < 15	8 (30.8)	18 (69.2)	
15 ≤ size < 20	4 (57.1)	3 (42.9)	
20 ≤ size	4 (80.0)	1 (20.0)	
Results of resection, *n* (%)			0.218
En bloc	9 (23.1)	30 (76.9)	
Piecemeal	8 (42.1)	11 (57.9)	
Location, *n* (%)			0.855
Bulb	2 (22.2)	7 (77.8)	
Second portion	15 (31.9)	32 (68.1)	
Third portion	0 (0)	2 (100)	
Macroscopic type, *n* (%)			0.950
Ip	2 (20.0)	8 (80.0)	
Is	7 (29.2)	17 (70.8)	
IIa or IIb	8 (33.3)	16 (66.7)	
Final pathology			0.345
Adenoma/LGD	14 (26.9)	38 (73.1)	
Adenoma/HGD and adenocarcinoma	3 (50.0)	3 (50.0)	

LGD: Low-grade dysplasia; HGD: High-grade dysplasia

Table 5 Clinicopathologic data and outcomes for 3 cases of incomplete resection

Patient	Age (yr)	Location	Tumor Size	Pathology	Resection type	Treatment method	Vertical/lateral margin	Result of follow-up biopsy	Follow-up (mo)
1	72	Bulb	20	Intramucosal adenocarcinoma	*En bloc*	EMR	-/+	-	29
2	71	Bulb	20	LGD	*En bloc*	EMR	-/+	-	27
3	75	2nd portion	10	LGD	*En bloc*	EMR	-/+	-	17

LGD: Low-grade dysplasia; EMR: Endoscopic mucosal resection.

lesions of approximately 10 mm[18,22,23]. Tomizawa *et al*[24] reported adenoma size, incomplete snare resection, and piecemeal resection were associated with duodenal adenoma recurrence by univariate analysis (multivariate analysis was not performed). Incomplete snare resection and piecemeal resection are likely consequences of larger lesions. However, others have reported incomplete resection, including piecemeal resection, was not associated with the long-term recurrence of SNADETs[25,26]. In the present study, one-third of patients underwent piecemeal EMR, but no recurrence was observed during follow-up. In a study on 75 duodenal adenomas treated by EMR, the residual tumor rate was 14.5% and the recurrence rate over a median follow-up of 59 mo was 10.9%[27]. However, all but one of these recurrences were successfully treated endoscopically and achieved favorable long-term outcomes.

Table 6 Long-term outcomes (*n* = 50 patients and 52 lesions)	
Recurrence, *n* (%)	0 (0%)
Death by duodenal neoplasm	0 (0%)
All-cause mortality	2 (3.6%)
Follow-up period median (range)	23 (6-100) mo
No. of follow-up endoscopies	
2	9
3 or 4	28
5 ≤	13

Although it is not clear how much effect piecemeal resection has on local recurrence, it appears piecemeal resection may not have a significant negative effect on the long-term outcomes of duodenal adenomas. Therefore, we believe that EMR, including EMR with piecemeal resection, offers an acceptable alternative to ESD for the treatment of duodenal adenoma.

Despite considerable technical advances in ER for superficial neoplasms of the GI tract, duodenal endoscopic treatment is considered a high-risk procedure that is more challenging than ER in other GI tract locations for several reasons[6-8]: (1) Endoscope and accessory maneuverability are restricted by the small-caliber, angulated, and fixed-in-place duodenal lumen; (2) Rich vascularity poses a bleeding risk; and (3) The risk of perforation is increased by a thin duodenal wall, retroperitoneal location, and surrounding structures. Although EMR techniques have not been standardized for SNADETs, the approach used should be similar to that adopted for polyps in other parts of the GI tract with added consideration of the thin duodenal wall. However, it is sometimes difficult to obtain successful results by conventional EMR due to insufficient lifting after submucosal injection. A new technique, underwater endoscopic mucosal resection (UEMR) was developed recently in the United States for the treatment of SNADETs, and its usefulness has been reported[28]. Subsequently, several studies were performed in Japan[29-31] to remove SNADETs of less than 20 mm by *en bloc* resection and to reduce treatment-related complications. During UEMR, superficial lesions float up into the snare as protruding lesions, and thus, are easily snared and removed, even when lesions are flat or sessile and difficult to remove by conventional EMR[32]. Theoretically, UEMR is safe because the underwater procedure decreases thermal damage to the duodenal wall and submucosa is cut shallower than during EMR. Additionally, post-UEMR defects are small and soft, and defects are easily closed using endoclips[32]. A retrospective observational study[33] on two different types of subjects, that is, prospectively collected consecutive 104 UEMR cases and 204 EMR cases as historical controls, demonstrated that the technical success rate of UEMR was significantly higher than that of EMR. However, *en bloc* resection and R0 resection rates of UEMR were significantly lower than those of EMR, and no significant difference in adverse events was observed. Further prospective study is warranted to evaluate the efficacy of UEMR.

Duodenal lesions of > 20 mm cannot usually be removed *en bloc* by EMR. Several recent studies of the efficacy of ESD for the treatment of SNADETs have reported *en bloc* and complete resection rates of 80%–100%[6,10,11,22]. However, even experts have reported duodenal ESD complication rates of 6.6% to 31.6% for intraprocedural perforation, 0% to 14.3% for delayed perforation, and 0% to 18.4 % for delayed bleeding[10,11,22,34]. Furthermore, reported emergency surgery rates range from 3.3 to 14.3 % in this technically difficult and dangerous situation. Of course, it is preferable to resect such lesions *en bloc* using ESD but performing duodenal ESD is exceptionally difficult, as evidenced by higher complication incidences. In contrast, EMR is recognized as a safer, easier, quicker procedure, with considerably lower risks of intraprocedural perforation (0%-2.7 %), delayed perforation (0%-2.0%), and emergency surgery (2.7%-4.0 %)[12-16,18]. In addition, several other factors should be borne in mind. (1) Mucosal resection–related perforations are not as easily recognized in duodenum as in other parts of the GI tract[35], any delay in the diagnosis of iatrogenic perforation increases the risk of subsequent surgery [26]; (2) Perforation of the duodenum, particularly of the 2nd portion, requires immediate surgery because bile and pancreatic juice have the deleterious effects on surrounding organs; and (3) The risk of delayed perforation in duodenum is also high[9,36], and this can result in serious consequences in the absence of prompt diagnosis and surgery. Thus, the risks of perforation associated with ESD require careful consideration. Furthermore, no head-to-head comparison of the long-term adenoma recurrence–free rates of ESD and EMR has been performed to date. In our opinion, the risks associated with ESD are greater than the benefits of *en bloc* resection in some cases. Given the considerable technical skills and time required for ESD, it is not routinely recommended for the endoscopic treatment of duodenal tumors, particularly for lesions < 20 mm.

Reported bleeding rates during or after ER of SNADETs vary, in part, because of the different definitions of bleeding used, but nevertheless, are consistently greater than those reported for ER of colorectal adenomas. Ahmad *et al*[37] reported a bleeding frequency of 33% for duodenal EMR, and Lé

pilliez *et al*[16] reported a frequency of 25%. In the present study, clinically significant bleeding, which was defined as any bleeding that requires intervention, occurred in 29.3% of lesions, which is similar to the results mentioned above. Klein *et al*[21] reported a higher EMR-related bleeding rate of 43%, which was probably due to a greater proportion of large lesions (29 lesions > 40 mm) in their cohort. Most of the bleeding cases (15/16) in the present study were intraprocedural bleedings. The thin muscular layer of the duodenum is easily perforated by transmural thermal injury during hemostasis procedures, and intraprocedural bleeding is generally considered an undesirable complication. However, Lépilliez *et al* [16] did not consider it a true complication, because it can often be controlled by endoscopic clip application, ablative therapy, or adrenaline injection without serious complication. In addition, as there is no standardized definition for intraprocedural bleeding, it is difficult to determine whether reported bleeding cases in various studies were clinically significant, and therefore, discussions on the management of intraprocedural bleeding during duodenal EMR tend to subjective. Our analysis showed lesion size was significantly associated with a higher risk of EMR-related bleeding, although multivariate analysis could not preformed because there were only 17 events. Even though patients that experienced bleeding required additional hospitalization, all bleeding cases were successfully managed endoscopically, and neither surgical intervention nor interventional radiology was required.

Furthermore, no case of intraprocedural or delayed perforation was encountered, and delayed bleeding occurred only in 1 case (1.7%), which had undergone prophylactic clip placement. Forty-eight lesions (82.8%) underwent prophylactic clip placement based on perceived higher risk because we believe clip placement reduces complications by protecting mucosal defects from pancreatic juice and bile[6,13,16,18,19]. Yamamoto *et al*[22] also reported the absence of bleeding after prophylactic clipping during duodenal ER. Although a larger study is required to precisely determine the effect of prophylactic clipping, results published to date support its use based on considerations of technical difficulties associated with location, size, or scope instability[9,16,18].

Previous studies have shown that 4.8–13.5% of cases in which lesions were initially diagnosed as duodenal adenoma by biopsy were finally diagnosed as adenocarcinoma after resection[13,16]. Okada *et al*[38] reported that HGD in biopsy samples and a lesion diameter of > 2 cm predict progression to adenocarcinoma and suggested that erythematous lesions and lesions with surface nodularity present the risk of progression and recommended their removal. In the present study, EMR resulted in 1.8% of lesions (1/55) being upgraded from LGD to HGD and 3.6% of lesions (2/55) being upgraded from LGD to intramucosal adenocarcinoma. This discrepancy between biopsy samples and resected specimens suggests that relatively large adenoma lesions and adenoma lesions exhibiting surface changes are better to treated by EMR rather than APC.

The major strength of our study is that it covers a 10-year span and benefits from meticulous, long-term follow-up in terms of determining clinical outcomes regarding the safety and efficacy of EMR for SNADETs and natural history after EMR. Our findings reinforce notions that the vast majority of SNADETs can be safely and curatively resected by EMR, even when resection is piecemeal, and that larger lesions size are associated with EMR-related bleeding, which has implications for risk management and surveillance strategies.

The limitations of our study are that it was a single center, retrospective study with a relatively small sample size, and some patients were lost during follow-up to other institutions. Nevertheless, the study documents both short-term outcomes, including complications, and long-term outcomes after EMR for SNADETs.

CONCLUSION

Summarizing, most SNADETs can be safely and effectively managed by EMR undertaken by an expert endoscopist, and EMR may be considered a first-line treatment for SNADETs due to the high incidence of fatal complications attributable to ESD in duodenum. We believe the risks of performing *en bloc* resection by ESD exceed its benefits in some cases, therefore, even piecemeal resection by EMR is a better proposition based on the excellent prognoses observed in this study.

ARTICLE HIGHLIGHTS

Research background

Superficial nonampullary duodenal epithelial tumors (SNADETs) are uncommon, but small early SNADETs are now being diagnosed more frequently, and thus, the demand for endoscopic resection (ER) has increased. However, the duodenum is the most challenging location in the gastrointestinal tract for ER.

Research motivation

Duodenal lesions that require ER are limited in number, and thus, although several reports have been

published on the topic, little information is available on the long-term clinical outcomes of ER for SNADETs.

Research objectives

The objective of this investigation was to evaluate the safety and efficacy of ER for the treatment of SNADETs and associated factors using a 10-year follow-up.

Research methods

This retrospective analysis was conducted on 56 consecutive patients with 58 lesions who underwent endoscopic mucosal resection (EMR; 57 lesions), and snare polypectomy (one lesion) for SNADETs from January 2011 to December 2020. Patient demographics, lesion characteristics, and procedural and technical data were collected, and clinical outcomes, including procedure-related complications, completeness of resection, and recurrence were analyzed.

Research results

Lesions consisted of 52 adenomas with low-grade dysplasia, 3 adenomas with high-grade dysplasia, and 3 intramucosal adenocarcinomas. There were 16 cases of intraprocedural bleeding (27.6%) and 1 case of delayed bleeding (1.7%), and these 17 cases were successfully managed endoscopically. No perforation or procedure-related death occurred. Larger lesion size was associated with an increased risk of EMR-related bleeding. During a median follow-up period of 23 mo (range 6–100 mo) no local recurrence occurred, despite the fact one-third of the patients (19 lesions, 32.8%) underwent piecemeal resection and 3 patients (3 lesions, 5.2%) that underwent *en bloc* resection had a pathologically determined positive lateral margin.

Research conclusions

The majority of SNADETs can be safely and curatively resected by EMR, even when resection is piecemeal. However, larger lesions are associated with EMR-related bleeding, which has implications for risk management and surveillance strategies.

Research perspectives

This study covers a 10-year period and benefits from meticulous, long-term follow-up in terms of determining clinical outcomes that reflect the safety and efficacy of EMR for SNADETs and natural history after EMR. Further larger-scale studies are needed to determine the long-term outcomes of ER for SNADETs.

FOOTNOTES

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