Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes CME

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Background and Aims: Large sporadic duodenal adenomas are uncommon but they harbor malignant potential, which requires consideration of definitive treatment. EMR is gaining acceptance as an effective and safe alternative to high-risk surgical procedures, but data on long-term outcomes are limited. Herein we describe the short- and long-term outcomes of these lesions in a tertiary referral center.

Methods: Prospectively collected data were analyzed to identify risk factors for adverse events and outcomes. Patient demographics, lesion characteristics, and procedural technical data were collected.

Results: From 2007 to 2015, 106 adenomas ≥10 mm were resected (mean patient age, 69 years; 54% male; median size, 25 mm; interquartile range [IQR], 19–40). Complete endoscopic resection was achieved in 96%. Intraprocedural bleeding occurred in 43% of cases and was associated with lesion size ($P < .001$), number of resected specimens ($P = .003$), and longer procedures ($P = .001$). Delayed bleeding occurred in 15% (56% did not require active intervention) and was associated with lesion size ($P = .03$). Perforation occurred in 3 patients. The 30-day mortality was 0%. Median follow-up was 22 months (IQR, 7–45). Histologically proven adenoma recurrence was identified and treated in 12 of 83 patients (14.4%) on first surveillance endoscopy. For the 53 patients for whom follow-up ≥12 months was available (median follow-up, 36 months; IQR, 24–51), 48 patients (90.6%) were free of adenoma and considered cured.

Conclusions: In a tertiary referral center, endoscopic resection of duodenal adenomas is a safe and effective alternative to surgery. Lesion size is strongly associated with adverse events, particularly intraprocedural bleeding and delayed bleeding. Good long-term outcomes are demonstrated. (Gastrointest Endosc 2016;84:688-96.)

(footnotes appear on last page of article)

INTRODUCTION

Duodenal polyps are uncommon and comprise a heterogeneous group including, most commonly, Brunner gland hyperplasia, adenomas, and submucosal lesions. They are found in 0.3% to 4.6% of patients undergoing upper GI endoscopy and are usually incidental findings.[1-4] Sporadic duodenal adenomas (SDAs), ie, adenomas not associated with genetic polyposis syndromes and not involving the major duodenal papilla, account for 7% of all duodenal polyps. They are most commonly found in the second part of the duodenum, and are usually solitary, flat sessile lesions.[5-8] SDAs harbor malignant potential similar to colonic adenomas and removal is therefore recommended. The risk of malignancy seems to increase with the size of the adenoma.[9-11] Similar to colonic adenomas, most appear to be small (<10 mm) and may be managed outside tertiary centers although adverse events are known to be more frequent for small SDAs than for colonic adenomas of similar size.[12] Large (≥10 mm) lateral spreading lesions of the duodenum (LSL-D) are a subgroup of SDAs. Little is known about their prevalence, characteristics, and outcomes after endoscopic treatment.

Traditionally, surgical procedures such as Whipple's pancreatectomy, pylorus-preserving pancreatectomy

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(PPP), or pylorus and pancreas-preserving duodenectomy (PPPD) were the mainstay of treatment for LSL-D. These procedures, although providing curative resection, are associated with significant morbidity (37%–41%) and mortality (1%–6%)[13-15] and thus, for noninvasive disease, endoscopic resection may provide a viable alternative. EMR is a proven effective and safe procedure for the removal of large colonic lateral spreading lesions and in recent years has also gained acceptance as a valuable tool in the treatment of LSL-D.[16-20] Complete endoscopic resection of duodenal adenomas can be achieved in 79% to 100% of cases at the index procedure.[1] Adenoma recurrence is encountered in 10% to 37% of cases and can be adequately managed with additional resection and/or ablative techniques. Significant adverse events (mainly bleeding) are seen in up to 33% of cases.[21,22] Several studies have demonstrated a correlation between lesion size and rates of complete resection, recurrence, and adverse events.[23-26] However, long-term data are limited and large lesions seldom comprise a significant portion of reported cohorts.

Herein we report on the immediate and long-term outcomes of a large cohort of patients with LSL-D referred to a tertiary center for endoscopic treatment.

METHODS

Study design

A retrospective analysis of a prospectively collected and maintained database was performed. Data collection included patient demographics and clinical data, lesion characteristics (location, size, morphological type, histologic diagnosis), procedure-related data (technical success, adverse events), and results of endoscopic and clinical follow-up. The study was approved by the institutional review board and registered (NCT02306603).

Patients

Patients who were referred for EMR of LSL-D between January 2007 and November 2015 were included. A comprehensive pre-resection evaluation was undertaken to ensure the procedure was clinically appropriate. The patient's general health, functional status, and medical comorbidities were assessed, and the lesion's size, location, histopathology if available, and relationship to the papilla were reviewed. All patients received a detailed explanation regarding the procedure, its risks, benefits, and alternatives, and provided written informed consent. Patients receiving anti-platelet agents or anti-coagulants were instructed to stop the medication 5 to 7 days before the procedure in accordance with established societal guidelines.[27]

Lesions

Large LSL-Ds were defined as those ≥10 mm in size with predominant Paris 0-IIa or 0-ls morphology. Giant LSL-Ds are defined as those >30 mm in size. The greatest dimension of the polyp was estimated by reference to an open polypectomy snare of known size.

Procedure

An experienced endoscopist or senior endoscopy fellow under direct supervision performed all EMR procedures. Endoscopy was performed after overnight fasting on the patients on the morning list. Sedation with midazolam, fentanyl, and propofol was used in 90 patients (86%). General anesthesia was used in the remaining 14% in whom technical complexity, predominantly related to lesion size, was anticipated. The previously well-described standard inject and resect EMR technique was used in all cases.[28,29] The type of endoscope used was influenced by lesion location and was selected by the endoscopist to ensure optimal access to the lesion (Table 1). Our preference was to use a pediatric colonoscope for the dual advantages of more favorable 6 o'clock orientation of the working channel and the additional working length. For lesions on the medial and anterior wall, a side-viewing instrument (duodenoscope) may provide better access and was often used as a backup in these instances. For complex and extensive resection, both instruments may have been necessary. For EMR we mainly used braided 15-mm oval snares. Thin-wire 10-mm snares were used for difficult nonlifting areas or to treat recurrent adenoma. Complete endoscopic resection was defined as no residual visible adenomatous tissue at the end of the EMR. We always aimed to achieve complete snare excision. Argon plasma coagulation (APC) was not used for treatment of visible residual adenoma. Postprocedural care involved 2- to 4-hour monitoring in the endoscopy suite, clear fluids overnight, and bi-daily proton pump inhibitors (PPI) for 6 weeks. Hospital admission for observation was undertaken at the discretion of the endoscopist, usually after large complex resections or if significant intraprocedural bleeding (IPB) was encountered during the procedure. Pathology was reported by specialist GI pathologists.

Adverse events and outcome definitions

In our department, the definition of IPB is standardized as persistent oozing or spurting of blood during the procedure that did not arrest spontaneously within 60 seconds or after water irrigation, and required endoscopic treatment. This was achieved with snare tip soft coagulation (STSC) or coagulation graspers (80W effect 4, Vio 300D; ERBE, Tubingen, Germany). Delayed bleeding (DB) was defined as any clinically significant bleeding occurring after the procedure and requiring presentation to the emergency department, hospitalization, or medical intervention. Perforation was defined as clinical evidence of muscularis propria injury or a frank hole in the bowel wall. First surveillance endoscopy (SE1) was performed at 4 to 6 months after resection. If no recurrence was present, further surveillance was performed yearly thereafter. If adenoma

TABLE 1. Patient and lesion characteristics and procedural data for the entire cohort (N = 106)

Characteristic	Value
Patient characteristics	
Mean age (years)	69
Female gender (%)	46
Mean ASA classification (range)	2 (1–4)
Major comorbidities (%)*	42
Anti-platelet medications, n (%)	22 (21)
Anti-coagulation medications, n (%)	2 (2)
Lesion characteristics	
Location, n (%)	
D1	8 (7)
D2	85 (81)
D3	13 (12)
Paris classification (%)	
0-IIa	70
0-Is	14
Median lesion size, mm (IQR)	25 (19–40)
Lesion size by group, n (%)	
10-20 mm	38 (36)
21-30 mm	29 (27)
31-40 mm	21 (20)
41-50 mm	10 (9)
>50 mm	8 (8)
Histology, n (%)	
TA/TVA + LGD	99 (93)
TA/TVA +HGD/IMC	6 (6)
Invasive cancer	1 (1)
Procedural data	
Endoscope type, n (%)	
Duodenoscope	19 (18)
Pediatric colonoscope	50 (47)
Gastroscope	12 (11)
Combination	14 (13)
Not reported	11 (11)
Median procedure time, min (IQR)	53 (39–73)
Anesthetic support (%)	
General anesthesia	16
Sedation	84
IPB, n (%)	46 (43)
Treatment for IPB, n (%)	
STSC	71 (67)
Coagulation forceps	8 (7)
Clips	18 (17)
Combination	9 (9)

ASA, American Society of Anesthesiologists; *IPB*, intraprocedural bleeding; *TA*, tubular adenoma; *TVA*, tubulo-villous adenoma; *LGD*, low-grade dysplasia; *HGD*, high-grade dysplasia; *IMC*, intramucosal cancer; *IQR*, interquartile range; *STSC*, snare tip soft coagulation.
*Major comorbidities include IHD with previous intervention, chronic lung disease, chronic kidney disease, major thromboembolic event.

recurrence was identified at SE1, further surveillance was performed after an additional 6 months and then yearly. Suspected adenoma recurrence was treated endoscopically by snare excision or ablative methods such as APC or STSC at the discretion of the endoscopist. Adenoma recurrence was defined as histologically proven adenoma from biopsy specimens obtained during surveillance endoscopy.

Statistical analysis

Descriptive statistics are presented as mean + range or median + interquartile range (IQR). Univariate analysis for the association between continuous variables and outcomes was tested with the Mann-Whitney test. Categoric variables were analyzed with the Pearson χ^2 test. Results were considered significant for a P value <.05. Multivariate forward feeding binary logistic regression was performed to single out independent predictors of resection outcomes. Data analysis was performed using SPSS (version 23; SPSS, Chicago, Ill).

RESULTS

Over 8 years to November 2015, 117 duodenal lesions were referred for EMR at our center. EMR was not attempted for 3 lesions and instead these patients were referred directly to surgery (suspicion of invasive disease [n = 2], later confirmed in the surgical specimen in both cases, and luminal stenosis limiting access [n = 1]). In 8 cases the excised specimen revealed a nonadenomatous pathology (lipoma [n = 2]; angiolipofibroma [n = 1]; gastric heterotropia [n = 2]; hamartoma [n = 2]; hyperplastic polyp [n = 1]). These were excluded from the analysis. One hundred six LSL-Ds were resected (mean patient age, 69 years; 54% male; median lesion size, 25 mm; IQR, 19–40 mm) (Fig. 1). Twenty-nine patients had a lesion encompassing ≥2/3 of the luminal circumference (lesion size, >40 mm). For lesions removed en bloc, endoscopic size estimation was similar to the size of the histologic specimen (mean, 15.3 mm vs 14.8 mm; P = 0.5). Overall, complete endoscopic resection was achieved in 102 of 106 lesions (96%) at the index procedure. Table 1 shows patient, lesion, and procedural characteristics for the entire cohort.

Patients

Forty-five patients (42%) had at least 1 major comorbidity. Mean American Society of Anesthesiology (ASA) score

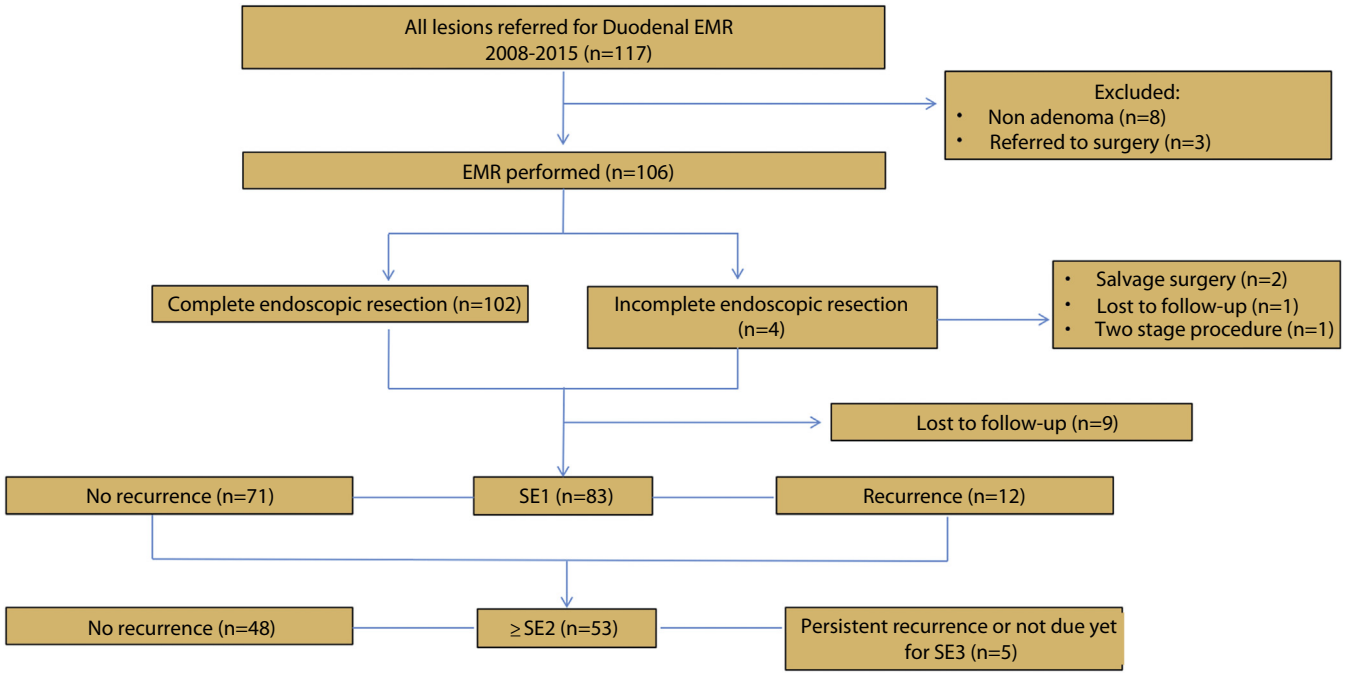

Figure 1. STROBE diagram. *SE*, surveillance endoscopy.

was 2 (range, 1–4). In addition, 22 patients (21%) were taking anti-platelet agents and 2 patients were on warfarin. There was no correlation between the presence of major comorbidity or use of anti-platelet/anti-coagulation medications and adverse events. Patient characteristics such as age and ASA classification were similar between patients who developed adverse events and those who did not.

Effect of pre-resection biopsy

Compared with pre-resection biopsy, EMR changed the histology in 30% of cases (upgraded in 27%, downgraded in 3%). However, there was no increased risk of adverse outcomes in lesions that underwent a previous biopsy versus those that did not (IPB, 47% vs 44%, $P = .28$; DB, 12% vs 22%, $P = .09$; perforations, 0% vs 3%, $P = .28$; incomplete endoscopic resection, 100% vs 95%, $P = .84$).

Bleeding

IPB occurred in 46 of 106 cases (43%) and was successfully managed endoscopically with STSC (n = 31), coagulation forceps (n = 3), clips (n = 8), or a combination thereof (n = 4). Clips were used earlier in our experience; however, 2 of 8 patients had a perforation. On univariate analysis, IPB was associated with lesion size ($P < .001$), number of resected specimens ($P = .005$), and longer procedures ($P = .001$). DB occurred in 16 patients (15%) (56% of these did not need active intervention). Endoscopic intervention was successful in 5 of 7 patients. One patient required angio-embolization and 1 patient went directly to emergent surgery to control massive bleeding. Seven patients required red blood cell transfusion (median, 2 units; IQR 1–3). On univariate analysis, DB was associated with lesion size ($P = .03$). DB was not associated with piecemeal resection or the presence of IPB ($P = .09$ for both comparisons). On multivariate analysis, lesion size was the only significant independent predictor for both IPB ($P = .001$) and DB ($P = .01$).

Perforation occurred in 3 patients. Two required surgery and 1 was successfully managed endoscopically with clip closure. One perforation was delayed, presenting 12 hours after the procedure. Overall, 46 patients (44%) were admitted to the hospital; 21 of these patients (45%) were admitted as a result of a procedure-related adverse event (median length of stay, 5 days; IQR, 2.5–9). The other 55% were admitted for observation only (median length of stay, 1 day; IQR, 1–1) with no further adverse sequelae. Overall admission was associated with larger lesion size ($P < .001$), longer procedures ($P < .001$), and the number of resected specimens ($P < .001$). However, no differences were observed between patients admitted for observation and those admitted for an adverse event. The 30-day mortality was 0%.

Follow-up

Eighty-three of 106 patients (79%) had at least 1 surveillance endoscopy (SE). Median follow-up for the entire cohort was 22 months (IQR, 7–45). Thirteen patients were not yet due for their first surveillance and 10 patients were lost to follow-up. Histologically confirmed recurrence/residual adenoma was seen and treated in 12 of 83 patients (14.4%) during SE1 (Fig. 1). Recurrence was treated by snare excision (n = 4), STSC (n = 1), or

TABLE 2. Univariate analysis of adverse events and outcomes

	No IPB	**IPB**	***P* value**
Median procedure time, min (IQR)	47 (36-61)	69 (47-96)	.001
Median number of resected specimens (IQR)	2 (1-4)	4 (2-7)	.005
Median lesion size, mm (IQR)	25 (15-30)	35 (25-45)	<.001
En bloc resection (%)		31	.09
Piecemeal resection (%)		49	
	No DB	**DB**	
Median procedure time, min (IQR)	51 (39-70)	67.5 (39-120)	.14
Median number of resected specimens (IQR)	3 (1-5)	4 (3-7)	.055
Median lesion size, mm (IQR)	25 (18-35)	35 (25-55)	.03
En bloc resection (%)		6	.09
Piecemeal resection (%)		19	
With IPB (%)		22	.09
No IPB (%)		10	
	No admission	**Admission**	
Median procedure time, min (IQR)	46 (36-56)	70 (55-96)	<.001
Median number of resected specimens (IQR)	2 (1-4)	4 (3-6)	<.001
Median lesion size, mm (IQR)	25 (15-30)	40 (25-50)	<.001
	No recurrence (SE1)	**SE1 recurrence**	
Median lesion size, mm (IQR)	30 (20-40)	35 (25-40)	.065
En bloc resection (%)		4.2	.008
Piecemeal resection (%)		18.6	
	Not clear of disease at latest SE	**Clear of disease at latest SE**	
Median lesion size, mm (IQR)	40 (25–60)	30 (25–50)	.1
En bloc resection (%)		92	
Piecemeal resection (%)		80	.17

Mann-Whitney and χ^2 tests were used to analyze continuous and categorical variables respectively. The comparison is made between cases that exhibited the outcome and those that did not and the variables associated with the specific outcome.
IQR, Interquartile range; *DB*, delayed bleeding; *IPB*, intraprocedural bleeding.

a combination of methods (n = 7). Two of the 12 patients (16.7%) had persistent histologically proven recurrence at SE2. The rest were considered cured on long-term follow-up. Piecemeal resection was associated with higher rates of histologically proven recurrence at SE1 compared with en bloc resection (18.6% vs 4.2%, $P = .008$). We found no correlation between histologically proven recurrence at SE1 and lesion size or the number of resected specimens. Fifty-three patients had at least 12 months of follow-up (≥2 SE; median follow-up, 36 months; IQR, 24–51). Forty-eight of 53 patients (90.6%) were free of adenoma and considered cured. Table 2 summarizes adverse events and outcomes for the entire cohort.

Comparison between small and large lesions

Compared with large LSL-Ds (<30 mm), giant LSL-Ds (≥30 mm) had significantly more IPB ($P = .002$), DB ($P = .02$), and number of hospital admissions ($P < .001$). We found no significant differences between the 2 groups in the rates of complete endoscopic resection ($P = .35$), histological recurrence at SE1 ($P = .15$), or long-term endoscopic cure ($P = .16$). Table 3 shows the comparison between small and large lesions.

DISCUSSION

In this study we sought to evaluate our experience with EMR for large and giant LSL-Ds. We were able to identify predictors of adverse events and report on long-term outcomes.

We observed that the final EMR histology changed in a significant number of cases in comparison with the

TABLE 3. Comparison between large LSL-Ds and giant LSL-Ds

	Lesion <30 mm (n = 55)	Lesion ≥30 mm (n = 51)	*P* value
Patient/procedure			
Mean age, years (range)	67 (58-73)	71 (66-79)	.02
ASA classification, mean (range)	2 (1-2)	2 (2-3)	.2
Median procedure time, min (IQR)	45 (35-50)	73 (55-96)	<.001
Adverse events (%)			
Intraprocedural bleeding	29	59	.002
Delayed bleeding	7.3	23.5	.02
Admission	20	63	<.001
Mortality	0	0	
Outcomes (%)			
Complete endoscopic resection	98	94	.35
Histologic recurrence at SE1	9.5	19	.15
Clear at last SE	95	83	.16

Mann-Whitney and χ^2 tests were used to analyze continuous and categorical variables, respectively.
IQR, Interquartile range; *SE1*, first surveillance endoscopy; *SE*, surveillance endoscopy.

pre-resection histology. Discrepancy between the pre-resection biopsy result and that of the resected EMR specimens has been reported in duodenal lesions.[30,31] Kakushima et al[32] reported a discrepancy rate of 41% in 56 duodenal lesions (36% upgraded and 5% downgraded histology in the EMR specimen compared with the pre-resection biopsy results). Although this did not result in a statistically significant difference in adverse event rates in our study, from our experience pre-resection biopsies often cause submucosal fibrosis, which makes resection more difficult. We therefore believe that biopsies should be avoided unless serious doubt exists regarding the nature of the lesion. Instead, pre-resection assessment of the mucosal surface of the lesion by an experienced endoscopist with high-definition endoscopy including enhanced modalities such as narrow-band imaging should be used. If necessary, a superficial biopsy specimen from an area between folds can be taken, or in the case of a focal abnormality, directly from this area. Biopsy specimens taken from the tops of folds create a risk of subsequent adherence between the 2 mucosal surfaces on either side of the folds with interposed submucosa and muscularis propria.[21] Previously described endoscopic features suggestive of more advanced pathology include the presence of a Paris 0-llc (depressed) component, a red and ill-glistened surface, and irregular mucosal or vascular patterns on magnifying endoscopy and narrow-band imaging.[33-35] High-quality photo documentation is important and may be used as a reasonable substitute for biopsy.

Bleeding

In a recent review of the literature, Basford and Bhandari[1] summarized data from 5 case series of duodenal EMR.[5,8,18,19,36] In those series, reported IPB ranged from 7% to 18% and DB occurred in 3.9% to 22% of procedures, all successfully managed endoscopically. In a series with large lesions, Eswaran et al[37] reported an overall bleeding rate of 8%; however, a distinction between IPB and DB was not made. Lack of a standard definition of IPB in these studies does not enable firm conclusions to be drawn as to whether these bleeding episodes were of similar severity or clinically significant. In our center, we define IPB as any oozing/spurting bleeding encountered during EMR that does not spontaneously arrest within 60 seconds including with water irrigation and requires endoscopic treatment. In our cohort, IPB occurred at a rate of 43% and was successfully treated endoscopically in all cases. This higher bleeding rate may be attributed to the presence of very large lesions within our cohort (median size, 25 mm; 29 lesions >40 mm). IPB was independently associated with lesion size (P = .001) but did not predict DB. DB occurred in 15% (56% of these did not need active intervention) and was also independently associated with lesion size (P = .01 for multivariate analysis). We did not find an association between the presence of major comorbidities or the prior use of anti-platelet/anti-coagulation agents and the rates of IPB or DB. However, we recognize that our cohort size may not be adequately powered to address this relationship.

Other adverse events

In our cohort, perforation occurred in 3 patients, 2 of whom required surgery. This is comparable with the reported rate in the literature (up to 3%).[18,37] The duodenal wall is relatively fixed and thin. Clipping (eg, to control bleeding) onto the exposed deep submucosa within the post-EMR defect may inadvertently cause deep mural

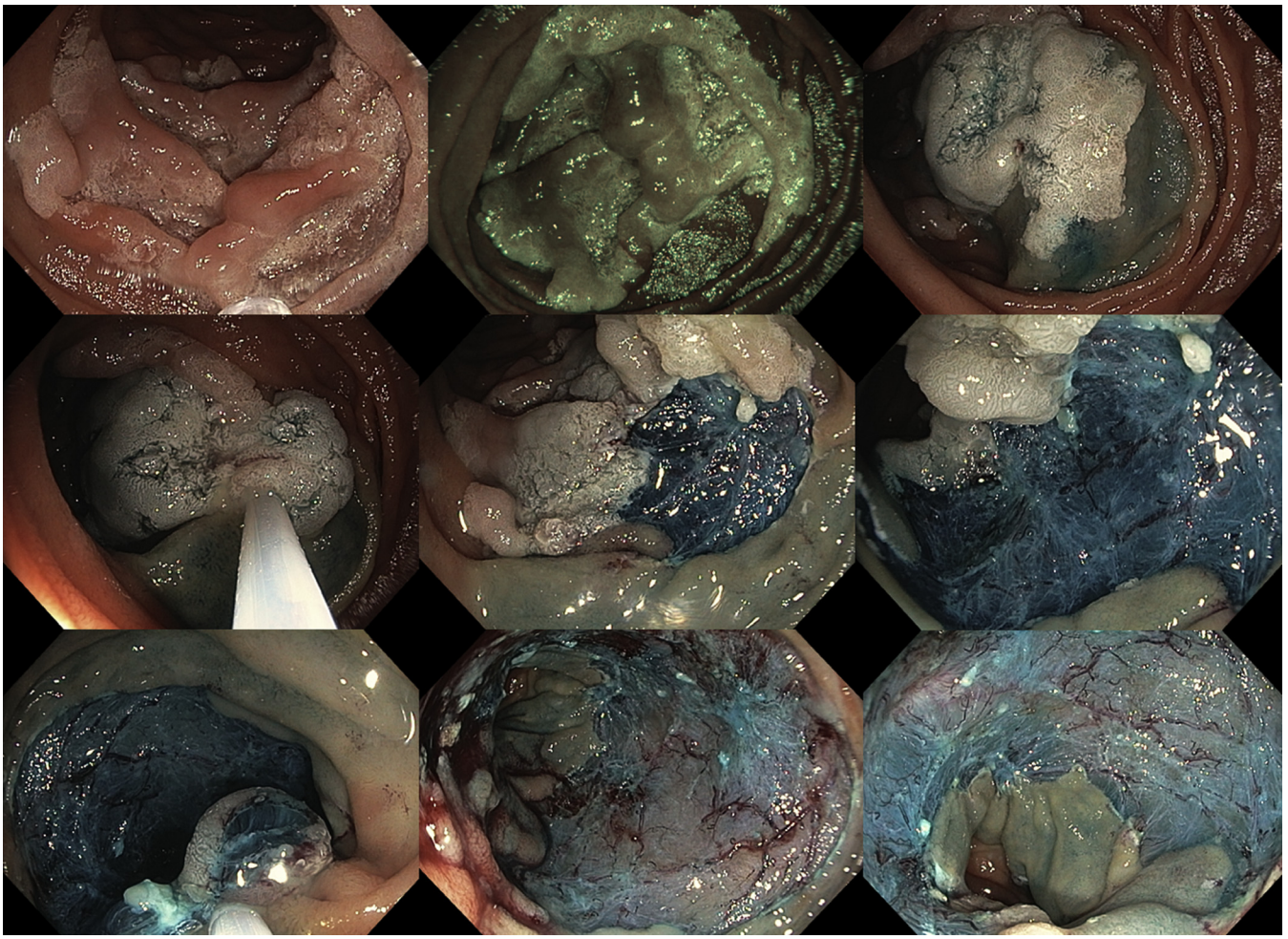

Figure 2. EMR of a nearly circumferential 60-mm duodenal adenoma. EMR inject and resect technique was used. The final mucosal defect was covered with Endoclot (Endoclot Plus Inc., Santa Clara, Calif, USA).

injury as a result of the traction force of the clip on the relatively fixed muscle layer of the duodenal wall. Great care should be exercised. Clipping onto intact mucosa (for defect closure or for closure over suspected deeper injury) is probably safe and may avoid the need for surgery in cases of small perforations.

The overall admission rate was 44%. Although this may seem like a relatively high number, in over half of the cases the patients were observed overnight as a precautionary measure and discharged the next day without any intervention or adverse event. Two patients early in our experience received salvage surgery because of incomplete removal of the adenoma in 1 case and persistent recurrence during surveillance in the second case. In both cases, local surgical excision was performed. The 30-day mortality was 0%.

Follow-up

SE1 was performed in 83 of 106 patients (79%). Histologically confirmed recurrence/residual adenoma at SE1 was seen and treated in 12 of 83 patients (14.4%). Fifty-three patients had ≥12 months of surveillance (median follow-up duration, 36 months). Previous reports on recurrence rates vary greatly (0%–36%). Lépilliez et al[18] reported no cases of recurrence during a mean follow-up of 15 months with 42% of patients having 1 follow-up endoscopy. Conversely, Abbass et al[24] reported 37% recurrence after a mean follow-up of 26 months, with a rate of 63% in lesions >2 cm in diameter. Alexander et al[19] reported recurrence in 25% of cases. All of these were successfully retreated with either snare resection or APC ablation. In a study by Apel et al,[5] recurrence occurred in 5 of 17 cases (29%) with successful treatment in 2 cases. In our study, piecemeal resection was associated with recurrence at SE1. Piecemeal resection is known to be associated with higher rates of recurrence after colonic EMR.[38] Because the resection technique is similar, this observation is not surprising. Taken together with the relatively high recurrence rates in other studies, this emphasizes the requirement for a structured surveillance program with adequate photo documentation and routine biopsies of any suspicious areas within the EMR

scar. However, recurrences are usually diminutive and easily treated at surveillance, resulting in a good overall curative outcome, which is not influenced by the index resection type (ie, piecemeal versus en bloc). In our cohort, for patients with long-term follow-up (≥12 months and ≥2 SEs [n = 53; median follow-up, 36 months]), 90.6% were free of adenoma and considered cured, and only 2 patients required salvage surgery (early in our experience) as a result of failed endoscopic treatment.

Comparison between large LSL-D and giant LSL-D

We defined giant LSL-D as those ≥30 mm. These lesions are nearly always removed piecemeal and require longer procedure times and greater expertise (Fig. 2). Previous series have also shown higher rates of adverse events and recurrence in larger lesions.[24] Compared with small lesions (<30 mm), larger lesions had significantly more IPB (59% vs 29%, $P = .002$), DB (23.5% vs 7.3% $P = .02$), hospital admissions (63% vs 20%, $P < .001$), and longer postprocedural hospital stay ($P < .001$). Conversely, outcomes such as achieving complete endoscopic resection and long-term recurrence rates were not statistically different between the 2 groups (Table 3). LSL-Ds are a relatively uncommon entity and our sample size may be underpowered for some of these comparisons. However, we believe that these observations suggest that lesion size may be an important factor predicting peri-procedural adverse events, but ultimately, in experienced tertiary centers, long-term outcomes are not affected. It is possible that experienced endoscopists trained in complex endoscopic resection and management of adverse events performing the procedure in a tertiary center is a more important factor in assuring a successful long-term outcome.

Limitations

Although a retrospective analysis may introduce some biases to the study, our patient, lesion, and procedural data are collected and maintained prospectively, mitigating this limitation to some extent. In addition, we recognize that our results may not be generalized. These data were accumulated in a large tertiary center specialized in complex endoscopic tissue resection, and our results mirror more than a decade of extensive experience in this field. However, equivalent specialized centers are now more common, and similar results can be reasonably expected. We believe that complex endoscopic resection, particularly in the duodenum, should be performed in large tertiary centers with an adequate case volume and endoscopists trained in complex resections and the management of associated adverse events. Adverse events are inevitable with wide-field EMR for LSL-D but, with experience, their frequency and severity can be minimized.

In conclusion, EMR of even very large LSL-Ds can be performed safely and effectively in a tertiary center by endoscopists trained in complex endoscopic resection and management of the associated adverse events. DB is a significant risk. The patient's comorbidities and life expectancy need to be continuously factored into the decision-making process. Recurrence is not uncommon but can be effectively treated during surveillance emphasizing the requirement for a structured surveillance program. Overall excellent long-term outcomes can be expected.

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Abbreviations: APC, argon plasma coagulation; ASA, American Society of Anesthesiology; DB, delayed bleeding; IPB, intraprocedural bleeding; IQR, interquartile range; LSL-D, lateral spreading lesions of the duodenum; PPI, proton pump inhibitors; PPP, pancreatectomy, pylorus-preserving pancreatectomy; PPPD, pylorus and pancreas-preserving duodenectomy; SDA, sporadic duodenal adenoma; SE, surveillance endoscopy; SE1, first surveillance endoscopy; STSC, snare tip soft coagulation.

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