

EMR of large, sessile, sporadic nonampullary duodenal adenomas: technical aspects and long-term outcome (with videos)

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Background: EMR is a viable alternative to surgery for removal of large mucosal neoplastic lesions of the entire GI tract. Few studies have, however, been published on the safety, efficacy, and technical aspects of EMR in the duodenum.

Objective: Our purpose was to evaluate the efficacy and safety of EMR of large (> 15 mm) duodenal adenomas.

Design: Retrospective evaluation of a defined patient cohort.

Setting: Tertiary academic referral center.

Patients: Patients with large (> 15 mm) sporadic nonampullary duodenal adenomas managed by a standardized technique who were referred by other specialist endoscopists for endoscopic treatment.

Methods: Five-year data from patients undergoing EMR for large duodenal adenomas were reviewed retrospectively. Immediate and delayed complications were recorded.

Results: Twenty-one lesions were removed by EMR in 23 patients (mean age 62.2 years, 13 female, 10 male). The mean size of lesions resected was 27.6 mm (median 20 mm, range 15-60 mm). Post-EMR histologic examination revealed mucosal adenocarcinoma in 1, low-grade tubulovillous adenoma (TVA) in 16, high- or focal high-grade TVA in 3 patients, and 1 with both high-grade TVA and carcinoid. EMR was performed successfully in 18 patients during a single session. Two patients required 2 sessions and 1 required 3 sessions for complete resection. The median follow-up was 13 months (range 4-44 months). During follow-up, 5 patients had minor residual adenomas that were treated successfully with snare resection and/or argon plasma coagulation. One patient had EMR site bleeding. There were no perforations.

Limitation: Retrospective study.

Conclusion: EMR for large sporadic nonampullary duodenal adenomas is a safe and effective technique. (Gastrointest Endosc 2009;69:66-73.)

Sporadic nonampullary duodenal adenomas are extremely uncommon.¹ The optimal treatment technique for large adenomas has not yet been defined. The majority of the published literature describes the experience with surgical techniques. Endoscopic resection by EMR of a nonampullary duodenal lesion was first described in

1992, but since then there have been few reports of endoscopic resection in the duodenum.²⁻⁴ The technique has not been standardized, and data on long-term outcomes are lacking. The aim of this study was to evaluate the short- and long-term outcomes of EMR of large, sessile, sporadic nonampullary adenomas in the duodenum.

Abbreviations: APC, argon plasma coagulation; TVA, tubulovillous adenoma.

DISCLOSURE: The authors report that there are no disclosures relevant to this publication.

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0016-5107/\$36.00
doi:10.1016/j.gie.2008.04.061

PATIENTS AND METHODS

The study was approved by the human ethics and research committee. The endoscopy database of a tertiary referral, university-affiliated hospital was reviewed to identify all patients with large nonampullary sessile duodenal lesions encountered over the preceding 5 years to December 2007.

Patient files and endoscopy reports were reviewed, and where necessary structured telephone interviews were performed. Data collected included lesion size and morphologic grade, histologic diagnosis, number of treatments, complications, and results of follow-up endoscopies. Only sessile lesions greater than 15 mm were included. Patients with polyposis syndromes were excluded.

Procedures were performed with the patient under sedation with a combination of midazolam, fentanyl, and propofol. Intravenous hyoscine 10 to 20 mg (Buscopan, Boehringer Ingelheim, Sydney, Australia) was given at the time of EMR when required to limit duodenal motility. The diameter of the polyp was estimated at the time of endoscopy by reference to an open polypectomy snare placed adjacent to the polyp. EUS was not routinely performed on these lesions. Instead, resectability was assessed at the time of the therapeutic procedure as detailed below.

Technique

All duodenal EMR procedures were performed by 2 experienced interventional endoscopists (M. J. B. and S. J. W.) using a standardized approach similar to that formally adopted for colon EMR in our center.^{5,6} The relationship between the lesion and the papilla was routinely assessed, including use of a side-viewing instrument if necessary. For lesions predominantly occupying the anteromedial wall of the duodenum, a duodenoscope was used, and for lesions on the lateral or posterior wall a pediatric variable-stiffness colonoscope was used (Olympus Optical, Tokyo, Japan).

EMR was performed by the well-recognized general principles of tangential submucosal injection of a large volume (>20 mL) normal saline solution in combination with dilute epinephrine (1 in 10,000) and indigo carmine (0.04%, Mayne Pharma, Melbourne, Australia).^{7,8} Freehand en bloc resection was then attempted for lesions of 15 to 20 mm (Figs. 1 and 2). Sequential piecemeal resection was performed for lesions greater than 20 mm with use of a combination of stiff-type snares, depending on lesion size and morphologic characteristics (20 mm SnareMaster, Olympus, Tokyo, Japan, or 15 mm × 30 mm AcuSnare [mini oval], 25 mm × 55 mm AcuSnare [standard oval], Cook Medical, Brisbane, Australia). For carpet-like lesions, the serrated snare (SnareMaster) was preferred to enhance tissue capture. The mini oval snare was used to remove any residual at the margin. For smaller or nodular lesions, the mini oval or standard oval snare was preferred.

The technique included the following:

- Minimizing the number of separate injections to decrease the likelihood of transmucosal fluid escape, which had been our anecdotal experience when multiple separate injection sites had been used (in excess of 5).
- In cases of piecemeal resection, commencing at one lateral margin and generally proximally, including a small 1- to 3-mm margin of normal mucosal tissue (Figs. 3 and 4).
- The polyp capture was performed by pushing down firmly with an open snare on the target tissue while

Capsule Summary

What is already known on this topic

- Duodenal adenomas are usually solitary, but they have a rate of malignant transformation ranging from 35% to 85%.
- Endoscopic resection of large, sessile nonampullary duodenal adenomas has been considered a high-risk procedure because of the thin duodenal wall.

What this study adds to our knowledge

- In a retrospective analysis of 21 patients who underwent EMR for sessile, sporadic nonampullary duodenal adenomas greater than 15 mm, 18 lesions were removed in a single session, with 3 requiring multiple sessions for complete resection.
- At a median follow-up of 13 months, 5 lesions resected piecemeal had remnant adenoma, but no recurrences were detected among patients treated with en bloc resection.

aspirating air as the snare was closed. Reinsufflation was then performed, and appropriate positioning of the snare was visually confirmed. In addition, the mobility of the mucosa relative to the muscularis propria was assessed by moving the snare back and forth several times. This was done for the dual purpose of ensuring that deeper layers had not been ensnared and that the lesion was freely mobile relative to the muscularis propria, making deep invasion unlikely (Video 1, available online at www.giejournal.org).

- Recognition of the critical role of the first snare resection to arrive in the correct plane as evidenced by a significant wide mucosal defect with a blue base.
- Once in the correct plane, tissue was removed sequentially from that point, always working within that initial tissue plane, analogous to surgical dissection.
- Attempt to resect the lesion in as few pieces as safely possible.
- For lesions that were greater than 40 mm or that occupied more than one wall of the duodenum, injection and resection of each wall or half segment was performed in turn to allow free access to the lesion and to enhance visualization (too large an initial injection may obscure the endoscopic view) and to minimize time for subsidence of the cushion from fluid diffusion.

Two different electrosurgical generators were used during the study. Before 2005, a Soring generator (Arco-3000, Quickborn, Germany), with a blended current of 60 watts cut and 30 watts coagulation, was used in 5 cases. After 2005, an ERBE electrosurgical unit (VIO 300, ERBE, Tubingen, Germany) set to Endocut Q, Effect 3, delivering a cut duration of 2 milliseconds and a cut interval of 1200 milliseconds was used.

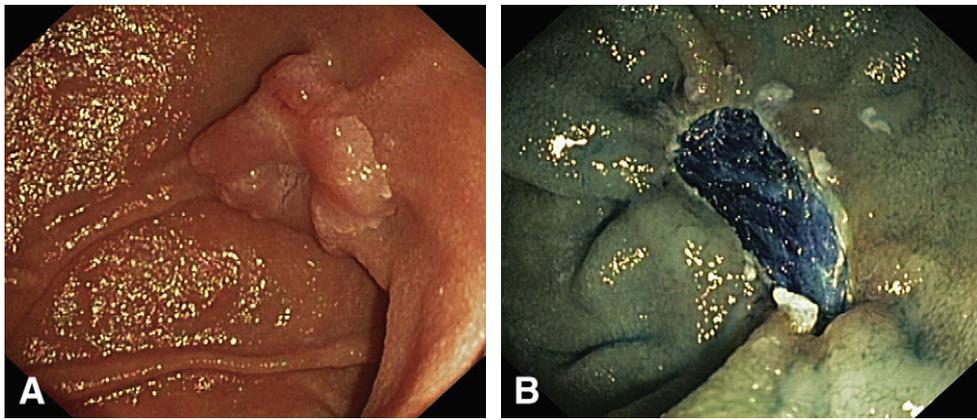


Figure 1. **A**, A 15-mm flat lesion on the lateral wall, with central depression. **B**, Complete en bloc snare resection with clean margins.

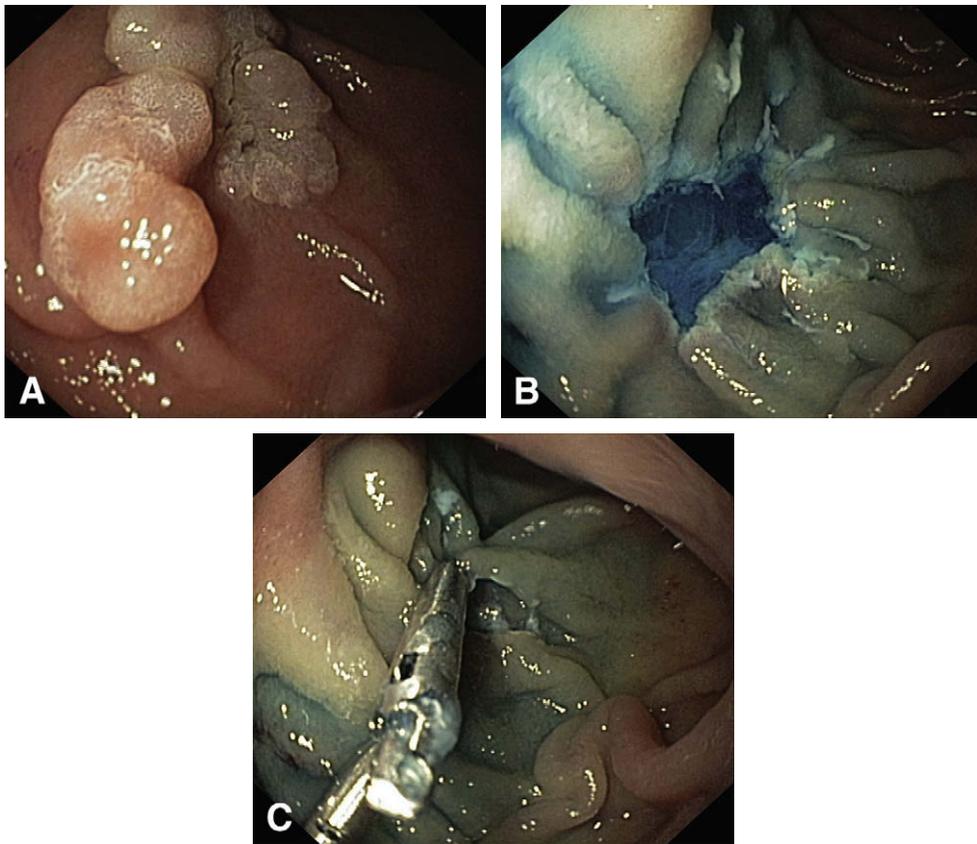


Figure 2. **A**, A 20-mm lesion on the posterior wall in a patient on obligatory antiplatelet therapy (drug-eluting coronary stent). **B**, After en bloc resection. **C**, Defect closed with 2 clips.

Postprocedural care and surveillance

Mucosal resection procedures were performed on outpatients between 8 and 10 AM. After an uncomplicated standard postendoscopy recovery, the patient remained in second-stage recovery for 4 to 6 hours on a clear liquid diet before final review by the proceduralist before discharge. If the patients were well at that point, they were allowed home on a clear liquid diet until the following

morning, after which a normal diet was to be resumed. Written information was provided for the patient and the family or carers on potential problems and the signs along with a contact number. All patients received twice-daily proton pump inhibitory therapy for 2 weeks after resection.

Every attempt was made to completely resect the lesion in a single session. Patients who had undergone

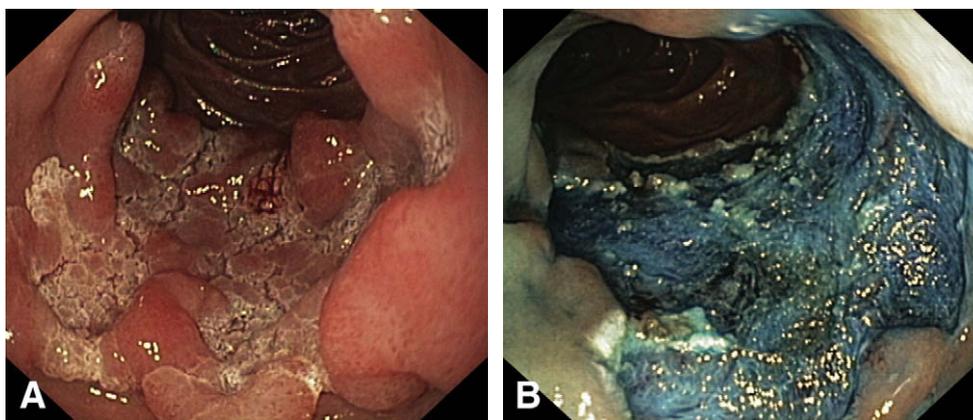


Figure 3. **A**, A 60-mm carpet-like lesion occupying two thirds of the duodenum. **B**, After piecemeal resection.

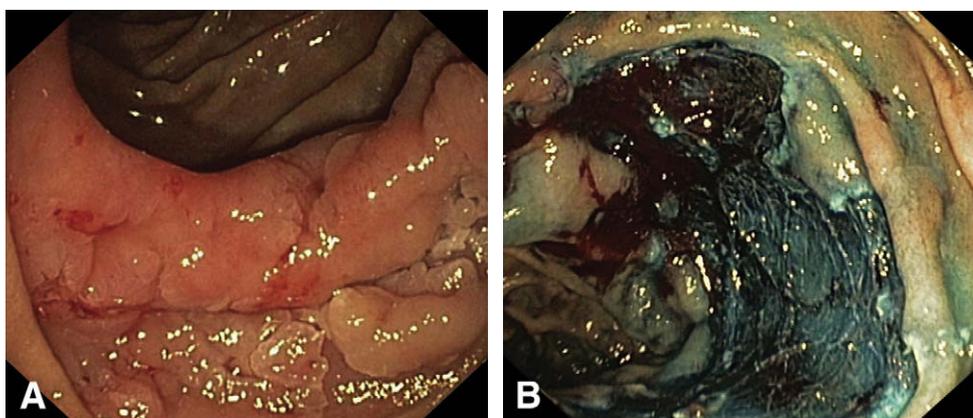


Figure 4. **A**, A 50-mm carpet-like lesion occupying one half of the duodenum. **B**, Defect after piecemeal resection. Minor venous oozing.

a technically successful and complete resection with endoscopically clear margins were scheduled for follow-up examinations in our unit at 3 and 12 months and then were advised to attend annually with the referring endoscopist. In cases where small amounts of residual adenoma were detected, these were resected with the mini oval snare without submucosal injection. Argon plasma coagulation (APC) was used if necessary but only to treat minute residuals that could not be removed with the snare. In cases where only a scar was detected, biopsies were performed for histologic confirmation.

Histologic assessment

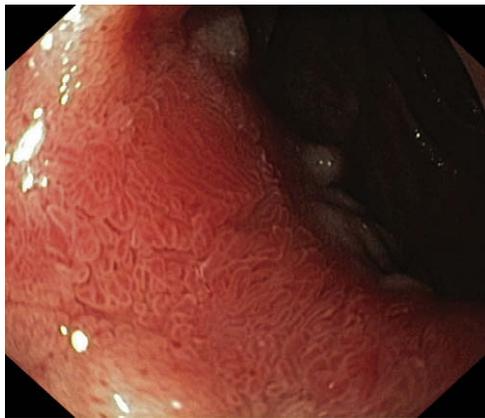
All tissue was retrieved for histologic analysis, and in the case of multiple fragments a disposable retrieval net was used (Roth retrieval basket, Endomed, Brisbane, Australia). All lesions resected en bloc, and the dominant parts of larger polyps resected piecemeal, were flattened and fixed with thin needles onto cork before pathologic fixation. All specimens were reviewed by specialist GI pathologists. Lesions with high-grade dysplasia or invasive carcinoma were reviewed in conjunction with the investigators.

RESULTS

We identified a total of 23 patients with large, sessile, sporadic nonampullary duodenal adenomas. Of these, 21 underwent EMR. All patients had been referred by 19 specialist endoscopists from outside our service. Baseline patient and polyp characteristics are shown in [Table 1](#). The mean lesion size was 27.6 mm (median 20 mm, range 15-60 mm). Two polyps were located at the junction of the first and second parts, and 19 were in the second part. EMR was performed on 21 lesions; 8 en bloc resection (mean size 15.6 mm) and 13 piecemeal (mean size 34.6 mm). All patients completed the endoscopic surveillance protocol. Two patients with 60- and 40-mm lesions had endoscopic features suggestive for invasion, including nonlifting sign and lack of mobility when manipulated with the snare; thus EMR was not attempted. In 1 patient EUS was suspicious for submucosal invasion, and the patient underwent surgery with deep submucosal invasion confirmed. The second patient (with a history of atrial fibrillation) had a major cerebral ischemic event before EUS could be performed, and EMR was not attempted.

TABLE 1. Baseline patient and polyp characteristics (n = 23)

Mean age (y ± SD)	62.2 ± 13.9
Female/male ratio	13:10
Symptoms	
Iron deficiency anemia	3
Abdominal pain	2
Nausea and vomiting	2
No symptoms	16

**Figure 5.** Scar site 3 months after resection of the lesion shown in Figure 3A. Note the prominent villi.

Histologic assessment after resection revealed mucosal adenocarcinoma in 1, low-grade tubulovillous adenoma (TVA) in 16, high or focal high-grade TVA in 3 patients and 1 with both high-grade TVA and a small 5-mm submucosal carcinoid that had been completely excised. EMR was performed successfully in 18 patients during a single session. Two patients required 2 sessions, and 1 required 3 sessions for complete resection. All 3 had extensive lesions occupying more than two thirds of the duodenal circumference, and one had also had multiple prior attempts at resection before referral with resultant submucosal fibrosis. Additional sessions were performed at 4 weekly intervals.

Clinical and endoscopic follow-up is available in 20 and pending in 1 patient. Sixteen patients have undergone scheduled examinations at 3 and 12 months, and 4 patients have completed 3 months of follow-up. The median follow-up is 13 months (range 4 to 44 months). In 15 patients, endoscopic examination at 3 months revealed regenerated mucosa, often displaying prominent villi (Fig. 5) and absence of the valves of Kerkring and other mucosal folds in the scar (Fig. 6) with luminal narrowing in cases of extensive resection. Biopsy specimens from

**Figure 6.** Abrupt termination of the mucosal folds in the scar at the site of resection of lesion seen in Figure 4A.

the sites in all patients were normal. In 5 patients (23.8%), minimal remnant tissue was seen, and all had developed in lesions that were resected piecemeal, ranging from 15 to 50 mm in size. Three were treated successfully with snare resection in combination with APC, and two were treated with APC alone and were then clear at a subsequent endoscopy at 3 months. Median follow-up is now 10 months in this group.

There were no perforations or clinically significant immediate bleeding. In 2 patients with a continuing need for antiplatelet therapy for coronary stents, prophylactic closure of the entire defect (Fig. 2C) or the site of a visible vessel with clips was performed (Fig. 7 and Video 2, available online at www.giejournal.org). One case of early bleeding developed within 48 hours of the procedure and was treated successfully with endoscopic clip therapy. No blood transfusions were required. One patient was admitted overnight with possible serositis and was treated with analgesia and intravenous antibiotics. An abdominal CT scan showed normal results, and the patient was discharged the following day.

DISCUSSION

This study describes the experience of a tertiary referral center in the endoscopic treatment of large, sessile, sporadic nonampullary duodenal adenomas with a standardized EMR technique. Such lesions are not common, and their endoscopic resection has traditionally been considered high risk because of the thin duodenal wall.⁹ Adenomas in the duodenum are usually solitary and similar to colon lesions. However, they have a high rate of malignant transformation ranging from 35% to 85%.¹⁰⁻¹³ Established treatment options are essentially surgical and include extensive duodenal segmental resection, submucosal excision after duodenotomy, or duodenopancreatectomy.¹⁴⁻¹⁸ However, as the results of the current study show, EMR in the duodenum can be performed

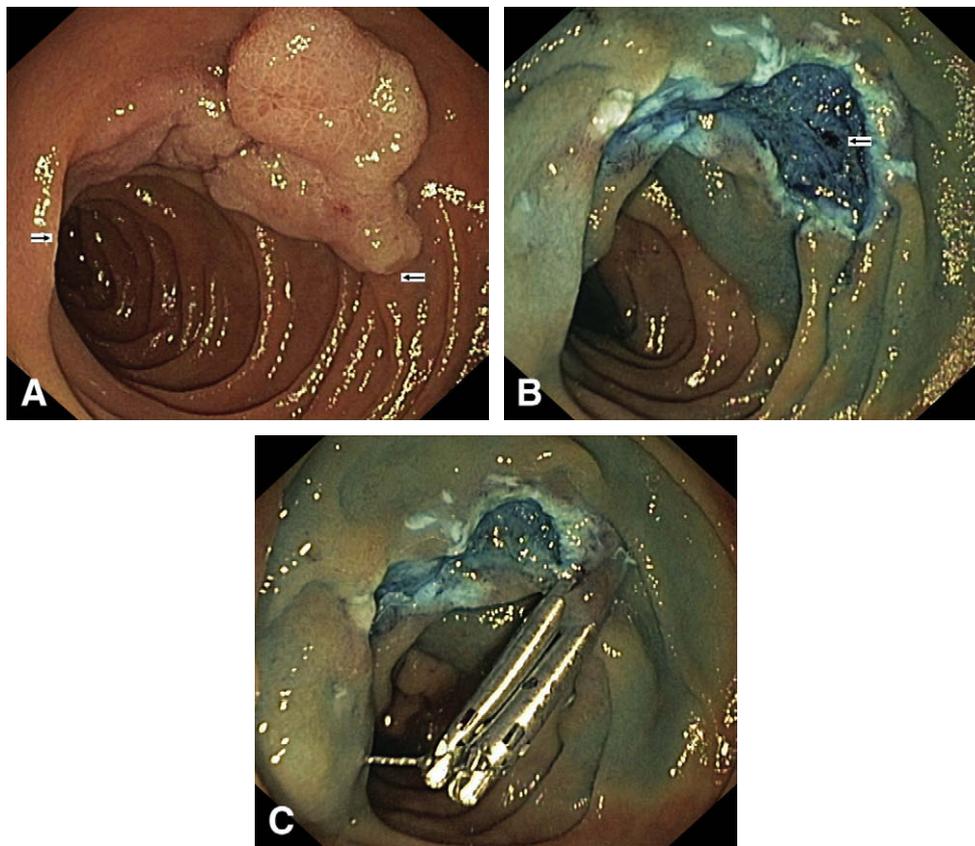


Figure 7. **A**, A TVA occupying 50% of the circumference on the anterolateral wall in the distal second part duodenum. **B**, Visible vessel in the right lateral aspect of the defect after resection. **C**, Two clips used to close the defect.

safely and successfully in a tertiary referral setting on day-only patients.

Overall, remnant tissue at the site of prior resection was found in 23.8% of our cases and occurred only in patients whose lesions were treated with piecemeal resection (5/13). All were subsequently treated with further snare resection in combination with APC or APC alone, and at a median follow-up of 10 months they had no evidence of remnant adenomas. Our findings in the duodenum are not dissimilar to those of the colon in which en bloc EMR of large lesions appears to be more effective in preventing recurrence.^{19,20} Currently, lesions larger than 20 mm cannot safely be removed en bloc, and residual remnant tissue remains a potential concern. Duodenal lesions resected piecemeal require careful surveillance. The recurrence rate observed in this study is within the range of published data for EMR of lesions elsewhere in the GI tract as well as surgically treated patients with duodenal adenomas.^{14,19,21-23}

Technique is critical in avoiding adenoma recurrence or residual. Inclusion of a small margin of normal tissue in the lateral aspect of the resection may minimize the rate of recurrence and avoid the problem of small residuals of neoplastic tissue at the margin of the defect. Also, careful sequential resection from the edge of the initial muco-

sal defect, working always from the edge of this advancing defect in combination with precise snare placement minimizes the potential for mucosal bridges within the defect. These are difficult to treat. These aspects of technique are not amenable to study within a randomized trial setting but seem logical. However, further long-term follow-up studies specifically examining this in the duodenum, and in particular using new technologies such as narrow-band imaging or high-magnification chromoendoscopy at the time of EMR to examine the resected margin, are required. It is likely that the safety and completeness of endoscopic resection of large duodenal adenomas is heavily dependent on the experience and expertise of the endoscopist.

Apel et al²⁴ have described their experience in 18 patients with duodenal adenoma treated with snare polypectomy and APC accumulated over a 13-year period. During a median follow-up period of 71 months, no patient had carcinoma. Our preference is to resect first rather than ablate. In contrast to mucosal resection where a clean blue submucosal plane can be clearly discerned, APC has no clear therapeutic end point other than “adequate” fulguration of residual neoplastic tissue, the assessment of which is obfuscated by the accumulation of a coagulum at the site of therapy.

When residual adenoma is treated in follow-up, submucosal injection is generally avoided because this can create a canyoning effect from submucosal fibrosis beneath the target tissue. Submucosal injection in these circumstances leads to fluid tracking laterally and preferentially elevating the normal mucosa around the target lesion but not beneath it. In this setting, the abnormal tissue is subsequently difficult to capture with the snare.

The pediatric variable colonoscope was preferred for posterior and lateral wall lesions because the working channel is oriented at the 6 o'clock position. This facilitates firm downward pressure on the lesion, and the resection technique is very similar to that of colon EMR. If a gastroscope were used, the working channel exits at the 9 o'clock position, and it is difficult to simultaneously apply firm pressure with the snare from this position in addition to maintaining adequate visualization of the lesion. Thus, this instrument is generally avoided for the treatment of these lesions. The use of a side-viewing instrument for the anteromedial duodenal wall allows en face viewing of the entire lesion. Such complete imaging is not always possible with a forward-viewing instrument. For extensive lesions, on occasion both instruments are needed, or it may be necessary to inject submucosally to elevate the lesion into the field of view.

Nonlifting or surface ulceration suggests submucosal invasion, and these lesions require further assessment with EUS and surgical treatment in the majority of cases. General guidelines on endoscopic treatment of sessile lesions in the GI tract suggest that lesions occupying more than a third of the luminal circumference should be considered for surgery, but the current study indicates that in certain cases lesions occupying more than 60% of the circumference can be effectively treated endoscopically provided the endoscopist has good access and the lesion elevates well with submucosal injection.

Complications of EMR include perforation, bleeding, and serositis. Immediate bleeding can often be controlled with endoscopic clip application. Because the duodenal wall is thin, it is our preference to anchor the clips on the adjacent normal mucosa to close the defect rather than clipping directly into it. An early bleeding rate of up to 33% has been reported in the duodenum, and it is the most common complication.³ One limitation of this study is the retrospective design with the potential for both the underreporting of complications and selection bias. Selection bias has been minimized by including all patients with large, sessile, sporadic nonampullary duodenal adenomas identified within the database over the study period. Because the discharge instructions after EMR included detailed information on potential complications, and because a point of contact and endoscopic follow-up at 3 and 12 months was performed at our institution, we believe that the likelihood of underreporting of major complications is small.

In conclusion, this study shows that the majority of lesions in the duodenum can be resected during a single outpatient procedure in a tertiary referral center with expertise in EMR technique. Careful endoscopic follow-up is essential to treat recurrence or residual that, although rare in complete en bloc resections, can occur in giant lesions resected piecemeal.

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Received February 26, 2008. Accepted April 19, 2008.

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