

# Endoscopic mucosal resection of sporadic duodenal nonampullary adenoma: outcomes of 130 patients with a long-term follow up in two tertiary French centers

Solène Hoibian<sup>a,b</sup>, Jean-Philippe Ratone<sup>b</sup>, Jean-Michel Gonzalez<sup>a</sup>, Erwan Bories<sup>b</sup>, Christian Pesenti<sup>b</sup>, Fabrice Caillol<sup>b</sup>, Jean-Charles Grimaud<sup>a</sup>, Marc Giovannini<sup>b</sup>, Marc Barthet<sup>a</sup>

Hôpitaux Universitaires de Marseille Nord, Chemin des Bourrely; Paoli-Calmettes Institute, Marseille, France

## Abstract

**Background** The long-term outcomes and safety of endoscopic mucosal resection (EMR) of sporadic duodenal adenoma (SDA), and the management of adverse events need to be confirmed.

**Methods** A bicentric retrospective study was performed including all patients who underwent EMR for SDAs from 2003-2016. The primary aim was to evaluate the efficiency of EMR for SDA. The secondary objectives were to assess safety, recurrence management, predictive factors for treatment success, and adverse events.

**Results** One hundred thirty patients (134 procedures) were included (median age 65 years, 49.3% male). The mean SDA size was 20.7 (range 5-50) mm. Of the SDAs, 58.2% were category 3 of the Vienna classification, 35.8% were category 4, and 5.9% were category 5. The median follow up was 25.0 (range 2-120) months. Complete mucosal resection was achieved for 129/134 lesions (96.2%), with *en bloc* resection in 59/134 (44%). Recurrence occurred in 28.6% of cases (30/105 procedures). Recurrence was successfully treated by new endoscopic procedures in 72.2% (13/18) and by surgery in 27.8% (5/18). Delayed bleeding occurred in 13.4% of cases (18/134) and was successfully managed endoscopically. The perforation rate was 3.7% (5/134); perforations were managed without surgery in 60% (3/5 patients) of cases.

**Conclusions** Endoscopic treatment of SDA appears to be effective and relatively safe in tertiary centers. All bleeding complications were endoscopically controlled, and perforation was rare. Recurrence was frequent but could be managed endoscopically. EMR is confirmed as a first-line treatment in cases of SDA, and surgery is useful only if repeated EMRs fail.

**Keywords** Duodenal adenoma, endoscopic mucosal resection, delayed bleeding, perforation, recurrence

*Ann Gastroenterol* 2020; 34 (1): 1-8

<sup>a</sup>Gastroenterology Unit, Hôpitaux Universitaires de Marseille Nord, Chemin des Bourrely (Solène Hoibian, Jean-Michel Gonzalez, Jean-Charles Grimaud, Marc Barthet); <sup>b</sup>Endoscopy Unit, Paoli-Calmettes Institute (Solène Hoibian, Jean-Philippe Ratone, Jean-Michel Gonzalez Erwan Bories, Christian Pesenti, Fabrice Caillol, Marc Giovannini), Marseille, France

Conflict of Interest: Marc Giovannini is a member of the advisory board for COOK MEDICAL™

Correspondence to: Solène Hoibian, Paoli-Calmettes Institute, Endoscopy Unit, 232 Boulevard de Sainte Marguerite, 13273 Marseille, France, e-mail: solene.hoibian@hotmail.fr

Received 24 June 2020; accepted 23 September 2020; published online 27 January 2021

DOI: <https://doi.org/10.20524/aog.2021.0581>

## Introduction

Endoscopic treatment of sporadic duodenal nonampullary adenomas (SDAs) remains a matter of debate. Because endoscopic submucosal dissection (ESD) has been ruled out by the European Society of Gastrointestinal Endoscopy (ESGE) recommendations, endoscopic mucosal resection (EMR) remains the first-line treatment of SDA [1,2]. SDAs are uncommon glandular benign epithelial tumors, largely asymptomatic and usually discovered incidentally. However, as a result of the widespread use of upper gastrointestinal endoscopy, SDAs have been detected with increasing frequency (0.4%) [3]. As SDAs have a malignant potential similar to that

of colonic adenomas [4,5], the aim of treatment is to prevent the occurrence of a duodenal adenocarcinoma, usually associated with a poor prognosis [6].

Endoscopic treatment is recommended for managing SDA when feasible and results in lower morbidity and mortality than surgery [7]. Curative endoscopic resection of a well-differentiated intramucosal adenocarcinoma without lymphovascular invasion is considered an option by the ESGE, though the risk of lymph node metastasis is poorly reported in the literature [2]. Conversely, surgery is necessary in cases of more aggressive or invasive carcinoma. The first case of endoscopic treatment of SDA was published in 1992 by Obata *et al* [8]. Currently, endoscopic treatment of SDA is mainly performed in tertiary referral centers, because it is a challenging procedure and major complications occur more often than for other sites [9,10]. The main complications are delayed bleeding (DB) (10-15%) and perforation (1-5%). Management of such complications is usually complex, and preventing their occurrence is a very important challenge. At present, ESGE recommends EMR and polypectomy, but not ESD, for endoscopic treatment of duodenal adenomas [2]. Although ESD achieves an excellent *en bloc* resection rate, a higher incidence of perforations has been described, and no benefit with regard to survival and long-term outcomes has yet been demonstrated [1,11-14]. Endoscopic diagnosis is required to differentiate resectable from unresectable lesions, notably because biopsy before resection appears to be insufficient [15-17].

Several series have described the outcomes of EMR for the endoscopic treatment of SDA. Short-term outcomes are good, with successful resection rates greater than 90%, and no death related to the spread of duodenal cancer has been described. However, piecemeal resection is often performed, and the recurrence rate varies widely [9,17,18]. Furthermore, long-term outcomes and the results of recurrence management have rarely been described. In addition, only a few cases of intramucosal and submucosal adenocarcinomas were included in these reports.

The latest series have found good outcomes with a long follow up, 563 days for Tomizaya *et al* and 83 months for Valerii *et al* [11,19-22]. Despite these favorable results for endoscopic treatment, long-term data are still limited, with only 1 study exceeding a median follow up of 24 months [21], even though it is well known that recurrence may occur after several months or years. The utility of iterative endoscopic resections also remains to be better defined. Nevertheless, despite its efficiency, open surgery remains a high-risk procedure with significant morbidity and mortality and must be used as a last resort [23].

The primary aim of this study was to assess the efficacy of endoscopic treatment of SDA in a large series with a comprehensive follow up. The secondary objectives were to assess safety, recurrence management, predictive factors for success and adverse events, and discrepancies between biopsy results and final pathology.

## Patients and methods

### Study design and data collection

This retrospective study was conducted in 2 tertiary centers. All patients undergoing endoscopic resection for a histologically proven SDA between December 2003 and March 2016 were included. Patients with genetic polyposis (familial adenomatous polyposis, Peutz-Jeghers syndrome, MUTYH) or ampullary adenoma, and those who had an endoscopic resection for nonadenomatous duodenal lesions were excluded.

We collected the following demographic and clinicopathological characteristics of the patients and lesions in computerized medical files: sex; date of birth; genetic syndrome; major comorbidity; American Society of Anesthesiologists score; result of a colonoscopy, if available; lesion size; Paris classification; location and number of lesions; invasion of the major papilla; depressed type of lesion; length of hospital stay; duration of procedure; lift quality after injection; results of biopsy; endoscopic ultrasonography; final histology according to the Vienna classification (VC) [24]; and complication rate. Major complications were defined as perforation or DB requiring red blood cell (RBC) transfusion or endoscopic treatment; other complications were defined as minor. In the case of several lesions, the characteristics of the largest are reported. The recurrence rate is also reported, as defined by persistence during endoscopic control of an adenomatous or adenocarcinomatous lesion.

The primary objective was to evaluate the long-term efficacy of endoscopic resection. Secondary objectives were to assess safety, recurrence management, predictive factors for success, failure or adverse events and concordance between biopsy results and final pathology. Safety was assessed by the following adverse events: the rate of per-procedural bleeding requiring instrumental treatment; the perforation rate; the DB rate; and the rate of other complications. Management recurrence was assessed by the need for and efficacy of a second endoscopic procedure, multiple endoscopic procedures or classical surgery.

### Endoscopic procedures

Endoscopic procedures were carried out by an experienced endoscopist with the patient under general anesthesia. A PENTAX MEDICAL™ gastroscopie with a large canal operator (EG-3490K), a PENTAX MEDICAL™ colonoscope (EC38-i10F2), a PENTAX MEDICAL™ duodenoscope (ED34-i0T), an OLYMPUS™ duodenoscope (PJF-160), and a PENTAX MEDICAL pediatric colonoscope (EC3490TFi) were used. CO<sub>2</sub> insufflation was systematically applied after 2010. All resections were performed after injection of saline solution or viscous solution mixed with adrenaline (1/10000). During this period, a 25-mm COOK MEDICAL™ snare, a hexagonal COOK MEDICAL™ snare, and a Monofil™ ultrasnare (10 and 15 mm) MEDWORK™ (Höchststadt, Germany) were employed. The choice of scope depended on the localization, stability and type of lesion. The electrosurgical

generator setting was endoQ effect 2 (ERBE elektromedizin, Tübingen, Germany). If there was any doubt, duodenoscopy was performed first to exclude an ampulloma.

In cases of suspicion of adenocarcinoma, endoscopic ultrasonography (EUS) was occasionally performed at the operator's discretion, in which case a PENTAX scope (EG38UTK, PENTAX, Tokyo, Japan) was used.

### Statistical analysis

The statistical analysis was carried out using PASW statistics version 17.02 (IBM SPSS Inc., Chicago, IL, USA). All variables are described in terms of the mean ( $\pm$ standard deviation) or median and range. Chi-squared and Fisher's exact tests were used to compare quantitative variables, and Student's *t*-test or Mann-Whitney test were applied for continuous variables. Multiple logistic regression with backward stepwise variable selection was utilized to identify independent predictors of outcomes of interest. Multivariate analyses were performed unless the number of events was insufficient, in which cases univariate analysis was performed.

### Ethical considerations

Approval was obtained from the local medical ethics committee.

## Results

### Patient, lesion, and endoscopic procedure characteristics

A total of 130 patients undergoing 134 procedures were included. The mean age was 65 (range 33-85) years, and 68 (50.7%) were female. In total, 102 of the patients underwent screening colonoscopy; colon cancer was found in 12.7% of cases and adenomatous polyps in 58.8%. Regarding associated genetic syndromes, 4 patients had hereditary nonpolyposis colorectal cancer syndrome.

Lesions were evaluated by EUS before resection in 19.4% of cases: all were staged as uT1N0 or uT0N0. The median size of the lesions was 20 (range 5-50) mm. Sixty percent of the lesions were larger than 20 mm, and 21.6% involved more than one quarter of the circumference.

EMR was performed in 98.5% of cases. Two lesions with insufficient lifting were resected by a hybrid technique of ESD and EMR, one because of an anterior attempt at resection. Both lesions had been biopsied before resection.

The mean duration of the procedure was 54 (range 14-144) min. *En bloc* resection was possible in 44% of cases, whereas 56% of the lesions were resected in a piecemeal fashion. *En bloc* resection was associated with the lesion size: <10 mm, 71.4%; 10-20 mm, 72.2%; 20-30 mm, 45.2%; 30-40 mm, 4%;  $\geq$ 40 mm 0% ( $P=0.0001$ ). Complete endoscopic resection was achieved

in 96.3% of cases. Two lesions required 2 sessions for complete resection.

Histological analysis revealed 36 tubular adenomas (26.9%) and 87 villous or tubulovillous adenomas (64.9%). A total of 58.2% of the lesions presented with low-grade dysplasia (Category 3 VC), 35.8% with high-grade dysplasia or noninvasive carcinoma (Category 4 VC), and 5.9% with intramucosal carcinoma (Category 5 VC).

For lesions removed *en bloc*, the endoscopic estimated size was close to the size of the histologic specimen (mean 15.5 mm vs. 13 mm;  $P=0.05$ ). Adenocarcinomas and high-grade dysplasia lesions were more likely to be associated with a villous component (80.4% and 90% vs. 38.9%;  $P=0.002$ ) in univariate analysis; in addition, they presented with a larger size than low-grade dysplasia lesions (23.9 mm and 23.9 mm vs. 18.8 mm;  $P=0.02$ ).

Regarding margins, 40.2% of the resected specimens had negative vertical and horizontal margins both; 52.2% of the horizontal margins were inconclusive because the resection was performed in a piecemeal fashion. Only 7.5% of the lateral margins were positive; 91.8% of the vertical margins were negative. In multivariate analysis, negative horizontal and vertical margins were associated with a small lesion size (odds ratio [OR] 0.94, 95% confidence interval [CI] 0.89-0.99;  $P=0.02$ ) and *en bloc* resection (OR 4.35, 95%CI 1.80-10.40;  $P=0.001$ ). The main characteristics of patients, lesions and endoscopic procedure are shown in Table 1.

### Main objective results: endoscopic treatment long-term efficiency

The median follow up was 25 (range 2-120) months, and a follow up greater than or equal to 1 year was achieved for 64.9% of the patients. A total of 105 procedures had at least 1 subsequent endoscopy (78.3%), after a median interval time of 7.5 (range 1-73) months.

Among the 105 patients undergoing follow-up endoscopy, 75 had no recurrence (71.4%). Thirty patients had a recurrence on surveillance endoscopy. In multivariate analysis, factors associated with endoscopic incomplete resection were a larger lesion size (OR 0.86, 95%CI 0.76-0.99;  $P=0.03$ ) and a depressed lesion type (OR 0.012, 95%CI 0.002-0.66;  $P=0.03$ ). In addition, clinical success was associated with *en bloc* resection in multivariate analysis (OR 2.20, 95%CI 1.11-3.94;  $P=0.05$ ). The main results concerning the primary endpoint are shown in the flowchart in Fig. 1.

Recurrence was found during the first follow-up endoscopy in 73.3% of cases ( $N=22/30$ ), and during the first year of follow up in 50% of cases ( $N=15/30$ ). Recurrences were endoscopically treated by EMR in 45.5% of cases, by EMR and argon plasma coagulation in 6.1%, by EMR and electrocoagulation in 6.1%, by argon plasma coagulation alone in 27.3% and by electrocoagulation alone in 15.2%. Among the 18/30 lesions for which the treatment was completed, recurrence was successfully managed endoscopically in 72.2% of cases (13/18), after a median number of 2 (range 2-4) resections (mean follow up 21.5 months). Surgical resection was needed in 27.8% (5/18)

**Table 1** Patient, lesion and endoscopic procedure characteristics

Characteristics	N	%
<b>Patients</b>		
Mean age	65 (33-85)	
Female	68/134	50.7
Median ASA	2 (1-4)	
Antiplatelet		21.6
Anticoagulant		9.7
<b>Histology</b>		
Villous or tubulovillous adenoma	87/134	64.9
Category 3 Vienna classification	78/134	58.2
Category 4 Vienna classification	48/134	35.8
Category 5 Vienna classification	8/134	5.9
<b>Lesion</b>		
Mean size (mm)	20,7 (5-50)	
<20	50/125	40.0
20-40	67/125	53.6
≥40	8/125	6.4
Depressed type	12/134	9.0
<b>Location</b>		
DI (bulb)	15	11,2
Genu superius	12	9,0
DII	82	61,2
Genu inferius	10	7,5
DIII	15	11,2
<b>Treatment</b>		
EMR	132/134	98.5
EMR+ESD	2/134	1.5
<i>En bloc</i>	59/134	44.0
Complete endoscopic resection	128/134	95.5
Ambulatory care	22/134	16.4
Mean hospital stay duration (days)	2 (1-18)	

American Society of Anesthesiologists; EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection

of cases. In these cases, endoscopy was considered a failure. According to multivariate analysis, a larger lesion size was a predictive factor for recurrence (OR 1.06, 95%CI 1.003-1.12; P=0.03). The main results of multivariate analysis for efficacy are shown in Table 2.

## Secondary endpoint results

### Safety and adverse events

The rate of major complications related to initial endoscopic treatment was 16.4% (N=22/134). DB occurred

**Table 2** Main results for efficacy

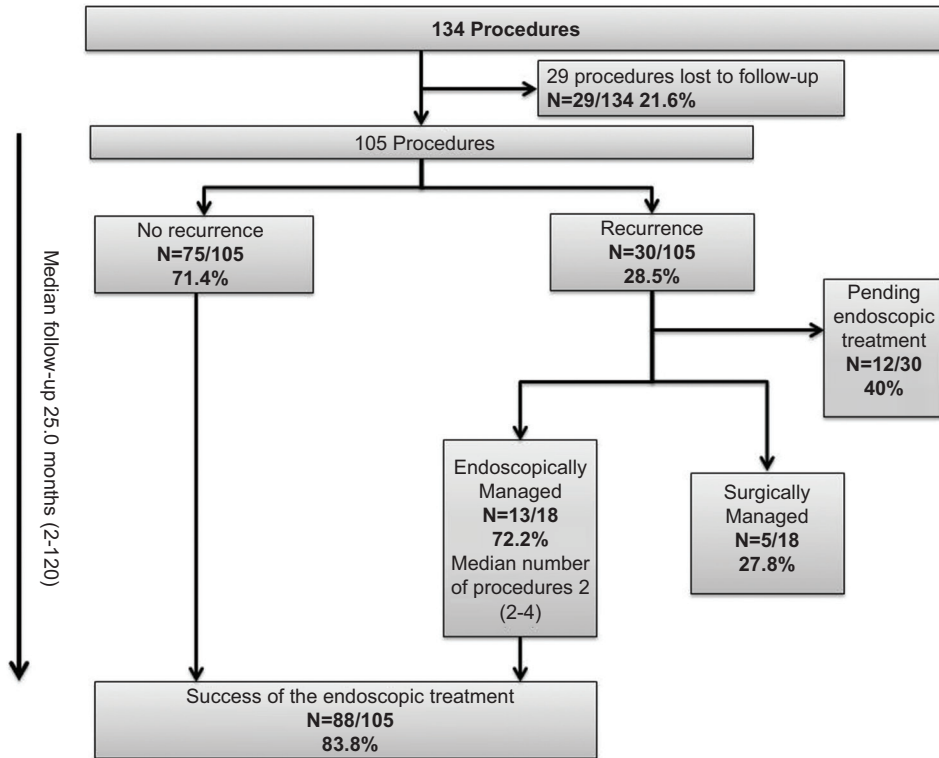
Multivariate analysis	OR (95%CI)	P-value
<b>Complete endoscopic resection</b>		
Size	0.86 (0.78-0.97)	0.01
Depressed type	9.92 (1.0-98.43)	0.05
Circumferential extension	2.25 (0.26-19.3)	0.45
<b>R0</b>		
Size	0.94 (0.89-0.99)	0.02
<i>En bloc</i> resection	4.35 (1.80-10.40)	P<0.01
<b>Recurrence</b>		
Size	1.06 (1.00-1.12)	0.03
Low-grade dysplasia	2.03 (0.88-10.35)	0.11
High-grade dysplasia	0.78 (0.27-2.28)	0.65
Adenocarcinoma	5.03 (0.96-26.43)	0.06
<i>En bloc</i> resection	0.38 (0.11-1.35)	0.13
<b>Success</b>		
<i>En bloc</i>	2.20 (1.11-3.94)	0.05
Size	0.02 (0.31-0.64)	0.42

OR, odds ratio; CI, confidence interval

in 13.4% of cases (18/134), and all were successfully managed endoscopically. Eighty-nine percent of DB episodes occurred during the first 3 postoperative days, and 81.2% occurred for lesions larger than 20 mm. Endoscopy was implemented in 93.9% of the cases, and active bleeding was found in 47%. Two and 3 hemostatic endoscopic treatments were each performed in one patient. Endoscopic hemostatic therapy was conducted in all cases to prevent bleeding recurrence. DB required RBC transfusion in 56.4% of cases (1-7 RBC), and 25% of the patients required monitoring in intensive care. In multivariate analysis, risk factors associated with DB were a large lesion size (OR 1.07, 95%CI 1.01-1.14; P=0.02), high-grade dysplasia (OR 5.79, 95%CI 1.04-32.13; P=0.03), and adenocarcinoma (OR 2.26, 95%CI 0.42-11.97; P=0.03).

Prophylactic hemostasis was applied in 61.9% of the procedures, mainly with clips used either alone (61.4%) or associated with other techniques. The rate of prophylactic hemostasis significantly increased from 50% of cases in 2003-2007 to 77.9% in 2013-2016. Multivariate analysis showed prophylactic clipping (OR 0.19, 95%CI 0.04-0.84; P=0.03) and the absence of visible vessels during the procedure (OR 0.19, 95%CI 0.04-0.84; P=0.03) to be protective factors for DB. The results of the multivariate analysis for delayed bleeding are shown in Table 3.

Perforation occurred in 3.7% (5/134) of patients. Of these, 40% (2/5) required emergency surgery for duodenal suture, 40% (2/5) had exclusive medical treatment with antibiotics, and 20% (1/5) underwent per-procedural endoscopic closure using conventional clips, without any symptoms. Eighty percent of perforations were delayed and occurred on the day of resection or on postoperative day 1. Other types of complications that occurred were 2 cases of acute pancreatitis (1 necrotizing, 1



**Figure 1** Flowchart showing success and recurrence

**Table 3** Delayed bleeding multivariate analysis

Multivariate analysis	OR (95%CI)	P-value
Size	1.07 (1.01-1.14)	0.02
Low-grade dysplasia	0.20 (0.02-2.25)	0.10
High-grade dysplasia	5.79 (1.04-32.13)	0.03
Adenocarcinoma	2.26 (0.42-11.97)	0.03
No visible vessel	0.12 (0.04-0.84)	0.05
Prophylactic clipping	0.19 (0.04-0.84)	0.03
Other prophylactic hemostasis technique	0.11 (0.10-1.25)	0.07
Gender	2.4 (0.64-9.09)	0.19

OR, odds ratio; CI, confidence interval

edematous), solitary fever in 1 patient, and abdominal pain without perforation in 2 patients.

During iterative resections for recurrence, the major complication rate was 6.3% (N=3/47) (2 cases of delayed bleeding and one of delayed perforation), with a minor complication rate of 4.2% (N=2/47). One patient experienced delayed perforation after argon plasma coagulation and, despite emergency duodenal surgery, died of multivisceral failure in intensive care.

In our series, we did not find a statically significant difference in the rate of complications according to the location of the adenoma. However, no major adverse events occurred for bulb lesions.

### Concordance between biopsy results and final histology

Previous results of biopsies were available in 64.2% of the cases. Discrepancy between the results of pre-resection biopsy and final histology was observed in 42.6% of cases: 32% of the lesions were upgraded and 10.6% downgraded. Biopsy did not detect the presence of adenocarcinoma.

### Discussion

To our knowledge, our bicentric retrospective study analyzing 134 procedures is the third largest series of endoscopic treatment for SDA and the largest series in a western country [11,19]. The median follow up of 25.0 months for 105 procedures allowed us to consider the great majority of recurrences, one of the main limitations of endoscopic resection. Only the study by Valerii *et al* had a longer follow up (59 months), though the cohort was much smaller (61 patients) [20]. The main results confirm that endoscopic treatment of duodenal adenoma is effective, with a complete initial resection rate of 96.3%; in addition, the success rate of endoscopic treatment was 83.8%, despite a high rate of resection by a piecemeal technique (56%), with a recurrence rate of 28.6%. These outcomes are similar to those in previous studies with high recurrence rates (20-37%) often managed endoscopically [9,11,17,19,20]. The long median follow up suggests that these results are lasting and that endoscopic

resection avoids surgery in the majority of cases. Nevertheless, management of recurrence is difficult because submucosal fibrosis limits lesion lifting. Our study highlights that several endoscopic procedures (mean 2.2 [1-4]), may be required before endoscopic treatment is considered to have failed. This is an important take-home message of our series. Overall, follow up is mandatory and must be organized. A follow-up endoscopy at 6 months after resection appears to be a good time to avoid false positives or false negatives. Lupu *et al* described ESD using countertraction with clips and rubber bands to treat recurrent duodenal superficial lesions with intense fibrosis [25]. This technique has to be appraised, and we hope that new possibilities such as this one will improve our outcomes. Several endoscopic series have described underwater EMR for SDA as an interesting technique, for primary resection but also in case of recurrence, because it is less affected by submucosal fibrosis than EMR [26-28].

The major complication rate (16.4%) was comparable to the literature and acceptable. DB (13.4%) was the most frequent, and all cases were successfully managed endoscopically. In multivariate analysis, DB was associated with a larger lesion size and the presence of high-grade dysplasia and adenocarcinoma. Protective factors included prophylactic clipping and the absence of visible vessels. The efficacy of prophylactic clipping is a major issue, because DB occurs frequently, increasing the length of hospital stay and the need for RBC transfusion. In our series, prophylactic hemostasis increased significantly between 2003-2007 (50%) and 2013-2016 (77.9%). It was associated with a nonsignificant decrease in the rate of DB, with DB episodes recorded in only 7.4% of cases in the years 2013-2016 vs. 16.7% in the years 2003-2007.

To prevent delayed complications, several closing and covering methods are proposed, with favorable clinical results, depending on the location and size of the mucosal defect, and scope stability. We can use through-the-scope (TTS) clips for small linear perforations (<1 cm) [29], a combined technique using TTS clips and an endoloop for larger perforations (10-30 mm) [30], and over-the-scope clips for defects from 10-30 mm [31]. Self-expandable metal stents are also an alternative for duodenal perforations [32]. Yahagi *et al* developed an interesting technique for closure of large defects using a clip with string [33].

As described for all endoscopic resections, per-procedural bleeding occurred in 5.8% of the cases and was significantly associated in univariate analysis with the lesion size, recurrence and a longer-duration procedure. Currently, we think per-procedural bleeding with exclusive endoscopic management must not be considered an adverse event or a limitation of endoscopic resection. Burgess *et al* reported similar results for colonic polyps when the size was larger than 20 mm; Klein *et al* also found a clear relationship between the lesion size and risk of per-procedural bleeding [15,18]. In the absence of multivariate analysis, the association between per-procedural bleeding and recurrence may be linked to common risk factors, such as lesion size.

Perforation is a rare complication, with an overall rate of 3.7% (only 1.5% in 2013-2016). No death was related to

perforation during the first session, even though 80% of the cases involved delayed perforations; 40% of the perforations required emergency surgery and 60% were managed with conservative treatment. The better tolerance of perforation might be explained by the realization of the procedures only with CO<sub>2</sub> after 2010. Nevertheless, duodenal perforation is a severe complication and may be fatal.

As a result, duodenal endoscopic resection must be performed by an experienced endoscopic team and in a hospital with an adapted intensive care unit and surgical team. In general, the size and position of the lesion might be a limitation for endoscopic resection, and Probst *et al* described a significant mortality rate for giant duodenal adenomas [34]. In these cases, benefits and risks have to be discussed with the surgical team.

In cases with suspicion of invasive adenocarcinoma, EUS might predict the depth of mucosal invasion in duodenal adenomas and possibly contraindicate endoscopic resection in cases of *muscularis* involvement [6]. Azih *et al* indicated that EUS can predict tumor *muscularis* invasion with a specificity of 88% and a negative predictive value of 90% [28]. In our series, only 19.4% of the lesions were evaluated by EUS, and all were correctly staged as T1. EUS must be performed only in case of any doubt on invasive adenocarcinoma more than a T1 lesion. As EUS staging does not differentiate intramucosal lesions and submucosal lesions, pit pattern analysis is the first, and probably the most important step before resection.

As previously reported, we noted some discrepancies between the results of biopsy and final histology [15-17]. We do not recommend performing a biopsy if the endoscopic diagnosis of adenoma is certain, because it can induce fibrosis and make the resection more difficult; furthermore, its accuracy is moderate to predict the degree of dysplasia. A biopsy can be of interest in cases of doubt with a benign lesion. This is an important take-home message for gastroenterologists because in our series, 64.5% of the lesions were biopsied before resection. Moreover, the endoscopic diagnosis, including magnified endoscopic, seems to be at least similar to or even more reliable than preoperative biopsy to determine the final histology, and our practice needs to evolve from systematic biopsy to accurate endoscopic diagnosis [35,36]. Kakushima *et al* found good sensitivity (80%) and specificity (72%) in detecting adenocarcinoma with endoscopic assessment (red color, depressed type, mixed type, and size >20 mm) [37].

Our series clearly had some limitations. The major limitation was the retrospective nature of the analysis. Another major limitation was the study duration of over 13 years. Indeed, endoscopic treatment has advanced, and we were able to observe better selection, resection and adverse event management in the last years of the study and to hope for even more in the future. Nevertheless, considering the rarity of sporadic duodenal lesions, the outcomes are interesting and prove good long-term efficiency in a western country, sometimes requiring several procedures in tertiary centers.

In conclusion, endoscopic treatment of SDA is effective with acceptable adverse events. Bleeding can be managed by endoscopy. Perforation is rare but serious. Recurrence is frequent, requires careful monitoring and is often successfully treated by a new endoscopic procedure.

## Summary Box

### What is already known:

- Recent rare large series proved that endoscopic mucosal resection is a successful technique for treating sporadic duodenal adenoma
- The complication rate is acceptable (compared to open surgery) but rigorous management is required
- Delayed bleeding is the most frequent adverse event; perforation is a rare complication, but can be life threatening and needs early and standardized management in an adapted surgery center

### What the new findings are:

- Recurrence was frequent (28.6%) and several endoscopic procedures may have been required before endoscopic treatment was considered to have failed
- Follow up was mandatory and had to be organized
- Delayed bleeding was associated with a larger lesion size and could be prevented by prophylactic hemostasis

## References

- Jung JH, Choi KD, Ahn JY, et al. Endoscopic submucosal dissection for sessile, nonampullary duodenal adenomas. *Endoscopy* 2013;**45**:133-135.
- Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, et al. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015;**47**:829-854.
- Jepsen JM, Persson M, Jakobsen NO, et al. Prospective study of prevalence and endoscopic and histopathologic characteristics of duodenal polyps in patients submitted to upper endoscopy. *Scand J Gastroenterol* 1994;**29**:483-487.
- Perzin KH, Bridge MF. Adenomas of the small intestine: a clinicopathologic review of 51 cases and a study of their relationship to carcinoma. *Cancer* 1981;**48**:799-819.
- Wittean BJ, Janssens AR, Griffioen G, Lamers CB. Villous tumours of the duodenum. An analysis of the literature with emphasis on malignant transformation. *Neth J Med* 1993;**42**:5-11.
- Oyasiji T, Alosi J, Tan W, Wilfong C, Wilkinson N. Duodenal adenocarcinoma: profile and predictors of survival outcomes. *Am Surg* 2015;**81**:1125-1133.
- Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. *Ann Surg* 1997;**226**:248-257.
- Obata S, Suenaga M, Araki K, et al. Use of strip biopsy in a case of early duodenal cancer. *Endoscopy* 1992;**24**:232-234.
- Lépilliez V, Chemaly M, Ponchon T, Napoleon B, Saurin JC. Endoscopic resection of sporadic duodenal adenomas: an efficient technique with a substantial risk of delayed bleeding. *Endoscopy* 2008;**40**:806-810.
- Navaneethan U, Hasan MK, Lourdasamy V, Zhu X, Hawes RH, Varadarajulu S. Efficacy and safety of endoscopic mucosal resection of non-ampullary duodenal polyps: a systematic review. *Endosc Int Open* 2016;**4**:E699-E708.
- Hara Y, Goda K, Dobashi A, et al. Short- and long-term outcomes of endoscopically treated superficial non-ampullary duodenal epithelial tumors. *World J Gastroenterol* 2019;**25**:707-718.
- Basford PJ, George R, Nixon E, Chaudhuri T, Mead R, Bhandari P. Endoscopic resection of sporadic duodenal adenomas: comparison of endoscopic mucosal resection (EMR) with hybrid endoscopic submucosal dissection (ESD) techniques and the risks of late delayed bleeding. *Surg Endosc* 2014;**28**:1594-1600.
- Ferlitsch M, Moss A, Hassan C, et al. Colorectal polypectomy and endoscopic mucosal resection (EMR): European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2017;**49**:270-297.
- Santos-Antunes J, Baldaque-Silva F, Marques M, Lopes J, Carneiro F, Macedo G. Real-life evaluation of the safety, efficacy and therapeutic outcomes of endoscopic submucosal dissection in a Western tertiary centre. *United European Gastroenterol J* 2018;**6**:702-709.
- Burgess NG, Metz AJ, Williams SJ, et al. Risk factors for intraprocedural and clinically significant delayed bleeding after wide-field endoscopic mucosal resection of large colonic lesions. *Clin Gastroenterol Hepatol* 2014;**12**:651-661.e1-e3.
- Kinoshita S, Nishizawa T, Ochiai Y, et al. Accuracy of biopsy for the preoperative diagnosis of superficial nonampullary duodenal adenocarcinoma. *Gastrointest Endosc* 2017;**86**:329-332.
- Singh A, Siddiqui UD, Konda VJ, et al. Safety and efficacy of EMR for sporadic, nonampullary duodenal adenomas: a single U.S. center experience (with video). *Gastrointest Endosc* 2016;**84**:700-708.
- Klein A, Nayyar D, Bahin FF, et al. Endoscopic mucosal resection of large and giant lateral spreading lesions of the duodenum: success, adverse events, and long-term outcomes. *Gastrointest Endosc* 2016;**84**:688-696.
- Tomizawa Y, Ginsberg GG. Clinical outcome of EMR of sporadic, nonampullary, duodenal adenomas: a 10-year retrospective. *Gastrointest Endosc* 2018;**87**:1270-1278.
- Valerii G, Tringali A, Landi R, et al. Endoscopic mucosal resection of non-ampullary sporadic duodenal adenomas: a retrospective analysis with long-term follow-up. *Scand J Gastroenterol* 2018;**53**:490-494.
- Bartel MJ, Puri R, Brahmabhatt B, et al. Endoscopic and surgical management of nonampullary duodenal neoplasms. *Surg Endosc* 2018;**32**:2859-2869.
- Rajkomar K, Kweon M, Khan I, Frankish P, Rodgers M, Koea JB. Endoscopic assessment and management of sporadic duodenal adenomas: The results of single centre multidisciplinary management. *World J Gastrointest Endosc* 2017;**9**:196-203.
- Lee CHA, Shingler G, Mowbray NG, et al. Surgical outcomes for duodenal adenoma and adenocarcinoma: a multicentre study in Australia and the United Kingdom. *ANZ J Surg* 2018;**88**:E157-E161.
- Schlemper RJ, Riddell RH, Kato Y, et al. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000;**47**:251-255.
- Lupu A, Faller J, Oung B, Wallenhorst T, Jacques J, Pioche M. Endoscopic submucosal dissection using countertraction with clips and rubber band allows safe en bloc resection of recurrent duodenal superficial lesions with intense fibrosis. *Endoscopy* 2020;**52**:E398-E399.
- Kiguchi Y, Kato M, Nakayama A, et al. Feasibility study comparing underwater endoscopic mucosal resection and conventional endoscopic mucosal resection for superficial non-ampullary duodenal epithelial tumor <20 mm. *Dig Endosc* 2020;**32**:753-760.
- Yamasaki Y, Uedo N, Takeuchi Y, et al. Underwater endoscopic

- mucosal resection for superficial nonampullary duodenal adenomas. *Endoscopy* 2018;**50**:154-158.
28. Shichijo S, Uedo N, Takeuchi Y, et al. Underwater endoscopic mucosal resection of residual duodenal tumor. *Endoscopy* 2019;**51**:E329-E330.
  29. Ansari D, Torén W, Lindberg S, Pyrhönen HS, Andersson R. Diagnosis and management of duodenal perforations: a narrative review. *Scand J Gastroenterol* 2019;**54**:939-944.
  30. Nakagawa Y, Nagai T, Soma W, et al. Endoscopic closure of a large ERCP-related lateral duodenal perforation by using endoloops and endoclips. *Gastrointest Endosc* 2010;**72**:216-217.
  31. Mori H, Ayaki M, Kobara H, et al. Suitable closure for post-duodenal endoscopic resection taking medical costs into consideration. *World J Gastroenterol* 2015;**21**:5281-5286.
  32. Bergström M, Arroyo Vázquez JA, Park PO. Self-expandable metal stents as a new treatment option for perforated duodenal ulcer. *Endoscopy* 2013;**45**:222-225.
  33. Yahagi N, Nishizawa T, Akimoto T, Ochiai Y, Goto O. New endoscopic suturing method: string clip suturing method. *Gastrointest Endosc* 2016;**84**:1064-1065.
  34. Probst A, Freund S, Neuhaus L, et al. Complication risk despite preventive endoscopic measures in patients undergoing endoscopic mucosal resection of large duodenal adenomas. *Endoscopy* 2020;**52**:847-855.
  35. Goda K, Kikuchi D, Yamamoto Y, et al. Endoscopic diagnosis of superficial non-ampullary duodenal epithelial tumors in Japan: Multicenter case series. *Dig Endosc* 2014;**26** Suppl 2:23-29.
  36. Kakushima N, Kanemoto H, Sasaki K, et al. Endoscopic and biopsy diagnoses of superficial, nonampullary, duodenal adenocarcinomas. *World J Gastroenterol* 2015;**21**:5560-5567.
  37. Azih LC, Broussard BL, Phadnis MA, et al. Endoscopic ultrasound evaluation in the surgical treatment of duodenal and peri-ampullary adenomas. *World J Gastroenterol* 2013;**19**:511-515.