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Endoscopic resection in subepithelial lesions of the upper gastrointestinal tract; experience of a tertiary referral hospital in The Netherlands.

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Abstract:
Objectives
Histological confirmation of subepithelial lesions (SELs) in the upper gastrointestinal tract remains challenging. Endoscopic resection of SELs is increasingly used for its excellent diagnostic yield and opportunity to do away with continued surveillance. In this study, we aimed to evaluate the indications, success-rates and complications of different endoscopic resections techniques for SELs in a large, tertiary referral hospital in Rotterdam, The Netherlands.
Methods
Data between October 2013 and December 2021 were retrospectively collected and analyzed. Main outcomes are R0-resection rate, en bloc resection rate, recurrence rate and procedure-related adverse events (Clavien-Dindo). Secondary outcomes are procedure time, need for surgical intervention and clinical impact on patient management.
Results
A total of 58 patients were referred for endoscopic resection of upper gastro-intestinal SELs. The median diameter of lesions was 20 mm (range 7-100mm). Median follow-up time was 5 months (range 0.4-75.7). Forty-eight (83%) procedures were completed successfully leading to en bloc resection in 85% and R0-resection in 63%. Procedure-related adverse events occurred in 6 patients (13%). Severe complications (CD grade 3a) were seen in 3 patients. Local recurrence rate for (pre)malignant diagnosis was 2%. Additional surgical intervention was needed in 7 patients (15%). A total of 32 patients (67%) could be discharged from further surveillance after endoscopic resection.
Conclusions
Endoscopic resection is a safe and effective treatment for SELs and offers valuable information in undetermined SELs in which repeated sampling attempts have failed to provide adequate tissue for diagnosis.

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Tables

Clinical and patient demographics of 58 patients referred for endoscopic resection of upper gastrointestinal SELs.	
Gender, male (n, %)	27 (47%)
Age (median, range)	58 (20-81)
Incidental findings (n, %)	27 (47%)
Indication for endoscopic resection (n, %)	
Suspected or proven (pre)malignant SEL	34 (59%)
Symptomatic lesion	10 (17%)
Undetermined SEL and patient-preference	12 (21%)
Previous incomplete endoscopic resection	2 (3%)
Tumor diameter in mm (median, range)	20 (7-100)
Tumor location	
Oesophagus	8 (14%)
Stomach	42 (72%)
Duodenum	8 (14%)
Pre-procedural determined layer of origin	
Muscularis mucosae	9 (16%)
Submucosa	19 (33%)
Muscularis propria	27 (47%)
Muscularis propria with extraluminal growth	3 (5%)
Follow-up, months (median, range)	4,9 (0.4-75.7)

Table 1 Clinical and patient demographics. SEL = subepithelial lesion, mm = millimeters.

Histopathological diagnosis in total study population	
Brunner's glands	1
Calcifying fibrous polyp	1
GIST (low-risk)	21
Hamartoma	1
Heterotopic pancreas	7
Inflammatory fibroid polyp	3
Leiomyoma	7
Leiomyosarcoma	2
Lipoma	3
Neuroendocrine tumor	
Low-grade (1)	6
Intermediate-grade (2)	2
Pyloric gland adenoma	1
Reactive cells	1
Unknown because of unsuccessful endoscopic resection	2

Table 2 Overview of histopathological diagnosis of included patients. GIST = gastrointestinal stromal tumor.

Overview of primary and secondary outcomes of endoscopic resection procedures			
	EFTR	**ESD**	**STER**
Total number of procedures	22	28	8
Tumor diameter, mm (median, range)	15 (9-25)	21.5 (7-100)	35 (10-60)
Technical success (n, %)	17 (77)	25 (89)	6 (75)
En bloc resection (n, %)	12 (71)	23 (92)	6 (100)
R0-resection (n, %)	13 (76)	13 (52)	4 (67)
R1-resection in premalignant diagnosis (n, %)	3 (18)	8 (29)	1 (17)
Local recurrence (n, %)	1 (6)	1 (4)	-
Procedure time, min (median, range)	35.5 (19-120)	72 (9-240)	138.5 (44-487)
Additional surgical intervention (n, %)	2 (9)	5 (18)	-
Post-procedural complications (n, %)	2 (9)	4 (14)	1 (13)

Table 3 Overview of primary and secondary outcomes of endoscopic resection procedures. EFTR = Endoscopic Full Thickness Resection. ESD = Endoscopic submucosal dissection. STER = Submucosal Tunneling Endoscopic Resection. R0 = pathological radical resection. R1 = pathological irradical resection.

Overview of procedure-related complications				
Clavien-Dindo classification	**EFTR**	**ESD**	**STER**	**Total**
No complications (n, %)	20 (91)	24 (86)	7 (88)	51 (88)
1 (n, %)	1 (5) *Post-ERCP pancreatitis*	2 (7) *Nausea and pain*	-	3 (5)
2 (n, %)	-	-	-	-
3 (n, %)	1 (5) – *Obstruction of common bile duct due to OTS-clip*	2 (7) *Additional endoscopy for bleeding*	1 (13) *Additional endoscopy for pain after dehiscence of mucosal access*	4 (7)
4 (n, %)	-	-	-	-
5 (n, %)	-	-	-	-

Table 4 Overview of procedure-related complications. EFTR = Endoscopic Full Thickness Resection. ESD = Endoscopic submucosal dissection. STER = Submucosal Tunneling Endoscopic Resection. OTS-clip = over the scope clip. ERCP = Endoscopic retrograde cholangiopancreatography.

Introduction

Subepithelial lesions (SELs) appear as a mass or bulge covered by normal-appearing mucosa and originate from the gastrointestinal wall [1]. Only 10-15% are (pre)malignant and require follow-up or even endoscopic or surgical resection [2].

As SELs are covered by normal-appearing mucosa, conventional endoscopy with biopsies are usually insufficient to obtain a definite diagnosis. Endoscopic ultrasonography (EUS) is the preferred primary diagnostic modality because of its ability to determine the lesion and the ability to obtain a tissue diagnosis by means of EUS-guided fine needle aspiration (EUS-FNA) or biopsy (EUS-FNB) [3, 4]. The reported diagnostic accuracy for EUS-FNA/B, however, varies widely.

Endoscopic resection can be used as diagnostic tool as well as a treatment for small SELs [2]. Different methods for endoscopic resection have been described including endoscopic mucosal resection (EMR), submucosal tunneling endoscopic resection (STER), endoscopic submucosal dissection (ESD) and endoscopic full-thickness resection (EFTR). Compared with surgery, endoscopic resection is less invasive, has short recovery time, and preserves the normal anatomy and function of the digestive tract [5].

Choice and success rate of the different endoscopic resection methods depends on the layer of origin, the location of a lesion and the experience of the endoscopist. The rates for complete resection vary between 85% and 98%, with reported adverse event rates around 5-10% [5-7]. Data on efficacy and complications of endoscopic en bloc resection limited and mainly derives from Asian countries [8].

Therefore, this retrospective study aims to evaluate the indications, success rates and complications of different endoscopic resection techniques in SELs in a large academic hospital in The Netherlands.

Methods

Patients and data collection

This study was approved by the Medical Research Ethics Committees United (MEC-U). Data of patients who underwent endoscopic resections for a SEL in the upper gastrointestinal tract at the Erasmus MC Cancer Institute (University Medical Center Rotterdam, The Netherlands) between October 2013 and December 2021 were analyzed. All consecutive adult (>18 years old) patients that underwent endoscopic resection for a SEL during this time period were included.

The following data were collected: patient demographics, lesion characteristics, such as size (mm), determined by EUS or endoscopy when available, procedure-related outcomes, histological data and follow-up data.

Outcome parameters

The main outcomes of this study are technical success rate of endoscopic resection, en bloc resection rate, pathological radical (R0) resection rate, procedure-related adverse events and recurrence rate. Technical success rate is defined as the percentage of procedures in which the intended endoscopic resection technique was completed successfully, without early termination of the procedure or the need for conversion to another technique or surgical intervention. En bloc resection rate is defined as number of lesions that are macroscopically completely and intact removed as described by the endoscopist. R0 resection indicates a microscopically margin-negative resection determined by the pathologist. Secondary outcomes are procedure time, need for surgical intervention and the clinical impact of endoscopic resection on patient management. The clinical significance of endoscopic resection is defined by the number of patients who can be discharged from further surveillance following a successfully completed procedure. Adverse events are graded according to the Clavien-Dindo scoring system [9].

Procedures and follow-up

The endoscopic resections described in this study were performed by two experienced endoscopists from the gastroenterology department with a colonic FTRD. The endoscopist determined the type of endoscopic resection based on lesion characteristics such as location, size and previous imaging.

After all endoscopic procedures, patients were observed in the recovery unit. When there were no signs of delayed complications, the patients were discharged on the same day. The patients are prescribed high dose proton pomp inhibitors orally (40mg twice daily for at least four weeks) and advised to keep a clear liquid diet for 12-24 hours as per local protocol.

All patients returned to visit the outpatient department within one to three weeks after the procedure for follow-up. Dependent of clinical and histopathological outcomes, patients were discharged from further follow-up or entered a surveillance program. When the histopathological diagnosis was GIST, NET or another malignant outcome, the decision for further management was discussed in a multidisciplinary sarcoma or neuro-endocrine tumor team considering features of the lesion such as size and histopathological risk assessment and comorbidities of the patient.

Results

A total of 58 patients with 67 SELs in the upper gastrointestinal tract were referred for endoscopic resection in the study period and included in this study.

Clinical and patient demographics are shown in Table 1.

The indications for endoscopic resection were distributed over 3 major groups; referral because of suspected or proven (pre)malignant diagnosis (e.g. GIST or NET) (n=34), a symptomatic lesion (n=10) or uncertain diagnosis despite previous attempts for tissue acquisition and preference of the patient for removal of the lesion instead of surveillance (n=12).

A total of 58 procedures were initiated, including 22 EFTRs, 28 ESDs, and 8 STER-procedures. The median diameter of all lesions was 20mm (range 7-100mm). Forty-eight out of 58 procedures (83%) could be successfully completed. En bloc resection was achieved in 41/48 patients (85%) and pathological radical (R0) resection in 30/48 patients (63%). Procedure-related adverse events were seen in 7 patients (12%). The overall local recurrence-rate after en bloc endoscopic resection was 4% (n=2) during a median follow-up of 5 months (range 0.4-75.7), one inflammatory polyp and one NET. Additional complementary surgical intervention was needed in 7 patients (12%).

Twenty-seven patients (47%) had benign histopathological outcome. Most of these patients (10/27, 37%) were referred for resection because a (pre)malignant diagnosis was suspected, followed by uncertain diagnosis despite previous attempts for histology as reason for resection (9/27, 33%). For this reason, benign lesions as heterotopic pancreas were resected.

A total of 31 patients (31/58, 53%) had definitive (pre)malignant histopathological diagnosis (GIST, NET or leiomyosarcoma) (table 2). Fifteen out of these 31 (48.4%) patients had prior histology with a (pre)malignant histopathological outcome. The other 16 patients were referred because a GIST or NET was suspected based on EUS-features or radiologic imaging. All confirmed GIST lesions were deemed very low to low risk based on mitotic count. Five out of 8 NETs were radically resected (R0, 62.5%). Of the 19 endoscopically resected GISTs, 10 were R0-resected (52.6%).

An overview of the outcomes for endoscopic resection are shown in table 3. An overview of procedure-related complications according to Clavien-Dindo classification is shown in table 4.

EFTR

The EFTR was successful in 17/22 patients (77%) with a median lesion size of 15mm (range 9-25). Most EFTR were performed in the stomach (n=14), the other 8 were performed in duodenum. Endoscopic en bloc resection was accomplished in 12 out of 17 procedures (71%) [Supplementary material: Figure I]. Three (18%) of the lesions that were not radically resected (R1) concerned a NET (n=3) (grade 1-2), but none recurred during a median follow-up time of 8 months (range 0.3-75.7).

In 5/22 patients EFTR was unsuccessful, because the lesion could not be pulled into the cap based on size or rigidity. Eventually, 2/5 patients with incomplete procedures were referred for surgical wedge excision of the lesions as there was a high suspicion of a malignant diagnosis, 2/5 patients were rescheduled for ESD leading to successful resection of GIST and 1 patient remains in surveillance to date (47 months follow-up).

Two patients (9%) experienced procedure-related complications. In both cases, the (pre)malignant lesions were located in duodenum, near the ampulla of Vater. Given the patients' comorbidities, surgical intervention was not viable and endoscopic resection was deemed to be the second best option. One patient developed a mild post-ERCP pancreatitis after pre-procedural placement of a protective stent in the common bile duct (Clavien-Dindo 1). Another patient developed obstruction of the common bile duct due to the position of the OTS-clip. Later, the OTCS-clip was removed. (Clavien-Dindo 3a).

ESD

Of 28 initiated ESD-procedures, 25 (89%) procedures were successful [Supplementary Material: Figure II] in lesions with a median size of 21.5 (range 7-100) . All ESD were performed in stomach. Three procedures were unsuccessful due to extraluminal growth (n=2) or because the lesion was too large to resect endoscopically (n=1). En bloc resection rate was 92% (23/25), the R0 resection rate was 52% (13/25). In patients with R1-resection, 8/12 lesions (29%) were low-risk GIST, other lesions were heterotopic pancreas (n=3/12) and an inflammatory polyp (n=1/12). Despite R1-resection of GIST, 5/8 patients were discharged because of benign characteristics and en bloc resection of the lesion. Local recurrence after ESD developed in one patient during a median follow-up time of 7 months (range 0.4-69.3), this was a grade I NET.

In one frail elderly patient, a symptomatic GIST was too large (60mm) to be removed after ESD through the mouth. Consequently, the tumor was left in the stomach following dissection, making the assessment of resection margins unfeasible. Resection margins could therefore not be evaluated. Surgical intervention was not considered an option for the patient. A follow-up visit was occurred two months after the intervention. The symptoms subsided and the patient remained in good health. Therefore, further monitoring was deemed unnecessary.

As shown in Table 4, 4 patients experienced post-procedural complications. Two patients presented with melena and needed additional endoscopy to treat the post-procedural bleeding (Clavien-Dindo 3a). Two patients needed hospitalization for observation of symptoms such as nausea or pain (Clavien-Dindo 1).

Additional surgery (n=5) was successfully performed in four patients with an unsuccessful endoscopic resection, resulting in radical resection of 3 GISTs and 1 leiomyoma, and in 1 patient with an R1- resection of a GIST.

STER

All patients underwent STER because the lesion was located in the esophagus. The lesions had a median size of 35mm (range 10-60mm). Of 8 procedures, 6 were successful (75%) and en bloc resection was achieved [Supplementary material: figure III]. Despite circumferential dissection, one lesion could not be removed because of fibrosis. The supplying blood vessels were transsected and the lesion was left in situ. Per-procedural biopsies showed leiomyoma. After three months the lesion decreased in size and the patient reported resolvement of dysphagia.

The lesions with irradical resection margins were all leiomyomas. However, radical resection could not be determined in one patient due to damaging of the lesion when passing through the upper esophageal sphincter. This was a low-grade leiomyosarcoma for which surveillance was advised in the referring hospital.

One patient was hospitalized after the procedure because of progressive thoracic pain caused by a post-procedural dehiscence of the mucosal access with spill into the submucosal tunnel. This dehiscence was closed by clipping a mucosal flap over the defect. The patient recovered swiftly with additional antibiotics (Clavien-Dindo 3a).

Clinical impact on patient management

An overview of the clinical impact of the endoscopic resections in this study is shown in figure 1.

Of 48 completed procedures, 32 patients (67%) were discharged from further surveillance after the procedure. The majority of these patients (20/32) had R0-resection of a histopathological benign lesion (n = 13) or low-risk (pre)malignant diagnosis (n = 7). In addition, 12 patients with R1-resections could also be discharged from further follow-up because of benign histopathological outcome (n=7), a diagnosis of low-risk GIST in a patient with severe comorbidities (n=1) or benign characteristics in the histopathological sample in combination with en bloc resection of the lesion (n=3). One discharged patient with R1-resection of low-risk GIST achieved additional surgical wedge excision showing no residual malignant cells in the histopathological sample. No local recurrence is known to have occurred in these patients during a median follow up time of 1 month (range 0.3-69.3).

A total of 16 patients (33%) entered a surveillance program. Three patients had irradical resection margins of GISTs, 3 other patients had low-grade NETs. The other 10 patients had radical resection margins, but the histopathological diagnosis (e.g. NET (n=6), large, recurrent or multiple GIST (n=3) or leiomyosarcoma (n=1)) entailed that the patient had to enter a surveillance program. During a median follow-up period of 7 months (range 0.4-69.3), one patient developed a local recurrence of a neuroendocrine tumor (NET) after undergoing ESD and one patient had local recurrence of a symptomatic inflammatory fibroid polyp after EFTR.

Discussion

Adequate tissue sampling is essential to achieve a diagnosis that distinguishes between (pre)malignant lesions requiring follow-up or resection, and non-neoplastic lesions, which require no additional surveillance. In addition, histological diagnosis is important for risk stratification and subsequent management of a NET and a GIST. Current tissue acquisition methods, however, have their limitations and optimal management strategy remains unclear, especially in small SELs [10]. This retrospective clinical data study in 58 patients with SELs demonstrates endoscopic resection could provide a safe and effective treatment with a technical success-rate of 83%, and adverse event rate of 12%, achieving en bloc resection and R0-resection in 85% and 63% respectively. In addition, in only 12% additional surgery was needed and 67% of patients could subsequently be discharged from further surveillance after successful endoscopic resection.

Guidelines suggest obtaining tissue with EUS-guided fine needle aspiration (EUS-FNA), fine needle biopsy (EUS-FNB) or mucosal incision-assisted biopsy (MIAB) [2, 10, 11]. In clinical practice, EUS-FNA and EUS-FNB are the most widely used but have a poor diagnostic yield especially in lesions <20mm[12-14]. Current literature suggests that MIAB-techniques result in higher diagnostic yield. [15-17]. However, the reported diagnostic yield of these techniques is limited in small (<20mm) lesions (47—79%) [12-14] and all available MIAB-techniques can result in local fibrosis, which may hamper future attempts of endoscopic resection using for instance submucosal tunneling [18-20]. This study indicates that endoscopic resection can be considered an effective diagnostic tool for small SELs with 36 out of 58 (62%) SELs being <20mm (range 7-100) [15, 16, 21].

Undiagnosed SELs often require intensive surveillance [2, 10], which may lead to a significant burden especially in young patients. In addition, previous data showed a low compliance (44.6%) for the recommended surveillance strategy [22]. In the most recent ESGE-guideline for the management of SELs, it is therefore suggested that resection is an option for undetermined SELs of < 20mm to avoid the need for intensive follow-up [10].

The challenge remains in setting correct eligibility criteria for choosing endoscopic resection. Since the current study was performed with clinical data from a tertiary referral hospital, specialized in GIST and NET treatment, most patients (59%) were referred for endoscopic resection because of a high suspicion or proven (pre)malignant SEL. Twelve patients (21%) were referred for endoscopic resection because of an undetermined SEL for which the patient expressed a preference to resection instead of surveillance. In this group with a median diameter of SEL of 18.5 mm (range 9-30 mm), the technical success-rate was 91.7% (11/12 procedures) with pathological (R0) resection rate of 54.5% (6/11 procedures). Long-term surveillance could be prevented in 8/11 patients because of benign histopathological outcome (n=6) or R0-resection of low-risk premalignant lesion (n=2). These results suggest that even though a R0-resection is not achieved, endoscopic resection can be safe and effective in managing small, undetermined SELs, as the majority are benign.

When considering the clinical impact of successful endoscopic resection, this study showed out of 48 successful endoscopic resections, 32 (67%) patients could be discharged from follow-up. There are no direct comparisons between a follow-up strategy and direct diagnostic excision strategy. However, the findings in this study might indicate that endoscopic treatment can contribute in preventing the patient from unnecessary diagnostic and therapeutic procedures through diagnosing an undetermined lesion or curation of a malignant lesion.

Surgical wedge excision is considered to be the gold standard in Western guidelines for treatment of (malignant) SELs. In agreement with previous studies the choice for an endoscopic resection technique was dependent on the diameter and location of the lesion, and local expertise [7, 23]. There are no previous studies directly comparing the different endoscopic resection techniques. In the current study, adverse events were seen in 12% (7/58 procedures), but these were only severe (CD >= 3) in 7% (4/58 procedures) and could be quickly resolved. These rates are consistent with previously reported adverse event rates, which range from 5-15% [7, 24]. The adverse event rates of endoscopic resection are comparable to laparoscopic resection techniques [25, 26]. Endoscopic resection can therefore be considered a safe, less invasive alternative for providing both diagnosis and treatment in SELs, with less procedure time, less blood loss and length of hospital stay [25, 27].

The optimal treatment of small GISTs still remains controversial. For intraluminal GISTs smaller than 20 mm, resection and surveillance are both acceptable alternatives. For lesions up to 35 mm, endoscopic resection may be an alternative to laparoscopic wedge excision [10, 28]. The current study shows high technical success rates for EFTR (77%), ESD (89%) and STER (75%), with en bloc resection rate of 71%, 92% and 100% respectively. These outcomes for ESD are in concordance with previous literature, but higher successful resection rates are reported for EFTR and STER [7, 29, 30]. A possible explanation for this could be that the average diameter of resected lesions in this study was relatively large which might have hampered successful performance of the EFTR- and STER-procedures. However, subgroup analysis demonstrated only an improved success rate for STER in lesions with diameter ≤30mm (n=4; 100%). Good visibility and the ability to successfully resect the lesion in EFTR and STER is limited by the maximum diameter of the cap size for EFTR and the upper esophageal sphincter in STER. Also, some SELs are fixed to the surrounding gastro-intestinal wall making it difficult to be captured into the cap. Reported complete resection rates in literature ranges from 74- 100%, with higher rates reported for lesions originating from the third wall layer and smaller of size [31, 32]. In ESD, the resection margin is close-fitted to the SEL and evaluation of the pathological margin is more difficult, which might explain the lower reported pathological resection rate of 52% found in the current study. However, no local recurrence was seen in the R1-resected lesions. Local recurrence rate for premalignant diagnosis in this study was only 2% during follow-up. In addition, it is implied R1-resection in GIST is not associated with a higher risk of local recurrence or lower survival outcome as long as an en bloc resection is achieved [33].

Although the present results support the feasibility and effectiveness of endoscopic treatment in SEL, it is appropriate to recognize several limitations of the study. The study is a retrospective evaluation of clinical data of an experienced referral tertiary center. Important data or nuances could be missed when these were not documented in the electronic health records. Even though most patients were discharged from further surveillance, the follow-up time in the remaining patients was modest. The possibility of long-term recurrence therefore cannot be completely ruled out. In addition, because the procedures were performed by experienced endoscopists in a tertiary, referral center, data cannot be transposed to smaller, regional centers with less experience for this specific indication.

In conclusion, endoscopic resection is an effective treatment for SELs and offers valuable information in undetermined SEL in a field with a low diagnostic accuracy of current techniques. In addition, in the current study two-third of the referred patients could be discharged from surveillance and unnecessary follow-up procedures were prevented. Eligibility criteria and the long-term recurrence rate for endoscopic resection are not yet well-established and need further investigation.

Figure 1	Clinical impact of endoscopic resections. GIST = gastro-intestinal stromal tumor. NET = neuro-endocrine tumor. R0 = pathological radical resection. R1 = pathological irradical resection.

Supplementary Figure I	EFTR-procedure for a gastric neuro-endocrine tumor **A.** Marked nodule lesser curvature. **B**. Resection surface above the above the deployed over-the-scope clip (OTSC) **C.** Full thickness resection of the lesion pinned down on foamboard.
Supplementary Figure II	ESD-procedure for a gastro-intestinal stromal tumor **A.** Gastric subepithelial lesion **B.** Submucosal dissection of the lesion. **C.** Resection surface. **D.** View of en bloc resection lesion.
Supplementary Figure III	STER-procedure of a leiomyoma **A.** View of subepithelial lesion in oesophagus **B.** Submucosal tunneling **C.** Dissection of lesion out of tunnel **D.** View of tunnel before closing the entry.

Figure Legends

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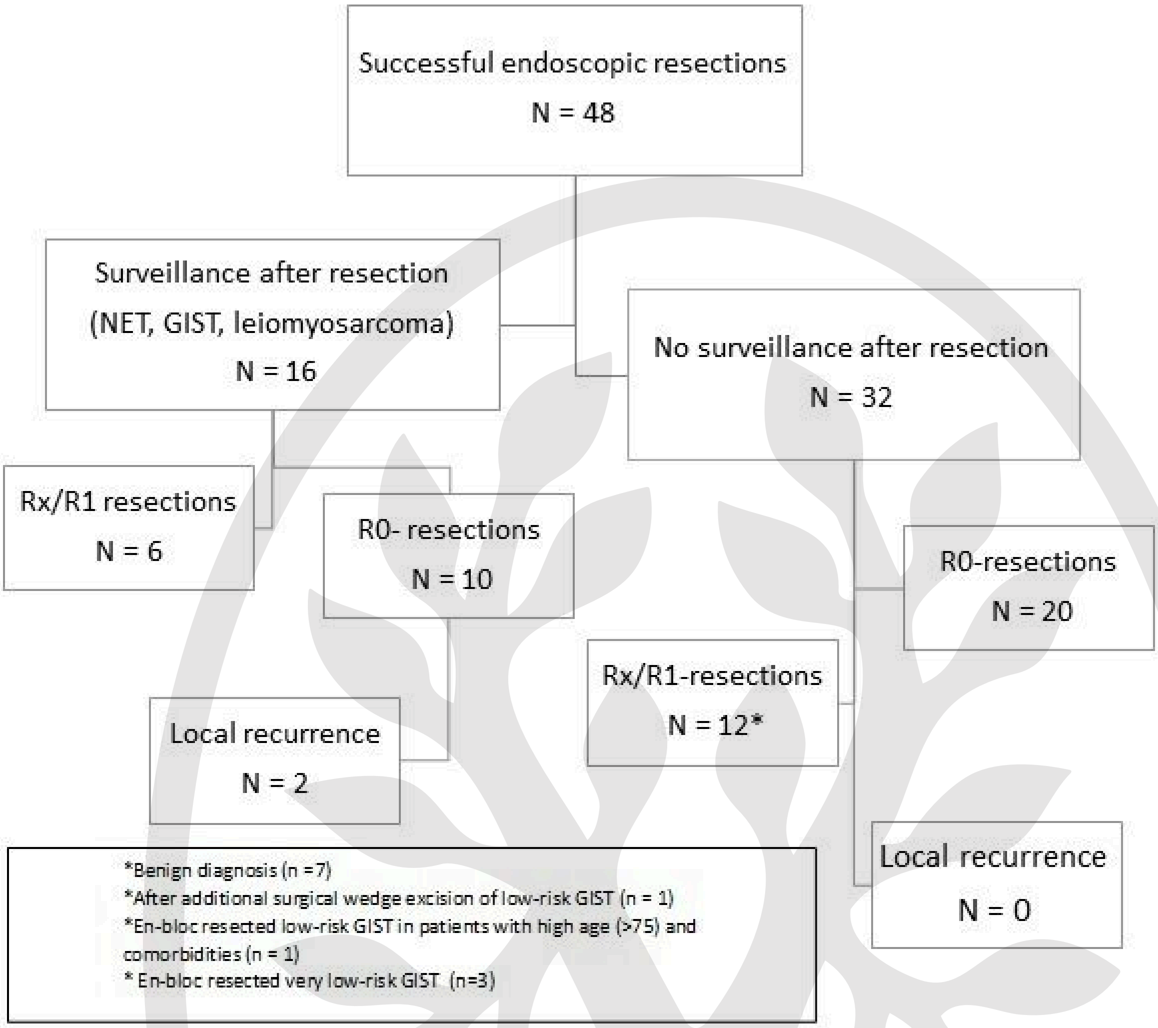
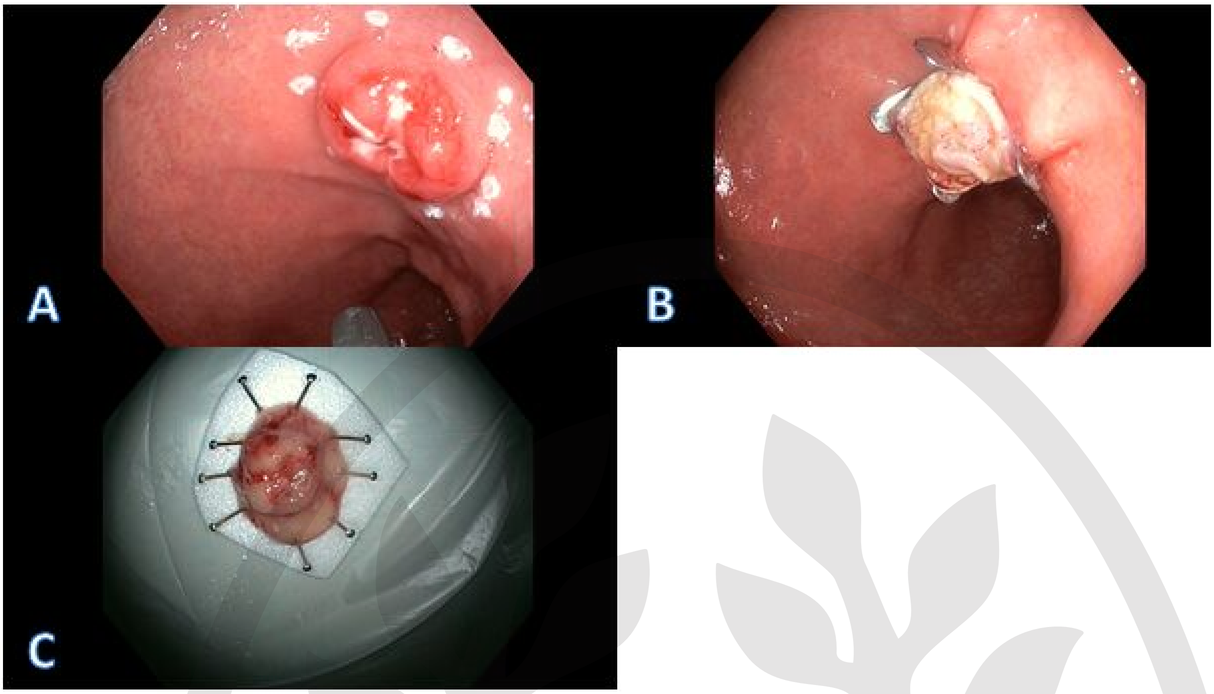

Successful endoscopic resections
N = 48
Surveillance after resection
(NET, GIST, leiomyosarcoma)
N = 16
No surveillance after resection
N = 32
Rx/R1 resections
N = 6
R0- resections
N = 10
R0-resections
N = 20
Rx/R1-resections
N = 12*
Local recurrence
N = 2
Local recurrence
N = 0
*Benign diagnosis (n =7)
*After additional surgical wedge excision of low-risk GIST (n = 1)
*En-bloc resected low-risk GIST in patients with high age (>75) and comorbidities (n = 1)
* En-bloc resected very low-risk GIST (n=3)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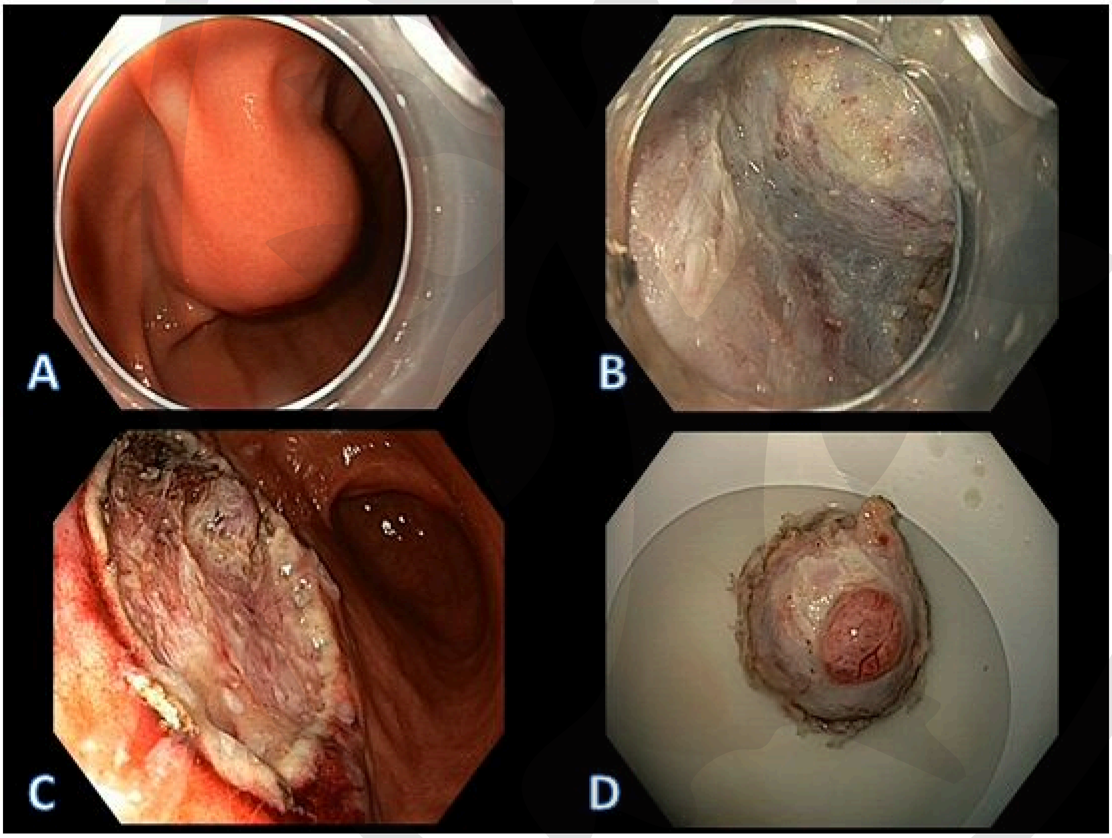
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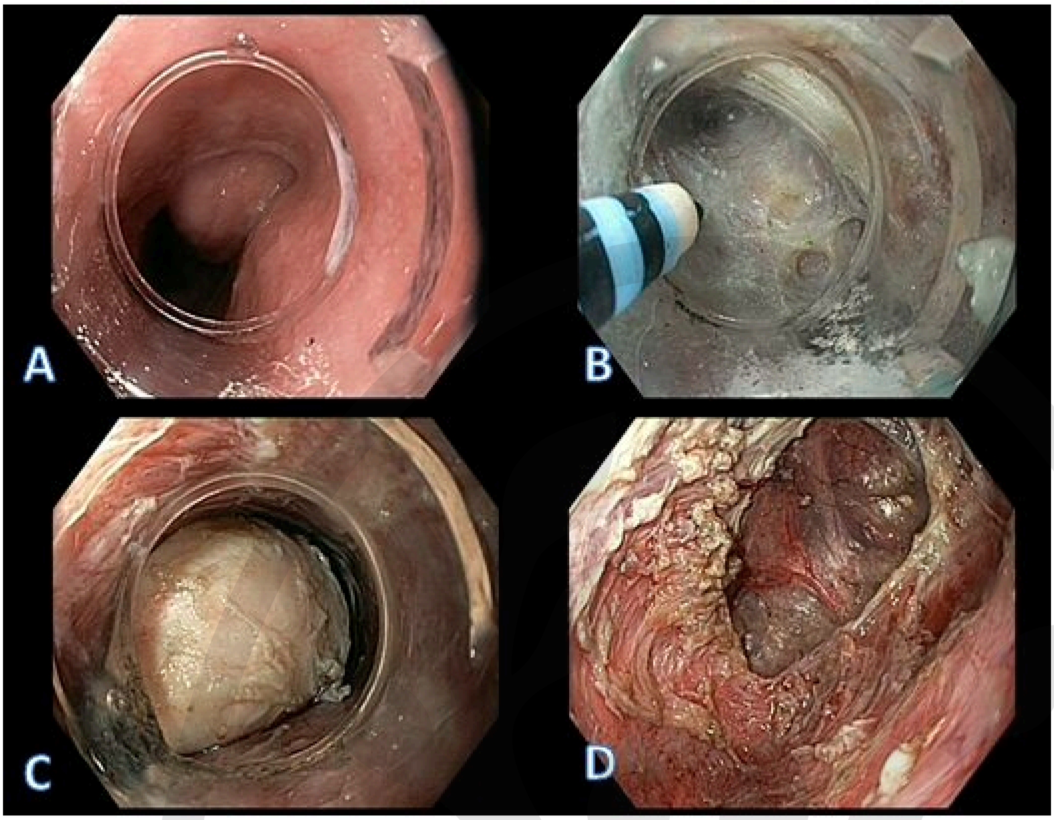
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