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Efficacy and safety of endoscopic resection for small submucosal tumors originating from the muscularis propria layer in the gastric fundus

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Abstract

Background Gastric small submucosal tumors (SMTs) are becoming increasingly common. However, the fundus of stomach is regarded as a difficult area for endoscopic resection (ER). In this study, we investigated the efficacy, safety, and long-term outcomes of ER for small SMTs of the gastric fundus in a large series of patients, research that was previously lacking.

Methods 537 consecutive patients with SMTs no more than 20 mm in diameter, occurring in the gastric fundus and originating from the muscularis propria layer, which were treated with endoscopic submucosal excavation or endoscopic full-thickness resection (EFTR) were included in this retrospective study at Zhongshan Hospital of Fudan University from January 2013 to September 2016. Clinicopathological, endoscopic, and follow-up data were collected and analyzed.

Results *En* bloc resection was achieved in 100% of patients, and complete resection was achieved for 530 (98.7%) lesions. Although the total rate of complications was 9.3%, few serious adverse events occurred in only three (0.6%) patients, including major pneumoperitoneum, major hydrothorax, and bleeding. Unlike lager tumor sizes and longer procedure times, endoscopist experience had a positive impact on decreasing the likelihood of complications. Based on statistical analysis, tumors with greater size near the cardia, which were treated by EFTR, were the significant contributors to longer operative times. A median follow-up of 32 months was available, and all patients were free from local recurrence or distant metastasis during the study period.

Conclusions Although the gastric fundus presents technical difficulties, ER is effective for the resection of small gastric SMTs with a high complete resection rate and rare serious adverse events.

Keywords Small submucosal tumors · Endoscopic submucosal excavation · Endoscopic full-thickness resection · Complications

Bing Li, Tao Chen and Zhi-Peng Qi have contributed equally to this paper.

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Gastrointestinal submucosal tumors (SMTs) are most commonly found in the stomach, as often as one in every 300 endoscopies [1]. Small tumors may be asymptomatic or only present with non-specific gastrointestinal symptoms, and are usually detected incidentally during upper gastrointestinal endoscopy [2]. Recently, with the widespread use of digestive endoscopy and advances in endoscopic ultrasonography (EUS), the frequency of diagnosing small SMTs, including gastrointestinal stromal tumors (GISTs) with malignant potential, has increased. According to guidelines set by the National Comprehensive Cancer Network (NCCN) [3], surgical referral should be considered for non-metastatic GISTs > 2 cm, whereas GISTs < 2 cm lacking high-risk features upon EUS can be followed up at 6–12 months. However, distinguishing GISTs from other SMTs with similar features using EUS is difficult. Furthermore, when the tumor grows, patients may lose the opportunity to receive minimally invasive treatment [4]. Therefore, the minimally invasive resection approach for these small SMTs is likely a better option.

Endoscopic resection (ER), including endoscopic submucosal excavation (ESE) and endoscopic full-thickness resection (EFTR), which are derived from endoscopic submucosal dissection (ESD), has been used to curatively resect gastric SMTs in an *en* bloc fashion [5, 6]. When the tumor is in the fundus, the dissection is more challenging and more time is consumed for the resection, due to retroflexion of the endoscope and specific anatomical features. Large consecutive studies analyzing small SMTs treated by ER techniques, particularly in gastric fundus, have not been reported. The aim of this study was to evaluate the feasibility of resection of small gastric SMTs using ESE and EFTR techniques in a large series of patients with long-term outcome measurements.

Methods

Patients

Between January 2013 and September 2016, a total of 537 consecutive patients with SMTs smaller than or equal to 20 mm of the gastric fundus originating from the muscularis propria (MP) layer and treated with ER (ESE or EFTR) were included in this study at the Zhongshan Hospital of Fudan University. All of the tumors were defined by endoscopic ultrasonography (EUS) and/or computed tomography (CT), which also evaluated the size of the lesions and metastasis before ER.

The inclusion criteria for ESE or EFTR of SMTs in gastric fundus were as follows: (1) the tumor originated predominantly in the muscularis propria layer, (2) SMTs were detected without metastasis using EUS and CT, (3) the tumors were considered to be potentially malignant with high risk features of EUS, such as the presence of cystic spaces and irregular borders, or predicted by EUS-FNA, (4) SMTs that could not be diagnosed conclusively by EUS and/or EUS-FNA and required histopathological review, (5) patients complained of upper gastrointestinal symptoms, and (6) patients were willing to have the tumor resected by ER, a decision that was made by the patients after they had been fully informed of the risks and benefits of different treatment strategies, including follow-up, ER, and surgery. Exclusion criteria were as follows: (1) disagreement regarding resection, (2) malignant tumor with metastasis, and (3) coagulation disorders. Patients were considered eligible for ESE when the tumor originated from the superficial MP. On the contrary, EFTR without laparoscopic assistance was performed when SMTs originated from the deep MP, showed predominantly extraluminal growth, or were adherent to the serosa as assessed by EUS or CT. In fact, the choice of ESE or EFTR for each patient was mainly determined by operators according to intraoperative situation.

Informed patient consent was also obtained before the procedures. The study and procedures were conducted in accordance with the ethical standards of the Helsinki Declaration of 1975. The study was approved by the Institutional Review Board of Zhongshan Hospital (No. 2009-135).

Procedures

All ESE and EFTR procedures were performed by two groups of operators (one with more than 25 cases of ER experience every year in the gastric fundus, the other with no more than 25 cases experience) who were all certified ER endoscopists. All patients were treated under intravenous anesthesia with airway intubation while the parameters of cardiorespiratory function, such as heart rate, blood pressure, and oxygen saturation, were continuously monitored. A single-channel endoscope or dual-channel endoscopy (GIF-Q260J or GIF-2T240, Olympus, Tokyo, Japan) was used during the procedures. A short, transparent cap (ND-201-11802; Olympus) was attached onto the tip of the endoscope to improve endoscopic visualization and to apply tension to the connective tissues during dissection. An IT-knife and/or a hook-knife (KD-611 and KD-620LR; Olympus) was used to dissect the submucosal layer and to peel the tumor. Other equipment included injection needles (NM-4L-1), snares (SD-230U-20), hot biopsy forceps (FD-410LR) (all from Olympus), and hemoclips (ROCC-D-26-195-C) (from Micro-tech, Nanjing, China).

ESE was performed as follows: (i) marker dots were made close to the lesion. (ii) Several milliliters of solution (100 mL saline, 5 mL 0.8% indigo carmine, and 1 mL epinephrine with the concentration of 1 mg/mL) were injected around the lesion using a 23-gauge disposable needle to lift the mucosa off. (iii) The mucosa was incised along the marker dots using the hook-knife or IT-knife. (iv) The hook-knife or IT-knife was used to peel the MP layer along the capsule of the lesions with covering mucosa and submucosa. After ESE, exposed vessels on the artificial ulcer were coagulated with argon plasma coagulation to prevent delayed bleeding, and clips were placed for deeply resected areas to prevent delayed hemorrhage or perforation.

EFTR was performed as follows (Fig. 1): (i), (ii), and (iii) were the same as ESE procedures. (iv) Active perforation was made by the hook-knife at one point around the lesion, then a circumferential incision was made as deep as the serosal layer surrounding the lesion by IT-knife. (v) Aspiration of the gastric fluid and completion of the full-thickness incision to the tumor was performed; a dual-channel gastroscope

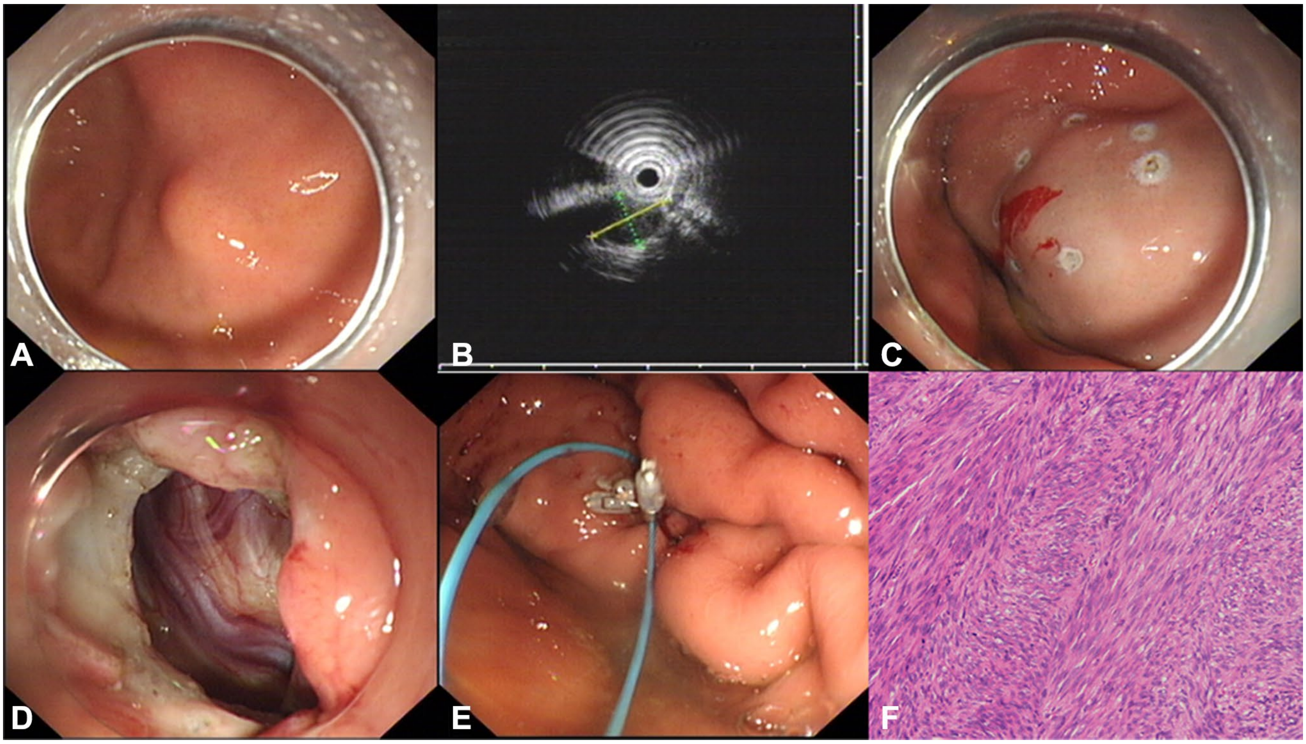

Fig. 1 EFTR operation process for treating SMTs in the gastric fundus. **A** Small submucosal tumor observed by endoscopy. **B** Same submucosal tumor observed by EUS. **C** Marker dots were made close to the lesion. **D** Gastric wall defect was presented after lesion was resected. **E** Metallic clips interrupted suture with endoloop were used to close the wall defect. **F** Pathological examination confirmed that the tumor was a gastrointestinal stromal tumor (HE stain, ×200)

was sometimes used with forceps grasping the tumor in the gastric cavity to prevent the tumor from falling into the peritoneal cavity. (vi) The gastric wall defect was closed by multiple metallic clips or with a metallic clip interrupted suture with endoloop, as reported previously [7]. In the presence of pneumoperitoneum, a 20-gauge needle was inserted into the right upper quadrant of the abdomen to percutaneously decompress the abdominal cavity during the procedure. In all patients, a nasogastric tube was routinely inserted after endoscopic resection.

Pathological examination

Tissue specimens were fixed using 10% formalin solution, embedded with paraffin, and sectioned for histopathological evaluation. *En* bloc resection was defined as excision of a tumor in one piece without fragmentation. Complete resection was defined as *en* bloc resection of a lesion with a tumor removed in a single piece, with the capsule intact [8]. In addition, the World Health Organization (WHO) classification of tumors of the digestive system was used for histopathological evaluation [9]. When the organization of a tumor was difficult to determine, immunohistochemistry was performed [10]. GISTs were risk stratified according to the National Institutes of Health (NIH) GIST risk stratification guideline based on tumor size, location, and mitotic rate [11].

Complications

Postoperative bleeding was defined as hematochezia or melena requiring an endoscopic hemostatic procedure anywhere between 0 and 14 days after completion of ER. Hydrothorax was defined when excess fluid accumulated in the pleural cavity and was confirmed by a chest X-ray (Fig. 2A). Pneumoperitoneum was defined as pneumatosis in the peritoneal cavity, which could be seen on an X-ray or CT scan (Fig. 2B). Minor pneumoperitoneum and minor hydrothorax had minimal clinical impact or symptoms and did not require therapeutic intervention, while major complications required intervention. Post-ESD electrocoagulation syndrome (PEECS), a minor complication, was defined as symptoms of fever (> 37.7 °C) and abdominal pain with localized tenderness that was observed after confirmation by radiological examination that there was no definite evidence of perforation within a few hours to 7 days after ER treatment [12]. Major pneumoperitoneum, major hydrothorax, and postoperative bleeding, all of which require therapeutic intervention, were defined as serious adverse events.

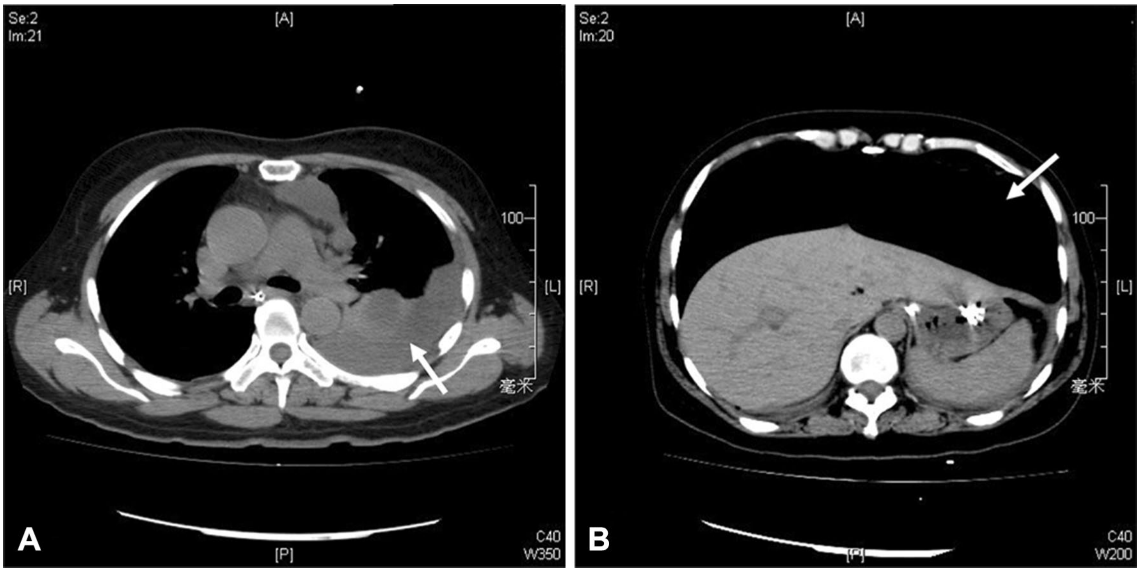

Fig. 2 ER-related complications. **A** Major hydrothorax was detected at 3 days after the endoscopic procedure via CT. **B** CT of a patient with major pneumoperitoneum showed large pneumatosis in the peritoneal cavity

Follow-up

All patients were followed up with standard endoscopy and at 3, 6, and 12 months during the first year after the initial procedure to observe the healing of the wound and to check for residual tumor or recurrence. Subsequently, patients were followed-up annually if no local recurrence was identified in two consecutive follow-up examinations. For patients with GISTs, contrast-enhanced CT scans were recommended every 6–12 months to evaluate the presence of lymph nodes or distant metastasis. Follow-up patient data were obtained from medical records. For patients from distant provinces and those unwilling to come back for follow-up, detailed telephone interviews, including symptoms and treatments or tests received at other hospitals were conducted.

Data collection and analysis

Clinicopathological, endoscopic, and follow-up data were collected and analyzed, including age, sex, tumor characteristics, histopathology, operation information, *en* bloc and complete resection rates, adverse events, local recurrence, and metastasis. Statistical analysis of independent risks for long operative time and ER-related complications were assessed using multivariate analyses. Commercial software (IBM SPSS Statistics 18; Chicago, IL, USA) was used for statistical analysis, and $p < 0.05$ was accepted to be statistically significant.

Results

Clinicopathological characteristics

In this large, consecutive study, 537 patients with a definite diagnosis of gastrointestinal SMTs smaller than or equal to 20 mm in the fundus of the stomach were evaluated (Table 1). The mean age was 56.6 ± 10.3-year old (median 58-years-old, range 21–82-year old) and the female:male ratio was approximately 2:1 (367:170). The mean tumor size was 10.0 ± 4.6 mm (median 10, range 2–20 mm). In addition, 252 (46.9%) tumors measured < 10 mm, and 285 (53.1%) measured 10–20 mm. Among all SMTs, 178 (33.1%) tumors were located in the fundus near the cardia, and 359 (66.9%) were located near the greater curvature. At the same time, 64 (11.9%) lesions showed extraluminal growth, while the other 473 (88.1%) did not. There were 332 (61.8%) GISTs, 196 (36.5%) leiomyomas, 8 (1.5%) calcifying fibrous tumors, and 1 schwannoma (0.2%). Among all GISTs ≤ 20 mm, the majority of the tumors (90.4%) were graded as very low risk, 17 (5.1%) were graded as low risk, 13 (3.9%) were graded as intermediate risk, and 2 (0.6%) were graded as high risk (Table 2). 208 (38.7%) patients had one or more symptoms, including epigastric pain, regurgitation, discomfort, bloating, eructation, nausea and vomiting, difficulty swallowing and others, which may be related to the gastric SMTs. Symptom distributions are included in Supplementary Table 1. 326 patients (60.7%) underwent ER by endoscopists with more than 25 cases of ER experience in the gastric fundus each year. The procedure time was over 45 min in 163

Table 1 Clinicopathological characteristics of 537 gastric fundus SMTs treated by ER

Patients	
Age, mean (median, range), year	56.6 ± 10.3 (58, 21–82)
Sex, male/female	170/367
Lesions	
Size, mean (median, range), mm	10.0 ± 4.6 (10, 2–20)
< 10 mm	252 (46.9%)
10–20 mm	285 (53.1%)
Location (near cardia)	
Yes	178 (33.1%)
No	359 (66.9%)
Extraluminal growth	
No	473 (88.1%)
Yes	64 (11.9%)
Histopathology	
GIST	332 (61.8%)
Leiomyoma	196 (36.5%)
Clarifying fibrous tumors	8 (1.5%)
Schwannoma	1 (0.2%)
Technique	
Surgical approach	
ESE	322 (60.0%)
EFTR	215 (40.0%)
Procedure time, mean (median, range), min	38.3 ± 21.8 (34, 10–210)
< 45 min	347 (69.6%)
≥ 45 min	163 (30.4%)
Endoscopist experience	
< 25 ERs/years	211 (39.3%)
≥ 25 ERs/years	326 (60.7%)
En bloc resection	537 (100%)
Complete resection	530 (98.7%)
Complications	50 (9.3%)
Pneumoperitoneum	20 (3.7%)
Minor pneumoperitoneum	19 (3.5%)
Major pneumoperitoneum	1 (0.2%)
Hydrothorax	13 (2.4%)
Minor hydrothorax	12 (2.2%)
Major hydrothorax	1 (0.2%)
PEECS	16 (3.0%)
Major bleeding	1 (0.2%)
Follow-up	
Recurrence	0 (0%)
Metastasis	0 (0%)

(30.4%) cases, while 347 (69.6%) cases were shorter than 45 min. In this study, all gastric fundus SMTs were resected, with a 100% *en* bloc resection rate, and complete resection was achieved in 530 of the 537 lesions (98.7%).

On the first postoperative day, patients resumed a liquid diet if they had no complaint of fever, dyspnea, chest pain, or abdominal pain. The mean post-operation hospitalization time was 3.3 ± 1.7 days (median 3, range 1–14).

Table 2 Pathological characteristics of 332 GISTs ≤ 20 mm treated by ER

Mitotic rate	
≤ 5 mitoses/50 HPF	317 (95.5%)
6–10 mitoses/50 HPF	13 (3.9%)
> 10 mitoses/50 HPF	2 (0.6%)
Risk stratification	
Very low	300 (90.4%)
Low	17 (5.1%)
Intermediate	13 (3.9%)
High	2 (0.6%)

Procedure time

In this study, the mean time required for the ESE or EFTR procedures was 38 ± 21.8 min (median 34, range 10–210 min). According to multivariate logistic analysis, tumor size (≥ 10 mm: OR 1.865; 95% CI, 1.249–2.785), location (near cardia: OR 1.551; 95% CI, 1.016–2.366), and surgical approach (EFTR: OR 2.893; 95% CI, 1.932–4.331) were significant risk factors for long operative times (Table 3). Other clinicopathological characteristics including age, sex, tumor location, extraluminal growth, histopathology, and endoscopist experience had no significant impact on the operative time required.

Complications

The total incidence of complications in this study was 9.3%, and serious adverse events presented in only 3 (0.6%) cases (Table 1). In detail, pneumoperitoneum occurred in 20 (3.7%) patients, including 1 patient with major pneumoperitoneum, which required puncture and 19 patients with minor pneumoperitoneum, which only required observation. Similar results occurred in 13 (2.4%) patients that suffered thoracic effusion; 1 patient with major thoracic effusion required thoracic drainage and the remaining 12 patients with minor effusion did not require intervention. There were 16 (3.0%) patients with PEECS who were administered intravenous antibiotics and fluids and whose oral food consumption was discontinued until symptoms improved. However, major bleeding occurred in only 1 patient (0.2%) who underwent endoscopic hemostatic procedures. There were no treatment-related deaths. A logistic regression model was used to identify predictors of ER-induced complications by incorporating demographic data, endoscopic tumor findings, and procedure-related factors. Multivariate logistic regression confirmed that tumor size (≥ 10 mm: OR 2.327; 95% CI, 1.071–5.055), procedure time (≥ 45 min: OR 3.375; 95%

Table 3 Multivariate analysis of research cohort

Factors	Procedure time ≥ 45 min			Adverse events of ER		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age						
< 60 years	1	–	–	1	–	–
≥ 60 years	1.226	0.821–1.831	0.320	0.678	0.327–1.408	0.298
Sex						
Male	1	–	–	1	–	–
Female	1.385	0.900–2.133	0.139	0.566	0.279–1.149	0.115
Tumor size						
< 10 mm	1	–	–	1	–	–
10–20 mm	1.865	1.249–2.785	0.002	2.327	1.071–5.055	0.033
Near cardia						
No	1	–	–	1	–	–
Yes	1.551	1.016–2.366	0.042	1.677	0.713–3.944	0.236
Extraluminal growth						
No	1	–	–	1	–	–
Yes	1.726	0.970–3.070	0.063	2.003	0.892–4.497	0.092
Histopathology						
GIST	1	–	–	1	–	–
Others	0.717	0.445–1.157	0.173	1.156	0.472–2.835	0.751
Surgical approach						
ESE	1	–	–	1	–	–
EFTR	2.893	1.932–4.331	< 0.001	1.390	0.659–2.931	0.387
Endoscopist experience						
< 25 ERs/years	1	–	–	1	–	–
≥ 25 ERs/years	1.355	0.903–2.034	0.143	0.350	0.157–0.777	0.010
Procedure time						
< 45 min	–	–	–	1	–	–
≥ 45 min	–	–	–	3.375	1.153–4.893	0.019

CI, 1.153–4.893), and endoscopist experience (≥ 25 ERs/years: OR 0.350; 95% CI, 0.157–0.777) were significant factors for ER-related complications (Table 3).

Follow-up results

Among 537 patients with SMTs of the gastric fundus treated with ER, 25 cases were not followed up, and the remaining cases were followed up for ≥ 12 months. The overall median follow-up period was 32 months (range 12–57 months). During follow-up, all patients were free from local recurrence and distant metastasis.

Discussion

At present, the management of SMTs mainly depends on tumor size; tumors less than 2.0 cm typically receive a recommendation for periodic follow-up. However, in the 2017 guidelines of the American Society for Gastrointestinal Endoscopy (ASGE) on subepithelial lesions [13], the words "we suggest" indicated a weaker recommendation for EUS surveillance for gastric GI stromal tumors < 2 cm in size, while "we recommend" appeared in the recommendation for tumors > 2 cm in size. That means that the strategy for the management of small gastric SMTs needs to be reconsidered after analyzing more studies of high quality. In our opinion, SMTs no more than 2 cm in the stomach should undergo resection by endoscopy if the patient agrees this option is best.

First, our research shows that GISTs, accounting for 61.8% of all SMTs, are the most common tumor in the gastric fundus when 60–70% of GISTs were found in the stomach [14]. Moreover, two cases were graded as high risk after postoperative pathological assessment. In fact, all GISTs have some malignant potential, regardless of their small starting size, as this type of tumor can increase in size consistently over time or even suddenly. A study showed that 13% of patients with GISTs less than 2 cm showed an increase in tumor size after a mean period of as little as 17.3 months of follow-up by EUS [15]. There was one case were the GIST increased from 1.8 cm at diagnosis to up to 10 cm after only 2 years, and the doubling time of the tumor was calculated to be 3.1 months. Even for GISTs with smaller diameters, the potential for proliferation and malignant transformation should not be ignored. In addition, once the tumor increases, patients will lose their opportunity to undergo minimally invasive treatment. Second, EUS and EUS-FNA, even as two of the most common diagnostic methods, have limitations in distinguishing GISTs from other SMTs. EUS is mandatory to confirm the subepithelial position of lesions, although EUS alone cannot identify the histological tumor subtype, nor can it predict the potential malignant behavior of gastric SMTs [16, 17]. Compared to EUS, although tissue specimens are acquired, EUS-FNA cannot properly evaluate high-risk lesions. A precise histopathological diagnosis can be difficult to achieve with EUS-FNA, because most GISTs are difficult to penetrate, exhibiting fibrosis that frequently prevents collection of sufficient material by aspiration [18]. Furthermore, the size of SMTs also restricts the application of EUS-guided techniques. According to a study by Akahoshi et al., the yield of sufficient tissue acquisition seems to be dependent on the tumor diameter, being 71%, 86%, and 100% for a tumor less than 2 cm, 2–4 cm, and more than 4 cm in diameter, respectively [19]. Therefore, tumors less than 2 cm in size can be difficult to be assess accurately by EUS-guided FNA (EUS-FNA). Moreover, substantial adverse events related to biopsies have also been described, with bleeding occurring in up to 22% of patients undergoing EUS-FNA [20]. Third, the majority of patients with small gastric SMTs prefer to undergo a resection operation as opposed to regular surveillance. The discomfort caused by endoscopic examination results in poor compliance, and the indefinite follow-up examinations can cause an enormous psychological burden. According to the experience of our center, around 70% of the patients that had SMTs smaller than 2 cm would choose to undergo lesion resection by ER within 6 months, rather than continuously monitor the SMT.

In this study, we paid attention to small SMTs originating from the MP layer, especially those located in the gastric fundus. This area of the stomach is a common location for SMTs, especially GISTs. Due to endoscopic retroflexion, the gastric fundus is regarded as a difficult area to perform ESE or EFTR. The endoscope needs to be retroflexed to reach the gastric fundus and the knife is therefore vertically oriented to the fundus, which can result in prolonged procedure times [21, 22]. In addition, the gastric fundus is thinner than other regions, and the diaphragm, the spleen, and many blood vessels surrounding the gastric fundus increase the risk of ER-related complications. Therefore, only the most skilled endoscopists should perform such procedures using the most advanced technology available.

Procedure time can reflect the degree of operation difficulty, in part. Based on multivariate analyses, our results also indicated that the procedure time tended to be longer when the tumor size was over 10 mm and lesions were near the cardia. The result that larger tumor sizes increase procedure time has been confirmed by other studies [23], while the observation that tumors near the cardia also increase procedure time is a new finding. We suspect this is because with submucosal tumors of the esophagogastric junction, the endoscopist is restricted by a narrow space and sharp angle, which is more prominent in this area compared to others in gastric fundus [24]. In addition, our data have shown that the surgical approach used also impacts the procedure time. The percentage of procedures requiring a long operative time over 45 min for ESE and EFTR was 21.7% and 43.3%, respectively, indicating that it was more common for EFTR procedures to be prolonged as compared to ESE. This could be because of the different characteristics of the SMTs treated by each ER approach. Moreover, it is necessary to close gastric defects after EFTR, using a metallic clip alone or a metallic clip interrupted suture with endoloop, which can add time to the procedure.

The results of this study show that ER techniques, ESE and EFTR, are safe and effective treatment options for SMTs of the gastric fundus. Although the overall rate of ER-related adverse events for SMTs in this area was 9.3% (50/537), major pneumoperitoneum, major hydrothorax, and postoperative bleeding which required therapeutic intervention occurred in only 3 (0.6%) patients. There were 19 (3.5%) patients with minor pneumoperitoneum, 12 (2.2%) with minor hydrothorax, and 16 (3.0%) with PEECS, and these minor adverse technical events had minimal clinical impact or symptoms. In this study, the reported ER-related serious complications rates were lower than other reports [25–27], which may because of the smaller tumor size and rich experience of the doctors in our center. For the same reasons, the minor complications, especially PEECS, also occurred in fewer patients compared to other studies [28]. According to our statistical analysis, tumor sizes ≥ 10 mm and longer ER duration times ≥ 45 min were associated with a significantly increased risk of ER-related complications, while endoscopist experience decreased this risk. Therefore, ESE and EFTR for SMTs located in gastric fundus should be performed only by endoscopists who are skilled and experienced, which should improve patient safety, especially for patients with larger lesions. These results also confirmed the importance of professional training for the endoscopist.

The results of the present study showed that ER provided a 100% *en* bloc resection and a 98.7% complete resection rate for gastric SMTs in fundus, which indicated that ER was a feasible and effective treatment option for small gastric SMTs. In this series, the overall median follow-up period was 32 months (range 12–57 months), and the long-term outcomes of ESE and EFTR for all SMTs in the present study were excellent; neither local recurrence nor distant metastasis has been observed.

Compared to other treatment strategies, this study and others on ER for small SMTs reveal that patients may benefit more. Other published reports on small SMTs also demonstrate that endoscopic resection has a high safety rate and efficacy, when the incidence of severe adverse events was 2.9–3.1% and complete resection rate obtained was up to 96.7% [29, 30]. Therefore, diagnosis and treatment in the same session are possible by endoscopic resection, and the need for a second, therapeutic procedure after diagnosis is eliminated [29]. After getting an accurate diagnosis and removal by ER, non-specific gastrointestinal symptoms and psychological burden of patients caused by small gastric SMTs may be relieved. In addition, ER of small SMTs can achieve similar oncological outcomes with the advantages of a shorter mean operation time, less blood loss, a shorter length of hospital stay, and lower costs than conventional surgery [31, 32]. That means, ER is an appropriate choice for patients with small gastric SMTs who prefer to resection over long-term surveillance.

A large consecutive series of cases were evaluated, but some limitations were still present. For one, the study design used was retrospective, and it was a single-center analysis, although the patients in our center are from different regions of China. In addition, ER was not compared with other conventional treatments. Thus, a prospective and randomized study is warranted. Moreover, a median of 32-month follow-up was insufficient to evaluate the long-term outcomes for potentially malignant SMTs, especially GISTs; a longer-term follow-up is currently in process. The purpose of this retrospective study is to sum up the experience of ER for the treatment of small SMTs, not to change the existing guidelines of clinical practice. We really hope our study could provide some references for peers who need to manage similar cases.

In conclusion, ER is effective for resection of SMTs of the gastric fundus originating from the muscularis propria layer and is associated with a 9.3% rate of complications, but only a 0.6% rate of serious adverse events. Tumor size, procedure time, and the experience of the endoscopist influence the development of ER-related complications. In addition, ER is feasible in the gastric fundus, although technological difficulties were present, evidenced by longer procedure times, which were correlated with tumor size, presence near the cardia, and the selected ER approach.

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Compliance with ethical standards

Disclosures Bing Li, Tao Chen, Zhi-Peng Qi, Li-Qing Yao, Mei-Dong Xu, Qiang Shi, Shi-Lun Cai, Di Sun, Ping-Hong Zhou, and Yun-Shi Zhong have no conflicts of interest or financial ties to disclose.

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