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Effect of endoscopic resection of gastrointestinal stromal tumors in the stomach under double-channel gastroscopy

A retrospective observational study

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Abstract

We aimed to investigate the safety and efficacy of endoscopic resection for the treatment of gastric gastrointestinal stromal tumors (GISTs) under single-channel gastroscopy and double-channel gastroscopy.

We identified 154 patients with GISTs of the stomach who underwent endoscopic resection and were retrospectively analyzed at our hospital between May 2016 and March 2020, including 49 patients by single-channel gastroscopy and 105 patients by double-channel gastroscopy. We observed the clinical efficacy, complications, and safety of endoscopic resection of gastric GISTs, and the data were evaluated retrospectively.

All patients underwent endoscopic resection successfully, without conversion to open surgery. In the single-channel gastroscopy group, 7 patients had lesions in the gastric cardia, 17 in the gastric fundus, 20 in the gastric corpus, and 5 in the gastric antrum. In the double-channel gastroscopy group, 13 patients had lesions in the gastric cardia, 34 in the gastric fundus, 46 in the gastric body, 10 in the gastric antrum, 1 in the pylorus, and 1 in the gastric angular incisure. The double-channel gastroscopy group had a shorter operation time than the single-channel gastroscopy group (59.9 ± 34.9 minutes vs 74.8 ± 26.7 minutes; $P = .009$ and $P < .01$, respectively), while they also had a lower perforation rate than the single-channel gastroscopy group (34.3% vs 51.0%; $P = .048$ and $P < .05$, respectively). No residual or recurrent lesions were discovered in any patients by gastroscopy reexamination.

Both single-channel gastroscopy and double-channel gastroscopy can provide safe, effective, feasible endoscopic resection. However, double-channel gastroscopy has some distinct advantages in endoscopic resection.

Abbreviations: CT = computerized tomography, EFTR = endoscopic full-thickness resection, ER = endoscopic resection, ESE = endoscopic submucosal excavation, EUS = endoscopic ultrasonography, GISTs = gastrointestinal stromal tumors, LECS = laparoscopic and luminal endoscopic cooperative surgery, MP = muscularis propria, STER = submucosal tunneling endoscopic resection.

Keywords: endoscopic full thickness resection, endoscopic submucosal excavation, gastric gastrointestinal stromal tumors, gastroscopy

1. Introduction

Gastrointestinal stromal tumors (GISTs) originate from the muscularis propria (MP) layer of the digestive tract. The gastric wall is mainly divided into mucosa, muscularis mucosa, submucosa, MP, and serosa. Among them, tumors originating in the muscularis mucosa are superficial and tend to grow toward the lumen of the digestive tract, which are easier to remove under endoscopy. In contrast, tumors originating in the MP are at a deeper location, are difficult to detect by conventional endoscopy and need to be diagnosed by endoscopic ultrasonography (EUS). Endoscopic resection (ER) of such tumors is difficult, and perforation easily occurs during resection. GISTs are potentially malignant, are common in the stomach and are indicated for resection.[1,2] According to American and European guidelines, the standard treatment for resectable GISTs is surgery.[3,4] However, surgical treatment has some connatural disadvantages, such as more blood loss, slower functional recovery, and higher hospital cost,[5,6] and these disadvantages may make some patients refuse surgical treatment. However, thanks to the

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development of digestive endoscopic technology, an increasing number of GISTs can be excised completely under endoscopy.[7] ER includes submucosal tunneling endoscopic resection (STER), endoscopic submucosal excavation (ESE), endoscopic full-thickness resection (EFTR), and laparoscopic and luminal endoscopic cooperative surgery (LECS), and it has become a standard treatment modality for early intraluminal GISTs.[8,9]

In recent years, with the help of single-channel gastroscopy and double-channel gastroscopy, ER has been applied to treat gastric GISTs in our hospital, including extraluminal or mixed growth type, and good therapeutic outcomes have been achieved. We aimed to investigate the safety, efficacy, and feasibility of ER in GISTs, especially those extraluminal growth types.

2. Materials and Methods

2.1. Patients

From May 2015 to March 2020, 154 patients were treated at the Endoscopy Center of the Affiliated Hospital of Qingdao University Laoshan district (Qingdao, China) with the use of single-channel gastroscopy or double-channel gastroscopy. The clinical data of 154 patients who underwent ER of gastric GISTs in our center were retrospectively analyzed. All patients were forbidden to take any anticoagulant drugs for at least 1 week and were subjected to preoperative examinations. EUS was carried out to determine the exact tumor size, growth pattern, and layer of the lesion, and abdominal computerized tomography (CT) scanning was carried out if necessary.[10] Patients with any high-risk features on EUS or CT scanning were excluded. Patients with serious heart diseases, lung diseases, before disturbances of blood coagulation were healed, malignant hematonosis, and other severe diseases were also excluded. All patients were informed of the procedure and received careful explanations about the necessity, relative risks, and possible complications of endoscopic treatment, and written informed consent was provided before ER. All patients were strictly fasted with respect to food and water before ER. The study protocol was approved and reviewed by the Institutional Review Board of the Affiliated Hospital of Qingdao University.

2.2. Medical devices

Single-channel gastroscopy (GIF-HQ290, Olympus Co. Ltd., Tokyo, Japan), double-channel gastroscopy (GIF-2TQ260 M, Olympus Co. Ltd., Tokyo, Japan), an electronic endoscopy system (Olympus LUCERA CV-290, Olympus Co. Ltd., Tokyo, Japan), a high-frequency electric coagulation and electrocution device (ERBE VIO 300D; ERBE Elektromedizin, Tübingen, Germany), an injection water pump (OFP-2, Olympus) and a CO2 air pump (UCR, Olympus) were used.

A flush knife (DK2618JB-20-; Fujifilm Holdings Co., Tokyo, Japan) or dual knife (KD-650L; Olympus), IT knife 2 (KD-611L; Olympus), Coagrasper (FD-410LR; Olympus) (for hemostasis), needle (NM-200 L-0523, Olympus), polypectomy snare (MTN-PFS-E-36/23 Micro-Tech, Nanjing, Co., Ltd., Nanjing, China), metal clips (ROCC-D-26-195 Micro-Tech, Nanjing, Co., Ltd., Nanjing, China) and resolution clips (M00522610, Boston Scientific Co, Natick, Massachusetts, USA), nylon loops (MAJ-340, Olympus), and transparent caps (D-201-13404, Olympus) were used. Propofol was given for general intravenous anesthesia under a tracheal cannula, and the patient was kept sedated with cardiorespiratory monitoring during surgery.

2.3. Endoscopic procedures

2.3.1. For small tumors, GISTs with a diameter of <15 mm could be treated using the suction-resection method. The suction-resection method was performed. First, a snare was inserted through 1 channel, and the handle of the pusher was still held by the assistant. Second, the endoscopist inserted the gastroscope with the snare until reaching the gastric lesion and placed the snare on the root of the tumor. After the lesion was sucked into the transparent cap, the assistant narrowed the snare, ligated the lesion fully, and resected the tumor with the help of an electrocution device. Finally, the lesion was withdrawn for pathological diagnosis, and the wound was closed with metal chips.

2.3.2. For large tumors, GISTs with a diameter of > 1.5 cm could be treated using ESE or EFTR. ESE and EFTR were performed using double-channel gastroscopy, flush knife or dual knife, polypectomy snare, IT knife and foreign forceps if necessary. EFTR procedures were performed. First, a dual knife or flush knife was used for marking at 2 to 3 mm from the tumor margin under soft coagulation mode, and methylene blue injection and normal saline were used for submucosal injection near the markers. Second, after injection with methylene blue and normal saline, the mucosa around the GISTs was cut along the markers to expose the GISTs. For deeper lesions, the mucosa could be excised by blocks with the use of snares to expose the lesions. Third, the surrounding gastric wall was excised carefully. After the GISTs were excised in at least two-third circles, they were pulled into the gastric cavity, grasped closely by foreign forceps, and then removed completely. Sometimes, the surrounding gastric wall was directly cut to produce an active perforation, an endoscope was inserted into the abdominal cavity to cut the extraluminal or mixed growth tumor, and it was excised completely in the abdominal cavity. Then, the perforation was closed as quickly as possible by pure-string sutures with nylon loops and metal clips. Some small perforations were closed only by metal clips. Finally, the GISTs were removed for pathological diagnosis, and the gas in the gastric cavity was sucked out.

Mild bleeding was treated successfully under flush water, knife, or hemostatic forceps. Bleeding caused by large vessels was cured by metal clips.

2.4. Histopathological evaluation

The excised lesions were subjected to formalin (10%) fixation and delivered to the Department of Pathology, followed by histopathological examination. Immunohistochemical staining of CD117, CD34, DOG-1, S-100, SOX10, SMA, desmin, and Ki-67 was performed. The mitotic index was calculated under 50 high-power field. The consensus from the National Institutes of Health[11] was used to guide the risk classification standard of GISTs.

2.5. Statistical analysis

All statistical analyses were performed using SPSS version 11.5 statistics software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean ± standard deviation, significant differences between groups were assessed by independent samples *t* test, significant differences between groups of categorical variables were assessed by chi-square test, and $P < .05$ was considered statistically significant.

3. Results

3.1. Tumors were excised completely under different endoscopy methods

All tumors were excised completely under endoscopy, including 83 tumors by ESE (Fig. 1A), 3 by STER (Fig. 1B), and 68 by EFTR (Fig. 1C). All of the perforations were closed by using metal clips, and large perforations (diameter >2 cm) were additionally given nylon ropes without conversion to LECS or open surgery. Bleeding in all patients was recorded during resection,

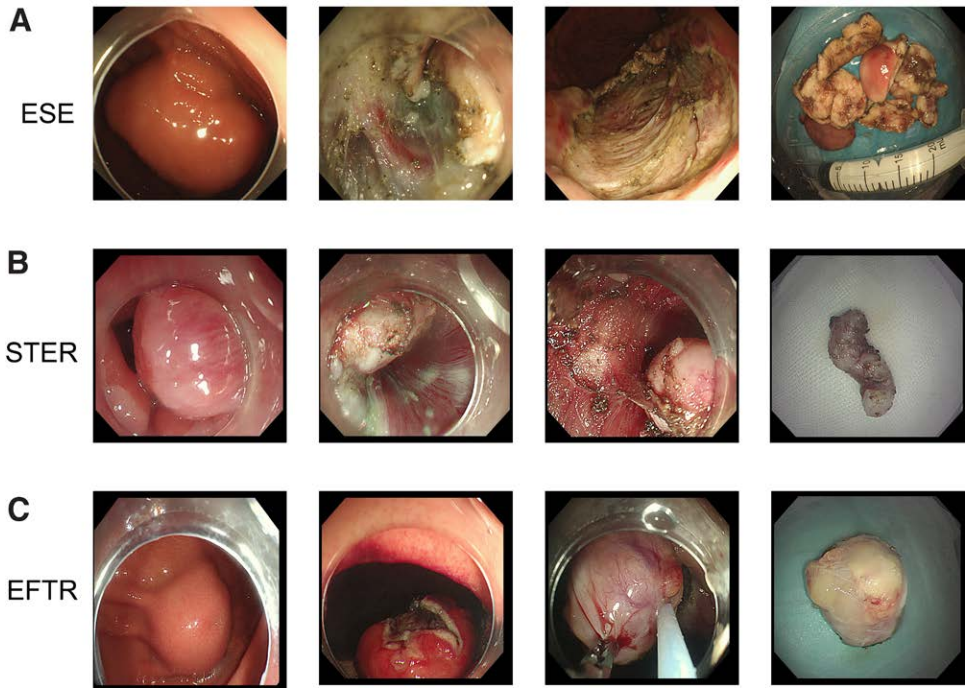

Figure 1. (A) The ER process of the single-channel gastroscopy technique. A large GIST was observed in the anterior wall of the gastric body, the root of the tumor was wholly exposed, and the wound of the gastric wall was clipped. After the tumor was cut into several small slices, all the tumor tissue was taken out. (B) The ER process of the double-channel gastroscopy technique. Abdominal CT showed that a GIST was located in the greater curvature of the gastric body. The greater omentum could be seen from the active perforation after the GIST was removed. In addition, the view of the GIST after resection. (C) The ER process of the double-channel gastroscopy. A GIST was observed in the greater curvature of the gastric body. The GIST was observed from the active perforation. The perforation was observed from the abdominal cavity. The perforation was closed by purse-string sutures with 2 nylon loops and several metal clips. In addition, the tumor was taken out. CT = computerized tomography, EFTR = endoscopic full-thickness resection, ER = endoscopic resection, ESE = endoscopic submucosal excavation, GIST = gastrointestinal stromal tumors, STER = submucosal tunneling endoscopic resection.

and hemostasis was treated successfully, with an average blood loss of <30 mL. In Figure 1A, there are 2 very large tumors (diameter 4.0–5.0 cm) that are separated from the gastric wall and too large to be taken out. It was also very difficult to cut them into small slices. So, after a little tissue was taken for biopsy, the rest of the tumor was fixed to the gastric wall by a nylon loop and clips.

3.2. Double-channel gastroscopy could be a safe, effective, feasible ER technique

The double-channel gastroscopy group had a shorter operation time than the single-channel gastroscopy group (59.9 ± 34.9 minutes vs 74.8 ± 26.7 minutes; $P = .009$, < .01), while this group had a lower perforation rate than the single-channel gastroscopy group (34.3% vs 51.0%, $P = .048$, <.05). The single-channel group had a longer follow-up time than the double-channel gastroscopy group (32.5 ± 12.1 vs 19.1 ± 12.4, $P = .000$, < 0.01; Table 1). In the double-channel gastroscopy group, ER of the gastric fundus had a higher perforation rate than the gastric cardia ($P = .011$, < .05) and gastric corpus ($P = .007$, < 0.05), while there was no statistically significant difference in the single-channel gastroscopy group (Table 2).

3.3. Pathological characteristics and risk classification

The results of immunohistochemistry showed that CD117 was positive in 71 patients (67.6%), DOG-1 was positive in 73 (69.5%), and CD34 was positive in 69 (65.7%). While SMA was positive in only 32 (30.5%) patients, S-100 was rare in 3 (2.9%) cases. In the risk classification, 93 patients (88.6%) were classified as very low risk, 8 (7.6%) as low risk, and 4 (3.8%) as moderate risk.

3.4. Postoperative management

Within 72 hours after the operation, nasogastric negative pressure drainage and bedrest were instituted, while eating or drinking were forbidden. Fluid infusion, nutritional support, proton pump inhibitors, hemostasis, and antibiotics were administered

Table 1

The summary of the 2 groups.

	Single-channel gastroscopy group	Double-channel gastroscopy group	*P*
Sex (male/female)	23/26	48/57	$P = .887 > .05$
Age, y (mean ± SD)	53.1 ± 10.4	56.1 ± 10.6	$P = .107, > .05$
Perforation, n (%)	25 (51.0)	36 (34.3)	$P = .048, < .05$
Operation time, min (mean ± SD)	74.8 ± 26.7	59.9 ± 34.9	$P = .009, < .01$
Tumor diameter, cm (mean ± SD)	1.8 ± 1.0	1.9 ± 1.4	$P = .724, > .05$
Postoperative day, d (mean ± SD)	5.1 ± 1.3	5.3 ± 1.5	$P = .549, > .05$

SD = standard deviation.

Table 2

The location and perforation rate of the study.

	Gastric cardia	Gastric fundus	Gastric corpus	Gastric antrum	Pylorus	Gastric angular incisure
Number, n (%)						
Group 1	7 (14.3)	17 (34.7)	20 (40.8)	5 (10.2)	0 (0.0)	0 (0.0)
Group 2	13 (12.4)	34 (32.4)	46 (43.8)	10 (9.5)	1 (1.0)	1 (1.0)
Perforation, n (%)						
Group 1	2 (4.1)	9 (18.4)	13 (26.5)	1 (2.0)	0	0
Group 2	3 (2.9)*	12 (21.0)	20 (19.0)	1 (1.0)†	0	0

Group 1 means the single-channel gastroscopy group; group 2 means the double-channel gastroscopy group. In group 2, compared to the tumors from gastric fundus.

*$P = .011$, <0.05.

†$P = .007$, <0.01.

as additional treatments if necessary. The clinical signs and symptoms of the patients were carefully monitored, along with symptoms such as fever, abdominal pain, melena, hematemesis, peritonitis, and the color of the fluid from nasogastric negative pressure drainage. The postoperative hospitalization time was 5.1 ± 1.3 days in the single-channel group and 5.3 ± 1.5 days in the double-channel group, and there was no statistically significant difference ($P > .05$; Table 1).

3.5. Follow-ups

Four patients were of moderate risk, so they received adjuvant therapy with imatinib after the operation, and they were referred to the Oncology Department for more treatment. In the first, third, and sixth months, as well as 1 year, after ER, all patients were required to receive gastroscopy reexamination to inspect the recovery status of the wound, and whether any residue or recurrence of the tumor had occurred was examined. The patients received abdominal ultrasonography and/or CT every year to exclude metastasis. During the follow-up months, there was no recurrence, metastasis, or death in any of the patients.

4. Discussion

Most patients with GISTs lack specific clinical symptoms or are asymptomatic in the early stages, and the tumors are frequently found incidentally with endoscopy or physical examination. An increasing number of GISTs smaller than 2 cm have been found in recent years.[12,13] Traditionally, most GISTs are treated by laparoscopic wedge resection or open surgery.[14,15] However, GISTs are different from gastric cancer because they have a distinct boundary with the surrounding normal tissues, and lymph node metastasis is infrequent.[16] As a result, they seldom require lymphadenectomy or a large resection margin. Compared with surgical resection, endoscopic treatment can provide an exact operation and reduce the harm to surrounding organs and tissue. ER has great advantages, including faster recovery, lower cost, and shorter hospital stay.[17,18] ER can provide a better quality of life to patients with the protection of normal gastric structures and digestive physiology.[19] The less invasive endoscopic techniques of ER for GISTs have been gradually accepted and used as an effective method for gastric GISTs in recent years,[20,21] and how to choose a suitable endoscopic approach mainly depends on the tumor location, size, and growth patterns.[22] Perforation is the main problem of ER,[23] especially tumors located in the middle of the gastric wall and tumors with extraluminal growth.[24] Our data have shown that the gastric fundus has a higher incidence of perforation than others in the double-channel gastroscopy group, which is similar to other research,[25] and this may be because the wall of the gastric fundus is thinner than others and the tumors located in the gastric fundus are not convenient to be excised. In the single-channel gastroscopy group, there was no statistically significant difference, which may be because the number of patients was not large enough.

The small perforations of ER are often closed by metal clips. However, using metal clips alone to close large perforations is very difficult.[26] Therefore, purse-string sutures with nylon loops and metal clips,[27] over-the-scope clip[28–30] and line-assisted complete closure methods[31] were used, and conversion to open surgery was seldom needed.[32] Moreover, regardless of accidental perforation or active perforation, it should be quickly repaired in a few minutes during the procedure to reduce the risk of pneumoperitoneum and peritonitis. In our study, all the perforations were closed by the application of metal chips or purse-string sutures with nylon loops and metal clips under gastroscopy.

In this retrospective observational study, we investigated gastric GISTs treated by single-channel gastroscopy and double-channel gastroscopy, and we found that double-channel gastroscopy has distinctive advantages in ER procedures compared with single-channel gastroscopy. First, in double-channel gastroscopy, the diameter of the channels is larger than that of the channel of single-channel gastroscopy, so it is more powerful and quick to remove fluid and smoke from the gastric cavity, which can reduce the risk of pneumoperitoneum and peritonitis. Second, keeping a clear view is very important. Sometimes active perforation is convenient to cut tumors with an extraluminal growth pattern. With 2-angle control turn-knobs, double-channel gastroscopy has a greater angle in ER procedures than traditional endoscopy, which allows the endoscopist to insert the endoscope into the abdominal cavity to treat the tumors more easily than single-channel gastroscopy and ensures that the other organs, nerves, and vessels are not hurt. Some special positional lesions can also be treated easily, which are located at the gastric fundus and gastric cardia, especially the greater curvature of the cardia. Third, the rate of perforation was high, as most of the tumors were probably from the 4th layer. When the extraluminal growth-type tumor is cut, after foreign forceps are inserted through 1 channel, a snare or knife can be inserted through another channel. After foreign forceps have caught the tumor, a snare or knife can be used to cut the tumor. This is impossible for single-channel gastroscopy. When we want to make the perforation larger, the IT knife is a good choice, which can protect the surrounding tissues and organs. However, double-channel gastroscopy has its own disadvantages. It has a larger diameter than normal gastroscopy, so it has some difficulty crossing the throat and pylorus, checking the gastric angular incisure, and inserting into the tunnel entry. Pathological risk classification is very important for the prognosis of GISTs.[33,34] In our study, most of the tumors were classified as pathologically very low or low risk of malignancy, and only 4 tumors were classified as moderate risk. Most of the patients were followed up for a long time to evaluate the efficacy and safety of ER measures for the treatment of gastric GISTs. Some surgeons worried about the residual tumor and the peritoneal implantation of the very large tumor, because before it was separated completely from the gastric wall, it was cut into several small

slices. To avoid these situations, we separated the tumor carefully without rupture, and the tumors were resected wholly to maintain the completeness of the wound. Therefore, the risk of residual and peritoneal implantation of the tumor is very low. There are limitations in our study. The follow-up period of several patients was limited in this study because the ER of these patients was completed in March 2020. The long-term efficacy of ER should be observed continuously.

Patients with hypertension, diabetes, advanced age, or long-term oral glucocorticoids are more prone to adverse events. A series of measures were carried out to mitigate the side effects. They were required to control the blood pressure and the blood glucose level. All patients were forbidden to take any anticoagulant drugs at least 1 week, and were subjected to preoperative examinations, including heart and lung function examination, blood tests was done to check the hemoglobin concentration and platelet count. The endoscopy doctors must pay attention to how to reduce the pneumoperitoneum, with the use of carbon dioxide air pump, shorten the operation time and abdominal puncture to deflate. According to the Wells criteria, assess the risk degree of venous thromboembolism before surgery, pay attention to the amount of fluid replacement and early bedside activity.[35,36] The change of circulating fibrin D-dimer was monitored. The pressure pump was used to massage the lower limbs. For those moderate or high probability, low-molecular-weight heparin can be used as appropriate.[35,36]

In conclusion, our data demonstrated that, with the help of single-channel gastroscopy and double-channel gastroscopy, ER is a feasible, safe, and minimally invasive treatment for the resection of gastric GISTs, including large-size GISTs and extraluminal or mixed growth pattern GISTs, and double-channel gastroscopy has its own distinct advantages in ER.

Author contributions

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Formal analysis: Xue-Guo Sun, Hui-Zi Liu, Bo Zhang, and Ti-Dong Shan.
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Supervision: Yue-Ping Jiang, Fu-Guo Liu, and Ti-Dong Shan.
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