Original Article

Comparison between laparoscopic and endoscopic resections for gastric submucosal tumors

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Abstract

Background/Aims: Open resection/laparoscopic resection (LR) is the traditional treatment of gastric submucosal tumor (G-SMT). The endoscopic resection (ER) technology provides good results for G-SMT treatment but lacks sufficient evidence-based evidence. This retrospective study aimed to compare the clinical efficacy of ER [endoscopic submucosal dissection (ESD), endoscopic submucosal excavation (ESE), and endoscopic full-thickness resection (EFR)] and LR [laparoscopic wedge resection (LWR) and laparoscopic subtotal gastrectomy (LSG)] for G-SMT.

Patients and Methods: From January 2013 to January 2017, data of patients with G-SMT with tumor diameter <5 cm were collected from the database of The Affiliated Hospital of Qingdao University and classified based on surgical methods. Demographics, tumor characteristics, surgical outcomes, complications and tumor recurrence were recorded and compared.

Results: Overall, 275 patients with G-SMT were enrolled: 152 underwent ER (ESD, $n = 65$; ESE, $n = 23$; EFR, $n = 61$) and 123 underwent LR (LWR, $n = 93$; LSG, $n = 30$). Age, sex, R0 resection rate, tumor location, type, recurrence and complications were not statistically significant ($P > 0.05$). The ER group had a significantly higher percentage of intraluminal tumor (94.1% vs 62.4%) and smaller tumor size (1.8 ± 0.8 vs 3.4 ± 1.2 cm) than the LR group. The ER group had less muscular tumors than the LR group (54.6% vs 70.7%). The ER group had no serosal tumor. The ER group had shorter hospitalization time, postoperative hospital stay and diet recovery time. The LR group had shorter operation time, less cost and less blood loss.

Conclusion: ER and LR are safe and effective treatments for SMT. For small intraluminally growing SMT, ER is better than LR.

Keywords: Clinical efficacy, endoscopic resections, gastric submucosal tumor, laparoscopic resections

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INTRODUCTION

Gastric submucosal tumor (G-SMT) can be divided into tumors based on its origin in the stomach wall: mucosa, submucosa and muscularis propria. Because the tumors on the muscularis propria are located in the deeper layers, especially those that do not grow in the lumen, endoscopic

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resection (ER) can hardly achieve safe and complete resection. Therefore, for most G-SMTs, laparoscopic resection (LR) is still the standard treatment.[1-3] The main laparoscopic surgical procedures include laparoscopic wedge resection (LWR), total gastrectomy and laparoscopic subtotal gastrectomy (LSG).[4,5] Among them, LWR is the most common laparoscopic surgery, in which the gastric tissue in the tumor is removed by a cutting and closing device, which is suitable for SMT of the anterior wall of the stomach. When the tumor is close to the pylorus or cardia, LWR can cause stenosis of the pylorus or cardia. Hence, LSG is recommended for this tumor type. This study included the most commonly used and the least damaging LWR and proximal or distal LSG.

With the development of endoscopic diagnosis and treatment techniques, endoscopic submucosal dissection (ESD), endoscopic submucosal excavation (ESE), and endoscopic full-thickness resection (EFR) have been used in the treatment of SMT derived from the muscularis propria, and the results appear to be satisfactory.[6-8] LR technology, especially LWR, which has lower trauma than traditional open surgery, has been shown to have good results in terms of efficacy, safety and length of hospital stay.[9,10] The National Comprehensive Cancer Network (NCCN) guidelines recommend that for 5-cm GSMT, LR is the preferred method.[11] However, because of the advanced equipment and complex technology required for these ER procedures, such ER reports are currently relatively limited. Therefore, we conducted a retrospective study to compare the clinical efficacy of ER (ESD, ESE, and EFR) and LR (LWR and LSG) for the treatment of SMT; in particular, their effectiveness, safety, complications, costs and indications were compared.

PATIENTS AND METHODS

Patients and study design

This study retrospectively collected data of G-SMT patients who underwent ER or LR from January 2013 to January 2017 from the database of The Affiliated Hospital of Qingdao University. All patients had a single tumor and no metastasis was detected by computed tomography before operation. According to the NCCN guidelines, all tumors were <5 cm. We excluded serious diseases in other organ systems and combined with other tumors. Patient demographic data, tumor characteristics, surgical outcomes, complications and tumor recurrence were recorded.

A total of 275 patients were enrolled in the study and were divided into ER and LR groups. There were 152 people in the ER group, of which 65 patients underwent ESD, 26 underwent ESE and 61 underwent EFR. Then, 123 patients with G-SMT were in the LR group, of which 93 underwent LWR and 30 underwent LSG.

All patients signed written informed consent before undergoing these procedures. The study was conducted in accordance with the principles of the Declaration of Helsinki of the World Medical Association. The study was approved by the Medical Ethics Committee of The Affiliated Hospital of Qingdao University.

Indications for endoscopic resection

All patients completed endoscopic ultrasonography to determine risk classification and depth of tumor invasion. Tumor was to be removed if the diameter of the tumor was >2 cms. When the diameter of the tumor was less than 2 cms, the tumor was to be removed, if the endoscopic ultrasonography detected combined adverse factors. The specific indications for each ER are as follows: (1) in ESD, the tumor is limited to the submucosal layer; (2) in ESE, the tumor originates from the muscularis propria (MP) and submucosa; and (3) in EFR, the tumor penetrates the MP layer toward the serosa without a massive extraluminal component.

Methodology of endoscopic resection

ESD

(1) Marking: A needle knife or argon plasma coagulation (APC) was used to mark the edge of the bulging lesion. (2) Submucosal injection: The marked submucosal positions were each injected with a solution consisting of 5 mL of indigo carmine, 1 mL of epinephrine and 100 mL of saline. (3) Incision of the lateral margin of the tumor: A hook knife or IT knife was used to cut the surrounding mucosa and submucosa along the marked points. (4) Dissection of the tumor: Complete dissection of the tumor was done using a hook knife or IT knife. (5) Wound treatment: After the tumor was removed, the small vessels visible on the wound surface were treated with APC, and if necessary, the hemostatic clip was used to suture the wound.

ESE

This ESD technique was used to cut the mucosa and submucosa, revealing the submucosal and muscularis propagating tumors and completely excavating the tumor in the muscularis propria along the edge of the lesion.

EFR

This ESD technique was carried out to separate the muscularis propria down to the serosal layer along the edge of the tumor. A needle knife or hook knife was used to penetrate the serosa, resulting in an "artificial perforation."

Under the direct vision of the gastroscope, the IT knife or hook knife was used to completely remove the tumor including the serosa, and the metal clip or Nylon rope purse was used to completely suture the wound.

Laparoscopic resection

Laparoscopic SMT resection was performed under endotracheal intubation and general anesthesia. According to the nature, location, size and growth pattern of the tumors, appropriate surgical procedures should be adopted. LWR was the main method for extraluminal growing tumors. To prevent stenosis after partial resection, for proximal or pyloric tumors, proximal or distal gastrectomy was mostly used.

Postoperative treatment

All patients diagnosed with gastrointestinal stromal tumor (GIST) by pathological diagnosis and immunohistochemistry were classified according to the 2011 NCCN GIST risk grading standard.[12] According to this standard, for patients with moderate to high risk, oral Gleevec (400 mg/day) should be given after surgery; for patients at moderate risk of nongastric origin, treatment should be administered for 3 years; for patients at moderate risk of gastric origin, treatment should be administered for 1 year; and for high-risk patients, treatment should be administered for more than 3 years.

Statistical analysis

Data analysis was performed using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA). Continuous values are expressed as mean ± standard deviation, and categorical values are presented as count and proportions. Student's *t*-test was used to test parameter data, and between-group comparisons involving categorical data were performed using χ^2 statistic corrected for continuity (Fisher's exact tests when appropriate). For all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 compares the baseline demographics and outcomes between the two groups. A total of 275 patients with G-SMT underwent surgery, of which 152 patients underwent ER and 150 patients (98.7%) underwent complete resection, and 123 patients were in the LR group and 120 patients (97.5%) underwent complete resection. There was no statistically significant difference in age, sex, and overall complications between the ER and LR groups. There were no recurrences in the two groups during the follow-up period. The average operative time in the ER group was shorter (81.8 ± 13.5 vs 141.7 ± 60.4 min), the intraoperative blood loss was significantly less (14.4 ± 15.8 vs 41.9 ± 56.3 mL), and total hospital stay, postoperative hospital stay, and postoperative feeding were shorter. Recovery time was shorter than that in the LR group, and the ER group incurred less cost (all $P < 0.05$).

Table 2 shows the results of pathological outcomes between the two groups. Most patients had GIST, and there was no statistical difference in the pathological type and growth position between the two groups. The intraluminal growing rate in the ER group was significantly higher than that in the LR group (94.1% vs 62.6%). The

Table 1: Comparison of baseline demographics and outcomes between the two groups

	ER (*n*=152)	LR (*n*=123)	*P*
Age, years	55.9±11.8	58.5±10.8	0.064
Sex, male: female	58:94	54:69	0.388
Length of stay (days)	7.3±2.0	11.7±3.9	<0.001*
Postoperative length of stay (days)	4.4±1.3	6.8±2.5	<0.001*
Recovery eating time, stay (days)	2.7±1.0	4.8±2.1	<0.001*
Hospitalization expenses (Yuan)	28542.0±6397.3	63610.0±211138.8	0.042*
Operative time, min	81.8±13.5	141.7±60.4	<0.001*
Estimated blood loss (mL)	14.4±15.8	41.9±56.3	<0.001*
R0 resection	150 (98.7%)	120 (97.5%)	0.659
Overall complication	28 (18.4%)	18 (14.6%)	0.422
Follow-up length (months)	12.3±6.6	29.5±11.2	<0.001*
Tumor recurrence	0 (0.0%)	0 (0.0%)	-

ER: Endoscopic resection; LR: Laparoscopic resection; ESD: Endoscopic submucosal; ESE: Endoscopic submucosal excavation; EFR: Endoscopic full-thickness resection. ER includes ESD (*n*=6), ESE (*n*=26), and EFR (*n*=61); LR includes laparoscopic subtotal gastrectomy (*n*=30) and laparoscopic wedge resection (*n*=93). *$P<0.05$

Table 2: Comparison of pathological outcomes between the two groups

	ER (*n*=152)	LR (*n*=123)	*P*
Pathology			
GIST	91 (59.9%)	81 (65.9%)	0.079
Leiomyoma	17 (11.2%)	15 (12.2%)	
Lipoma	6 (3.9%)	2 (1.6%)	
Schwannoma	5 (3.3%)	11 (8.9%)	
Neurofibroma	4 (2.6%)	4 (3.3%)	
Ectopic pancreas	20 (13.2%)	9 (7.3%)	
Neuroendocrine tumor	7 (4.6%)	1 (0.8%)	
Lymphoma	2 (1.3%)	0 (0.0%)	
Tumor location			
Upper 1/3	59 (38.8%)	23 (32.5%)	0.134
Mid 1/3	61 (40.1%)	87 (52.0%)	
Lower 1/3	32 (21.1%)	13 (15.4%)	
Tumor growth pattern			
Intraluminal growing	143 (94.1%)	77 (62.6%)	<0.001*
Extraluminal growing	9 (5.9%)	46 (37.4%)	
Tumor size (cm)	1.8±0.8	3.4±1.2	<0.001*
Infiltration depth			
Mucosa and submucosa	69 (45.4%)	23 (18.7%)	<0.001*
Muscularis propria	83 (54.6%)	87 (70.7%)	
Serosa	0 (0.0%)	13 (10.6%)	

ER: Endoscopic resection; LR: Laparoscopic resection; GIST: Gastrointestinal stromal tumor. *$P<0.05$

tumors in the ER group were significantly smaller than those in the LR group (1.8 ± 0.8 vs 3.4 ± 1.2 cm). There was a statistically significant difference in the depth of tumor invasion between the ER and LR groups ($P < 0.05$). There was no infiltration of the serosal tumor in the ER group. The proportion of tumors infiltrating the mucosa and submucosa and the muscularis propria was 45.4% and 54.6%, respectively. In the LR group, the infiltration in the muscularis propria accounted for 70.7%, and infiltration in the mucosa and submucosa was slightly more than that in the serosal layer, which was 18.7% and 10.6%, respectively.

Table 3 shows the tumor size and risk classification of patients with GIST. There were 91 patients in the ER group and 81 patients in the LR group. There was no statistical difference between these two groups. The GIST in the ER group was smaller than that in the LR group (1.9 ± 0.8 VS 3.6 ± 1.2 cm). The number of low-, medium-, and high-risk patients in the ER group was 83, 6 and 2, respectively, and that in the LR group was 72, 6 and 3, respectively. There was no statistical difference between these two groups. All medium- and high-risk patients were treated with Gleevec. There was no recurrence during the follow-up period.

Table 4 shows the complications among the surgical groups. There was no significant difference in the overall complication rate among the groups. A total of 65 patients in the ER group underwent ESD, 6 patients had intraoperative perforation, and 4 patients had delayed perforation on the first day after surgery. Moreover, 26 patients underwent ESE, 4 patients underwent intraoperative perforation and 1 had subcutaneous emphysema. In all, 61 patients underwent EFR, and all patients had active perforation, 2 patients had upper gastrointestinal bleeding after operation, 4 patients had abdominal infection, 1 patient had chest infection, 1 patient with esophageal stenosis underwent laparoscopic surgery because of the large and hard tumor, and the operation in 1 patient was converted to laparoscopic surgery because of the difficulty of tumor dissection. Although these two cases were negative in postoperative pathological margin, this was recorded as non-R0 resection in ER group. Moreover, 93 patients underwent LWR, including 6 cases of abdominal infection, 3 cases of chest infection, 1 case of deep vein thrombosis and 5 cases of postoperative gastric dysfunction; 1 case was converted to open surgery to complete the resection because of a large tumor close to the cardia. Thirty patients underwent partial gastrectomy, of which three had abdominal infection and one had postoperative gastric dysfunction; two cases were converted to open surgery because of the difficulty of tumor resection. Similarly, the three patients who were converted to open surgery were recorded as non-R0 resection.

Table 3: Tumor size and risk classification of patients with GIST

	ER (*n*=91)	LR (*n*=81)	*P*
Tumor size (cm)	1.9±0.8	3.6±1.2	<0.001*
Risk			
Low	83 (91.2%)	72 (88.9%)	0.818
Medium	6 (6.6%)	6 (7.4%)	
High	2 (2.2%)	3 (3.7%)	
Tumor recurrence	0 (0.0%)	0 (0.0%)	-

GIST: Gastrointestinal stromal tumor; ER: Endoscopic resection; LR: Laparoscopic resection. *$P<0.05$

DISCUSSION

In this study, the ER and LR groups pathologically confirmed that the incision margin was negative; both groups almost reached R0 resection. The ER and LR groups did not have serious complications, indicating that these two approaches are safe and effective treatments for SMT. Compared with LR, ER has more obvious advantages: shorter operation time and hospitalization time, less human resources needed during operation, less overall cost and less influence on postoperative gastric function.

In the past, for the treatment of G-SMT, especially gastric stromal tumor, the traditional surgical method is open resection or LR.[1,2,13] However, most G-SMTs, including GIST, usually bulge in the stomach wall. Unlike gastric cancer, GIST rarely causes lymph node metastasis, and its incidence is about 1.1%–3.4%.[14,15] Therefore, the surgical treatment of SMT is mainly complete tumor resection (R0 resection), neither expanding the scope of resection nor cleaning lymph nodes.[16,17] Therefore, it is a more reasonable choice to reduce trauma as much as possible on the basis of complete resection of the tumor, which is the theoretical basis of ER.

For G-SMT originating from the mucosa and submucosa, ESD can generally remove the lesion completely, and the incidence of complications is low. However, for SMT originating from the muscularis propria, when the lesion is deep and protruding to the serosa or growing close to the serosa, the risk of perforation during ESD resection is higher, limiting the application of ESD.[18] ESE is based on the development of ESD technology, especially for the shallow layer of muscularis propria tumors growing into the lumen. Its main complications are bleeding and perforation. It is impossible to safely and effectively resect tumors located in the deep muscularis propria or with serious adhesion to the serosa. The main complication of ESD and ESE in this study was perforation. Notably, four patients

Table 4: Complications between the various surgical groups

	ESD (*n*=65)	ESE (*n*=26)	EFR (*n*=61)	LWR (*n*=93)	LSG (*n*=30)	*P*
Overall complication	13	5	10	12	6	0.767
Intraoperative perforation	6	4	-	-	-	
Delayed perforation	4	0	0	0	0	
Delayed bleeding	0	0	2	0	0	
Abdominal infection	3	0	4	6	3	
Chest infection	0	0	1	3	0	
Aerothorax	0	0	1	0	0	
Subcutaneous emphysema	0	1	0	0	0	
DVT	0	0	0	1	0	
Change the way of surgery	0	0	2	1	2	
Gastric dysfunction	0	0	0	5	1	

ESD: Endoscopic submucosal; ESE: Endoscopic submucosal excavation; EFR: Endoscopic full-thickness resection; LWR: Laparoscopic wedge resection; LSG: Laparoscopic subtotal gastrectomy; DVT: Deep vein thrombosis

who underwent ESD had perforation after operation. They were discharged from the hospital after conservative treatment such as fasting, gastrointestinal decompression, acid suppression, hemostasis and antibiotics. Compared with intraoperative perforation, postoperative perforation is not easily detected in time. We also found that four patients had delayed perforation. Fortunately, all four perforations were diagnosed and further processed on the day of the occurrence. If the delayed perforation cannot be diagnosed in time, it can lead to serious complications such as mediastinal emphysema and diffuse peritonitis. For such patients, it is mainly important to closely observe the disease changes to achieve early diagnosis; if conservative medical treatment is ineffective, endoscopic clipping or surgical treatment should be promptly considered.

On the basis of ESD, EFR is a technique that actively causes digestive tract perforation during the resection of lesion and then repairs the wall of digestive tract after resection of lesion, which further enlarges the depth of ESE treatment. This technology makes the growth depth of SMT no longer a limiting factor for endoscopic treatment.[19,20] The most common complication of EFR in this study was postoperative infection. This is because EFR has active perforation, and the EFR operation time is generally longer; hence, blood and exudates from the perforation easily leak into the abdominal cavity, because the abdominal cavity cannot be washed and aspirated, which more likely causes complications such as peritonitis, pneumothorax, pneumoperitoneum and abdominal abscess.[21] Although infection is the main complication, it was not more than in the LR group, and we reviewed these four cases of abdominal infection, which are tumors close to the cardia or pylorus. It can be said that the location and size of tumor growth are closely related to abdominal infection.

In this study, first, we observed that the ER group had less blood loss during operation, earlier recovery of diet and short postoperative hospital stay. This is because the resection scope in the ER group is small to retain the normal gastric structure as far as possible. This has almost no effect on gastric function, and patients can have a better quality of life, which is also an important advantage of ER minimally invasive surgery. Second, ER is more accurate in locating tumors than LR. Accurately locating tumors without endoscopy is sometimes difficult with laparoscopic surgery, which may result in the removal of more normal gastric tissue. Especially, for tumors protruding from the gastric cavity, with laparoscopy, it is more difficult to distinguish tumors from normal gastric tissue, which also increases the possibility of postoperative gastric dysfunction.

Although ER technology has the above advantages in the treatment of G-SMT, ER surgery requires a senior operator. With incorrect operation, active perforation occurs and is often accompanied by tumor damage, which increases the possibility of peritoneal implantation. Peritoneal implantation has a higher risk of recurrence, resulting in poor prognosis, which is the reason why the NCCN guidelines do not regard ER technology as the main treatment of GIST at present.[11] In this study, no relapse was reported during the follow-up period. At the same time, this study found that the recurrence rate of ER in the treatment of GIST within 5 years ranged from 0% to 6.7%.[22-24] It can be seen that ER surgery has a good long-term effect on GIST treatment.

This study has some limitations. First, this study is based on the characteristics of retrospective research, and there is inevitably a certain choice bias. Second, because EFR is a newer technology, the ER group has a short follow-up period and we cannot evaluate its long-term efficacy. In the future, designing a prospective randomized trial of ER and LR would be a more ideal experimental protocol.

In summary, this study shows that both ER and LR are safe and effective methods for SMT treatment. Compared

with LR, ER has no abdominal wall damage, less pain, less gastric tissue resection, no gastric dysfunction and lower cost. We believe that in institutions with rich endoscopic treatment experience, ER is better than LR for small and intraluminal SMT.

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Conflicts of interest

There are no conflicts of interest.

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