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ORIGINAL ARTICLE

A comparative study of treatment of gastrointestinal stromal tumors with laparoscopic surgery: a retrospective study

Bin He[1,2], Su Yan[1], Rui Li[1], Hongqing Qiu[2], Jianchen Tu[2]

[1]Department of Gastroenterology, The First Affiliated Hospital of Soochow University, Suzhou, China; [2]Department of Gastroenterology, Zhangjiagang Hospital Affiliated to Soochow University, Zhangjiagang, China

Summary

Purpose: *The purpose of this study was to analyze the clinical efficacy and complications of endoscopic submucosal dissection (ESD) and laparoscopic resection of stromal tumors, and to explore the clinical value and complications of stromal tumors treated with ESD.*

Methods: *146 patients with gastric stromal tumors (GSTs) treated in our hospital from January 2012 to January 2016 were retrospectively analyzed. Patients were divided into the ESD group and the laparoscopic surgery group (LS). The operation time, postoperative recovery time of diet, postoperative exhaust time, etc were observed and analyzed. All the measurement indexes were described as mean ± standard deviation. The t-test of two independent samples was used for the hypothesis test. Chi-square test was used for comparison of the percent data between the two groups and p<0.05 indicated significant difference.*

Results: *The postoperative diet recovery time, postoperative exhaust time, hospital stay and hospitalization cost of the ESD group were better compared with the LS group (p<0.001). There was no significant difference in operative time between the ESD and LS group (p>0.05), while the operation time in ESD group was longer than in the LS group (p<0.05). The operation time of gastric body and antrum stromal tumors was shorter than in the ESD group group (p<0.05). There were no significant differences in tumor diameter, mitotic number and Flether classification between the groups (p>0.05). No significant difference in the incidence of postoperative bleeding, incision infection and recurrence rate was noticeable between the groups (p>0.05).*

Conclusions: *Endoscopic treatment of GSTs is safe and feasible, and may be better than laparoscopic resection.*

Key words: *endoscopic submucosal dissection, gastric stromal tumor, laparoscopic surgery, safety*

Introduction

GSTs are the most common mesenchymal tumors of the digestive tract and can occur in any of its parts, but most often in the stomach [1,2]. It is a potential malignancy of non-directional differentiation, its biological characteristics are not yet clear, and surgical removal of the lesion is still the most effective treatment. According to the prognosis of GSTs, they are divided into benign, with undetermined malignant potential and malignant ones. Previously, for GSTs without distant metastases, surgical or laparoscopic resection of the lesions was the preferred treatment [3]. GSTs are mostly benign tumors, but some of them, especially those originating from the muscularis propria, are potentially malignant. It is generally believed that GSTs originating from the gastrointestinal mucosa and submucosa can be treated endoscopically, while for those originating from the muscularis mucosa are difficult to be completely removed under endoscopy, bearing the hazard of perforation.

With the continuous development of endoscopic digestive techniques, a variety of such tech-

Correspondence to: Su Yan, MD. Department of Gastroenterology, The First Affiliated Hospital of Soochow University, 188 Ten Catalpa Street, Suzhou 215006, Jiangsu, China.
Tel: +86 015950972578, E-mail: 15950972578@163.com
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niques have been used in the diagnosis and treatment of GSTs. ESD and endoscopic full-thickness resection (EFTR) are the two methods reported recently to having successfully treated the GSTs, including cases with large lesions which were completely resected [4-6]. To explore the clinical value of ESD in stromal tumors and complications, the clinical data of 62 cases of GSTs treated with ESD and 84 cases of GSTs treated with laparoscopy in our hospital from January 2012 to January 2016 were retrospectively and comparatively analyzed.

Methods

Patients

A total of 146 patients with stromal tumor of gastric muscularis propria diagnosed by EUS from January 2012 to January 2016 in the First Affiliated Hospital of Soochow University and Zhangjiagang Hospital were enrolled, including 92 males and 54 females, aged from 25 to 76 years (median 54). This study was approved by the ethics committee of the First Affiliated Hospital of Soochow University and Zhangjiagang Hospital. Signed informed consents were obtained from all participants before the study. Sixty-two patients were placed in the ESD group, among them 62 males and 26 females, with an average age of 51.55±9.30 years and tumor size 1.5-5.3 cm with an average of 3.4±1.1 cm. Eighty-four patients were placed in the LS group, including 56 males and 28 females, with an average age of 53.38±8.72 years and tumor size 1.5-6.0 cm with an average of 3.7±1.3 cm. There were no significant differences in gender, age and tumor size between groups ($p>0.05$), which were comparable. The inclusion criteria were as follows: 1) single lesion; 2) all patients underwent minimally invasive resection, including laparoscopic and endoscopic treatment; 3) removed lesions were sent for biopsy and immunohistochemistry; 4) preoperative blood routine tests, blood coagulation, hepatitis B surface antigen, pre-transfusion tests, ECG, abdominal CT and other tests were performed; 5) all patients and their families were informed of the treatment risks and signed informed consent. The main clinical manifestations of the patients in this study were upper abdominal pain, melena and abdominal discomfort.

Endoscopic ultrasonography

Endoscopic ultrasonography (EUS) was performed on the GSTs with normal surface mucosa of digestive tract found by endoscopy to ascertain the level and nature of the lesions.

ESD treatment methods and steps

1) Mark: electrocoagulation mark was made by the needle knife on the margin of the prominent lesion. 2) Injection: multiple injections of normal saline (including indigo carmine and epinephrine) into the mucosa outside the marked points. 3) Incision: cut of the mucosa along the mark with a needle knife. 4) Stripping: cut of the submucosa by a needle knife with head flexion. Lesions were stripped along their margin after exposure to the muscularis propria lesions or complete resection of the lesion with snare at the end of dissection. For tumors close to the muscularis that cannot be completely stripped, snare trap was used for removal as much as possible and most of the lesions were subjected to electrosurgical excision. Careful observation whether there was residual tumor on the wound surface and endoscopic wounds without any visible tumor were considered as a complete resection. 5) Wound treatment: argon plasma coagulation (APC) was used for the visible small blood vessels. A metal hemostatic clip was used to close the wound if necessary. Laparoscopic treatment was used when the lesions were located in the anterior wall of the stomach, and laparoscopic wedge resection of the stomach was then performed. For patients whose lesions were located in the posterior stomach wall, firstly the posterior stomach wall was flipped up, and then the wedge resection was performed.

The instruments used in the ESD group were: OlympusGIF-Q260J gastroscope, Olympus EU.M30 ultrasound system, and ERBEICC including 200 high frequency electric cutting device, APC300 argon ion coagulator, KD-620LR type HOOK knife, KD.61. 1L IT knife, NM.200U.0423 (23G) injection needle, FD-410LR electrothermal biopsy forceps, HX-610-135L hemostatic clip, HX-1IOQR hemostatic clip body, SP.210U-25 electric snare, and D.201.10704 transparent cap.

Evaluation of clinicopathological factors

The operation time, postoperative diet recovery time, postoperative exhaust time, hospitalization time, hospitalization cost, postoperative pathological results, surgical complications and prognosis of patients from both groups were evaluated and analyzed. Flether classification was done according to a previous study [5].

Statistics

SPSS 16.0 statistical software package (Chicago, IL, USA) was used for statistical analyses. All quantitative indicators were described as mean ± standard deviation (SD) and the hypothesis test was analyzed by the two independent samples of the *t*-test. Percentage data between groups were analyzed by the x^2 test and $p<0.05$ indicated statistically significant difference (*$p<0.05$, **$p<0.01$, and ***$p<0.001$).

Results

General data

A total of 146 patients with stromal tumor of gastric muscularis propria diagnosed by EUS from January 2012 to January 2016 were enrolled, including 92 males and 54 females, aged from 25 to 76 years (median 54). Sixty-two patients were placed in the ESD group; among them, 36 were males and 26 females, with a mean age of

51.55±9.30 years and tumor size 1.5-5.3 cm (mean 3.4±1.1). Eighty-four patients were assigned in the LS group, including 56 males and 28 females, with a mean age of 53.38±8.72 years and tumor size 1.5-6.0 cm (mean 3.7±1.3). There were no significant differences in gender, age and tumor size in both groups (p>0.05), which were comparable. The results are shown in Table 1.

Table 1. Patient characteristics

Characteristics	*ESD* *n (%)*	*LS* *n (%)*
Age (y), mean±SD	51.55±9.30	53.38±8.72
Sex		
Male	36 (58)	56 (61)
Female	26 (42)	28 (39)
Location		
Fundus ventriculi	19 (31)	27 (32)
Corpora ventriculi	32 (52)	38 (45)
Sinuses ventriculi	11 (17)	19 (23)

Results of treatment-related indicators

There was no significant difference in operation time between ESD and LS group (p=0.062). However, the postoperative recovery time of diet in the ESD group was significantly shorter than in the LS group, and the difference was statistically significant (p<0.001). Postoperative exhaust time in ESD group was significantly shorter compared with the LS group (p<0.001). The hospitalization time and hospitalization cost in the ESD group were also significantly better than in the LS group (p<0.001). The results are shown in Table 2 and Figure 1.

Results of operation time

The operation time of stromal tumors in fundus ventriculi treated with ESD was significantly longer than that in the LS group (p=0.028). However, the operation time of stromal tumors in corpora ventriculi and sinuses ventriculi treated with ESD were shorter compared to those treated with LS

Table 2. Results of treatment related indicators (mean±SD)

	Operation time(min)	*Hospitalization time(d)*	*Hospitalization cost (yuan)*	*Postoperative exhaust time(d)*	*Postoperative recovery time of diet(d)*
ESD	104.44±42.09	8.09±1.63	19837.67±3688.09	3.09±0.88	3.61±0.75
LS	117.56±40.88	9.90±1.85	27523.55±5314.54	4.67±1.28	4.83±1.03
p	0.062	<0.001	<0.001	<0.001	<0.001

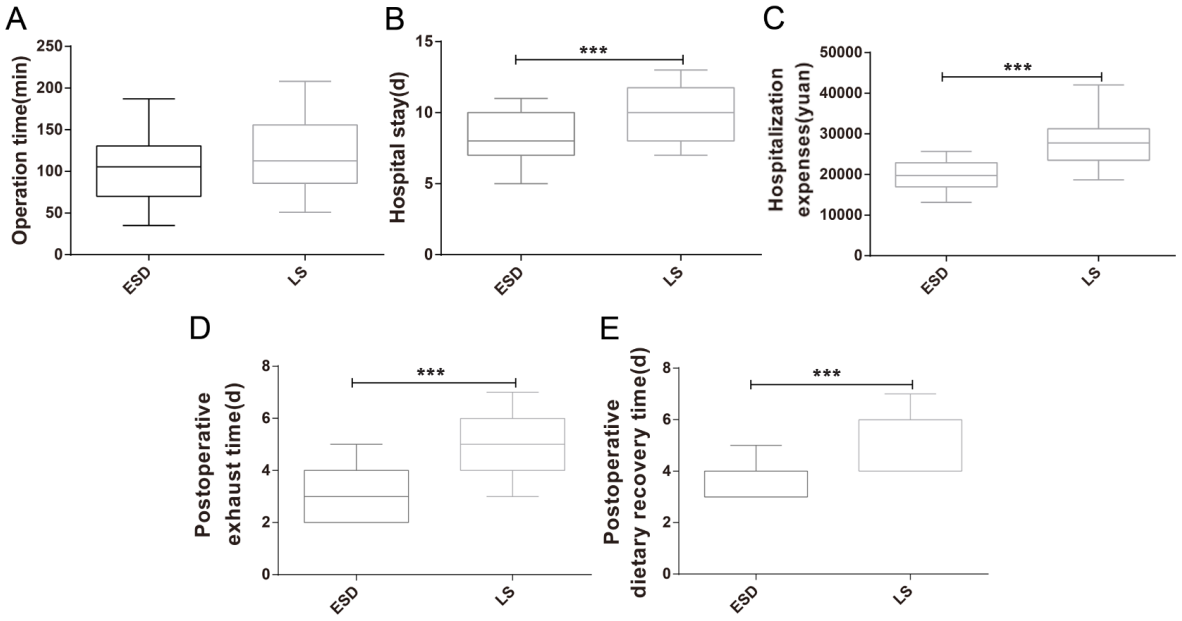

Figure 1. A: There was no difference in the operation time between ESD group and LS group. **B:** ESD group had significantly shorter hospitalization time than LS group. **C:** ESD group had less significantly hospitalization cost than the LS group. **D:** ESD group had significantly faster postoperative exhaust time than LS group. **E:** ESD group had significantly earlier postoprative recovery time of diet than LS group. ***p<0.001, compared between ESD group and LS group.

with statistically significant differences (p=0.0258 and p=0.002, respectively). The results are shown in Table 3 and Figure 2.

Results of postoperative pathological indicators

There was no significant difference in the pathology of the stromal tumors between ESD and LS group (p>0.05). Postoperative pathological results also showed no significant differences in tumor size, nuclear fission number and Flether grade between the two groups (p>0.05). Patients with high risk of Flether grade in both groups were treated with radical surgery and the results are shown in Table 4.

Postoperative adverse events and prognostic outcomes

In the postoperative adverse events, no significant differences in the incidence of postoperative bleeding and incision infection between ESD and LS group were noticed (p>0.05). The follow-up time was more than 1 year, and there was no significant difference in the recurrence rate of stromal tumors between ESD and LS group. The results are shown in Table 5.

Table 3. Results of operation time (mean±SD; min)

Therapeutic groups	*Fundus ventriculi*	*Corpora ventriculi*	*Sinuses ventriculi*
ESD	138.47±40.83	91.40±32.61	83.72±35.97
LS	112.48±36.35	111.86±41.01	135.89±43.34
p	0.028	0.026	0.002

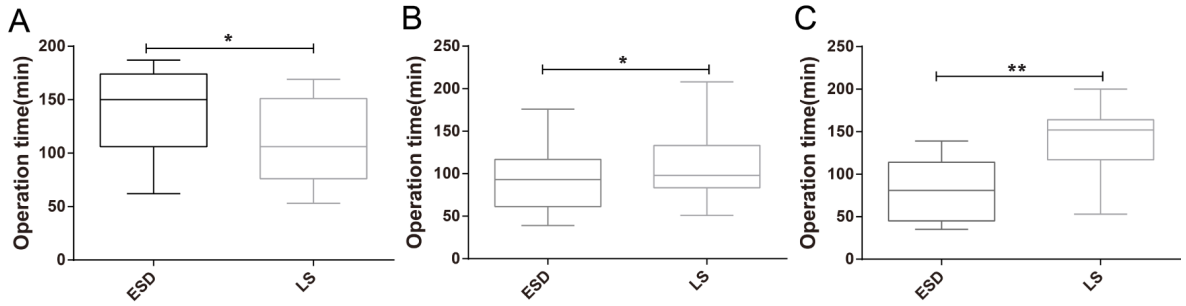

Figure 2. A: ESD group had significantly longer operation time than LS group in stromal tumors of fundus ventriculi. **B:** ESD group had significantly longer operation time than LS group in stromal tumors of corpora ventriculi. **C:** ESD group had significantly longer operation time than LS group in stromal tumors of sinuses ventriculi. *p<0.05, **p<0.01 compared between ESD and LS groups.

Table 4. Results of postoperative pathological indicators

Indicators	*ESD* *n (%)*	*LS* *n (%)*	*p value*
Size (cm), mean±SD	3.4±1.1	3.7±1.3	0.09
Flether classification			
Very low risk	47 (76)	57 (68)	0.29
Low risk	5 (8)	7 (8)	0.95
Moderate risk	6 (10)	11 (14)	0.52
High risk	4 (6)	9 (10)	0.37
Nuclear fission number			0.59
≤5	36 (58)	45 (53)	
>5	26 (42)	39 (47)	

Table 5. Adverse events and prognostic outcome

Advesre events / outcome	*ESD*	*LS*	*p value*
Postoperative bleeding	2	3	0.91
Incision infection	1	2	0.74
Postoperative recurrence	4	5	0.90

Discussion

The term "Gastrointestinal stromal tumors (GISTs)", the most common myometrial-derived mesenchymal tumor of the digestive tract, was first coined by Mazur and Clark in 1983 [7]. Stromal tumors can occur anywhere from the esophagus to the rectum. Most stromal tumors <2 cm in diameter are easily missed due to lack of specific clinical manifestations. The widespread use of endoscopy and extensive use of EUS have provided a new dimension for diagnosis and treatment [8]. EUS can further clarify the origin, size, echogenicity, growth pattern and other characteristics of the tumor for submucosal lesions found by endoscopy.

All GSTs had non-directional differentiation characteristics and potentially malignant risks [9,10], and their malignant potential was mainly associated with tumor size, location and fission numbers [11-13]. Therefore, there is still a need for early resection of GSTs <2 cm in diameter. For small lesions, long-term follow-up may increase the psychological burden of patients, while if the lesion is larger, surgical resection would lead to big trauma, and lesions <5 cm can be removed by minimally invasive treatment. It has been reported that lesions <2 cm in diameter were currently advocated for early resection [14].

The preferred treatment of gastric muscularis stromal tumors is still surgery [3,15], and as GSTs tumors rarely present lymph node metastasis, dissecting the surrounding lymph nodes is generally not necessary, providing thus a good foundation for laparoscopic surgery. Endoscopic surgery could avoid the trauma caused by open surgery, and its procedure is through the laryngeal passage to avoid postoperative incision healing and other issues. ESD can remove the lesion from the basal lamina of the gastrointestinal mucosa to avoid the problems of residual lesions caused by simple resection [16].

This study showed that the hospitalization time in the endoscopic treatment group was significantly shorter than that in the laparoscopy group ($p<0.001$) for lesions <5 cm in diameter. Postoperative recovery time of diet and postoperative exhaust time were shorter than the laparoscopic group ($p<0.001$). The results suggested that patients undergoing endoscopic treatment of GSTs recovered faster than those in the surgical group. At the same time, hospitalization cost in the endoscopic group was also less than in the laparoscopic group ($p<0.001$), suggesting that the endoscopic treatment of GSTs helps patients save hospitalization costs. However, there was no significant difference in the operation time between the two groups ($p>0.05$).

The operation time of stromal tumors of fundus ventriculi in the ESD group was significantly longer than that of the laparoscopic group ($p<0.05$), while no significant difference in the operation time in the other two parts between the two groups was noticed. We consider that longer stripping time and stopping bleeding repeatedly could contribute to extended operation time.

In this study, no significant difference was found in Flether grade or tumor diameter between patients in the ESD and LS group, suggesting that ESD can achieve resection results similar to laparoscopic surgery and will not be limited by the scope of resection, thus leading to increased long-term recurrence rate in patients.

The main complications of endoscopic treatment were intraoperative and postoperative bleeding and perforation. With the skilled application of metal hemostatic clips and nylon rope purse suture technology, the endoscopic process turned to a minimally invasive treatment. He et al. [5] reported on 31 cases of larger GISTs (including 6 cases of esophageal and 25 cases of gastric GISTs) where they studied ESD. Among them, in 6 (19.35%) cases with perforation, the metal clip or nylon ring closed successfully without further surgery. There were no significant differences in the incidence of postoperative bleeding and incision infection in this study between the ESD and LS group ($p>0.05$).

In most reports on ESD of stromal tumors, the postoperative follow-up time ranged from several months to dozens of months, generally being 3 years. In this study, each patient was followed up for at least 1 year and the longest was up to 58 months. The mean follow-up time was similar to that reported by Novitsky et al. in the long-term efficacy of laparoscopic treatment of GSTs [17]. Our successful surgical resection rate was 100%, with many of the tumors being >5 cm in diameter, no serious postoperative complications occurred, indicating that the long-term of this approach is safe and reliable treatment for GSTs. The final follow-up results showed that the recurrence rate of tumors in the ESD group and the LS group were similar, indicating that endoscopic treatment of GSTs did not increase the risk of recurrence compared with surgery.

Although compared with laparoscopic treatment, minimally invasive endoscopic treatment had the advantages of less trauma, shorter hospitalization time and faster recovery. However, perforation or bleeding that was difficult to stop during the endoscopic treatment still required laparoscopic treatment to help closure or hemostasis, so laparoscopic gastrectomy combined with surgery is expected to become a new trend.

Some of the limitations of this study are noteworthy. This is a retrospective, single-center study. Limited sample size is another limitation of this study. Thus, prospective and multicenter studies with increased sample size are needed in the future.

Conclusions

In summary, endoscopic treatment of GSTs is safe and feasible, while reducing the patient's economic and psychological burden. This minimally invasive treatment performed early can avoid the progression of disease, significantly improve the prognosis of patients, and achieve good results.

Conflict of interests

The authors declare no conflict of interests.

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