

# Endoscopic band ligation versus endoscopic submucosal dissection and laparoscopic resection for small gastric stromal tumors

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## Abstract

**Background and aim** Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. Previous studies have addressed the safety and feasibility of endoscopic band ligation (EBL) for the treatment of small gastric GISTs. However, published reports comparing EBL with other interventions are limited. This current study evaluates the efficacy of EBL and compares EBL to both endoscopic submucosal dissection (ESD) and laparoscopic resection (LAP) for small gastric GISTs less than 15 mm.

**Methods** A total of 339 patients who underwent endoscopic therapy or laparoscopic resection for gastric GISTs between 1998 and 2012 were retrospectively identified and collected from medical records in our hospital. The parameters measured for each procedure type includes clinicopathological characteristics, length of stay, hospitalization expense and surgical outcomes.

**Results** Among the 147 patients included in our study, 72 (48.98 %) received EBL, 27 (18.37 %) received ESD, and 48 (32.65 %) received LAP. The demographic and clinical

characteristics of the patients such as gender, age, tumor site and size were well balanced between the study groups. There was also no significant difference in follow-up time between the study groups. The mean operating time was significantly shorter in the patients receiving EBL than patients receiving ESD and LAP ( $p < 0.001$ ). The estimated blood loss was significantly different between the three groups ( $p < 0.001$ ). Complications occurred in 1.39 % of the patients receiving EBL, 18.52 % of the patients receiving ESD and 4.17 % of the patients receiving LAP ( $p = 0.004$ ), and recurrence rate in 15.00, 9.10 and 11.76 %, respectively ( $p = 0.705$ ). There was also significant difference about mean hospital stay and hospital cost between three groups ( $p < 0.001$ ).

**Conclusion** Our results show a significant advantage in the short-term outcome for EBL compared to ESD and LAP. However, long-term randomized controlled trials are needed to compare the three methods for the treatment of small GISTs.

**Keywords** Endoscopic band ligation · Endoscopic submucosal dissection · Laparoscopic resection · Gastrointestinal stromal tumors

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Gastrointestinal stromal tumors (GISTs) represent the most common mesenchymal gastrointestinal tumor with low malignant potential. Although tyrosine kinase inhibitors (TKIs) have revolutionized the treatment of advanced GISTs [1, 2], complete surgical resection remains the main treatment for primary GISTs with no evidence of metastasis [3]. All GISTs 20 mm or larger should be resected; however, the management of incidentally encountered GISTs smaller than 20 mm remains controversial [3]. Laparoscopic resection has been proven to be a reasonably safe and effective

procedure in most patients with small- and medium-sized gastric GISTs [4–6]. Recently reports have demonstrated various endoscopic approaches to resect small GISTs, but because of its inherent risks of positive margins, tumor spillage and potential perforation, its role remains uncertain. One promising endoscopic technique is endoscopic band ligation (EBL). EBL is one of the first-line choices for the management of gastroesophageal varices and variceal hemorrhage in cirrhosis [7]. Furthermore, EBL is also considered to show promise as an effective and safe treatment for gastric small GISTs [8–10]. In contrast, Yang and his colleagues believe that surgical resection should be taken into consideration for all small gastric GISTs [11]. Consequently, there is controversy regarding the safety and efficacy of EBL for small gastric GISTs. Although, EBL has been demonstrated to be an effective technique for the resection of small gastric GISTs, there is no published comprehensive comparison between EBL and other interventions for gastric GISTs. Laparoscopic resection (LAP) is the preferred treatment for patients with gastric GISTs who do not have a contraindication to this approach [12–15], and endoscopic submucosal dissection (ESD) represents the correct diagnostic and definitive treatment for submucosal tumors among various endoscopic approaches [16–18]. Therefore, we carried out the present study to evaluate and compare EBL technique with ESD and LAP for small gastric stromal tumors.

## Materials and methods

We retrospectively reviewed and collected the medical records of 367 patients diagnosed with primary gastric GISTs between June 2003 and October 2014 in our hospital. Among these patients, 339 patients received endoscopic or surgical resection for their gastric GISTs. However, only 147 subjects fulfilled our criteria and were enrolled in this current study. The inclusion criteria were as follows: (1) Gastric GISTs diagnosed by endoscopic ultrasonography or confirmed by pathology; (2) gastric GISTs less than 15 mm in size; (3) patients underwent either EBL, ESD or LAP. The exclusion criteria were as follows: (1) GISTs with remote metastasis and (2) serious accompanied diseases such as advanced malignant tumor and organ failure. Study subject flow diagram for screening and grouping is illustrated in Fig. 1. Standard demographic and clinicopathologic data were collected including sex, age, symptoms, tumor site, size and pathological results. Operation details including operating time, estimated blood loss, complications, length of hospital stay and hospitalization expense were recorded; date of last follow-up, recurrence, and survival were also collected and analyzed. Complications were defined as perforation or massive hemorrhage. The hospitalization expense mainly consists

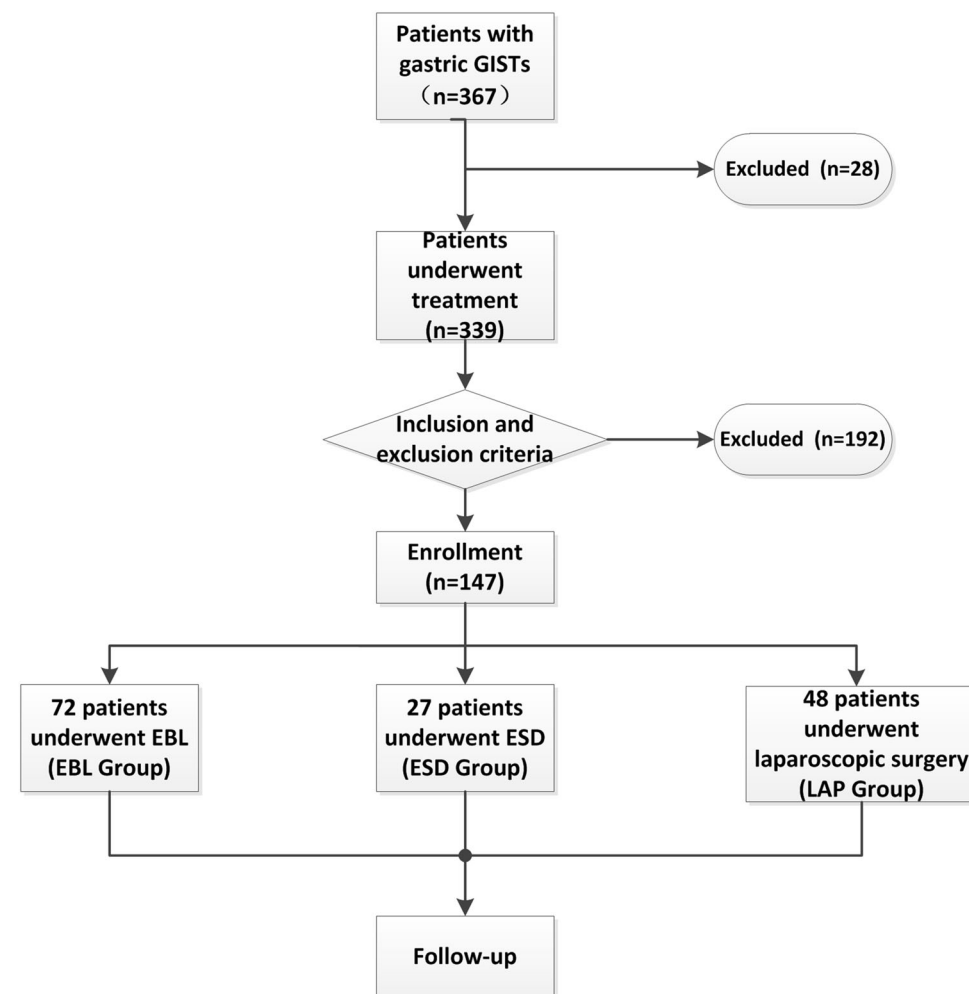
of the cost of surgical treatment (including extra procedures required as a part of a treatment) and cost of peri-operative care. The patients were usually assessed by endoscopy in 3, 6 and 12 months after the treatments to evaluate the evidence of recurrence or residual tumor. Recurrence was defined as biopsy-proven recurrent GIST or a lesion deemed suspicious on cross-sectional imaging. All endoscopic resections were performed by experienced endoscopists using the standard method such as EBL and ESD. All patients were informed of the benefits and risks of the procedure and signed the written informed consent document prior to each procedure.

Categorical data are presented as number of cases. Continuous data are reported as mean (SD), median and range. Statistical differences between groups were assessed by means of Fisher's exact test for categorical data and by Student's *t* test or the Mann–Whitney *U* test for continuous data. Disease-free survival was analyzed using Kaplan–Meier tests. All analyses were performed using SPSS 13.0 (IBM, Armonk, NY, USA). Values with  $p < 0.05$  were considered statistically significant in all cases.

## Results

Among the 147 patients included in our study, 72 (48.98 %) received EBL, 27 (18.37 %) received ESD, and 48 (32.65 %) received LAP according to the doctors' individual decision and patients' different choices of treatment. As shown in Table 1, the demographic and clinical characteristics of the patients were well balanced between the study groups. The mean age for the included patients was  $52.56 \pm 10.95$  years ( $53.44 \pm 10.3$  in the EBL group,  $49.15 \pm 10.31$  in the ESD group and  $53.17 \pm 12.04$  in the LAP group,  $p = 0.199$ ). Most tumors (80.95 %) were located at the gastric fundus. The mean tumor size for the included patients was  $11.31 \pm 3.12$  mm ( $10.68 \pm 3.66$  in the EBL group,  $11.78 \pm 2.67$  in the ESD group and  $12.02 \pm 2.21$  in the LAP group,  $p = 0.053$ ). There was no significant difference in follow-up period between the study groups. Surgical characteristics and clinical outcomes of patients with small gastric GIST treated with different methods (EBL, ESD and LAP) are summarized in Table 2. The mean operating time was significantly shorter in the patients receiving EBL than patients receiving ESD and LAP ( $17.11 \pm 4.97$  vs.  $65.26 \pm 28.78$  and  $90.81 \pm 77.89$  min,  $p < 0.001$ ). The estimated blood loss was also significantly different between the three groups ( $0.07 \pm 0.59$  ml in the EBL group vs.  $12.04 \pm 18.25$  ml in the ESD group and  $18.33 \pm 18.80$  ml in the LAP group,  $p < 0.001$ ). Complications occurred in 1.39 % of the patients receiving EBL, 18.52 % of the patients receiving ESD and 4.17 % of the

**Fig. 1** Study subject flow diagram for screening and grouping



**Table 1** Demographic and clinical characteristics of patients with small gastric GIST treated with different methods (EBL, ESD and laparoscopic resection)

Variables	Total (n = 147)	EBL (n = 72)	ESD (n = 27)	LAP (n = 48)	p value
Gender—no. (%)					0.927
Male	61 (41.50)	31/72 (43.06)	11 (40.74)	19 (39.58)	
Female	86 (58.50)	41/72 (56.94)	16 (59.26)	29 (60.42)	
Age (years)	52.56 ± 10.95	53.44 ± 10.3	49.15 ± 10.31	53.17 ± 12.04	0.199
Tumor site—no. (%)					
Gastric fundus	111 (75.51)	61 (84.72)	20 (74.07)	30 (62.50)	0.108
Gastric body	30 (20.41)	9 (12.50)	5 (18.52)	16 (33.33)	0.130
Gastric antrum	6 (4.08)	2 (2.78)	2 (7.41)	2 (4.17)	0.775
Tumor size (mm)	11.31 ± 3.12	10.68 ± 3.66	11.78 ± 2.67	12.02 ± 2.21	0.053
Follow-up					
Median, range	6, (3–53)	6, (3–53)	7, (3–24)	6, (3–59)	0.764
	(n = 68)	(n = 40)	(n = 11)	(n = 17)	

EBL patients underwent EBL treatment, Group ESD patients underwent ESD treatment, Group LAP patients underwent laparoscopic resection

patients receiving LAP ( $p = 0.004$ ). The mean hospital stay was significantly shorter in the patients receiving EBL than patients receiving ESD and LAP ( $6.47 \pm 3.90$  vs.

$10.04 \pm 3.89$  and  $11.44 \pm 3.75$  days,  $p < 0.001$ ). The mean hospital cost was also significantly lower in the patients receiving EBL than patients receiving ESD and

**Table 2** Surgical characteristics and clinical outcomes of patients with small gastric GIST treated with different methods (EBL, ESD and laparoscopic resection)

Variables	EBL (n = 72)	ESD (n = 27)	LAP (n = 48)	p value
Operating time (min)	17.11 ± 4.97	65.26 ± 28.78	90.81 ± 77.89	0.000
Estimated blood loss (ml)	0.07 ± 0.59	12.04 ± 18.25	18.33 ± 18.80	0.000
Complications <sup>a</sup> —no. (%)	1 (1.39)	5 (18.52)	2 (4.17)	0.004
Hospital stay (days)	6.47 ± 3.90	10.04 ± 3.89	11.44 ± 3.75	0.000
Hospital cost (RMB)	11,968 ± 6710	24,211 ± 6974	37,300 ± 10,895	0.000
	(n = 37)	(n = 21)	(n = 34)	
Recurrence rate—no./total no. (%)	6/40 (15.00)	1/11 (9.10)	2/17 (11.76)	0.705

EBL patients underwent EBL treatment, Group ESD patients underwent ESD treatment, Group LAP patients underwent laparoscopic resection

<sup>a</sup> Complication is defined as perforation or massive hemorrhage

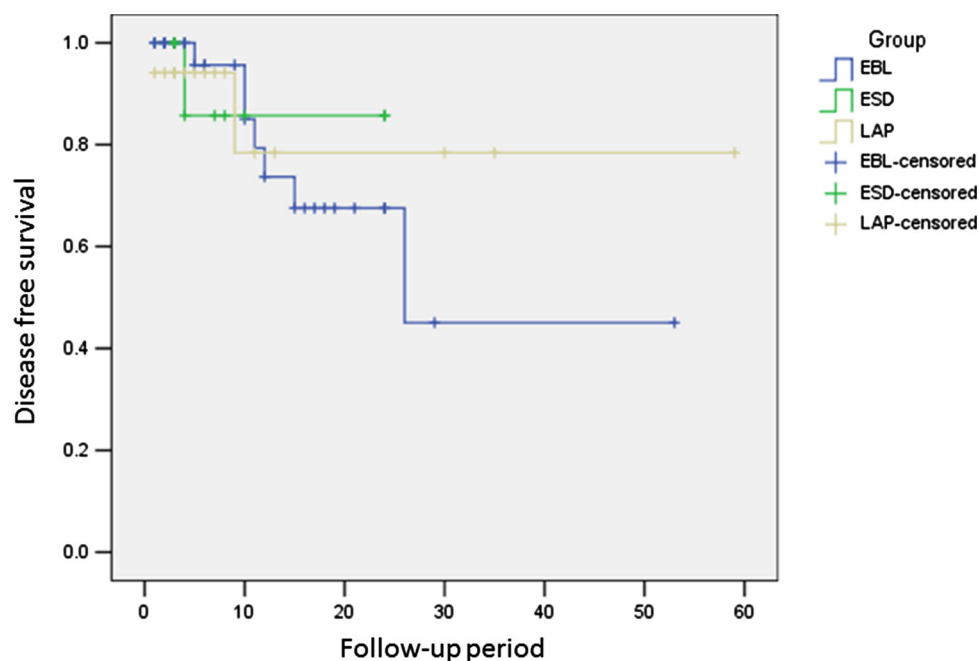
LAP (RMB 11968 in the EBL group vs. 24211 in the ESD group and 37300 in the LAP group,  $p < 0.001$ ). However, the recurrence of EBL, ESD and LAP group patients during the follow-up period was 15.00, 9.10 and 11.76 %, respectively ( $p = 0.705$ ). Kaplan–Meier curves for disease-free survival also showed no statistically significant difference between the study groups (Fig. 2). No tumor-related death was reported in our study.

## Discussion

GISTs are the most common mesenchymal neoplasms of the gastrointestinal tract. The age-adjusted yearly incidence rate of GISTs was 6.8 per million in the Surveillance, Epidemiology and End Results data from 1992 to 2000,

with 54 % men and 46 % women [19]. GISTs are associated with a broad range of presentations. Many are identified clinically because they cause symptoms and some are identified at autopsy. Small GISTs that are smaller than 20 mm usually do not produce any symptoms and are detected incidentally during abdominal exploration, endoscopy or radiologic imaging [20]. Due to the wide use of gastrointestinal endoscopy, small GISTs are frequently detected and diagnosed. Surgery is the standard of care for non-metastatic GISTs equal to or greater than 20 mm [3]. However, there is no standard of care for small non-metastatic GISTs less than 20 mm. There are several potential treatment methods including EBL, ESD and LAP. Previous research has demonstrated that EBL with systematic follow-up by endoscopic ultrasonography is an effective and safe treatment for small GISTs [8–10]. ESD

**Fig. 2** Kaplan–Meier curves for disease-free survival showed that there is no significant difference between the study groups ( $p = 0.923$ )



is also indicated as the correct diagnostic and definitive treatment for patients with small tumor size (<20 mm) accompanied by high success rate of 90 % and the low incidence of complications [16–18]. Similarly, published patient reports and retrospective analyses in the literature have shown that laparoscopic or laparoscopic-assisted resections for gastric GISTs are not only possible but are also associated with low recurrence rates, short hospital stay and low morbidity [4–6, 21].

Currently, there is controversy regarding the optimal treatment and management of small GISTs. One study by Yang et al. [11] found that small gastric GISTs less than 20 mm also have malignant potential. Thus, they recommended surgical resection of all small gastric GISTs once diagnosed. This controversy spawned due to the lack of clinical data showing definitive evidence to identify an optimal treatment and guide the management of small GISTs (<20 mm) discovered incidentally on endoscopy.

In this present study, we evaluated the efficacy of EBL, ESD and LAP for treatment of small gastric GISTs and made comparison between these three alternative methods. As demonstrated by our data, demographic and clinical characteristics of patients are similar between EBL, ESD and LAP groups. However, we found that EBL was prior to ESD and laparoscopic resection for small GISTs in terms of operating time, estimated blood loss and complications. Thus, it can be seen that EBL was an easier and faster method accompanied by high safety. In addition, the hospital stay and hospital cost of patients in EBL group were also reduced compared to that of the other two groups. Furthermore, we did not find significant difference about recurrence of patients with small gastric GIST treated with different methods (EBL, ESD and LAP). Kaplan–Meier curves for disease-free survival also showed no statistically significant difference between the study groups.

One of the major limitations is the retrospective nature of our study. Recurrence rate may be biased because about half of the patients are lost to follow-up. Another limitation is the relatively short follow-up period, which is about 10 months on average. It is possible that if the follow-up period was quite longer, more recurrence would occur in the EBL group. Thus, endoscopic surveillance at regular intervals should be considered and continued.

To our knowledge, this is the first clinical study comparing the three methods, EBL, ESD and laparoscopic resection, in the treatment of gastric GISTs less than 20 mm with no metastasis. Our results indicated that EBL possesses a lower complication rate and a comparable recurrence rate compared with those of ESD and LAP. Furthermore, EBL has many other advantages over ESD and LAP, including shorter operating time, less blood loss, lower hospital cost and shorter hospital stays. Taking these data together, EBL is superior to ESD and LAP for small

gastric GISTs with a lower complication and a comparable recurrence rate compared with those of ESD and LAP.

## Conclusion

Our results show a significant advantage in the short-term outcome for EBL compared to ESD and laparoscopic resection. However, randomized controlled clinical trials and long-term follow-up studies are needed to compare the three methods in the treatment of small localized GISTs.

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**Author contributions** Side Liu and Yan Meng designed the study. Yue Li and Cunli Cao recorded the data. Yan Meng analyzed the data. Yan Meng and Yue Li drafted the manuscript. Shujie Song provided advice for the study. All authors have read and approved the submitted version of the paper.

## Compliance with ethical standards

**Disclosures** Prof. Side Liu and Yan Meng, Chunli Cao, Shujie Song, and Yue Li have no conflicts of interest or financial ties to disclose.

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