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Endoscopic semi-blunt dissection technique is safe and effective for treating gastric submucosal tumors from the muscularis propria

Liming Zhang^{1*†}, Rui Zhao^{1†} and Junxuan Zhang¹

Abstract

Background Needle knives are the most commonly used instrument during endoscopic treatment for gastric submucosal tumors (SMTs). The conventional resection method involves fully extending the needle-shaped knife head, which allows it to more easily penetrate the muscularis propria while stripping the muscle layer of the tumor. We propose a semi-blunt dissection method that can effectively reduce damage to the muscularis propria.

Methods A total of 113 patients who underwent endoscopic resection of gastric SMTs originating from the muscularis propria were retrospectively analyzed. The conventional method consisted of 73 patients; The other group consisted of 40 patients underwent the semi-blunt dissection method.

Results There was no significant difference between the two groups in age, sex, or lesion location. The intraoperative operational variable, the maximum diameter of gastric muscularis propria damage, was significantly greater in conventional method group than the other group (1.06 ± 0.48 cm vs. 0.46 ± 0.09 cm, $p < 0.001$). There was also no significant difference between the two groups in terms of histological diagnosis, postoperative complications and the percentage of histologically positive resection margins.

Conclusion The semi-blunt dissection method has certain advantages in the endoscopic resection of gastric tumors originating from the muscularis propria, including a small extent of gastric muscularis propria damage and a shorter postoperative hospital stay.

Keywords Endoscopic dissection, Gastrointestinal stromal tumors, Submucosal tumors

[†]Liming Zhang and Rui Zhao co-first authors.

*Correspondence:

Liming Zhang
zhangliming_endo@163.com

¹Endoscopy Center, Peking University People's Hospital, Beijing, China



Introduction

Gastrointestinal stromal tumors (GISTs) and leiomyomas originating from the muscularis propria of the gastric wall are the most common gastric submucosal tumors (SMTs). However, imaging methods such as endoscopic ultrasound (EUS) and computed tomography (CT) have difficulty differentiating these two tumors. In recent years, many guidelines have recommended resecting GISTs after they have been histologically diagnosed, regardless of the tumor diameter [1–4]. According to the Chinese SMT consensus, for patients whose tumors measure ≤ 2 cm in diameter, are suspected of being a GIST or neuroendocrine tumor with a low risk of recurrence and metastasis and can possibly be completely resected, direct endoscopic resection can be performed [5]. In recent years, endoscopic treatment has been gradually used for resecting gastric SMTs. The majority of gastric tumors originating from the muscularis propria are resected via endoscopic resection, with a complete resection rate ranging from 92.4% ~ 100% [6–11].

Needle knives are the most commonly used instrument during endoscopic treatment. Based on the growth characteristics of the tumors originating from gastric muscularis propria, the conventional resection method involves fully extending the needle-shaped knife head, which allows it to more easily penetrate the muscularis propria while stripping the muscle layer of the tumor. In practice, we found that during the operation, when the needle knife is retracted, the metal surface of the knife tip can be placed against the loose tissue for high-frequency electric dissection, while the endoscope can be used to carry the head end of the plastic knife handle along the fissure created by the high-frequency electric incision for blunt push dissection, reducing damage to the muscularis propria. This method is named the semi-blunt dissection method.

No studies have compared the treatment efficacy and safety of conventional methods and semi-blunt dissection. This study compared the treatment efficacy and safety of the two methods for treating gastric tumors originating from the muscularis propria, especially GISTs.

Materials and methods

Participants

A total of 113 patients who underwent endoscopic resection of gastric SMTs originating from the muscularis propria between 2017 and 2022 were retrospectively analyzed. This study was approved by the Ethics Committee of Peking University People's Hospital.

The inclusion criteria for the study were as follows: (1) age ≥ 18 years; (2) SMT evaluated by endoscopy, EUS or CT assessment revealing that the tumor originated from the muscularis propria, that at least half of the tumor was

protruding into the gastric cavity, and (3) the tumor had a diameter ≥ 10 mm or ≤ 40 mm.

The exclusion criteria for the study were as follows: (1) Upper gastrointestinal lesions measured by EUS < 10 mm or > 40 mm; (2) $\geq 1/2$ of the tumor protruded out of the gastric cavity; (3) Portal hypertension; (4) A history of upper gastrointestinal surgery. (5) Patients that took c-kit inhibitor (for GISTs) were excluded.

Procedure

Two physicians with more than five years of experience in endoscopic submucosal excavation performed the operation. An Olympus 290 endoscope was used, and the treatment instrument, a DualKnife (KD-650 L/U/Q, Olympus) was used throughout the whole procedure without replacement. This procedure was performed under anesthesia with tracheal intubation. The process includes: 1) Lesion marking; 2) A small submucosal injection; 3) Mucosal incision; 4) Removal of the submucosa around the tumor to expose the edge of the muscularis propria tumor; 5) Careful removal of the tumor, minimizing the damage to the muscularis propria. At this point, different methods were used for Group A and Group B (Fig. 1). The conventional method was used for Group A, which consisted of 73 patients; the knife head was fully extended during the cutting and peeling process, after which the remainder of the conventional surgical protocol was conducted. Group B, which consisted of 40 patients, underwent the semi-blunt dissection method. First, if the capsule had no ulcerations, the knife head was retracted. Then, the contact surface of the metal tip of the knife head was pressed to the cutting surface with slight pressure, and a high-frequency current was applied to create a blunt separation fissure on the cutting surface, while the plastic knife handle was used for blunt pushing and dissection. This method was used when the boundary of the tumor was clear and the tissues beneath the tumor were loose. The remaining surgical procedures were performed according to the conventional method. 6) Full-thickness wound (gastric wall damage is defined as gastric muscularis propria perforation) were closed with titanium clips and/or Ligation device (a kind of nylon loop) by endoscopic suturing. If the wound couldn't be closed by endoscope, laparoscopic suturing with threads were employed. 7) Removal of the resection specimen through the oral cavity. 8) Other operations: Peritonocentesis was performed for pneumoperitoneum causing a significant increase in abdominal pressure. In some patients, dental floss suspended was used to expose the submucosal dissection surface and the edges of tumors fully encased within the muscularis propria.

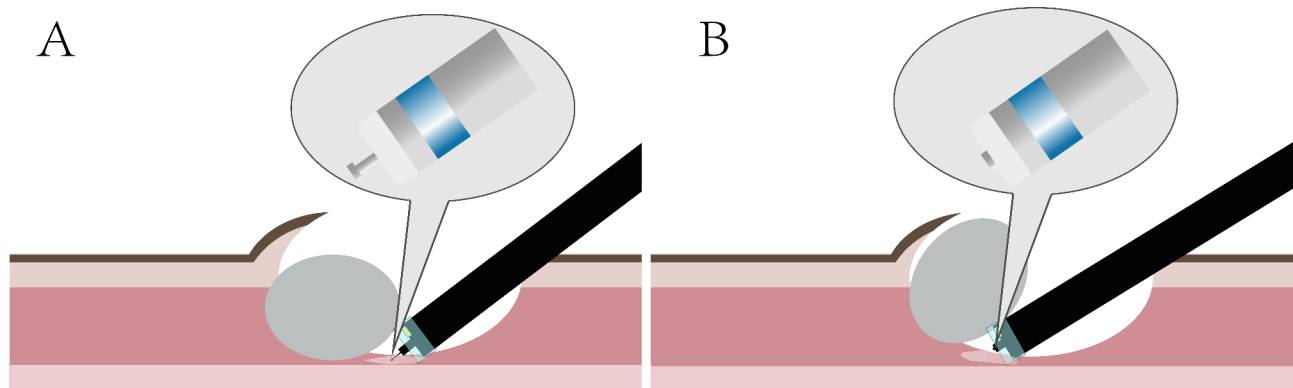


Fig. 1 **A**. The knife head was fully extended during the cutting and peeling process; **B**. The knife head was retracted. The contact surface of the metal tip of the knife head was pressed to the cutting surface with slight pressure, and a high-frequency current was applied to create a blunt separation fissure on the cutting surface, while the plastic knife handle was used for blunt pushing and dissection

Histological diagnosis

After the specimen was fixed in formalin, it was divided into 3 mm sections to determine the maximum tumor diameter and resection margin. Histopathological results were confirmed by hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) staining. For GISTs, the tumor risk was categorized according to the modified Fletcher classification. The histological examinations were performed by a pathologist with more than 8 years of experience.

Definitions

(1) Histological resection: R0 resection was defined as a resection with a clear edge under the microscope; R1 resection was defined as a gross tumor resection with a positive tumor edge under the microscope; R2 resection was defined as residual tumor visible to the naked eye. (2) Complete endoscopic resection was defined as resection of the entire tumor without residual tumor; this included endoscopic R0 and R1 resection. (3) Delayed bleeding was defined as postoperative bleeding, vomiting or black stools, and a decrease in hemoglobin of 20 g/L. (4) Recurrence: a submucosal tumor-like bulge found under endoscopy; a clearly visible tumor on CT scan; and biopsy results at the resection site suggestive of recurrent tumor cells.

Follow up

Patients with a pathological diagnosis of GIST underwent endoscopy at 4 and 12 weeks after surgery, endoscopy and CT examination at 24 weeks after surgery, and endoscopy and CT examination every year thereafter. Patients with pathologically diagnosed leiomyoma underwent endoscopy at 4 and 12 weeks and then endoscopy and CT examination every year thereafter.

Statistical analysis

SPSS 22.0 software was used for the statistical analysis. Categorical variables were expressed as counts and composition ratio, and were compared using the Chi-square test or Fisher exact test as appropriate, and the t test was used to compare variables depicted as mean values. $P < 0.05$ was considered to indicate statistical significance.

Results

Perioperative patient characteristics and histology of gastric submucosal tumors (Table 1).

The conventional method was used for Group A, which consisted of 73 patients; Group B, which consisted of 40 patients, underwent the semi-blunt dissection method. There was no significant difference between the two groups in age, sex, or lesion location. The intraoperative operational variable, the maximum diameter of gastric muscularis propria damage, was significantly greater in Group A than in Group B (1.06 ± 0.48 cm vs. 0.46 ± 0.09 cm, $p < 0.001$); there was no statistically significant difference between the two groups in terms of endoscopic or laparoscopic suturing methods. Postoperatively, the average length of hospitalization in Group A was longer than that in Group B (7.66 ± 2.90 days vs. 5.80 ± 1.96 days, $p < 0.001$); there was no significant difference between the two groups in terms of postoperative fever duration; there was no incidence of delayed bleeding or perforation in either group. No recurrence was observed during the follow-up period. On histological evaluation, the maximum pathological size of the resected lesions in Group B was significantly greater than that in Group A (1.95 ± 1.43 cm vs. 1.26 ± 0.70 cm, $p = 0.006$); there was no significant difference between the two groups in terms of histological diagnosis and the percentage of histologically positive resection margins.

Perioperative patient characteristics and histology of GISTs (Table 2).

Table 1 Comparison of the clinical and pathological data of the different dissection methods before, during, and after treatment

	Group A conventional method (n = 73)	Group B semi-blunt (n = 40)	p
Preoperative			
Sex (male), number (%)	30 (41.1)	12 (30.0)	0.315
Age (years)	57.8 ± 9.0	54.5 ± 10.8	0.673
Lesion location, number (%)			0.324
Below the cardia	13 (17.8)	8 (20.0)	
Gastric fundus	20 (27.4)	6 (15.0)	
Body of stomach	40 (54.8)	26 (65.0)	
Intraoperative			
Maximum diameter of gastric muscularis propria damage (cm)	1.06 ± 0.48	0.46 ± 0.09	< 0.001
Suturing method, number (%)			0.088
Endoscopic suturing	67 (91.8)	40 (100)	
laparoscopic suturing	6 (8.2)	0 (0)	
Complete endoscopic resection, number (%)	73 (100)	40 (100)	1
Postoperative			
Postoperative hospital stay (days)	7.66 ± 2.90	5.80 ± 1.96	< 0.001
Postoperative fever duration (days)	2.03 ± 1.71	1.50 ± 0.78	0.056
Delayed bleeding, number (%)	0 (0)	0 (0)	1
Delayed perforation, number (%)	0 (0)	0 (0)	1
Relapse, number (%)	0 (0)	0 (0)	1
Average follow-up time (months)	43.40 ± 19.96	46.80 ± 24.58	0.456
Histology			
Histological diagnosis, number (%)			0.428
Leiomyoma	36	22	
Gastrointestinal stromal tumor	37	16	
Pathological measurement of the maximum lesion diameter(cm)	1.26 ± 0.70	1.95 ± 1.43	0.006
Histological margin grade, number (%)			0.081
R0	60 (82.2)	38 (95.0)	
R1	13 (17.8)	2 (5)	
R2	0 (0)	0 (0)	

The conventional method was used for Group A, which consisted of 37 patients; Group B underwent the semi-blunt dissection method consisted of 16 patients. For the 53 patients with GISTs, there was no significant difference in age, sex, or lesion location between the two groups. The maximum diameter of gastric muscularis propria damage in Group A was significantly greater than that in Group B (1.20 ± 0.49 cm vs. 0.48 ± 0.07 cm, $p < 0.001$). There was no significant difference between the two groups in terms of the use of endoscopic or laparoscopic suture methods. The average duration of hospitalization in Group A was significantly longer than that in Group B (8.43 ± 3.55 days vs. 6.25 ± 1.98 days, $p = 0.006$). There was no significant difference in terms of postoperative fever duration between the two groups. There was no occurrence of delayed bleeding or perforation and no recurrence during the follow-up period. In the histological evaluation, there was no significant difference between the two groups in terms of histological diagnosis, maximum pathological diameter of the resected

lesion, or the percentage of histologically positive resection margins.

Discussion

In our study, the semi-blunt dissection group has smaller gastric muscularis propria damage, and shorter length of hospitalization, the associated costs were reduced.

There are many reports on the endoscopic treatment of gastric tumors originating from the muscularis propria, most of which have focused on the comparison of endoscopic and laparoscopic resection [12–16]; however, few reports have compared different endoscopic resection methods.

Blunt dissection is commonly used in surgical operations and refers to the use of the handle of the scalpel, hemostatic forceps or fingers to separate the soft tissues. Blunt dissection is often used to strip loose connective tissues such as those seen in normal tissue gaps, loose adhesions, benign tumors or cysts in the extraperitoneal space. This procedure can prevent accidental injury to nerves and blood vessels and reduce the loss of

Table 2 Comparison of clinical and pathological data before, during, and after treatment of patients with different dissection methods for GISTs

	Group A conventional method (n = 73)	Group B semi-blunt (n = 40)	p
Preoperative			
Sex (male), number (%)	14 (37.8)	4 (25.0)	0.530
Age (years)	56.9 ± 9.6	53.0 ± 7.3	0.848
Lesion location, number (%)			0.406
Below the cardia	7 (18.9)	4 (25.0)	
Gastric fundus	11 (29.7)	2 (12.5)	
Body of stomach	19 (51.4)	10 (62.5)	
Intraoperative			
Range of gastric muscularis propria damage (cm)	1.20 ± 0.49	0.48 ± 0.07	< 0.001
Suturing method, number (%)			0.545
Endoscopic suturing	34 (91.9)	16 (100)	
laparoscopic suturing	3 (8.1)	0 (0)	
Complete endoscopic resection, number (%)	37 (100)	16 (100)	1
Postoperative			
Postoperative hospital stay (days)	8.43 ± 3.55	6.25 ± 1.98	0.006
Postoperative fever duration (days)	2.91 ± 2.27	2.00 ± 0.85	0.104
Delayed bleeding, number (%)	0 (0)	0 (0)	1
Delayed perforation, number (%)	0 (0)	0 (0)	1
Relapse, number (%)	0 (0)	0 (0)	1
Average follow-up time (months)	40.28 ± 16.35	43.80 ± 19.55	0.558
Histology			
Histological diagnosis, number (%)			0.066
Very low risk	28	8	
Low risk	9	8	
Pathological measurement of the maximum lesion diameter (cm)	1.25 ± 0.68	1.25 ± 0.91	0.986
Histological margin grade, number (%)			0.112
R0	24 (64.9)	14 (87.5)	
R1	13 (35.1)	2 (12.5)	
R2	0 (0)	0 (0)	

tissue function. There are few reports about the application of blunt dissection in endoscopic treatment, and the methods vary. Most such studies are case reports, and one reported that during dissection, the tissue under the tumor was directly stripped using titanium clips supplemented by a rubber band. However, this method is only suitable for cases where there is only a small part of tumor left during dissection and the tissue under the tumor is relatively loose or the locations where the operating can be difficult [17]. Another case reported the use of a lab-made scissor-like blunt dissection instrument for the incision and dissection of the esophageal submucosal tunnel. Yet another case report described aspiration of a gastric fundus lesion into a transparent cap during lesion dissection, which itself was performed using the anterior and posterior movement of the endoscope coupled with pushing of the transparent cap [18]. Blunt dissection of the esophageal submucosal tunnel through the transparent cap has also been reported [19]. Compared with blunt dissection alone, the semi-blunt dissection method

used in this study involves high-frequency, shallow electrocautery to create a gap for blunt dissection with the plastic knife handle, facilitating rapid blunt dissection; even at the edge of the tumor, slightly compact connective tissue can also be isolated using this method. At the same time, appropriate selection of parameters enables coagulation of the small blood vessels at the cutting surface, which reduces the risk of bleeding relative to blunt dissection alone, keeps the dissection wound clear, and reduces the difficulty of subsequent dissection and the risk of perforation.

In the analysis of all patients, the maximum diameter of the resected lesions in Group A was smaller than that in Group B (1.26 ± 0.70 cm vs. 1.95 ± 1.43 cm, $p = 0.006$), but the maximum diameter of gastric muscularis propria damage in Group A was greater than that in Group B (1.06 ± 0.48 cm) vs. 0.46 ± 0.09 cm, $p < 0.001$). For larger lesions, there was less gastric muscularis propria damage in Group B than in Group A, and the difference was statistically significant. The procedure used

for Group A patients involved the creation of a sharp incision. Because the tumor was embedded in the muscularis propria of the stomach with little tissue between the tumor margin and the healthy tissue, submucosal injection was difficult, and puncture was highly likely, as the needle-like knife was kept protruded to make the sharp incision. At this time, use of an insulated-tip (IT) knife with a magnetic tip could reduce the risk of perforation of the muscularis propria, but it will increase the cost for the patient. In Group B, careful, sharp incisions were performed when the tumor boundary was not clear. When the tumor boundary was clear and the tissues beneath the tumor were loose, the needle knife head was retracted, and semi-blunt dissection was performed, which not only reduced the risk of the knife tip piercing the muscularis propria but also allowed the wound to close easily; furthermore, there was no need to substitute for an IT knife, keeping the costs to the patient relatively low. The average postoperative hospitalization time for Group B was shorter than that for Group A (5.80 ± 1.96 days vs. 7.66 ± 2.90 days, $p < 0.001$). Because of the small wound area in group B, the wound was easy to close, the patient did not need to be on the postoperative diet as long, the hospitalization time was shortened, and the associated costs were reduced. Among the 53 patients with GISTs, Group B patients also experienced less damage to the gastric wall (1.20 ± 0.49 cm vs. 0.48 ± 0.07 cm, $p < 0.001$) and a shorter mean duration of hospitalization (8.43 ± 3.55 days vs. 6.25 ± 1.98 days, $p = 0.006$), suggesting that the semi-blunt dissection method for GISTs can also reduce the wound surface area, shorten the length of hospitalization, and reduce the cost for patients.

When excising muscularis propria tumors, novice doctors often experience a greater psychological burden when a perforation occurs. The proposed method is more suitable for such doctors in excising muscularis propria tumors under endoscopic surgery because of the increased safety following retraction of the knife tip [20]. The operation method is relatively simple, the risk of perforating the muscularis propria during surgery is low, closure is easy, the generation of a large amount of pneumoperitoneum is avoided, and the length of hospital stay is reduced.

Across the entire patient cohort, the R1 resection rate did not significantly differ between Groups A and B (17.8% vs. 5%, $p > 0.05$). Among the 53 GIST patients with higher resection margin requirements, there was also no significant difference in the R1 resection rate (35.1% vs. 12.5%, $p > 0.05$), and there were no patients in the two groups who underwent R2 resection. This finding suggested that the effect of the two resection methods on the resection margin was not significantly different. In most cases, the reasons for histological resections of grades other than R0 included capsule injury caused by the

use of an electrosurgical knife during endoscopic resection. Many studies have reported that in the treatment of gastric tumors originating from the muscularis propria, the rate of endoscopic R1 resection is greater than that of laparoscopic resection, but in previous studies of endoscopic resection of GISTs, the overall postoperative recurrence rate was not high (0–2.7%) [21–26]. While another study showed that lesion size and mitosis but not R1 resection were risk factors for recurrence [27]. In this study, none of the patients who underwent R1 resection, including those with GISTs, experienced recurrence or metastasis during follow-up, which is consistent with the findings of previous studies. However, all the patients with GIST pathologies in this study had a very low risk of recurrence. Therefore, the results of this study suggest only that the effects of the two endoscopic treatment methods on the resection margin in patients with very low recurrence risk, including those with low recurrence-risk GISTs, are not significantly different. Higher recurrence-risk GIST undergone R1- endoscopic resection were needed to be included in further research.

There are still some limitations in this study. This was a single-center retrospective study; future prospective studies are needed to further evaluate the efficacy and safety of semi-blunt dissection. Among SMTs, GISTs are more likely to be malignant than leiomyomas and therefore should be the greater focus of studies on the effect of endoscopic treatment. The number of GIST patients enrolled in this study was small and should be increased in future studies. In addition, the GIST patients enrolled in this study all had a low or very low risk of recurrence, so it is difficult to fully assess the true treatment efficacy and recurrence risk of the two treatment methods for resecting intermediate-risk GISTs. Follow-up studies are needed to further enroll patients who have undergone endoscopic resection for intermediate-risk GISTs and compare the two endoscopic treatment methods.

In conclusion, the semi-blunt dissection method has certain advantages in the endoscopic resection of gastric tumors originating from the muscularis propria, including a small extent of gastric muscularis propria damage and a shorter postoperative hospital stay.

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None.

Author contributions

LZ was involved in the concept and design of study; LZ and RZ were involved in the data curation; LZ, RZ and JZ were involved in statistical analysis; LZ and RZ were involved in drafting the manuscript; all authors were involved in writing—review and editing; LZ was involved in the supervision of study. All authors have made an intellectual contribution to the manuscript and approved the submission. All authors read and approved the final manuscript.

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Data availability

The dataset data used to support the findings of this study are available from the corresponding author at email address upon request.

Declarations

Ethics approval and consent to participate

The study protocol has been approved by the Ethical Committee of the Peking University People's Hospital with an approval number (2024PHB480) and performed according to the Declaration of Helsinki. Ethical Committee of the Peking University People's Hospital waived need for written informed consents due to the retrospective nature of this study.

Consent for publication

Not applicable.

Conflicts of interest

All authors have no have no conflicts of interest to disclose.

Competing interests

The authors declare no competing interests.

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