



## Hyperechoic demarcation line between a tumor and the muscularis propria layer as a marker for deciding the endoscopic treatment of gastric submucosal tumor

Yu ZHANG<sup>§1</sup>, Zhen WANG<sup>§1</sup>, Ting JIN<sup>3</sup>, Kai-qiang LI<sup>1</sup>, Ke HAO<sup>1</sup>, Wei ZHANG<sup>1</sup>, Bao-ying FEI<sup>†‡2</sup>

<sup>(1)</sup>Department of Gastroenterology, Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College, Hangzhou 310014, China

<sup>(2)</sup>Department of Gastroenterology, Tongde Hospital of Zhejiang Province, Hangzhou 310012, China

<sup>(3)</sup>Department of Gastroenterology, the First People's Hospital of Xiaoshan District, Hangzhou 311200, China

<sup>†</sup>E-mail: mmizjpph90@163.com

Received June 7, 2016; Revision accepted Sept. 17, 2016; Crosschecked July 19, 2017

**Abstract:** Minimally invasive endoscopic resection has been rapidly adopted as a new technique for treating patients with gastric submucosal tumors (SMTs) originating in the muscularis propria (MP) layer. This study was conducted to evaluate the information obtained from endoscopic ultrasonography (EUS) to determine the appropriate endoscopic dissection method for treating SMTs originating in the MP layer. Between February 2014 and May 2016, a total of 50 patients with gastric SMTs originating in the MP layer were enrolled in this study. The clinical features of the patients and their endoscopic, EUS, and histopathologic findings, as well as their postoperative follow-up data, were analyzed in this retrospective study. The mean age of the patients was (55.0±10.2) years, and the male/female ratio was 17:33. Endoscopic submucosal dissection (ESD) was performed on 43 patients and an endoscopic full-thickness resection (EFR) was performed on seven patients. The most frequent location for an SMT was in the upper body region of the stomach ( $n=16$ ), and the most common pathological diagnosis was a gastrointestinal stromal tumor (GIST) ( $n=32$ ). The overall rates for complete resection were 95.3% (41/43) and 100.0% (7/7) when the SMTs were treated by ESD and EFR, respectively. The presence of a complete tumor capsule was significantly associated with a complete resection ( $P=0.001$ ). Of the cases treated by ESD, nine patients developed perforation, one of whom required laparoscopic surgery. The remaining patients were closed with clips or purse-string sutures. The presence of an MP2-type tumor ( $P=0.018$ ) and a wide connection with the MP layer ( $P=0.044$ ) were significantly associated with perforation. A preoperative evaluation of the integrity and the location of a tumor capsule and the length of the tumor connection with the MP layer by EUS can improve the complete resection rate and reduce the occurrence of intraoperative complications. Tumors with a complete capsule originating from the superficial MP layer or with a narrow connection with the MP layer are appropriate candidates for treatment by ESD.

**Key words:** Gastric submucosal tumor; Endoscopic submucosal dissection; Endoscopic full-thickness resection; Muscularis propria

<http://dx.doi.org/10.1631/jzus.B1600256>

**CLC number:** R573.9

### 1 Introduction

Gastric submucosal tumors (SMTs) originating in the muscularis propria (MP) layer are usually

asymptomatic, and thus are accidentally discovered during endoscopic procedures. A portion of gastric SMTs are gastrointestinal stromal tumors (GISTs), which comprise the most common type of gastrointestinal mesenchymal tumors, and have a high potential for malignancy (Hedenbro *et al.*, 1991; Hwang *et al.*, 2006). Until recently, small gastric SMTs originating in the MP layer were primarily treated

<sup>‡</sup> Corresponding author

<sup>§</sup> The two authors contributed equally to this work

ORCID: Yu ZHANG, <http://orcid.org/0000-0003-1387-3962>

© Zhejiang University and Springer-Verlag Berlin Heidelberg 2017

with surgical techniques (Nishimura *et al.*, 2007; von Schonfeld, 2009; Ryu *et al.*, 2011). However, minimally invasive endoscopic resection has gradually become recognized as an alternative method for treating these patients. Endoscopic submucosal dissection (ESD) is an effective technique for completely resecting SMTs originating in the submucosal layer, and is associated with fewer complications than other treatment methods. However, gastric SMTs originating in the MP layer are located deep within the lesion, and the higher incidence of perforation and bleeding limits the use of ESD to remove them (Park *et al.*, 2004; Lee *et al.*, 2006; Zhou *et al.*, 2011; Bialek *et al.*, 2012; Chun *et al.*, 2013; Hobel *et al.*, 2014; Meng *et al.*, 2015). Laparoscopic-assisted endoscopic full-thickness resection (EFR) is a technique in which an iatrogenic perforation of the gastric wall is created for the purpose of removing a deep gastric lesion for patient treatment or to obtain a precise pathological diagnosis (Jeon *et al.*, 2010; Ye *et al.*, 2014). Technological improvements have allowed endoscopic resection to become the preferred option for treating SMTs originating in the MP layer because it allows the patient to retain the normal structure and function of their stomach, and it improves their long-term quality of life. However, endoscopic surgery does have some drawbacks, such as the risks of incomplete resection, perforation, and bleeding. Several feasibility studies have shown that when used to treat SMTs originating in the MP layer, standard ESD achieves a complete resection in 64% to 75% of cases (Park *et al.*, 2004; Lee *et al.*, 2006; Bialek *et al.*, 2012; Chun *et al.*, 2013; Hobel *et al.*, 2014; Meng *et al.*, 2015) and produces perforation in 0% to 20% of cases (Probst *et al.*, 2009; Jeon *et al.*, 2010; Shi *et al.*, 2011; Zhang *et al.*, 2011; Bialek *et al.*, 2012; Hobel *et al.*, 2014). Therefore, when choosing an endoscopic procedure, a preoperative evaluation is important for avoiding both unnecessary surgery and the subsequent procedures.

Endoscopic ultrasonography (EUS) is one of the most valuable diagnostic tools for differentiating gastric SMTs. Additionally, it provides valuable information for guiding future management of a patient, by probing the lesion's size, origin, margins, and echo structure (Chak, 2002). Several studies have recently introduced EUS as a method for the locoregional staging of gastric cancers, and planning the therapeutic management of such patients (Brand *et al.*,

2002; Polkowski *et al.*, 2004; Kwee and Kwee, 2007; Mocellin *et al.*, 2011). Because EUS has matured as a clinical methodology, it may now be possible to use this technique for selecting the most appropriate treatment for SMTs originating in the MP layer. In this study, we used EUS to observe SMTs originating in the MP layer, and then to evaluate the following parameters: membrane integrity, origin (originating in the superficial or deep MP layer), spatial relationship between the tumor capsule and the serosa layer, ratio of the length of the muscular connection, and the semi-circumference of the tumor capsule. This information was used to select the best type of endoscopic treatment, and to assess whether a complete resection could be achieved, the risk of complications, and the prognosis for the patient.

## 2 Materials and methods

### 2.1 Patients and study design

Between February 2014 and May 2016, a total of 50 patients (17 males, 33 females; median age 55.0 years, range 35–72 years) with gastric SMTs originating in the MP layer were enrolled in this study conducted at Zhejiang Provincial People's Hospital and Tongde Hospital of Zhejiang Province, Hangzhou, China. Each of the enrolled patients had provided their written informed consent to undergo ESD or EFR after receiving detailed verbal and written information concerning the EUS examination, ESD procedure, EFR procedure, and alternative treatment options. Prior to treatment, all patients were examined by EUS, and patients with an SMT that originated in the MP layer and did not display an extraluminal growth pattern were considered to be suitable for ESD. The data were retrospectively collected.

### 2.2 Standard endoscopy and EUS

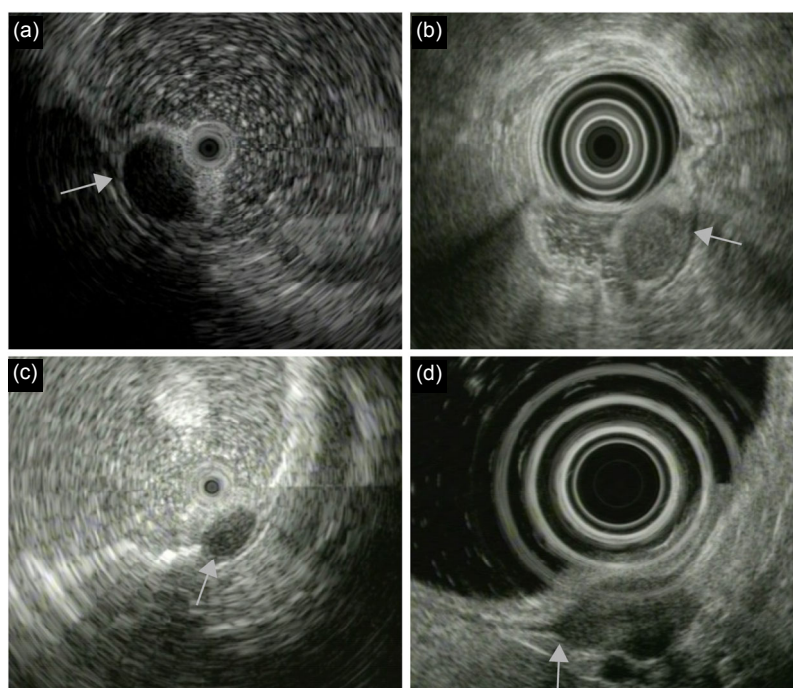
Each patient underwent a conventional endoscopic examination performed by an endoscopist who used a conventional white-light endoscope (GIF-Q260J or GIF-H260Z; Olympus Optical Co., Ltd., Tokyo, Japan). Each tumor was assessed for its size, shape, location, appearance, and mobility, and its location was recorded as being in one of the following regions: cardia, fundus, upper body, mid body, lower body, or antrum. EUS was performed with a

radial-scanning echo endoscope (GF-UM2000 or UM-DP12-25R micro probe; Olympus Optical Co., Ltd., Tokyo, Japan), and the following parameters for each lesion were recorded: echo intensity, echo uniformity, origin level, size, and boundaries. Evaluations included: (1) the largest tumor diameter; (2) the tumor growth pattern (intraluminal vs. extraluminal); (3) tumor capsular integrity; (4) location of the tumor capsule in the fourth layer; (5) the ratio of the length of the muscular connection and the semi-circumference of the tumor capsule; and (6) the vessels surrounding the tumor. The superficial MP layer was defined as the upper half of the fourth layer, while the deep MP layer was defined as the lower half of the fourth layer. Tumors that showed the hyperechoic line of their capsule to be located in the superficial MP layer or deep MP layer were classified as MP1 type and MP2 type tumors, respectively (Figs. 1a–1c). Tumors with a capsule that was tightly adhered to the serosa layer were classified as a serosa-type tumor (Fig. 1d). A narrow muscular connection was defined as the length of the connection area with the fourth layer being  $<40\%$  of the tumor capsular semi-circumference,

while a wide muscular connection was defined as that length being  $\geq 40\%$  (Figs. 1a and 1b).

### 2.3 ESD and EFR procedures

Endoscopic treatment: all ESD and EFR procedures were performed under conditions of general anesthesia and endotracheal intubation. (1) ESD: when the target lesion was identified, marking dots for guiding the incision were placed 3–5 mm outside the tumor using an argon plasma coagulation (APC) probe and epinephrine-saline-dye solution. After uplifting the lesion, an insulated-tip knife, hook-knife, or other type of electric knife was used to make a mucosal incision along the line of dots and dissect each lesion from the MP layer. (2) EFR: the ESD technique was used to separate the tumor until the serosa layer. Next, the full-thickness tumor, its underlying serosa, and the peritumoral gastric tissues were gradually resected using an insulated-tip knife. These tissues were resected by creating an iatrogenic perforation of the gastric wall for subsequent removal of the tumor. Clips or purse-string sutures were used for closure of the gastric wall defect.



**Fig. 1** Degrees of invasive depth and muscular connection of SMTs as visualized by endoscopic ultrasound

(a, b) MP1-type tumor: tumor capsule is in the upper half of the fourth layer; (c) MP2-type tumor: tumor capsule is in the lower half of the fourth layer; (d) Serosa-type tumor: tumor capsule is tightly adhered to the fifth layer. Narrow connection with the MP layer: length of the muscular connection is  $<40\%$  of the tumor capsular semi-circumference (a); Wide connection with the MP layer: length of the muscular connection is  $\geq 40\%$  of the tumor capsular semi-circumference (b, c, d). The gray arrow points to the tumor capsule: the hyperechoic demarcation line between the tumor and the MP layer

## 2.4 Pathological examinations and follow-up assessments

Endoscopically or surgically resected tissue specimens were fixed in 10% formalin, and then microscopically examined for cell type, depth of invasion, resection margins, nuclear atypia, and mitotic index. Immunohistochemical analyses of the c-Kit (CD117), CD34, smooth muscle actin (SMA), DOG-1, Ki-67, Desmin, and S-100 protein markers were performed to classify each tumor subtype. Each resection margin was classified based on the general criteria for cancer involvement in a resection margin (Edge and Compton, 2010). A status of “complete resection” was assigned when a full pathological examination showed that the horizontal and vertical resection margins were negative for tumor cells, and there was no evidence of lymphovascular invasion.

Each patient was scheduled to be followed up by conventional endoscopy at 3, 6, and 12 months after treatment to observe the healing of the artificial ulcer and to rule out tumor recurrence. Subsequently, each patient also received a follow-up examination every year to check for local tumor recurrence, lymph node swelling, and any evidence of distant metastasis.

## 2.5 Statistical analyses

All data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Values are presented as mean±standard deviation (SD), median value, or a percentage. Continuous data were evaluated using the *t*-test and comparisons of categorical data were performed using Fisher's exact test. *P*-values of <0.05 were considered statistically significant.

## 3 Results

### 3.1 Patients' tumor characteristics

The patients' characteristics and clinicopathologic features of the lesions are summarized in Table 1. The mean age of the patients was 55.0 years (range 35–72 years) and the male/female ratio was 17:33. The mean follow-up duration for the study subjects was (11.9±6.8) months (range 3–25 months). The most frequent locations of the SMTs were in the upper body region of the stomach (16 (32%)) and the fundus (15 (30%)). The final histologic examinations

revealed that 32 patients (64%) had a GIST and 16 patients (32%) had a leiomyoma. The tumors had a mean maximum diameter of 1.5 cm (range 1.0–3.0 cm). Of the 50 lesions, 7 (14%) displayed extraluminal growth and 43 (86%) displayed intraluminal growth. Forty-eight tumor capsules (96%) were complete and 2 (4%) were incomplete. EUS assessments of the depth of invasion and area of muscular connection showed that the numbers of MP1, MP2, and serosa tumors were 14 (28%), 29 (58%), and 7 (14%), respectively. Thirty tumors (60%) showed a wide muscular connection and 20 tumors (40%) had a narrow muscular connection. Forty-three lesions (86%) were initially treated by ESD, and the remaining 7 lesions (14%) were treated by EFR as a curative procedure.

### 3.2 Tumor resection rate

The clinical outcomes of the study subjects treated by ESD or EFR are summarized in Table 2. A successful complete resection was achieved for 41 of 43 patients (95.3%) treated by ESD. One patient in whom the ESD operation was incomplete underwent a laparoscopic operation to remove the residual tumor. Another patient with a GIST had a microscopic incomplete resection, but refused additional surgical management. All 7 lesions (100%) treated by EFR were completely resected. We analyzed the factors associated with a complete resection, including the tumor's location and size, and features seen by gastroscopy, EUS, and histologic examination. Two tumors with an incomplete capsule could not be fully resected by ESD.

The parameters associated with a complete tumor resection by ESD are shown in Table 3. The integrity of the tumor capsule was significantly correlated with the complete resection rate ( $P=0.001$ ).

### 3.3 Complications

The intraoperative perforation rate among patients treated by ESD was 20.9%. No major postoperative complications occurred and no patient developed major hemorrhage. Nine patients developed an endoscopically visible perforation during their ESD procedure, eight of whom were closed by purse-string suture or metal clips and one received laparoscopic surgery. Furthermore, the tumor (laparoscopic procedure) was located on the cardia region of the stomach, which made it very difficult to close the

**Table 1 Patients' characteristics and clinicopathologic features of the endoscopically diagnosed tumors (n=50)**

Parameter	Value
Patients' characteristics	
Sex (female/male)	33/17
Age (year)	55.0±10.2
Follow-up duration (months)	11.9±6.8
Endoscopic findings	
Tumor mobility	
Mobile lesion	35 (70%)
Fixed lesion	15 (30%)
Location	
Fundus	15 (30%)
Cardia	8 (16%)
High body	16 (32%)
Middle body	5 (10%)
Lower body	2 (4%)
Antrum	4 (8%)
Endoscopic ultrasound findings	
Growth pattern	
Intraluminal	43 (86%)
Extraluminal	7 (14%)
Tumor capsular integrity	
Complete	48 (96%)
Incomplete	2 (4%)
Tumor capsular location	
MP1	14 (28%)
MP2	29 (58%)
Serosa	7 (14%)
Tumor diameter	
≤2.0 cm	36 (72%)
>2.0 cm	14 (28%)
Connection with the MP layer	
Narrow	20 (40%)
Wide	30 (60%)
Pathological diagnosis	
GIST	32 (64%)
Leiomyoma	16 (32%)
Neurogenic tumor	2 (4%)
Treatment method	
ESD	43 (86%)
EFR	7 (14%)

Data are presented as number (percentage), mean±SD, or number. MP1: tumor capsule is in the upper half of the fourth layer; MP2: tumor capsule is in the lower half of the fourth layer; Serosa: tumor capsule is adhered to the fifth layer; ESD: endoscopic submucosal dissection; EFR: endoscopic full-thickness resection

gastric wall by endoscopic methods. Therefore, an additional laparoscopic operation was performed to complete the closure. Each of the nine lesions had a complete capsule which was located in the deep MP

**Table 2 Clinical outcomes of ESD and EFR for the study subjects**

Clinical outcome	Case number	
	ESD (n=43)	EFR (n=7)
Resection		
Complete resection	41 (95.3%)	7 (100%)
Incomplete resection	2 (4.7%)	0 (0%)
Complication		
Major hemorrhage	0 (0%)	1 (14.3%)
Perforation	9 (20.9%)	0 (0%)
Additional surgery	2 (4.7%)	2 (28.6%)

Data are presented as number (percentage)

**Table 3 Parameters for predicting a complete resection of a gastric SMT treated by ESD**

Parameter	Complete resection		P-value
	Yes (n=41)	No (n=2)	
Tumor capsular integrity			<b>0.001</b>
Complete	41 (100%)	0 (0%)	
Incomplete	0 (0%)	2 (100%)	
Tumor capsular location			0.450
MP1	14 (100%)	0 (0%)	
MP2	27 (93.1%)	2 (6.9%)	
Tumor diameter			0.885
≤2.0 cm	33 (97.1%)	1 (2.9%)	
>2.0 cm	8 (88.9%)	1 (11.1%)	
Connection with the MP layer			0.280
Narrow	20 (100%)	0 (0%)	
Wide	21 (91.3%)	2 (8.7%)	

Data are presented as number (percentage). Bold number indicates a statistically significant P-value

layer, and had a wide connection with the MP layer. In one of the perforation cases, the length of the tumor's muscular connection was about 60% of its capsular semi-circumference. Two patients treated by EFR were switched to a laparoscopic operation. One of the patients developed major bleeding caused by accidental injury of the serosa artery. The bleeding resulted in blurred endoscopic vision, and could not be stopped with metal clips; however, it was finally managed with a laparoscopic operation. The second patient had a very large iatrogenic perforation, and could not be closed endoscopically.

Some parameters for predicting perforation are shown in Table 4. A tumor's capsular location and its length of connection with the MP layer showed significant positive correlations with the occurrence of perforation ( $P=0.018$  and  $P=0.044$ , respectively).

**Table 4 Parameters for predicting perforation of a gastric SMT treated by ESD**

Parameter	Perforation		P-value
	No (n=34)	Yes (n=9)	
Location in stomach			0.183
Upper third	16 (61.1%)	7 (38.9%)	
Middle third	14 (93.3%)	1 (6.7%)	
Lower third	4 (80%)	1 (20%)	
Tumor capsular integrity			0.621
Complete	32 (78%)	9 (22%)	
Incomplete	2 (100%)	0 (0%)	
Tumor capsular location			<b>0.018</b>
MP1	14 (100%)	0 (0%)	
MP2	20 (69%)	9 (31%)	
Tumor diameter			0.657
≤2.0 cm	26 (76.5%)	8 (23.5%)	
>2.0 cm	8 (88.9%)	1 (11.1%)	
Connection with the MP layer			<b>0.044</b>
Narrow	19 (95%)	1 (5%)	
Wide	15 (65.2%)	8 (34.8%)	
Pathological diagnosis			0.122
GIST	17 (68%)	8 (32%)	
Leiomyoma	15 (93.8%)	1 (6.2%)	
Neurogenic tumor	2 (100%)	0 (0%)	

Data are presented as number (percentage). Bold number indicates a statistically significant P-value

#### 4 Discussion

ESD has been increasingly used to treat gastric SMTs originating in the MP layer. This is due to the small amount of trauma and rapid patient recovery time associated with the technique, as well as its broader acceptance by doctors and patients for producing results equivalent to those achieved with open surgery. However, this technology remains in an experimental stage, and no studies have addressed its safety, long-term results, or the most appropriate indications for its use. Most of the current studies on endoscopic resection of SMTs originating in the MP layer have been conducted on a small scale and investigated its practicability and feasibility. However, because deeper dissections are being performed, the use of ESD to perform a complete resection and the associated risks of complication are factors that require further investigation.

The complete resection rate is an important index for evaluating the effectiveness of ESD as a

treatment modality. In two studies which used similar inclusion criteria and methods, Chun *et al.* (2013) reported that the complete resection rate for SMTs originating in the MP layer of SMTs was 74.3%. These authors also reported that a positive rolling sign (tumor having a narrow muscle connection or no muscle connection) and a tumor size >2 cm were closely related to the complete resection rate. Bialek *et al.* (2012) reported a complete resection rate of 68%, and showed that the region connected with the MP layer was a factor correlated with a complete resection. In the current study, we achieved a complete resection rate of 95.3% (41/43 cases) when using ESD to treat tumors. We also found that an incomplete tumor capsule was negatively associated with the complete resection rate, whereas the connection between the tumor and the MP layer, the depth of tumor invasion, and tumor size did not correlate with the complete resection rate. Tumors with an incomplete capsule were more likely to extend to the resection edges, both vertically and horizontally. Also, the tumor tissue was more tightly connected with the surrounding tissue, and thus was more difficult to completely remove by endoscopic methods.

The most common complications of ESD are perforation and bleeding. Bialek *et al.* (2012) reported a 5.4% perforation rate when resecting SMTs originating in the MP layer. Those authors also reported that the tumor's connection with the MP layer was a factor related to complications, but did not specify the degree of contact with the MP layer or the depth of muscle invasion that correlated with the complication rate. In the present study, the perforation rate for SMTs originating in the MP layer and treated by ESD was 20.9% (9/43 cases), and this was much higher than the rates reported in other studies. This may have partially resulted from a large number of patients having tumors with a deeper than usual invasion level. However, it should be noted that using ESD to treat SMTs originating in the MP layer is a difficult process, and a perforation rate as high as 20% has been reported (Probst *et al.*, 2009). In the present study, the presence of an MP2-type tumor and a wide muscular connection appeared to be factors associated with the occurrence of complications. The perforation rate for tumors with a wide muscular connection was significantly higher than that for tumors with a narrow muscular connection (34.8% vs. 5.0%;  $P=0.044$ ).



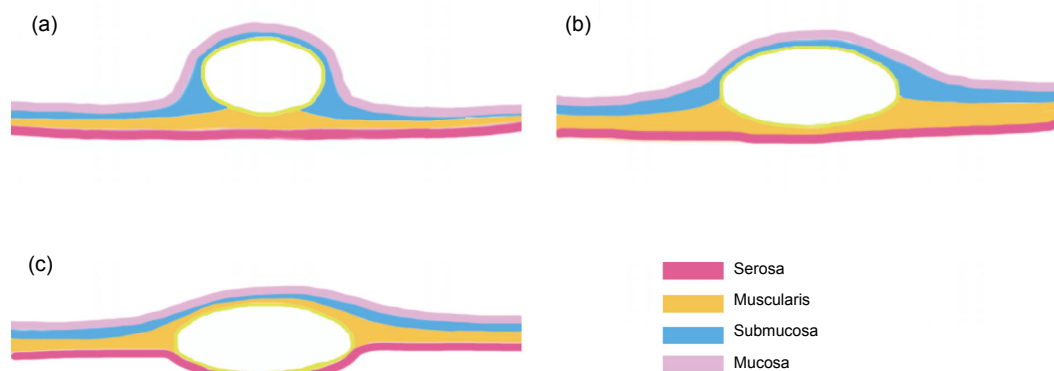
Chun *et al.* (2013) studied 35 SMTs which originated in the MP layer, and reported that perforation was more likely to occur when ESD was used to treat an immobile tumor (40% vs. 0% for highly mobile tumors), whereas the tumor's connection with the fourth layer was not related to the perforation rate. A wide muscular connection was a common finding among growing intraluminal tumors originating in the deep MP layer (Fig. 2b), and also among growing subserosal tumors (Fig. 2c). Moreover, there is a high probability of causing a perforation when treating such tumors. Tumors with a wide muscular connection have a capsule that is closely linked with the muscle tissue, and thus require dissection of a large MP layer, as well as repeated electrocoagulation procedures that can damage the MP. As a result, it is often difficult to separate the tumor from the MP layer without causing perforation. Additionally, rupturing the tumor capsule may lead to tumor recurrence or metastasis.

In the current study, the perforation rate among MP2-type tumors (31%) was significantly higher than that of MP1-type tumors (0%;  $P=0.018$ ). Theoretically, as the tumor invasion depth increases, the proportion of underlying muscle tissue decreases, and the chances of perforation also increase. In contrast to MP1-type tumors (Fig. 3b), MP2-type tumors have only a small underlying muscular layer and a much larger adjacent MP layer (Fig. 3c), and thus may become perforated more frequently. Our observations emphasize the role played by EUS in selecting appropriate patients for ESD. The EUS findings regarding tumor muscular connections, tumor capsule

location, and tumor capsule integrity are helpful for predicting the occurrence of complications and the probability of a complete endoscopic resection.

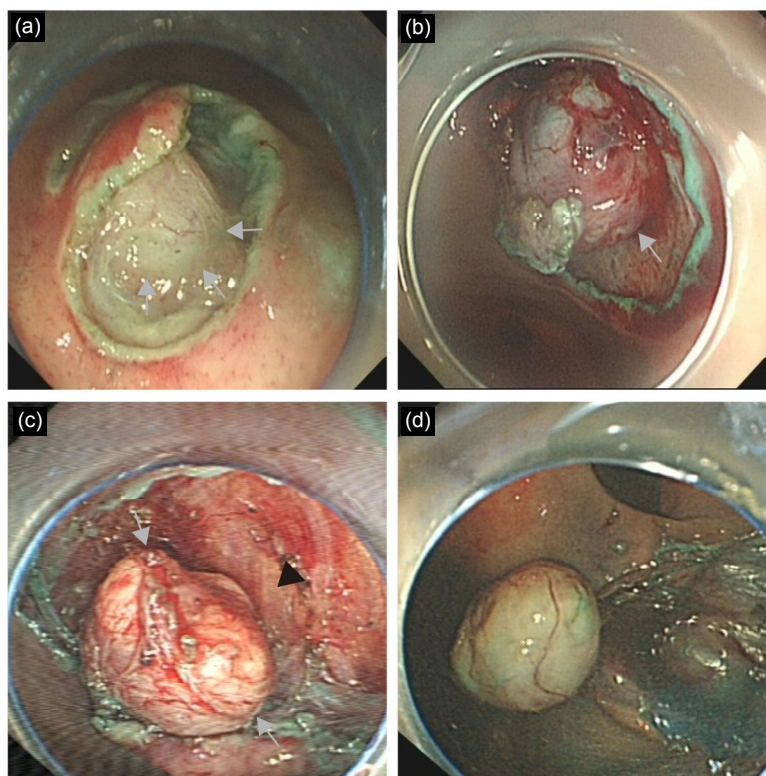
When using ESD to treat gastric SMTs originating in the MP layer, we found that some SMTs had a wide muscular connection and were located close to the serosa layer, and thus perforation was unavoidable when treating them by endoscopic resection. A growing subserosal tumor always shows an extraluminal growth pattern on EUS, and is easily diagnosed. In such cases, it was necessary to perform EFR to remove the underlying MP or serosa that was adherent to the tumor, by creating an iatrogenic perforation on the gastric wall. All seven SMTs in our study originating in the MP layer, were tightly adhered to the serosa layer, and had a wide muscular connection.

There is no standard for selecting an endoscopic resection method for treating small gastric SMTs that originate in the MP layer, because it is difficult to preoperatively diagnose these lesions and assess their malignant potential. Although in recent years, endoscopic resection technology has rapidly progressed and gradually replaced open surgery, its higher incidence of complications and rates of incomplete resection still demand attention. Thus, EUS plays an important role due to its ability to predict the occurrence of resection complications and the likelihood of achieving a successful endoscopic resection prior to actually performing the procedure. In this study, we analyzed EUS findings to investigate the appropriate indications for treatment with endoscopic resection, and then to select the most suitable resection method. We found that tumors which originated



**Fig. 2 Schematic illustrations of SMTs with different invasion depths and muscular connections**

(a) MP1-type with a narrow muscular connection; (b) MP2-type with a wide muscular connection; (c) Serosa-type with a wide muscular connection



**Fig. 3** Endoscopic images obtained during ESD of gastric SMTs

(a) A tumor capsule adjacent to the MP layer (gray arrows). (b) Narrow connection with the MP layer (gray arrow) as observed following dissection of the submucosal layer. (c) Wide connection with the MP layer (gray arrows) and underlying MP layer (black arrow head) as observed following a circumferential incision around the tumor. (d) A thin fibrous capsule, as commonly observed around a lesion after complete resection

in the superficial MP layer or had a narrow connection with the MP layer showed higher complete resection rates with almost no accompanying complications, and thus appeared to be ideal candidates for treatment with ESD. However, ESD should not be selected as a method for treating tumors which have an incomplete capsule. The current study has several limitations that should be mentioned. First, it had a retrospective rather than prospective design, and included a small number of patients. Second, not all patients who underwent endoscopic resection completed their long-term follow-up visits.

In conclusion, the results of this retrospective study suggest that EUS findings regarding the integrity and location of the tumor capsule and the length of the tumor muscular connection help to improve the complete resection rate and to reduce the occurrence of intraoperative complications. Therefore, the hyperechoic demarcation line between a tumor and the MP layer does contribute to the qualification of patients with a gastric SMT for ESD.

### Contributors

Bao-ying FEI designed the work that led to submission. All ESD and EFR operations were performed by Bao-ying FEI. Yu ZHANG was responsible for data statistics and paper writing. Zhen WANG analyzed the data and modified the paper. Ting JIN, Kai-qiang LI, Wei ZHANG, and Ke HAO were involved in data collation and proofreading.

### Compliance with ethics guidelines

Yu ZHANG, Zhen WANG, Ting JIN, Kai-qiang LI, Ke HAO, Wei ZHANG, and Bao-ying FEI declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

### References

Bialek, A., Wiechowska-Kozłowska, A., Pertkiewicz, J., *et al.*, 2012. Endoscopic submucosal dissection for treatment of gastric subepithelial tumors (with video). *Gastrointest.*



- Endosc.*, **75**(2):276-286.  
<http://dx.doi.org/10.1016/j.gie.2011.08.029>
- Brand, B., Oesterhelweg, L., Binmoeller, K.F., et al., 2002. Impact of endoscopic ultrasound for evaluation of submucosal lesions in gastrointestinal tract. *Dig. Liver Dis.*, **34**(4):290-297.  
[http://dx.doi.org/10.1016/S1590-8658\(02\)80150-5](http://dx.doi.org/10.1016/S1590-8658(02)80150-5)
- Chak, A., 2002. EUS in submucosal tumors. *Gastrointest. Endosc.*, **56**(4 Suppl.):S43-S48.
- Chun, S.Y., Kim, K.O., Park, D.S., et al., 2013. Endoscopic submucosal dissection as a treatment for gastric subepithelial tumors that originate from the muscularis propria layer: a preliminary analysis of appropriate indications. *Surg. Endosc.*, **27**(9):3271-3279.  
<http://dx.doi.org/10.1007/s00464-013-2904-9>
- Edge, S.B., Compton, C.C., 2010. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann. Surg. Oncol.*, **17**(6):1471-1474.  
<http://dx.doi.org/10.1245/s10434-010-0985-4>
- Hedenbro, J.L., Ekelund, M., Wetterberg, P., 1991. Endoscopic diagnosis of submucosal gastric lesions. The results after routine endoscopy. *Surg. Endosc.*, **5**(1):20-23.  
<http://dx.doi.org/10.1007/BF00591381>
- Hobel, S., Baumbach, R., Dautel, P., et al., 2014. Single centre experience of endoscopic submucosal dissection (ESD) in premalignant and malignant gastrointestinal neoplasia. *Z. Gastroenterol.*, **52**(2):193-199.  
<http://dx.doi.org/10.1055/s-0033-1356065>
- Hwang, J.H., Rulyak, S.D., Kimmey, M.B., 2006. American Gastroenterological Association Institute technical review on the management of gastric subepithelial masses. *Gastroenterology*, **130**(7):2217-2228.  
<http://dx.doi.org/10.1053/j.gastro.2006.04.033>
- Jeon, S.W., Jung, M.K., Kim, S.K., et al., 2010. Clinical outcomes for perforations during endoscopic submucosal dissection in patients with gastric lesions. *Surg. Endosc.*, **24**(4):911-916.  
<http://dx.doi.org/10.1007/s00464-009-0693-y>
- Kwee, R.M., Kwee, T.C., 2007. Imaging in local staging of gastric cancer: a systematic review. *J. Clin. Oncol.*, **25**(15):2107-2116.  
<http://dx.doi.org/10.1200/JCO.2006.09.5224>
- Lee, I.L., Lin, P.Y., Tung, S.Y., et al., 2006. Endoscopic submucosal dissection for the treatment of intraluminal gastric subepithelial tumors originating from the muscularis propria layer. *Endoscopy*, **38**(10):1024-1028.  
<http://dx.doi.org/10.1055/s-2006-944814>
- Meng, F.S., Zhang, Z.H., Shan, G.D., et al., 2015. Endoscopic submucosal dissection for the treatment of large gastric submucosal tumors originating from the muscularis propria layer: a single center study. *Z. Gastroenterol.*, **53**(7):655-659.  
<http://dx.doi.org/10.1055/s-0034-1399463>
- Mocellin, S., Marchet, A., Nitti, D., 2011. EUS for the staging of gastric cancer: a meta-analysis. *Gastrointest. Endosc.*, **73**(6):1122-1134.  
<http://dx.doi.org/10.1016/j.gie.2011.01.030>
- Nishimura, J., Nakajima, K., Omori, T., 2007. Surgical strategy for gastric gastrointestinal stromal tumors: laparoscopic vs. open resection. *Surg. Endosc.*, **21**(6):875-878.  
<http://dx.doi.org/10.1007/s00464-006-9065-z>
- Park, Y.S., Park, S.W., Kim, T.I., et al., 2004. Endoscopic enucleation of upper-GI submucosal tumors by using an insulated-tip electro-surgical knife. *Gastrointest. Endosc.*, **59**(3):409-415.  
[http://dx.doi.org/10.1016/S0016-5107\(03\)02717-2](http://dx.doi.org/10.1016/S0016-5107(03)02717-2)
- Polkowski, M., Palucki, J., Wronska, E., et al., 2004. Endosonography versus helical computed tomography for locoregional staging of gastric cancer. *Endoscopy*, **36**(7):617-623.  
<http://dx.doi.org/10.1055/s-2004-814522>
- Probst, A., Golger, D., Arnholdt, H., et al., 2009. Endoscopic submucosal dissection of early cancers, flat adenomas, and submucosal tumors in the gastrointestinal tract. *Clin. Gastroenterol. Hepatol.*, **7**(2):149-155.  
<http://dx.doi.org/10.1016/j.cgh.2008.09.005>
- Ryu, K.J., Jung, S.R., Choi, J.S., et al., 2011. Laparoscopic resection of small gastric submucosal tumors. *Surg. Endosc.*, **25**(1):271-277.  
<http://dx.doi.org/10.1007/s00464-010-1173-0>
- Shi, Q., Zhong, Y.S., Yao, L.Q., et al., 2011. Endoscopic submucosal dissection for treatment of esophageal submucosal tumors originating from the muscularis propria layer. *Gastrointest. Endosc.*, **74**(6):1194-1200.  
<http://dx.doi.org/10.1016/j.gie.2011.07.039>
- von Schonfeld, J., 2009. Endoscopic submucosal dissection for early gastric cancer. *Z. Gastroenterol.*, **47**(12):1264-1266.  
<http://dx.doi.org/10.1055/s-0028-1109815>
- Ye, L.P., Yu, Z., Mao, X.L., et al., 2014. Endoscopic full-thickness resection with defect closure using clips and an endoloop for gastric subepithelial tumors arising from the muscularis propria. *Surg. Endosc.*, **28**(6):1978-1983.  
<http://dx.doi.org/10.1007/s00464-014-3421-1>
- Zhang, Y., Zhou, P., Xu, M., et al., 2011. Endoscopic diagnosis and treatment of gastric glomus tumors. *Gastrointest. Endosc.*, **73**(2):371-375.  
<http://dx.doi.org/10.1016/j.gie.2010.10.023>
- Zhou, P.H., Yao, L.Q., Qin, X.Y., et al., 2011. Endoscopic full-thickness resection without laparoscopic assistance for gastric submucosal tumors originated from the muscularis propria. *Surg. Endosc.*, **25**(9):2926-2931.  
<http://dx.doi.org/10.1007/s00464-011-1644-y>

## 中文概要

**题 目:** 超声内镜下肿瘤与固有肌层之间的高回声线在指导内镜黏膜下剥离术治疗起源于固有肌层的黏膜下肿瘤中的价值

**目的:** 近年微创内镜技术作为治疗起源于固有肌层的黏膜下肿瘤的新型方式迅速发展。本研究旨在通过观察超声内镜下起源于固有肌层的肿瘤包膜完整性及所处位置(位于浅肌层或深肌层)、与浆膜层的位置关系和肿瘤与固有肌层紧密接触长度占肿瘤包膜长度的比例来评估完整切除率、穿孔及出血等并发症发生率、预后情况,进一步指导内镜下治疗方式的选择。

**创新点:** 首次提出通过超声内镜术前评估肿瘤包膜的完整性、在固有肌层中所处的位置及与固有肌层连接的长度选择内镜下治疗方式,可以提高完整切除率及降低术中并发症的发生。

**方法:** 收集浙江省人民医院及浙江省立同德医院

2014年02月至2016年6月接受内镜治疗的胃固有肌层肿瘤患者资料,总结并分析其临床特点、内镜及超声内镜表现、临床结果及术后随访资料。

**结论:** 肿瘤包膜的完整性与完全切除率密切相关。起源于深肌层以及与固有肌层为宽连接的黏膜下肿瘤在内镜黏膜下剥离术(ESD)中穿孔可能性较大。通过超声内镜术前评估起源于固有肌层的胃黏膜下肿瘤包膜的完整性、所处的位置以及与固有肌层连接的长度,有助于提高完整切除率和减少术中并发症的发生。

**关键词:** 胃粘膜下肿瘤; 内镜黏膜下剥离术; 内镜下全层切除术; 固有肌层