Application of NOTES combined with ESD for the treatment of an exogenous gastric stromal tumor: A case report and review of the literature

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Abstract. The present study aimed to investigate the safety and feasibility of natural orifice transluminal endoscopic surgery (NOTES) combined with endoscopic mucosal dissection (ESD) as a treatment for the exogenous growth of gastric stromal tumors of the serosal layer. The clinical data of one patient presenting with the growth of an exogenous gastric stromal tumor of the serosal layer admitted to the Department of Gastroenterology, Taihe Hospital, were reviewed. The patient's condition was evaluated pre-operatively, and NOTES combined with ESD were performed under general anesthesia. PubMed, EMbase, Wanfang data, the China National Knowledge Infrastructure and other databases, combined with the published literature were also searched to evaluate the safety and feasibility of this type of treatment for gastrointestinal stromal tumors (GISTs). In the present study, the duration of the surgery was 110 min, intraoperative blood loss was approximately 5 ml, and the lesion was completely stripped. After 5 days, the patient resumed a normal diet. After 45 days, the wound healing of the gastroscope was complete. An abdominal CT scan revealed that the tumor had been completely removed. In general, the endoscopic treatment of GISTs has a number of advantages; however, large lesions limit its application. Laparoscopic and endoscopic techniques have expanded the indications for GIST surgery to reduce contamination and tumor dissemination risks. NOTES technology is a novel direction for the treatment of GISTs, and its combination combined with ESD is safe and feasible. On the whole, as demonstrated herein, NOTES combination with ESD is safe and feasible for the treatment of GISTs originating from the gastric serosa or extraluminal growth type, particularly when the lesion is <3.5 cm in diameter. This method may thus be worthy of clinical promotion.

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Introduction

Gastrointestinal stromal tumors (GISTs) are a group of tumors originating from the gastrointestinal mesenchymal tissue and are the most common mesenchymal tumors of the digestive tract (1); gastric stromal tumors account for 60-70% of tumors of the digestive tract (1). GISTs occur in the fundus and stomach, and exhibit malignant tendencies (2). Surgery, including open and laparoscopic resection are the primary treatment options for GIST. The laparoscopic treatment of GISTs is safe and effective, and is suitable for the greater curvature or anterior wall lesions of the stomach (3,4). However, tumors with intraluminal growth and a small diameter, and lesions located in the cardia or pylorus are difficult to locate. Excessive normal gastric tissues may be removed, leading to gastric stenosis. Thus, the completely effective application of this technique remains to be discussed (4).

The endoscopic resection of GISTs has become the mainstream treatment option, particularly for tumors with a diameter of <3.5 cm (5). Endoscopic mucosal resection (EMR) is simple, safe and effective procedure, has few complications, and is easy to master. This method can be used for the radical resection of small lesions originating from the muscularis, particularly those without lymph node and hematogenous metastasis. Intrinsic muscular layer GISTs are treated with endoscopic mucosal dissection (ESD), endoscopic submucosal excision (ESE) and endoscopic full-thickness resection (EFR), all of which allow full tumor resection (6). However, given their origin from the deep muscular or serosal layer, perforation is often difficult to avoid, and endoscopic treatment is associated with the risk of residual marginal tumor cells and the destruction of the tumor capsule.

Natural orifice transluminal endoscopic surgery (NOTES) was developed in 2007, and does not involve skin puncture, but

requires the insertion of a soft endoscopic device through the body's natural orifices, such as the esophagus, stomach, vagina and rectum into the abdominal cavity or in the body cavity for surgery (7,8). This method has been applied for the treatment of GISTs; however, the number of applied cases is limited and the experience is not yet broad. For GISTs originating from the serosal layer, there is no standard treatment plan which is being followed at this stage. The present study describes a case of a gastric stromal tumor treated with NOTES combined with ESD, and provides a literature review in order to evaluate the safety and feasibility of this technique.

Case report

General information and medical history. The patient depicted in the present study was a 32-year-old married female admitted to the Department of Gastroenterology, Taihe Hospital due togastric eminence. The patient was first examined at the outpatient clinic due to intermittent upper abdominal pain and bloating. An endoscopic examination revealed chronic superficial gastritis with erosion, and gastric antrum elevation and endoscopic ultrasound (EUS) examination was recommended (Fig. 1A). Oral medications (unknown) were prescribed, and the symptoms were alleviated, but recurred after the drug was stopped. During the first hospital visit to the outpatient department, a computed tomography (CT) scan of the upper abdomen was performed (Fig. 2A). The greater curvature of the gastric antrum showed small nodules, possibly enlarged lymph nodes. The presence of a stromal tumor was excluded. Given that the lesions were small, no further examinations and treatments were performed. Following an EUS examination, a bulge in the gastric antrum was still observed (Fig. 1B and C). The patient's mucosa was clear, and the possibility of stromal tumors was high. A relative of the patient had passed way due to gastric cancer within the year the lesion was discovered. The patient requested the lesion to be removed and was admitted to the hospital. A physical examination revealed a temperature of 36.6˚C, a pulse rate 70 beats/min, respiratory rate (R) 18 breaths/min and a blood pressure of 118/65 mmHg. Epigastric tenderness was observed without other positive signs. For the lesions, the combined results of EUS and the CT scan suggested the presence of an exogenous stromal tumor possibly of the serosal layer in origin. On the basis of minimal invasiveness, surgical costs and post-operative cosmetic effects, the surgical protocol was customized as ESD surgery combined with NOTES surgery. A full communication with the patient and family members was performed prior to the surgery. An informed written consent was signed, and a hospital ethics committee certification was obtained. The results of the pre-operative examination of the patient are presented in Table I.

Instruments and methods used

Surgical instruments. A GIF-H260 electronic endoscope (Olympus Corporation) was used to observe the lesion and complete the surgery through the endoscope. Prior to the surgery, the front end of the endoscope should be worn with a transparent cap. The UM-3R ultrasound probe (frequency, 12 and 20 MHz; Olympus Corporation) was used to complete the ultrasound examination to assess the size and level of the lesion. During the surgery, an NM-200L-0421 injection needle (Olympus Corporation) was used to complete the submucosal injection. A KD-650L dual knife (Olympus Corporation) was used to remove the lesion, and the SD-5L-1 snare (Olympus Corporation) was used to assist in the removal of the lesion. During the surgery, FD-430L thermal biopsy forceps (Olympus Corporation) and high-frequency electrocutting device (Erbe Elektromedizin GmbH) were used to assist in the treatment of the wound and complete hemostasis. After the lesion was removed, the wound was sealed with the HX-610-135 metal titanium clip (Olympus Corporation) during this period.

Surgical methods. The patient underwent endoscopic surgery following tracheal intubation and general anesthesia (sevoflurane 1%, penehyclidine hydrochloride 0.5 mg, propofol 100 mg) (Fig. 1D-I). An endoscopic examination revealed a proximal 1.5x1.8 cm bulge in the stomach, and the mucosal surface was smooth. The edge of the lesion was marked with a Dual knife. Approximately 3 ml of indigo carmine and 1 ml of adrenaline were mixed with 100 ml of normal saline, and a submucosal injection was then performed at the marked point. After the lesion was fully lifted, the mucosa was excised from the submucosa by Dual knife edge, and the submucosa and lamina propria were separated. No lesions were observed. It was thus assessed that the lesion was located in the serosal layer and growing out of the cavity. NOTES was employed to enter the abdominal cavity. Specifically, the muscularis and serosal layer were cut. The endoscope was then inserted into the abdominal cavity. The peritoneal serosal surface revealed a bulge of approximately 1.5x1.8 cm in size with a congested surface. The lesion was completely removed along the base of the bulge. The wound was treated by electrocoagulation and then closed with titanium clip. A gastrointestinal decompression tube was implanted after the surgery. The specimen had a size of approximately 1.5x1.8 cm and was sent for histopathological examination. The surgery was uneventful and adhered to the guidelines for tumor resection (9). The duration of the surgery 110 min, and intraoperative blood loss was 5 ml.

Post-operative treatment. Post-operatively, for the patient, gastrointestinal decompression was continued, and the post-operative feeding protocol (9), hemostasis, antibiotics (cefmetazole sodium, 2.0 g, b.i.d., for 2 days), nutritional support and fluid replacement therapy were administered. Vigilance was maintained for complications, such as abdominal pain, peritonitis, bleeding and perforation.

Literature review search strategy. PubMed (https://pubmed.ncbi.nlm.nih.gov/), EMbase (https://www.embase.com), the Chinese National Knowledge Infrastructure (https://www.cnki.net/) and Wanfang database (http://www.wanfangdata.com.cn/index.html) were searched to collect clinical research on the treatment of gastric stromal tumors with NOTES and ESD. The search time was from the establishment of the library until August, 2020. English and Chinese studies were included, and the following search terms were used: 'Gastric submucosal tumor, gastric stromal tumor, serosal layer, endoscopy, ESD, NOTES'. On this basis, the references included in the preseant study were traced to obtain the relevant information.

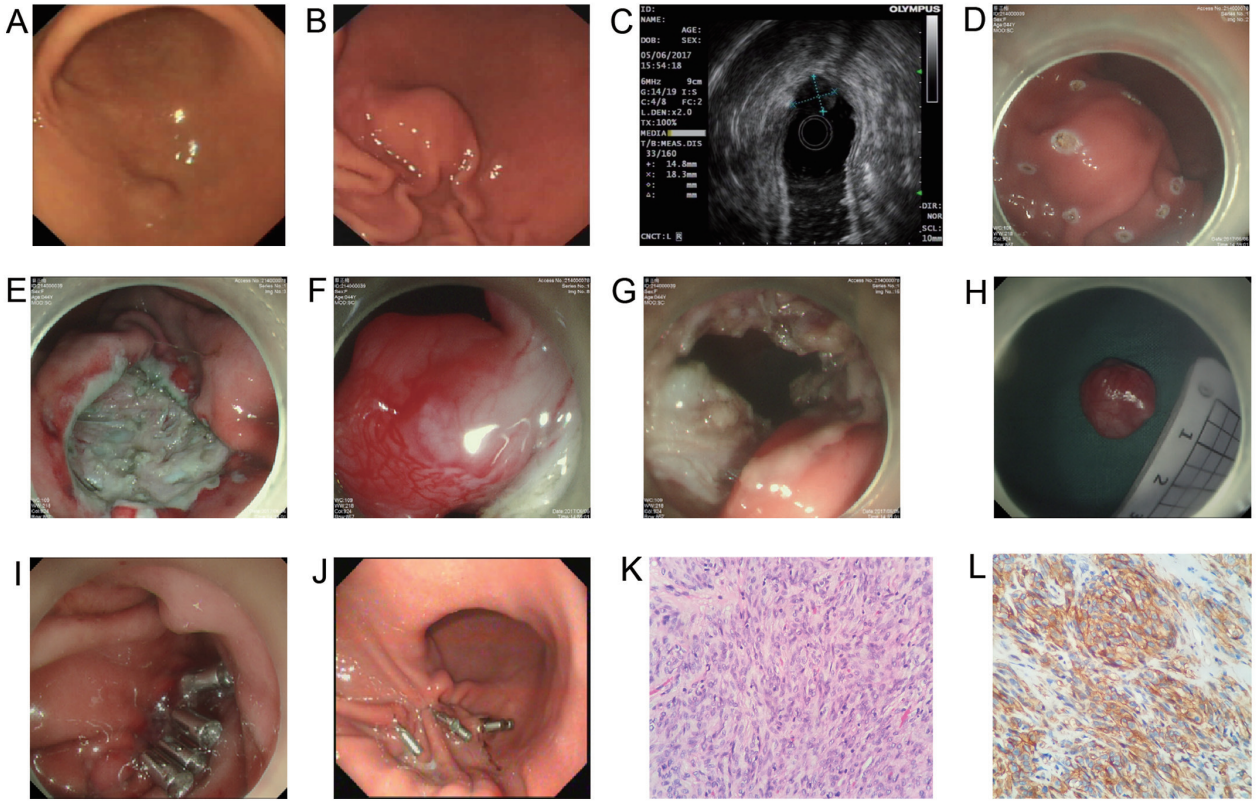

Figure 1. Endoscopy and surgery-related images. (A) A bulge of approximately 0.5x0.4 cm in the gastric antrum with a smooth surface was found by endoscopy. (B) The gastric antrum still had a lesion after 1 year. (C) The lesion was evaluated by EUS: The lesion exhibited low to medium echo level, originate from the intrinsic muscularis, and had a cross-sectional size of approximately 1.8x1.4 cm. (D) The lesion margin was marked before ESD surgery. (E) The mucosa to the submucosa was cut and the submucosa and lamina propria were separated; and no obvious lesions were observed. (F) Patient underwent NOTES, the endoscope entered the abdominal cavity, and the gastric serosal surface was approximately 1.5x1.8 cm with pedicle bulging, and the surface was congested obviously. (G) Complete removal of the lesion along the base of the bulge. (H) The size of the specimen was approximately 1.5x1.8 cm, and the whole specimen was sent for medical examination. (I) Electrocoagulation treatment wounds after surgery; metal clips were used to close the wounds. (J) The gastroscopy was reviewed to observe the lesions, at 45 days after the surgery. (K) Post-operative pathological images of the patient (a large number of spindle cell tumors, H&E staining; x40 magnification). (L) Immunohistochemical CD117-positive staining (x40 magnification). EUS, endoscopic ultrasound; ESD, endoscopic submucosal dissection; NOTES, natural orifice transluminal endoscopic surgery.

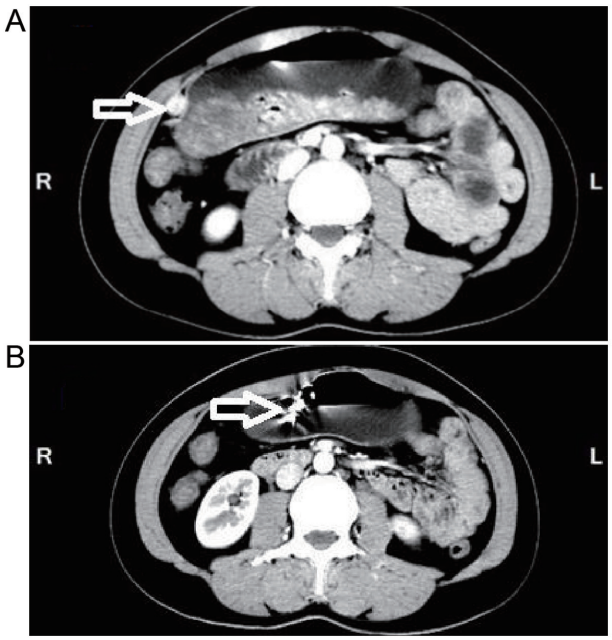

Figure 2. Comparison of CT examination results of the patient before and after surgery. (A) Lesions found on CT before surgery (shown by white arrow). (B) The lesion disappeared after surgery, and the titanium clips in the gastric cavity remained (shown by white arrow). CT, computed tomography.

Inclusion and exclusion criteria. The inclusion criteria were as follows: The lesion is a gastric stromal tumor. When the lesion originated from the serosal layer or the muscularis, the modality of treatment is NOTES, endoscopy (including ESD, EFR, ESE and STER) or laparoscopy, or a combination of the two. All cases have complete clinical and pathological data. The exclusion criteria were as follows: Repeated or replicated publication of the literature, animal studies, or studies of early or precancerous lesions; reviews, abstracts, systematic reviews and letters from readers.

Patient treatment

High power field (HPF) findings. The macroscopic appearance must satisfy the following: One polyp sample, no pedicle and a gray surface on the section. Histopathological diagnosis includes the following: Gastric stromal tumor, very low risk, tumor size of 1.5x1.5x1.3 cm, mitotic count <50 HPF.

The report of the biopsy revealed the following: Gastric stromal tumor, very low risk, the tumor size is 1.5x1.5x1.3 cm, and the mitotic image is <5/50 HPF. Immunohistochemistry (performed by the hospital pathology department) revealed the following: CD117 (+), CD34 (part +), Desmin (-), DOG1 (+), S-100 (-), SDHB (-), SMA (-) (Fig. 1K and L).

Table I. Summary of patient partial examination results.

Item	Result
ECG	Sinus rhythm, ST segment changes (ST IIIIIaVF horizontal type down 0.05 mV)
Hepatobiliary spleen and pancreas	Calcification of the right lobe of the liver, rough wall of the gallbladder, no obvious abnormalities in the spleen and pancreas.
Endoscopy and EUS	GF (July 16, 2016): Greater curvature of the gastric antrum shows a 1.0x0.8 cm bulge, with smooth surface. Diagnosis: gastric antrum bulge (recommended ultrasound gastroscopy). EUS (June 5, 2017): The lesion is in the middle and hypoechoic, of muscularis layer origin, the cross-sectional size is ~1.8x1.4 cm, the remaining layer structure is clear, no enlarged lymph nodes are seen around. Imaging diagnosis: gastric submucosal mass. GF (July 20, 2017): Scars are observed in the greater curvature of the stomach. 5 titanium clips are observed, 3 titanium clips were removed. The stomach is normal, and the peristalsis is good. Imaging diagnosis: chronic superficial gastritis with erosion, duodenal inflammation, portal inflammation.
Upper abdomen enhanced CT	December 22, 2016: The thick antrum shows the nodules, and it is close to the stomach wall, and the boundary is clear. The size is ~1.3x1.5 cm. Diagnosis: Greater curvature shows nodules of the antrum, large lymph nodes, stromal tumors to be ruled out. July 19, 2017: Post-operative gastric stromal tumor: The intensive nodules on the greater curvature were removed, no obvious nodules and masses were found locally, and no obvious enlarged lymph nodes were found in the abdominal cavity and retroperitoneum.

EUS, endoscopic ultrasound; GF, gastroscope.

Outpatient treatment and follow-up. Post-operatively, the patient had no obvious abdominal pain, abdominal distension or any other type of discomfort. No bleeding, perforation or other symptoms occurred. The patient recovered at 3 days after surgery and was discharged after 5 days. Outside the hospital, the patient gradually transitioned from liquid to semi-solid to normal diet and was advised to pay attention to rest, avoid fatigue, and continue oral acid suppression and mucoprotective medication. The patient was under a weekly telephone follow-up. Apart from short-term abdominal discomfort outside of the hospital, no adverse reactions occurred. At 45 days following the surgery, the residual titanium clips were observed by a CT scan (Fig. 2B). The wounds were completely healed, as shown by the endoscopic examination, and residual titanium clips remained (Fig. 1J).

Literature search results. Literature explicitly describing ESD combined with NOTES was not retrieved. Different methods of minimally invasive treatment of GIST was classified into single endoscopic treatment, endoscopic combined with laparoscopic treatment, and NOTES treatment of GIST. The data were summarized and analyzed. Individual endoscopic treatments of GIST from different studies are presented in Table II. In addition, studies using NOTES for the treatment of GIST are presented in Table III.

Discussion

Submucosal tumors (SMTs) can originate from the mucosal muscle layer, submucosa or muscularis propria (23). With the popularity of endoscopy, the diagnostic rate is gradually increasing. Common types of SMT include lipoma, leiomyoma and stromal tumor. SMTs originating from the muscularis propria are mostly GISTs. SMTs have different biological characteristics and the treatment options include follow-up, endoscopic resection, laparoscopic resection and surgical treatment (24). GISTs have malignant potential, and the malignancy accounts for approximately 25% (25). The need for treatment is dependent on the location and size of the tumor and clinical manifestations and the risk stratification of clinical malignancies (26). GISTs which are <2 cm in diameter do not require treatment, but must be closely monitored to ensure that the lesion does not increase in size (4). Moreover, GISTs with a diameter >5 cm or lesions causing obstruction and bleeding require surgery (27). Surgery or endoscopic resection is the primary treatment option (28).

Among the endoscopic techniques for the clinical treatment of GISTs, ESD is the most widely used and can achieve complete resection (29). EFR is a derivative of ESD that can completely remove lesions from all layers, including the serosal layer (30). Furthermore, this method is recommended

Table II. Common endoscopic procedures combined with laparoscopic treatment procedures for GISTs.

Author/(Refs.)	Year	Procedure name	Abbreviation	Procedure	Duration of surgery (min)	Peri-operative bleeding (ml)	Tumor diameter (cm)	Complication	Indications/ advantages	Limitation
Cai *et al* (10)	2015	Laparoscopic wedge resection.	LWR	According to the location of tumor, wedge resection or local gastrectomy should be performed. The resected tumor is taken out through abdominal incision.	106±40.1	67.3±80.5	3.5±1.9	3 Cases of delayed gastric emptying, 1 case of lung infection.	Suitable for excision of GIST, particularly <5 cm lesions.	It is difficult to identify the edge of the tumor from the serosalsurface. Unintentional removal of healthy gastric tissue may occur. Surgery near the esophagogastric junction or pylorus may lead to stricture or obstruction of the stomach inlet or outlet.
Matsuda *et al* (11)	2017	Laparoscopic endoscopic cooperative surgery.	LECS	The lesions are located by endoscopy, and wedge resection or local gastrectomy is performed according to the location of the tumor. The resected tumor is taken out through abdominal incision.	190.2±66.8	15.1±38.6	NA	NA	Suitable for all sizes and location of GIST, combined with endoscopic techniques and laparoscopic gastrectomy to prevent excessive gastric resection and postoperative gastric deformation.	Advanced endoscopic and laparoscopic techniques and skilled collaboration between internal and external surgeons are required; long operation time may increase digestive fluid spillover and abdominal infection risk.
Nunobe *et al* (12)	2012	Inverted laparoscopic endoscopic cooperative surgery.	Inverted LECS	The process from marking to artificial perforation is similar to classic LECS. In order to prevent the tumor from contacting visceral tissue, the gastric wall is lifted in the tangential direction by suture. Thus, the serosal layer is opened around the submucosal incision with ESD or laparoscope equipment and the tumor is removed. After removing the specimen, the gastric wall defect is sutured using a laparoscope.	N/A	N/A	N/A	N/A	The procedure was developed to prevent the contents of the stomach from spilling into the clean abdominal cavity.	Repeated intervention to the tumor may cause tumor recurrence and there is still a risk of gastric contents entering the abdominal cavity.
Ye *et al* (13)	2018	Laparoscopic exogastric wedge resection.	LEWR	The gastroscope passes through the cardia, identifies the site in gastric cavity to avoid stenosis. This procedure prevents excessive normal gastric tissue resection and uses a laparoscope to perform a wedge-shaped resection of the stomach wall from the distal end.	108.35±47.23	31.83±38.85	2.97±2.02	2 Cases of fever, symptomatic relief.	First choice of treatment of gastric submucosal tumor.	Need to open the anterior wall of the stomach. The duration of the surgery is prolonged, blood loss is increased and risks are amplified. Post-operative recovery time is prolonged, gastric juice enters the abdominal cavity and the risk of abdominal infection increases.

Table II. Continued.

Author/(Refs.)	Year	Procedure name	Abbreviation	Procedure	Duration of surgery (min)	Peri-operative bleeding (ml)	Tumor diameter (cm)	Complication	Indications/ advantages	Limitation
Ye *et al* (13)	2018	Laparoscopic transgastric wedge resection.	LTWR	If the location of the GIST is found to be unsuitable for LEWR, including posterior wall lesions or incomplete exposure after gastric rotation, the LTWR method is used to locate the lesion via endoscope and the gastrectomy is performed on the anterior wall of the tumor. After the tumor is removed, a wedge-shaped resection is performed sequentially along the normal stomach wall with a laparoscope and the gastric incision is sutured with a laparoscopic linear suturing device	149.44±49.78	82.22±119.87	3.27±1.36	1 Case of fever, symptomatic relief.	LTWR should be considered for growths in gastric posterior wall, intraluminal growths and lesions close to EGJ.	
Mahawongkajit *et al* (14)	2020	Non-exposed	NEWS endoscopic wall-inversion surgery	After the tumor is located under the endoscope, the seromuscular layer is opened underlaparoscopic surgery, and the tumor is sutured along the incision line, and then the tumor is inwardly turned into the gastric cavity which is then removed by endoscopy.	207.5±30.7	1.5±0.8	2.1±0.5	N/A	The resection line can be determined with high accuracy without causing peritoneal contamination, and the tumor can be prevented from being exposed to the peritoneal cavity, and SETs with a maximum diameter of <3 cm are feasible. Removal of the tumor in the mouth by total removal of stomach wall, thus avoiding the risk of intraperitoneal seeding.	If the size of the lesion is <3 cm, NEWS is preferred, and the patient sample size is small.

Table II. Continued.

Author/(Refs.)	Year	Procedure name	Abbreviation	Procedure	Duration of surgery (min)	Peri-operative bleeding (ml)	Tumor diameter (cm)	Complication	Indications/ advantages	Limitation
Hajer *et al* (15)	2018	Non-exposure technique	CLEAN-NET	Endoscopic examination of gastrointestinal stromal tumors which is then marked with electrocautery, followed by injection of methylene blue dye into the lesion, surrounding the serosal muscle incision. Stapling is done around the wound, elevation of submucosa away from the gastric wall. Resection of the tumor with a stapling device, then suturing the mucosal surface of the stomach wall eventually suturing the serosal surface of the stomach wall.	120-180 (average, 150)	N/A	3.0-4.5 (average, 3.75)	N/A	Applicable to tumors >4 cm in diameter, extraluminal growth tumors, fully protect gastric function.	The sample size is small, only 2 cases.
Kikuchi *et al* (16)	2017	Closed laparoscopic and endoscopic cooperative surgery.	Closed LECS	Endoscopic submucosal dissection around the lesion and the serosal surface was marked by laparoscopy. Laparoscopic suture of the stomach wall was made along the marked line and the lesion was enclosed in the stomach. Endoscopic dissection was continued and the tumor was taken out through the mouth.	253±45	18±55	2.41±0.76	Abdominal abscess in one patient	Without contamination and tumor cells spreading into the abdominal cavity.	The number of cases is small, the follow-up time is short, and the long-term effect is unknown.
Okumura *et al* (17)	2017	Lift-and-cut method	N/A	First, the seromuscular layer around the tumor was removed. As the mucosa and submucosa are stretchable, the tumor was elevated into the abdominal cavity. Following elevation, the gastric tissue under the tumor was cut in the submucosa with a linear stapler.	65-302 (average, 126)	0-200 (average, 10)	1.0-7.7 (average, 3.3)	N/A	Minimize gastric tissue resection and reduce the chance of contaminating the abdominal cavity.	Single-center study biased, long follow-up time, no prospective study compared to other surgical methods.

Table II. Continued.

Author/(Refs.)	Year	Procedure name	Abbreviation	Procedure	Duration of surgery (min)	Peri-operative bleeding (ml)	Tumor diameter (cm)	Complication	Indications/ advantages	Limitation
Dong *et al* (18)	2014	Modified laparoscopic intragastric surgery.	MLIGS	The position of the tumor was confirmed under endoscopy. The laparoscopic lamp was placed in the cavity using the trocar at the navel, and the other two trocars were inserted into the abdominal wall and the stomach wall. The gastroscope was monitored by a laparoscope, and the operation was performed in the gastric cavity. The tumor tissue was taken out with the forceps and the wound was closed by titanium clip.	85±25.77	20±10.35	2.75±1.07	Abdominal pain for 1.875±1.46 days	MLIGS and EFR are effective in treating the muscularis propria gastric stromal tumor, and they are non-invasive.	N/A
Moriyama *et al* (19)	2012	Robot-assisted laparoscopic resection.	N/A	The Da Vinci surgical system (da Vinci; Intuitive Surgical Inc.) was used to make an incision 30 mm above the umbilicus and introduced an Alexis wound retractor to establish a pneumoperitoneum. The 3-arm Da Vinci was used to control the surgical instruments with the right and left arms, and the endoscope was attached to the central arm. The omentum was dissected and the stomach was elevated to the abdominal wall. Using an electric knife the tumor was dissected, the tumor was removed, and the gastric and abdominal wall was closed.	190	<50	3.4	N/A	Simplify the process of laparoscopic resection, making it easier to perform gastric incision and suture.	The sample size is small, and some institutions do not have this equipment.

GIST, gastrointestinal stromal tumor; N/A, not available.

Table III. Summary of NOTES treatment for GISTs.

Author/(Refs.)	Year	Procedure	Abbreviation	n	Procedure	Surgery time (min)	Peri-operative bleeding	Post-operative examination	Complication	Technique advantages
Lee *et al* (20)	2013	Transgastric NOTE speritoneoscopy.	TGP	5	Mucosa is marked and a submucosal tunnel is established. The distal end is opened, balloon is dilated. Biopsy forceps is used for abdominal nodule biopsy and the incision is closed.	10.44±2.42	N/A	4 Cases of peritoneal cancer and 1 case of tuberculosis.	N/A	Simple technology, short operating time, less complications, low sedation requirements, no need for general anesthesia.
		Endoscopic full-thickness resection	EFTR	5	Mark the lesions, establish tunnels, remove lesions in tunnels, close mucosal incisions.	18.80±9.41 Resection time	N/A	3 Cases of GIST and 2 cases of schwannomas.	1 Case of abdominal pain, symptomatic treatment.	
Mori *et al* (21)	2011	Hybrid natural orifice transluminal endoscopic surgery.	Hybrid NOTES	6	Under the endoscope, balloon was fixed at the bulb of the duodenum, and it was fixed with 60-70 ml of gas to make the stomach filled. The ESD method was then used to peel off the muscle layer, causing active perforation ~1 cm outside the tumor, and the endoscope entered the abdominal cavity. EFR after inversion; laparoscopic observation of lesions, tumor removal was done from the mouth, laparoscopic suture of the stomach wall was performed.	180-360 (average 288)	N/A	GIST	N/A	Operation is not affected by the disease, can adjust the position; reduce the economic burden of the patient, mental and psychological pressure, shortcomings and operation time.
Nakajima *et al* (22)	2009	Hybrid transvaginal NOTES	NA	2	Under the assistance of laparoscope, endoscopic treatment was performed following the establishment of a channel through the vagina.	365 and 170	Almost no bleeding	1 Case of hemorrhagic lipoma, 1 case of GIST	N/A	Abdominal incision is avoided, the disadvantage is that the operation is cumbersome.

GIST, gastrointestinal stromal tumor; NOTES, natural orifice transluminal endoscopic surgery; ESD, endoscopic mucosal dissection; N/A, not available; EFR, endoscopic full-thickness resection.

for lesions derived from the muscularis propria and the serosal layer (31). However, EFR has a number of complications, such as perforation and bleeding, and needs to be performed by highly skilled surgeons. ESE is also a derivative of ESD and is widely used in the treatment of GISTs derived from the muscularis propria, particularly for intraluminal lesions (32). This technique can maintain the physiological integrity of the digestive tract and reduce complications, but it also requires a highly skilled surgeon. During the surgery, the tumor must be excised from the submucosa or inner muscle layer along the external edge of the tumor, and the capsule of the tumor must remain intact. STER technology is close to endoscopic myotomy (POEM) (33), which involves a tunnel to treat multiple lesions (34). However, the space inside of the tunnel is limited, and the operation and removal of large lesions are difficult. This condition also increases the risk of perforation, and the possibility of tunnel wall damage during operation is high. STER is recommended for treating tumors originating from intrinsic muscle layer, but not for those arising from muscularis propria. EMD can better expose the lesions, which is beneficial to the examination of disease compared with STER.

Longitudinal incision is used to simplify the surgical procedure and reduce the chances of perforation for lesions originating from the muscularis propria. Furthermore, this technique is rarely used, and the follow-up time is short. Long-term effects of this procedure are unknown. Suction treatment of exogenous GIST has the advantage of reducing the risk of perforation. However, this technique cannot be used when the lesions do not move towards the endoscope during the extraction, thereby limiting its clinical promotion. In conclusion, endoscopic GIST treatment has many advantages, including postoperative gastric structural integrity, short hospital stay, relatively simple sedation, low operating cost, and low manpower requirement. However, when the lesion is large, the tumor complete resection rate is low, the risk of perforation is increased, and a risk of tumor peritoneal implantation occurs when the perforation is large.

On the bases of the characteristics of laparoscopic and endoscopic techniques, scholars have proposed laparoscopic and endoscopic combined surgery (LECS) for the treatment of GISTs. Various surgical techniques have also been developed. Classical LECS includes endoscopic mucosal resection and laparoscopic surgery. The technique uses ESD or EMR to perform mucosal resection under the guidance of an endoscope and uses a laparoscopic incision for the closure of the surgical site, thus achieving minimally invasive treatment (35). LECS can be used to avoid the excessive resection of the stomach wall and maintain its structural and physiological integrity. However, a risk of peritoneal spread of tumoris possible. This technique is currently used for gastric GISTs with a diameter ≤5 cm and is not recommended for large and/or ulcerated GISTs with a diameter >5 cm (36). However, this procedure is suggested for larger-sized GISTs (37).

Domestic and foreign scholars have improved classic LECS, including laparoscopic-assisted endoscopic resection, endoscopic assisted wedge resection, reverse LECS, non-exposure technique (CLEAN-NET), non-exposure endoscopic gastric wall inversion (NEWS), laparoscopic-assisted endoscopic total resection (LAEFR) and clean non-exposure techniques. The above-mentioned techniques are mainly performed to avoid the spread of tumor cells following gastric wall incision and the contamination of the abdominal cavity by gastric contents (38). Laparoscopic and endoscopic techniques have expanded the indications for GIST surgery and have reduced the chances of contamination and tumor spread.

NOTES technology enters the body cavity through the natural cavity for exploration, biopsy and various surgical operations. This method proposes a novel direction for GIST treatment. At present, technology faces various difficulties, including surgical indications, choice of surgical pathway, incision closure, infection control during treatment, and patient acceptance, prior to their clinical application. For GIST, scholars have proposed mixed NOTES; however, most of these techniques are limited to small-sample clinical studies and lack large-sample, multicenter, prospective randomized controlled trials.

Although the future of NOTES remains unknown, surgeons have made a positive attempt for this method. Cases have been rigorously screened, the location and origin of the lesions have been fully evaluated, and reasonable treatment plans and countermeasures have been formulated. Full communication must be ensured before surgery to obtain the informed consent of patients and their families.

As the tumor of the patient in the present study was small, traction technology was not used upon entry of the gastroscope into the abdominal cavity. Instead, the endoscope was used to pull the tumor directly into the stomach and ESD was then used to remove it. After the tumor was removed, metal clips were used to seal the wound under the endoscope as the wound was fairly small. From past experience, it was learnt that closing with metal clips alone is often difficult when the tumor exceeds 3.5 cm. In this case, suturing the wound with nylon rope or combining the procedure with laparoscopy to remove the tumor may be necessary.

Basing on the above experience, the surgeon believes that NOTES combined with ESD is safe and feasible. The current endoscopic resection diameter of <3.5 cm GIST has become the norm. With the experience of flat ESD, NOTES combined with ESD is safe and feasible treatment for plasma membrane-originating GIST, particularly for exogenous lesions <3.5 cm in diameter. Relative laparoscopic surgery has the following advantages: Small trauma, no influence on the appearance of the patient (cosmetic), a low treatment cost, short hospital stay, quick recovery after surgery, and few complications, and thus is worthy of clinical promotion. The procedure may also have the following disadvantages: The lesion is difficult to locate, the technique is difficult, and high technical requirements from the surgeon are necessary. Larger sample, multicenter, prospective, randomized controlled trials are thus required to further assess the safety and feasibility of this technique.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article or are available from the corresponding author on reasonable request.

Authors' contributions

XBL, SBL and SJ conceived and designed the study. ZYG, CTS and XBL searched and collected the data. XBL, SP and BZS contributed to data extraction and data analysis. SJ and PL provided surgical and pathological information. XBL and ZYG wrote the manuscript. CTS, SJ and SBL reviewed and revised the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Taihe Hospital Ethics Committee. Informed consent was obtained from the patient.

Patient consent for publication

Written informed consent for publication was obtained from the participant.

Competing interests

The authors declare that they have no competing interests.

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