

Endoscopic full-thickness resection for gastric gastrointestinal stromal tumor originating from the muscularis propria

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SUMMARY

OBJECTIVE: This study retrospectively reviewed 46 cases of gastric gastrointestinal stromal tumors treated by endoluminal endoscopic full-thickness resection (EFR) microsurgery in our gastrointestinal endoscopy center. We aimed to evaluate the EFR for the treatment of gastric gastrointestinal stromal tumors originating from the muscularis propria.

METHODS: A total of 46 patients with gastric gastrointestinal stromal tumors originated from the muscularis propria layer from January 2012 to June 2015 were treated with EFR. The patients were followed up with gastroscopy and computed tomography (CT) for evaluation of therapeutic effect and safety.

RESULTS: EFR was successfully accomplished to remove all tumors in 46 patients. The mean procedure time was 82.5±39.8min (56-188min). Except in 3 leiomyomas, pathological examination confirmed gastrointestinal stromal tumor (GIST) in 43 cases. None of the patients had occurred bleeding, peritonitis and other complications after EFR. Thereafter, all patients were followed up with gastroscopy after 1, 6, 12 months.

CONCLUSIONS: EFR is effective and safe for patients with gastric gastrointestinal stromal tumors originated from muscularis propria layer and has the advantage of less invasive treatment and higher tumor resection rate. It should be considered for further application.

KEYWORDS: Gastrointestinal neoplasms. Gastrointestinal stromal tumors. Neoplasms, connective tissue. Stromal cells. Gastrectomy. Gastroscopy. Laparoscopy.

INTRODUCTION

The gastric submucosal tumor less than 3cm in most benign tumors, but gastrointestinal stromal tumor (GIST) currently regarded as a potentially malignant tumor. Stromal tumors arising from the muscularis propria are located in deeper layers, especially those that do not grow within cavities¹. The main treatment is complete tumor resection¹⁻³. Recently,

endoscopic full-thickness resection (EFR) has been applied as a treatment for gastrointestinal submucosal tumors (SMTs).

We used EFR for complete resection of gastric gastrointestinal stromal tumors from the muscularis propria and have summarized the effect of treatment.

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MATERIAL AND METHODS

Patients

From January 2012 to June 2015, 46 cases of gastric gastrointestinal stromal tumors, originating from the muscularis propria layer, were confirmed by endoscopic ultrasound (EUS) and computed tomography (CT) at The Affiliated Yantai Yuhuangding Hospital of Qingdao University. No metastasis of gastric gastrointestinal stromal tumors was found. The patients consisted of 21 males and 25 females at ages 23–65 years (median age 47.6±13.2 years). All the cases were single occurrences. The tumors were 1.2–4.5cm in size and located in the fundus (n = 36), the gastric corpus (n = 9), the gastric antrum (n = 1). Each patient's written informed consent was obtained. This retrospective study was approved by the Ethics Committee of The Affiliated Yantai Yuhuangding Hospital of Qingdao University.

Instruments

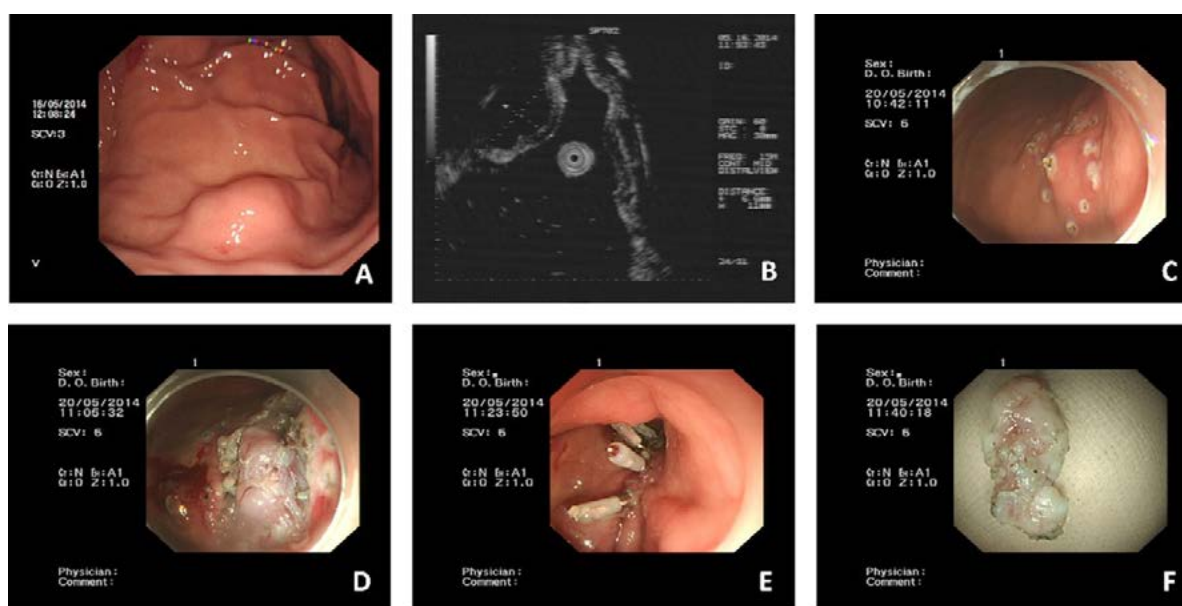
We selected these instruments to extend our previous study^{4,5}. The following instruments were used: Electronic gastroscope (Olympus GIF-Q260J, Olympus company, Japan), hyaline cap (D-201-11304, Olympus company, Japan), spiculiform cutting knife (KD-1 L-1, Olympus company, Japan), IT knife (KD-611 L, Olympus company, Japan), hook knife (KD-620 LR, Olympus company, Japan), injection needle

(NM-200 L-0525, Olympus company, Japan), snare (AS-1-S, ASJ-1-S, COOK company, United States), hot biopsy forceps (FD-410 LR, Olympus company, Japan), hemostatic clip (HX-610-90, Olympus company, Japan; HX-600-135, Olympus company, Japan; Boston Resolution™, Boston company, United States), high frequency electric knife (ERBE VIO 200S, ERBE company, Germany) and, Argon Plasma Coagulation instrument (ERBE APC2, ERBE company, Germany).

EFR Method

EFR method was done as previously described^{4,5}. Pneumoperitoneum will happen inevitably as gas will spill into the abdominal cavity in the process of tumor resection and suture of gastric defects in if EFR full-thickness resection of gastrointestinal mucosa lead to gastric perforation, the used of CO₂ in solution in water can reduce postoperative abdominal distension. The key to successful treatment of EFR is the endoscopic therapeutic perforation occurred as a mend. Under endoscopic guidance, the incisions on the gastric body from the two ends to the middle were fully closed with titanium clips, and the gastric wound was sealed. For wounds that were too large to seal directly, negative pressure was applied to suck the omentum into the gastric cavity, and the titanium clips were used to seal the wound by clipping the omentum to the gastric mucosa (Figure 1). When the serosa was cut all

FIGURE 1: PROCESSES OF EFR FOR GIST ORIGINATED FROM MUSCULARIS PROPRIA.



(A) Protruding submucosal lesion in the gastric body. **(B)** Endoscopic ultrasound showing that the lesion arose from the muscularis propria. **(C)** Endoscopic view of the submucosal tumor and labeling margins with argon plasma coagulation. **(D)** Application of the IT knife to isolate the stromal tumor along its periphery. **(E)** Sealing of a perforation with multiple titanium clips. **(F)** Resected tumor with the mucosa removed

around the GIST tumor, the lesion can fall within the peritoneal cavity. For tumors larger than 4 cm, we use double-channel gastroscope to avoid that.

Sample processing

Post-EFR pathological diagnosis was made by focusing on cell types. The immunohistochemical tests for CD34, CD117, Dog-1, S-100, and SMA. Mitotic counts per 50 highpower fields were evaluated in GISTs.

Postoperative treatment

After EFR surgery, a gastrointestinal decompression drainage tube was placed. Postoperative medication included nothing perorally, gastrointestinal decompression drainage for 24 hours, and drug therapy, such as a proton pump inhibitor and broad-spectrum antibiotic intravenous administration, for 3 days. Patients were discharged with proton pump inhibitor therapy for 2 months.

Statistical analysis

Statistical analysis was performed with SPSS for Windows Version 17.0 software (SPSS Inc., Chicago, IL, USA). Data were analyzed using the two-tailed Student's *t* test. $P < 0.05$ was considered significant. Data are expressed as mean \pm standard error of the mean (SEM).

RESULTS

Clinicopathological characteristics and outcomes of EFR are summarized in Table I. Among all enrolled patients, 46 tumors were located in the gastric fundus with 36 cases, 9 cases were in the gastric corpus, and 1 case was in the gastric antrum. All lesions were confirmed as originating from the muscularis propria or close to the serosa by endoscopic ultrasonography examination.

The EFR success rate was 100%. The median operation time was 82.5 minutes (range, 56-188minutes; SD, 39.8minutes). Mean size (the maximum diameter) of resected tumors was 2.6 (range, 1.2-4.5) cm. Pathological diagnosis showed 43 GISTs, 3 leiomyomas. Among the 43 GISTs, 33 cases were benign, 8 cases were a very low risk of malignancy, and 2 were at low risk of malignancy (Mitotic counts per 50 highpower fields \leq 5). All specimens were border-free.

Effects of tumor sizes affecting the entire EFR process were then assessed by subgroup analysis (Table

II). EFR for GISTs larger than 2 cm took longer times.

No procedure-related death was found. No single case had severe complications, such as GI bleeding, peritonitis, or abdominal abscess. The length of hospital stay in the EFR ranged from 4 to 11 d, with a mean of 5.5 ± 1.6 d. The mean follow-up time was 1,6,12 months. No tumor residual or recurrence has been found yet.

DISCUSSION

Most GISTs, including GISTs, grow intraluminally and rarely metastasize to local lymph nodes. Laparoscopic wedge resection with a linear stapler is the mainstay to manage those GISTs^{6,7}.

In recent years, based on endoscopic submucosal dissection and endoscopic submucosal excavation and due to improvements in the application of titanium clips under endoscopy, EFR treatment of gastrointestinal tumors arising from the muscularis propria has become possible. The key to EFR procedure is the successful closure of wall defect after resection to prevent peritonitis and surgical intervention.

In the present study, we retrospectively reviewed those cases of gastric gastrointestinal stromal tumors treated by EFR therapy in our center.

Successful treatment using EFR required successful repair of the perforation, thus avoiding the need for additional surgical repair and postoperative peritonitis(8-10). The most common method for re-

TABLE 1: CLINICOPATHOLOGICAL CHARACTERISTICS AND OUTCOMES OF EFR

Characteristic	Value
Patients (n)	46
Gender (male/female)	21/25
Age (years)	47.6 \pm 13.2 (23-65)
Gastric fundus	36
Gastric corpus	9
Gastric antrum	1
Size (cm)	1.2-4.5
Mean operation time (minutes)	82.5 \pm 39.8min(56-188min)
Titanium clips (n)	7.1 \pm 4.0 (3-18)
GISTs, malignancy (n)	43
Benign	33
Very low risk	8
Low risk	2
Mild risk	0
High risk	0
Leiomyoma (n)	3

TABLE 2: EFFECTS OF TUMOR SIZES AFFECTING THE ENTIRE EFR PROCESS

	Tumor size (cm)				P value
	< 1.0	1.0-2.0	2.0-3.0	> 3.0	
Number	21	18	5	2	
Gender (male/female)	10/11	7/11	4/1	0/2	.580
Location					.785
Gastric fundus	17	15	3	1	
Gastric corpus	3	3	2	1	
Gastric antrum	1	0	0	0	
Operation time (minutes)	40.9 ± 20.9	49.3 ± 20.1	96.0 ± 36.3	137.50 ± 46.1	.000
Titanium clips (n)	6.9 ± 3.8	7.1 ± 4.1	9.9 ± 4.3	16.0 ± 6.5	.361
GISTs					.001
Benign	20	16	5	2	
Risk of malignancy	15	14	4	0	
Very low	5	1	1	1	
Low	0	1	0	1	
Mild	0	0	0	0	
High	0	0	0	0	

pairing perforations was titanium clip repair. Several clips can close small defects^{11,12}.

Immediate closure of the gastric wall defects using metallic clips was performed in all 46 patients who received EFR. Consistent with the reports of Liu et al.¹³ gastric muscularis propria originating GISTs were mostly found at the gastric fundus. Also consistent with had been previously presented⁴. In addition, a novel over-the-scope clip (OTSC) system may be suitable for closure of various GI perforations¹⁴. OTSCs are increasingly used in the treatment of acute gastrointestinal perforations and fistulas^{15,16}. Furthermore, OTSCs are also used in submucosal tunneling endoscopy for resection of SMT in recent series¹⁷.

According to our experience, a too big GIST is not suitable for EFR. Incision of large lesions is associated with the potential high risk of suturing difficulty, long operative times, and complications during and after surgery. Preoperative computed tomography is very important, especially in patients with large lesions. In one patient with a partly nonintracavity GIST of 3.8 cm, EFR was successfully carried out in 138minutes; however, the tumor body was retrieved in a piecemeal manner. Outcomes of our study demonstrated that GISTs are most common in GISTs, which is similar to previous studies^{18,19}.

We found that the complete resection rate in our EFR group was 100%, with a 0% recurrence rate. Lying in a semi-reclining position, administration of an-

tibiotics and proton-pump inhibitors and nasogastric decompression can prevent peritoneal infection effectively²⁰. In the present study, none of the patients in our EFR group experienced peritonitis or intra-abdominal abscess. Our outcomes of EFR for gastric GISTs are encouraging, because of active perforation being performed and GISTs being successfully resected, as well as observing no severe post-EFR complications in all 46 patients.

Our study was limited by the Short-term follow-up. Because of the biological characteristics of GISTs, the follow-up period was relatively shorter in our study. Long-term follow-up is essential to assess complete removal and recurrence of GISTs.

CONCLUSION

In conclusion, we consider that in the treatment of the gastric gastrointestinal stromal tumor, full-thickness endoscopic resection is safe. We suggest that this technique can replace some surgical and it should be applied more widely in clinical practice to convey advantages.

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Disclosure Statement: The authors declare to have no conflicts of interest.

RESUMO

OBJETIVO: Este estudo revisou retrospectivamente 46 casos de tumores gástricos estromáticos gastrointestinais tratados por microcirurgia endoluminal endoscópica de ressecção completa (EFR) em nosso centro de endoscopia gastrointestinal. Pretendemos avaliar a EFR para o tratamento de tumores gastrointestinais estromáticos originários da muscularis própria.

MÉTODOS: Um total de 46 pacientes com tumores gástricos estromáticos gastrointestinais originários da camada muscular própria, de janeiro de 2012 a junho de 2015, foi tratado com EFR. Os pacientes foram acompanhados com gastroscópio e tomografia computadorizada (TC) para avaliação de efeitos terapêuticos e segurança.

RESULTADOS: A EFR foi realizada com sucesso para remover todos os tumores em 46 pacientes. O tempo médio de procedimento foi de 82,5±39,8 min (56-188 min). Exceto em três leiomiomas, exame patológico confirmou tumor estromal gastrointestinal (Gist) em 43 casos. Em nenhum paciente ocorreu sangramento, peritonite e outras complicações após EFR. Posteriormente, todos os pacientes foram acompanhados com gastroscópio após um, seis e 12 meses.

CONCLUSÕES: A EFR é eficaz e segura para pacientes com tumores gastrointestinais originários da camada muscular própria e tem a vantagem de ser um tratamento menos invasivo e com maior taxa de ressecção tumoral. Deve ser considerada para posterior aplicação.

PALAVRAS-CHAVE: Neoplasias gastrointestinais. Tumores do estroma gastrointestinal. Neoplasias de tecido conjuntivo. Células estromais. Gastrectomia. Gastroscopia. Laparoscopia.

REFERENCES

- Miettinen M, Majidi M, Lasota J. Pathology and diagnostic criteria of gastrointestinal stromal tumors (GISTs): a review. *Eur J Cancer*. 2002;38(Suppl 5):S39-51.
- Singer S, Rubin BP, Lux ML, Chen CJ, Demetri GD, Fletcher CD, et al. Prognostic value of KIT mutation type, mitotic activity, and histologic subtype in gastrointestinal stromal tumors. *J Clin Oncol*. 2002;20(18):3898-905.
- Ponsaing LG, Hansen MB. Therapeutic procedures for submucosal tumors in the gastrointestinal tract. *World J Gastroenterol*. 2007;13(24):3316-22.
- Huang LY, Cui J, Liu YX, Wu CR, Yi DL. Endoscopic therapy for gastric stromal tumors originating from the muscularis propria. *World J Gastroenterol*. 2012;18(26):3465-71.
- Huang LY, Cui J, Wu CR, Zhang B, Jiang LX, Xian XS, et al. Endoscopic full-thickness resection and laparoscopic surgery for treatment of gastric stromal tumors. *World J Gastroenterol*. 2014;20(25):8253-9.
- DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. *Ann Surg*. 2000;231(1):51-8.
- Joensuu H, Fletcher C, Dimitrijevic S, Silberman S, Roberts P, Demetri G. Management of malignant gastrointestinal stromal tumours. *Lancet Oncol*. 2002;3(11):655-64.
- Ikeda K, Sumiyama K, Tajiri H, Yasuda K, Kitano S. Evaluation of a new multitasking platform for endoscopic full-thickness resection. *Gastrointest Endosc*. 2011;73(1):117-22.
- Wang L, Ren W, Fan CQ, Li YH, Zhang X, Yu J, et al. Full-thickness endoscopic resection of nonintracavitary gastric stromal tumors: a novel approach. *Surg Endosc*. 2011;25(2):641-7.
- Mori H, Kobara H, Fujihara S, Nishiyama N, Ayagi M, Matsunaga T, et al. Establishment of the hybrid endoscopic full-thickness resection of gastric gastrointestinal stromal tumors. *Mol Clin Oncol*. 2015;3(1):18-22.
- Agrawal D, Chak A, Champagne BJ, Marks JM, Delaney CP. Endoscopic mucosal resection with full-thickness closure for difficult polyps: a prospective clinical trial. *Gastrointest Endosc*. 2010;71(6):1082-8.
- Kopelman Y, Siersema PD, Nir Y, Szold A, Bapaye A, Segol O, et al. Endoluminal compression clip: full-thickness resection of the mesenteric bowel wall in a porcine model. *Gastrointest Endosc*. 2009;70(6):1146-57.
- Liu BR, Song JT, Qu B, Wen JF, Yin JB, Liu W. Endoscopic muscularis dissection for upper gastrointestinal subepithelial tumors originating from the muscularis propria. *Surg Endosc*. 2012;26(11):3141-8.
- Matthes K, Jung Y, Kato M, Gromski MA, Chuttani R. Efficacy of full-thickness GI perforation closure with a novel over-the-scope clip application device: an animal study. *Gastrointest Endosc*. 2011;74(6):1369-75.
- Haito-Chavez Y, Law JK, Kratt T, Arezzo A, Verra M, Morino M, et al. International multicenter experience with an over-the-scope clipping device for endoscopic management of GI defects (with video). *Gastrointest Endosc*. 2014;80(4):610-22.
- Mennigen R, Senninger N, Laukoetter MG. Novel treatment options for perforations of the upper gastrointestinal tract: endoscopic vacuum therapy and over-the-scope clips. *World J Gastroenterol*. 2014;20(24):7767-76.
- Ye LP, Zhang Y, Mao XL, Zhu LH, Zhou X, Chen JY. Submucosal tunneling endoscopic resection for small upper gastrointestinal subepithelial tumors originating from the muscularis propria layer. *Surg Endosc*. 2014;28(2):524-30.
- Jeong ID, Jung SW, Bang SJ, Shin JW, Park NH, Kim DH. Endoscopic enucleation for gastric subepithelial tumors originating in the muscularis propria layer. *Surg Endosc*. 2011;25(2):468-74.
- Feng Y, Yu L, Yang S, Li X, Ding J, Chen L, et al. Endoluminal endoscopic full-thickness resection of muscularis propria-originating gastric submucosal tumors. *J Laparoendosc Adv Surg Tech A*. 2014;24(3):171-6.
- Zhou PH, Yao LQ, Qin XY. Endoscopic submucosal dissection for colorectal epithelial neoplasm. *Surg Endosc*. 2009;23(7):1546-51.

