Cancer Management and Research

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Endoscopic Submucosal Dissection of Gastrointestinal Stromal Tumours: A Retrospective Cohort Study

This article was published in the following Dove Press journal:
Cancer Management and Research

Ruonan Jiao*
Si Zhao*
Wei Jiang
Xin Wei
Guangming Huang

Medical Center for Digestive Diseases, The Second Affiliated Hospital of Nanjing Medical University, Nanjing, People's Republic of China

*These authors contributed equally to this work

Background: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms. Endoscopic submucosal dissection (ESD) has been used to remove submucosal tumours for many years. However, whether ESD can be recommended for the treatment of GISTs is still controversial. Therefore, we evaluated the efficacy and safety of ESD for treating GISTs.

Patients and Methods: We retrospectively analysed 75 GIST patients who underwent ESD in our hospital from January 2016 to December 2018, and the demographic data, clinical presentation of tumours, operative parameters, postoperative complications and length of hospital stay were analysed.

Results: Seventy-five patients successfully underwent en bloc resection, and 74 (98.7%) patients underwent complete resection of the lesions, with an average tumour size of 1.7 cm (range 0.3–6.0 cm). The median operation time was 84.8 min (range 20–180 min). Forty-two (56.0%) patients underwent endoscopic purse-string suture with no conversions to an open operation. The median postoperative length of hospitalization was 6.6 days (range 3–14 days). Out of a total of 75 GIST patients, 48 (64.0%) were considered very low risk, 19 (25.3%) were low risk, 5 (6.7%) were mild risk, and 3 (4.0%) were high risk. The median follow-up was 24.0 months (range 6–45 months). During hospitalization and follow-up, no complications, recurrence or metastasis occurred.

Conclusion: Based on our study from a medical centre, ESD is a safe and effective method for treating GISTs. However, further studies are needed.

Keywords: endoscopic submucosal dissection, gastrointestinal stromal tumour, prognosis

Background

Gastrointestinal stromal tumours (GISTs), originating from the interstitial cells of Cajal or their precursors, are the most common mesenchymal neoplasms. GISTs account for approximately 1–2% of gastrointestinal (GI) tract tumours with an estimated clinical incidence of 10 per one million population.[1,2] In general, GISTs can arise throughout the entire length of the GI tract, but the stomach and small intestine are the most common tumour locations, with approximate constituent ratios of 60% and 35%, respectively.[3] Pathogenetically, oncogenic mutations in KIT and/or platelet-derived growth factor receptor α (PDGFRA) may be the leading cause of GISTs, indicating that these tumours have potentially malignant behaviour.[4] Patients with GISTs tend to be diagnosed incidentally by gastroscopy, and gastrointestinal bleeding is a typical symptom of GISTs.

Correspondence: Guangming Huang
Email hgmnjmu@hotmail.com

submit your manuscript | www.dovepress.com
DovePress
http://doi.org/10.2147/CMAR.S252459

According to the current National Comprehensive Cancer Network (NCCN) guidelines, the mainstay of therapy for GISTs without metastasis is surgical resection with microscopically negative margins, including open or laparoscopic surgery.[5] However, some disadvantages inevitably exist, such as multiple complications, disruption of the integrity of the normal GI tract, and prolonged hospital stays.[6]

Most recently, with the rapid development and maturity of endoscopic techniques, an increasing number of GISTs are being removed by less invasive procedures, providing the opportunity for complete resection. In this respect, endoscopic resection appears to have advantages over surgery, including minimal trauma, shorter operative time, less intraoperative blood loss, and shorter postoperative hospital stays. Accumulating evidence has suggested that endoscopic submucosal dissection (ESD) is an effective and feasible method for treating early GISTs, especially for patients who cannot tolerate surgery or who have a tumour <2 cm.[7–9] An et al applied the ESD technique to successfully resect 168 GISTs located in the muscularis propria (MP) layer with a mean tumour size of 1.5 cm. Throughout the study, delayed bleeding occurred in 2 patients (1.2%) while no local recurrence or distant metastasis was observed during the follow-up period.[10] Even so, data regarding clinical outcomes based on clinicopathological features have not been reported in detail and are still controversial. Therefore, we conducted a retrospective study on ESD for GISTs to evaluate the efficacy and safety of ESD.

Patients and Methods

Patients

We conducted a retrospective study comprising 75 patients with GISTs who underwent ESD in the Medical Center for Digestive Diseases, the Second Affiliated Hospital of Nanjing Medical University between January 2016 and December 2018. The inclusion criteria were as follows: (1) had a postoperative pathological diagnosis of GIST; (2) had no distant metastases or other malignancies; and (3) agreed to provide informed consent and underwent ESD after learning the advantages and disadvantages of ESD; (4) patients who were unable to tolerate anaesthesia with tracheal intubation, or those who had previous coagulopathy, and those who were converted to open surgery during ESD were excluded.

ESD Procedure

ESD was performed under intravenous general anaesthesia. Preoperative gastroscopy (GIF-Q260J, CF-H260AI, Olympus) and ultrasound endoscopy (EG-530UR2, Fujifilm) were used to determine the tumour size, tumour quality and depth of invasion. Electrocoagulation marks were made with a dual knife (KD-650L, Olympus) or hybrid knife (KD-620LR, Olympus), 0.5–1.0 cm from the edge of the lesion. Multipoint injections of methylene blue and normal saline at the outer edge of the marked site were made to lift up the lesions and separate them from the intrinsic base layer, which is beneficial for ESD to ensure complete en bloc resection of the lesions from the mucosal layer and submucosa, and effectively reduce complications such as bleeding and perforation. The mucosa around the lesion was cut along the outer edge of the marked point, and the submucosal injection (NM-200L, Olympus) was repeated to ensure that the lesion site was well lifted; then, the lesion was completely peeled along the submucosa. If a small amount of bleeding was seen in the wound after dissection, haemostasis was achieved by electrocoagulation (FD-410LR; Olympus) and thermal biopsy forceps (SD-410LR, Olympus). If the wound area was too large, a purse-string suture with an endoloop (MAJ-254; Olympus) and clips (HX-610-135L, Olympus) were placed by dual-channel gastroscopy (GIF-2TQ260M; Olympus). After tightening the endoloop, the wound surface was closed simultaneously from the edge to the centre. All operations were performed by physicians who ranked higher than deputy physicians.

Postoperative Management

After the operation, patients who underwent gastric or duodenal surgery were placed in a semi-recumbent position, and fasted for 72 h. Gastrointestinal decompression, infection prevention, and acid suppression were routinely performed. The blood test results were reviewed, and normal gastrointestinal angiography was performed. For patients who had perforations during surgery, metal clips were placed under endoscopy to close wounds or purse-string sutures for wound closure, and the fasting time could be appropriately extended. Patients took proton pump inhibitors (PPIs) orally for 4 weeks after discharge from the hospital. Patients with mild- or high-risk GISTs were recommended to receive adjuvant imatinib therapy according to NCCN guidelines.

All resected specimens were subjected to immunohistochemical analysis. Immunohistochemical staining (CD117, CD34, DOG-1, SMA, S-100, Desmin, and Ki-67) was carried out to diagnose GISTs. The mitotic index at 50 HPF was recorded, and the size and location of the tumour were used to evaluate the risk of GIST. The risk classification standard of GISTs refers to the consensus from the National Institutes of Health.

Data Collection and Some Definitions

The following information was obtained: baseline and clinicopathological data including patient demographics, tumour size and location, operative parameters (duration, frequency of en bloc resection and endoscopic purse-string suture), postoperative complications, length of hospital stay and pathological data. En bloc resection was defined as the removal of the entire tumour in one piece under endoscopy. Complete resection referred to tumours removed en bloc with no residual tumour microscopically. In this study, complications were identified as perioperative or delayed bleeding, peritonitis, or perforation requiring surgical intervention. Intraoperative perforation that did not require surgical intervention and could be closed by endoscopic methods was not considered a complication.

Follow-Up

We conducted postoperative follow-up through outpatient service review or via telephone. Endoscopic monitoring and/or abdominal CT were/was performed to observe wound healing at 1, 3 or 6, and 12 months for the first year and then annually thereafter.

Statistical Analysis

All statistical analyses were conducted with SPSS version 23.0 software (SPSS Inc, Chicago, IL, USA). Continuous variables were expressed as the median (range) and categorical data were reported as number (n) and percentage (%).

Results

Patient Characteristics

The study included 25 males and 50 females, with a median age of 58.3 years (range: from 32 to 83 years) at diagnosis. The median body mass index (BMI) of the patients with GISTs was 23.3 (range: from 17.2 to 34.5). The most frequent locations were the gastric fundus (57.3%), followed by the body (20.0%), and the cardia (12.0%). There were 67 (89.3%) GIST patients with clinical symptoms, and abdominal pain (38.7%) and discomfort (26.7%) were the most common symptoms. The other common clinical symptoms were abdominal distention, gastrointestinal bleeding, acid reflux, belching or retrosternal pain, shapeless stool, and retrosternal discomfort. The average diameter of all lesions was 1.7 cm (range: from 0.3 to 6.0 cm). The clinicopathological features of the GIST patients are listed in Table 1.

Therapeutic Outcomes and Complications of ESD for GIST Patients

The therapeutic outcomes of ESD for GIST patients are shown in Table 2. All of the patients underwent ESD successfully, with a median procedure time of 84.8 min

Table 1 Patient Characteristics

Characteristic	
Age (years)	
Median	58.3
Range	32–83
Gender	
Male	25 (33.3)
Female	50 (66.7)
BMI (kg/m^2)	
Median	23.3
Range	17.2–34.5
Tumor location	
Esophagus	1 (1.3)
Cardia	9 (12.0)
Fundus	43 (57.3)
The junction	3 (4.0)
Body	15 (20.0)
Antrum	2 (2.7)
Duodenum	1 (1.3)
Colon	1 (1.3)
Tumor size (cm)	
Median	1.7
Range	0.3–6.0
Symptom	
Abdominal pain	29 (38.7)
Abdominal distention	4 (5.3)
Abdominal discomfort	20 (26.7)
Gastrointestinal bleeding	5 (6.6)
Acid reflux, belching or retrosternal pain	6 (8.0)
No symptom	8 (10.7)
Others	3 (4.0)

Abbreviation: BMI, body mass index.

Table 2 Therapeutic Outcomes and Complications of ESD for GIST Patients

Therapeutic Outcome/Complication	n (%)
En bloc resection	75 (100)
Complete resection	74 (98.7)
Endoscopic purse-string suture	42 (56.0)
Duration of procedure (min)	
Median	84.8
Range	20–180
Postoperative length of stay (days)	
Median	6.6
Range	3–14
Postoperative complication	
Bleeding/Perforation	0 (0)
Pathologic diagnosis	
Very low risk	48 (64.0)
Low risk	19 (25.3)
Mild risk	5 (6.7)
High risk	3 (4.0)
Mitotic index	
≤5/50HPF	71 (94.6)
5~10/50HPF	2 (2.7)
≥10/50HPF	2 (2.7)
Immunohistochemical staining	
CD117(+)	73 (97.3)
CD34(+)	75 (100)
DOG-1(+)	75 (100)
SMA(+)	52 (69.3)
S-100(+)	22 (29.3)
Desmin(+)	34 (45.3)
Ki-67	
≤5%	64 (85.3)
>5%	11 (14.7)
Recurrence	0 (0)

(range: 20–180 min). The rate of en bloc resection was 100%. Of the 75 lesions, 74 (98.7%) lesions that were removed with ESD showed complete resection without residual tumour microscopically. A total of 42 (56.0%) patients received endoscopic purse-string sutures. The median postoperative length of hospital stay was 6.6 days (range: 3–14 days). Microscopically, the mitotic index was calculated as equal to or less than 5/50 HPF in 71 (94.7%) patients and more than 5/50 HPF in 4 (5.3%) patients. There were 48 (64.0%) GIST patients considered very low risk, 19 (25.3%) patients considered low risk, 5 (6.7%) patients considered mild risk, and 3 (4.0%) considered high risk. In terms of immunohistochemical staining, the positive rates of CD117, CD34, DOG-1, SMA, S-100 and Desmin expression were 97.3%, 100%, 100%, 69.3%, 29.3% and 45.3%, respectively. Ki-67 expression was greater than 5% in 11 (14.7%) GIST patients, and equal to or less than 5% in 64 (85.3%) patients. During hospitalization, no severe complications such as bleeding peritonitis or perforation after ESD were observed.

Follow-Up Outcomes

The median follow-up was 24.0 months (range 6–45 months). During the follow-up period, gastroscopy, abdominal ultrasonography, or CT was performed, and no recurrence or metastasis was observed.

Discussion

GISTs are among the most common gastrointestinal subepithelial tumours. Some GISTs have a certain degree of malignant potential, and often cannot be diagnosed accurately before surgical or endoscopic treatment.[11] Resection is usually recommended when a GIST is found, due to the potentially malignant nature of the tumour. Resection can not only confirm the diagnosis, but also cure the disease if the lesion is completely removed.[12] ESD is a minimally invasive endoscopic/surgical technique for the radical resection of advanced lesions, including early gastrointestinal (GI) cancer. Surgery (laparoscopic or open) can be avoided if the ESD procedure achieves complete resection; otherwise, open surgery would be needed for resection. Recently, ESD has been increasingly recommended as the treatment of choice for GIST removal.[10,13] However, more clinical evidence is required to support the effectiveness of ESD for GISTs. The short-term outcomes of our study showed that complete resection by ESD was achieved in 75 lesions (98.7%), and no complications occurred. These short-term outcomes were consistent with previously published findings from a number of studies evaluating the use of ESD for the treatment of GISTs.[10,13-15] Compared with published studies, our study included a larger sample size to assess the safety and efficacy of ESD for GISTs, which increases the evidence and support for the use of ESD to treat GISTs. According to these outcomes, ESD is a feasible treatment option for GISTs. The risk of local recurrence or distant metastasis associated with ESD for GISTs is a major concern for some doctors. Recently, a number of studies using ESD to treat GISTs have

shown that the recurrence rate ranged from 0 to 6.7%.[7,10,13,16-23] In 3 of these studies with a mean/median follow-up period of ≥ 7 months, the recurrence rate ranged between 2.67% and 6.7%.[13,21,22] In our study, no patients experienced local recurrence or distant metastasis during a median follow-up period of 24 months. The differences in the rate of recurrence might be explained by the single-centre retrospective design, different inclusion criteria in different studies and different pathological grades of GISTs. Complete resection might be a pivotal factor for a low recurrence rate in patients with GISTs. Our experience with complete resection for GISTs can be concluded as follows. First, the size of the GISTs should be small. Reports have shown that ESD is a feasible, safe, and effective treatment for patients with gastrointestinal submucosal tumours (SMTs) ≤5 cm in diameter, especially those ≤2 cm.[9] If the tumour is too large, it is very difficult to remove the tumour en bloc with ESD, and the possibility of complications will be higher, because of the limitations of the gastrointestinal space and longer endoscopic resection time.[1,2] Second, the submucosal injection was repeated to ensure that the lesion site was well lifted, which might prevent the tumour mass from rupturing, and then the lesion was completely peeled along the submucosa. Third, GISTs need to be fully evaluated by endoscopic ultrasound (EUS) or/and computed tomography (CT) scans before ESD surgery. Chen et al[24] reported that CT features may be more useful than EUS features for predicting the tumour mitotic index, and preoperative imaging features can help predict the prognosis of patients with gastric GISTs. Exophytic/mixed growth pattern, irregular tumour shape, distant metastasis, and adjacent tissue invasion or serosal invasion identified by EUS and CT often predicts a high risk for complications. Whether these patients undergo ESD surgery requires careful evaluation. According to previous studies, the mitotic index is an important prognostic factor for GISTs.[25] Several studies found that even small GISTs (< 2.0 cm) with a high mitotic index have malignant potential.[26–28] In this study, we found that 2 (2.7%) GISTs had an index of 5–10 per 50 HPF, and 2 (2.7%) GISTs had an index of ≥ 10 per 50 HPF. For some patients with GISTs, classified as intermediate or high risk, adjuvant therapy (imatinib, etc.) and/or additional surgery are recommended to decrease the rate of recurrence after ESD.[29]

However, this study had some limitations. First, it is a single-centre, retrospective cohort study with possible selection bias. Second, most GIST cases occurred in the past 4 years, so we cannot comment on the long-term results. Finally, our department is a key clinical specialty clinic in Jiangsu Province, Ministry of Health Digestive Endoscopy Physician Diagnosis and Treatment Technology Training Base, and every ESD operations was performed by an experienced endoscopist. Therefore, the results in this study might not apply to all centres or hospitals. Thus, larger randomized, controlled, multicentre studies are needed to evaluate the efficacy and safety of ESD for GISTs.

Conclusions

These findings indicate that ESD might be an effective and safe therapeutic method for resecting GISTs. However, larger, long-term, randomized controlled, multicentre trials are needed.

Abbreviations

GISTs, Gastrointestinal stromal tumors; GI, gastrointestinal; NCCN, National Comprehensive Cancer Network; ESD, endoscopic submucosal dissection; MP, muscularis propria; EUS, endoscopic ultrasound; CT, computed tomography; BMI, body mass index; PDGFRA, platelet-derived growth factor receptor α; PPIs, proton pump inhibitors; SMTs, submucosal tumors.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics

Our study is retrospective, all patients have agreed to provide written informed consent before endoscopic therapy. The study was approved by the Ethics Committee of the Second Affiliated Hospital of Nanjing Medical University (2019KY117). And all research methods and processes are in accordance with the regulations of the Second Affiliated Hospital of Nanjing Medical University. We declare that all the patient data are confidential and in compliance with the Declaration of Helsinki.

Consent for Publication

All the listed authors have approved the submitted manuscript.

Acknowledgments

We thank all the clinicians who participated in the clinical study. We also appreciate Nature Research Editing Service

and American Journal Experts (AJE) for English language editing.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests.

References

1. Menge F, Jakob J, Kasper B, Smakic A, Gaiser T, Hohenberger P. Clinical presentation of gastrointestinal stromal tumors. *Visc Med*. 2018;34(5):335–340. doi:10.1159/000494303
2. Darnell A, Dalmau E, Pericay C, et al. Gastrointestinal stromal tumors. *Abdom Imaging*. 2006;31(4):387–399. doi:10.1007/s00261-004-0092-8
3. Buchs NC, Bucher P, Gervaz P, Ostermann S, Pugin F, Morel P. Segmental duodenectomy for gastrointestinal stromal tumor of the duodenum. *World J Gastroenterol*. 2010;16(22):2788–2792. doi:10.3748/wjg.v16.i22.2788
4. Chen W, Kuang Y, Qiu HB, et al. Dual targeting of insulin receptor and KIT in imatinib-resistant gastrointestinal stromal tumors. *Cancer Res*. 2017;77(18):5107–5117. doi:10.1158/0008-5472.CAN-17-0917
5. Casali PG, Abecassis N, Aro HT, et al. Gastrointestinal stromal tumours: ESMO-EURACAN clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2018;29(Suppl 4):iv267. doi:10.1093/annonc/mdy320
6. Kim HH. Endoscopic treatment for gastrointestinal stromal tumor: advantages and hurdles. *World J Gastrointest Endosc*. 2015;7(3):192–205. doi:10.4253/wjge.v7.i3.192
7. He Z, Sun C, Zheng Z, et al. Endoscopic submucosal dissection of large gastrointestinal stromal tumors in the esophagus and stomach. *J Gastroenterol Hepatol*. 2013;28(2):262–267. doi:10.1111/jgh.12056
8. Chen T, Lin ZW, Zhang YQ, et al. Submucosal Tunneling Endoscopic Resection vs Thoracoscopic Enucleation for Large Submucosal Tumors in the Esophagus and the Esophagogastric Junction. *J Am Coll Surg*. 2017;225(6):806–816. doi:10.1016/j.jamcollsurg.2017.09.002
9. He G, Wang J, Chen B, et al. Feasibility of endoscopic submucosal dissection for upper gastrointestinal submucosal tumors treatment and value of endoscopic ultrasonography in pre-operation assess and post-operation follow-up: a prospective study of 224 cases in a single medical center. *Surg Endosc*. 2016;30(10):4206–4213. doi:10.1007/s00464-015-4729-1
10. An W, Sun PB, Gao J, et al. Endoscopic submucosal dissection for gastric gastrointestinal stromal tumors: a retrospective cohort study. *Surg Endosc*. 2017;31(11):4522–4531. doi:10.1007/s00464-017-5511-3
11. Nishida T, Blay JY, Hirota S, Kitagawa Y, Kang YK. The standard diagnosis, treatment, and follow-up of gastrointestinal stromal tumors based on guidelines. *Gastric Cancer*. 2016;19(1):3–14. doi:10.1007/s10120-015-0526-8
12. Chen X, Cao H, Wang S, et al. Endoscopic submucosal dissection for silent gastric Dieulafoy lesions mimicking gastrointestinal stromal tumors: report of 7 cases-a case report series. *Medicine*. 2016;95(36):e4829. doi:10.1097/MD.0000000000004829
13. Meng Y, Li W, Han L, et al. Long-term outcomes of endoscopic submucosal dissection versus laparoscopic resection for gastric stromal tumors less than 2 cm. *J Gastroenterol Hepatol*. 2017;32(10):1693–1697. doi:10.1111/jgh.13768
14. Tan Y, Tan L, Lu J, Huo J, Liu D. Endoscopic resection of gastric gastrointestinal stromal tumors. *Transl Gastroenterol Hepatol*. 2017;2:115. doi:10.21037/tgh.2017.12.03
15. Yu C, Liao G, Fan C, et al. Long-term outcomes of endoscopic resection of gastric GISTs. *Surg Endosc*. 2017;31(11):4799–4804. doi:10.1007/s00464-017-5557-2
16. Lee IL, Lin PY, Tung SY, Shen CH, Wei KL, Wu CS. Endoscopic submucosal dissection for the treatment of intraluminal gastric subepithelial tumors originating from the muscularis propria layer. *Endoscopy*. 2006;38(10):1024–1028. doi:10.1055/s-2006-944814
17. Bialek A, Wiechowska-Kozlowska A, Pertkiewicz J, et al. Endoscopic submucosal dissection for treatment of gastric subepithelial tumors (with video). *Gastrointest Endosc*. 2012;75(2):276–286. doi:10.1016/j.gie.2011.08.029
18. 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):3141–3148. doi:10.1007/s00464-012-2305-5
19. Chu YY, Lien JM, Tsai MH, et al. Modified endoscopic submucosal dissection with enucleation for treatment of gastric subepithelial tumors originating from the muscularis propria layer. *BMC Gastroenterol*. 2012;12:124. doi:10.1186/1471-230X-12-124
20. Sun C, He Z, Zheng Z, et al. Endoscopic submucosal dissection for gastrointestinal mesenchymal tumors adjacent to the esophagogastric junction: we need to do more. *J Laparoendosc Adv Surg Tech A*. 2013;23(7):570–577. doi:10.1089/lap.2012.0462
21. Meng Y, Cao C, Song S, Li Y, Liu S. Endoscopic band ligation versus endoscopic submucosal dissection and laparoscopic resection for small gastric stromal tumors. *Surg Endosc*. 2016;30(7):2873–2878. doi:10.1007/s00464-015-4571-5
22. Balde AI, Chen T, Hu Y, et al. Safety analysis of laparoscopic endoscopic cooperative surgery versus endoscopic submucosal dissection for selected gastric gastrointestinal stromal tumors: a propensity score-matched study. *Surg Endosc*. 2017;31(2):843–851. doi:10.1007/s00464-016-5042-3
23. Guo Y, Jing X, Zhang J, et al. Endoscopic removal of gastrointestinal stromal tumors in the stomach: a single-center experience. *Gastroenterol Res Pract*. 2019;2019:3087298. doi:10.1155/2019/3087298
24. Chen T, Xu L, Dong X, et al. The roles of CT and EUS in the preoperative evaluation of gastric gastrointestinal stromal tumors larger than 2 cm. *Eur Radiol*. 2019;29(5):2481–2489. doi:10.1007/s00330-018-5945-6
25. Akahoshi K, Oya M, Koga T, Shiratsuchi Y. Current clinical management of gastrointestinal stromal tumor. *World J Gastroenterol*. 2018;24(26):2806–2817. doi:10.3748/wjg.v24.i26.2806
26. Soreide K. Cancer biology of small gastrointestinal stromal tumors (<2 cm): what is the risk of malignancy? *Eur J Surg Oncol*. 2017;43(7):1344–1349. doi:10.1016/j.ejso.2017.01.240
27. Tokumoto N, Tanabe K, Misumi T, Fujikuni N, Suzuki T, Ohdan H. The usefulness of preoperative 18FDG positron-emission tomography and computed tomography for predicting the malignant potential of gastrointestinal stromal tumors. *Dig Surg*. 2014;31(2):79–86. doi:10.1159/000357149
28. Yang J, Feng F, Li M, et al. Surgical resection should be taken into consideration for the treatment of small gastric gastrointestinal stromal tumors. *World J Surg Oncol*. 2013;11:273. doi:10.1186/1477-7819-11-273
29. Joensuu H. Adjuvant treatment of GIST: patient selection and treatment strategies. *Nat Rev Clin Oncol*. 2012;9(6):351–358. doi:10.1038/nrclinonc.2012.74