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ORIGINAL ARTICLE

Safety of laparoscopic local resection for gastrointestinal stromal tumors near the esophagogastric junction

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Abstract

Purpose Laparoscopic local resection for gastrointestinal stromal tumors (GISTs) near the esophagogastric junction (EGJ) increases the risk of injuring the EGJ. We investigated the safety of laparoscopic local resection for GISTs near the EGJ according to the distance from the EGJ to the tumor edge.

Methods We retrospectively evaluated 40 patients who had undergone laparoscopic local resection for GISTs near the EGJ between January 2009 and December 2019. After excluding 1 patient who had undergone right colectomy at the same time, 39 patients were classified according to distance of the GIST from the EGJ in the Near group (0–2.0 cm; $n=16$) and the Far group (2.1–5.0 cm; $n=23$).

Results We found no marked differences in the operation time, blood loss, length of postoperative hospital stay, or postoperative complication rate in the two groups. Anastomotic leakage occurred with a tumor located on the EGJ. Three tumors recurred in the Near group, and all of them were located on the EGJ.

Conclusion Except for GISTs located on the EGJ, laparoscopic local resection for GISTs near the EGJ can be performed safely with few postoperative complications and a low risk of recurrence.

Keywords Gastrointestinal stromal tumors · Esophagogastric junction · Laparoscopic local resection · Complication · Recurrence

Introduction

Gastrointestinal stromal tumors (GISTs) are gastric submucosal tumors. Although GISTs arise most commonly in the stomach, GISTs in general are rare [1]. Surgery is the first choice of treatment for resectable stomach GISTs. Such surgery entails complete resection of the tumor with a negative gross margin without disrupting the capsule of the tumor. Because stomach GISTs rarely progress to lymph node metastasis, laparoscopic local resection is typically performed [2, 3]. However, when GISTs arise near the esophagogastric junction (EGJ), local resection carries a risk of deformity and stenosis of the EGJ or may cause gastroesophageal reflux disease; thus, surgery for such GISTs is considered difficult [4, 5]. In attempts to avoid injuring the EGJ, the resection margin may be positive if resection of nearby GISTs is insufficient.

Some reports have verified the safety and effectiveness of laparoscopic local gastrectomy for GISTs near the EGJ [4–6]. We have performed laparoscopic local resection of such GISTs regardless of the distance from the EGJ. When GISTs are very close to the EGJ, local resection is more difficult because the resection or suturing lines often extend to the EGJ. The incidence of complications can therefore increase when the tumor is located close to the EGJ. Furthermore, an insufficient resection margin around the EGJ as a result of efforts to avoid injuring the EGJ may lead to local recurrence of nearby GISTs.

No report has yet compared the safety of laparoscopic local resection based on the distance of GISTs from the EGJ [4, 5, 7, 8]. Therefore, in the present study, we newly assessed the incidence of complications and recurrence of GISTs near the EGJ in patients who had undergone

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laparoscopic local gastrectomy according to the distance from the EGJ to the oral edge of the tumor.

Methods

Patients

We retrospectively reviewed a prospectively compiled surgical database to identify 99 consecutive patients who underwent laparoscopic local resection for primary GISTs at Kobe University Hospital between January 2009 and December 2019. We then extracted the 40 patients whose GISTs were located near the EGJ. Such GISTs were defined as tumors for which the distance from the EGJ to the tumor edge was within 5 cm. When the distance from the EGJ to the tumor oral edge was expected to be within 5 cm by preoperative esophagogastroduodenoscopy, we routinely measured the distance using endoscopic measuring forceps.

To evaluate the intraoperative parameters and postoperative outcomes related to laparoscopic local resection for the GIST itself, one patient who had undergone combined surgery with right colectomy was excluded. The remaining 39 patients were then divided into 2 groups according to the distance from the EGJ to the oral edge of the tumor. Those in whom the distance was ≤ 2 cm were classified as the Near group ($n = 16$), and those in whom the distance was > 2 cm were classified as the Far group ($n = 23$). The patient flow diagram of this study is shown (Fig. 1).

Informed consent was obtained from all patients for the use of the clinical data in this study, and the study was approved by the Kobe University Institutional Review Board (no. B210039).

Surgical technique

During laparoscopic surgery, the surgeon stood on the patient's right-hand side, the assistant on the left side, and the endoscopist between the legs of the patient. An umbilical incision was made with the standard cut-down technique, and the first trocar was then inserted. Carbon dioxide was insufflated through this port, and the pressure

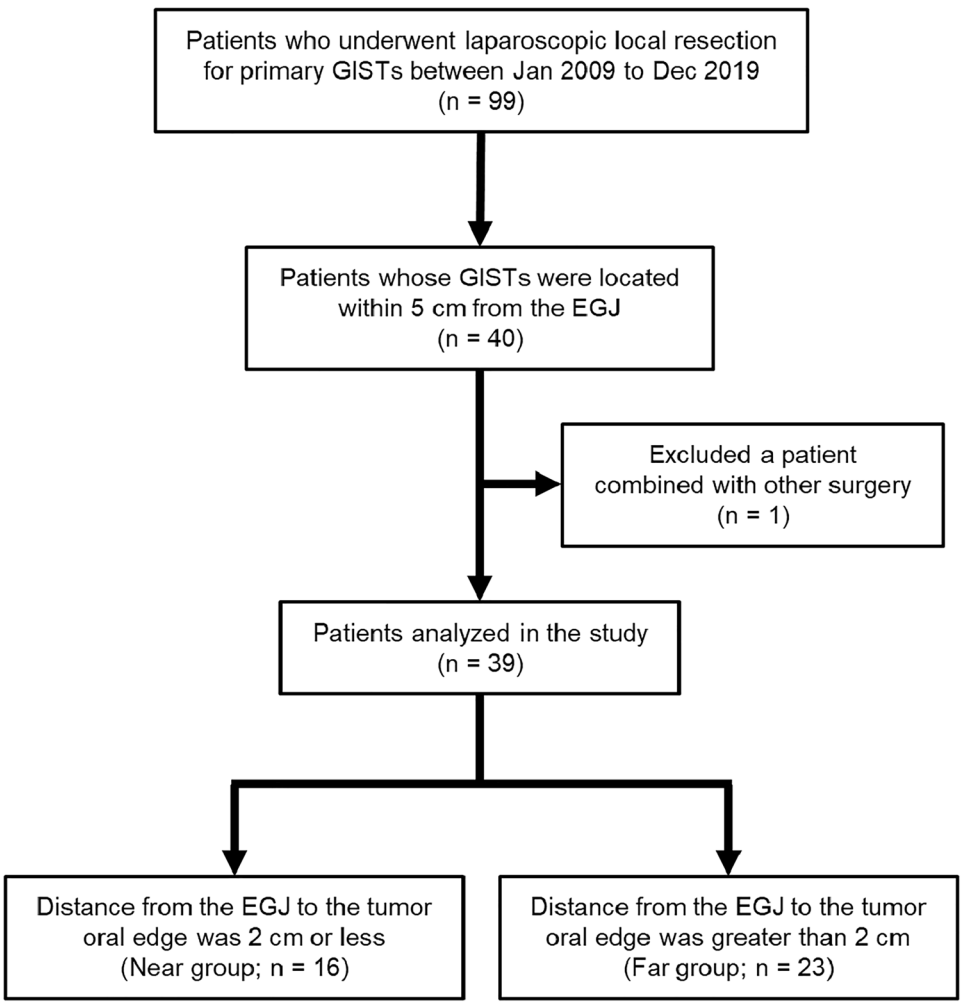

Fig. 1 Patient flow diagram. *EGJ*, esophagogastric junction; *GIST*, gastrointestinal stromal tumor

was maintained at 10 mmHg. The endoscope was inserted through this port. Three other ports were established in the upper left, upper right, and lower right regions of the abdomen, and an additional port was inserted in the lower left region if necessary.

Until July 2014, laparoscopic wedge resection (LWR) was performed for all GISTs in the stomach. Since August 2014, laparoscopic and endoscopic cooperative surgery (LECS) has been performed for GISTs in the stomach with endogastric and transgastric growth patterns, and LWR continues to be performed for such GISTs with an exogastric growth pattern.

The location of the tumor was confirmed intraoperatively by esophagogastroduodenoscopy. If necessary, blood vessels and any part of the omentum around the tumor were divided with laparoscopic coagulation shears. In LECS, we injected physiological saline into the submucosa around the tumor, keeping a 2 mm margin from the tumor edge. We then used a FlushKnife BTS (Fujifilm, Tokyo, Japan) to make an incision in the stomach wall all around to the submucosa endoscopically and laparoscopic coagulation shears to incise the remaining layers laparoscopically. In LWR, we used laparoscopic coagulation shears to incise the full-thickness layer of the gastric wall over half or one-third of the circumference of the tumor laparoscopically. During the incision of the gastric wall, we observed by endoscopy whether or not a sufficient margin from the tumor edge could be secured. To prevent incision of the tumor, we placed stay sutures on the normal area of the gastric wall outside the tumor margin, and a plastic bag was inserted into the abdominal cavity to collect the specimen.

We then resected the tumor using laparoscopic coagulation shears or linear staplers. During the resection, an endoscope was inserted into the stomach as a bougie of the EGJ. We were also careful not to injure the EGJ during the procedure. The resected specimen was placed in the plastic bag immediately after resection. We then laparoscopically viewed the area around the suture or the staple line to confirm the absence of bleeding or leakage. At the same time, we confirmed by endoscopy that no bending or stenosis of the EGJ had occurred. We closed the defect of the gastric wall with 3–0 polyglactin (Vicryl™) sutures or linear staplers.

Indications for postoperative adjuvant chemotherapy

Postoperative adjuvant chemotherapy was actively recommended for all patients classified as high risk according to the modified Fletcher classification [9]. Thus, once informed consent was obtained, postoperative adjuvant chemotherapy was performed.

Statistical analyses

To perform statistical analyses of the patients' background characteristics and surgical data, we used the JMP software program version 14.0 (SAS Institute Inc., Cary, NC, USA). Data for continuous variables were calculated as the means ± standard deviations, and Student's *t* test was used for comparisons between the groups. Categorical variables were calculated as numbers and percentages of patients and compared in Fisher's exact test. A P value < 0.05 was considered statistically significant.

Results

The background characteristics and surgical procedures for all 39 patients in the Near and Far groups are summarized in Table 1. We found no statistically significant differences between the two groups in terms of the sex, age, tumor size, preoperative pathological diagnosis, growth pattern, or pathological horizontal margin. However, we found a significant difference in tumor localization between the groups ($P < 0.01$): all tumors located in the greater curvature were found in patients in the Far group, and the number of tumors located on the posterior wall was greater in the Far group than in the Near group.

The intraoperative parameters and postoperative outcomes are summarized in Table 2. The surgical procedure selected did not differ markedly between the two groups, and we found no significant difference in the conversion rate between the groups, although one patient in the Near group required conversion to an open procedure. We found no marked differences in the operation time, amount of blood loss, length of postoperative hospital stay, or postoperative complication rate between the groups. However, the time until the start of oral intake was significantly longer in the Near group (3.9 ± 1.4 days) than in the Far group (3.2 ± 0.7 days; $P = 0.047$), and the recurrence rate was also significantly higher in the Near group (18.8%) than in the Far group (0%; $P = 0.038$). All three cases of recurrence were in the Near group.

Of the 39 GISTs near the EGJ, 4 were located on the EGJ. Clinical characteristics and outcomes are showed in Table 3. Three of them had experienced tumor recurrences. Two recurrences were liver metastases, and the other resulted from peritoneal dissemination. The remaining tumor that did not recur instead caused anastomotic leakage.

Discussion

In most cases, resection or suturing with a linear stapler unavoidably involves the EGJ when the distance between the tumor edge and the EGJ is within 2 cm. Therefore, we

Table 1 A comparison of the characteristics of patients in the Near and Far groups

Factors	All ($N=39$)	Near group ($n=16$)	Far group ($n=23$)	P value
Sex				0.5
Male	17 (43.6%)	8 (50%)	9 (39.1%)	
Female	22 (56.4%)	8 (50%)	14 (60.9%)	
Age (years)	67.4 ± 11.1	71.5 ± 10.0	64.6 ± 11.1	0.31
Tumor size (cm)	3.8 ± 1.5	4.2 ± 2.0	3.5 ± 1.0	0.15
Distance from the EGJ (cm)	2.9 ± 1.4	1.5 ± 0.8	3.8 ± 0.8	< 0.0001*
Preoperative pathological diagnosis				0.49
GIST	35 (89.7%)	15 (93.8%)	20 (87.0%)	
Unknown	4 (10.3%)	1 (6.3%)	3 (13.0%)	
Tumor location				0.001*
EGJ	4 (10.3%)	4 (25.0%)	0 (0%)	
Greater curvature	7 (17.9%)	0 (0%)	7 (30.4%)	
Lesser curvature	6 (15.4%)	2 (12.5%)	4 (17.4%)	
Anterior wall	13 (33.3%)	9 (56.3%)	4 (17.4%)	
Posterior wall	9 (23.1%)	1 (5.7%)	8 (34.8%)	
Tumor growth pattern				0.93
Endogastric	20 (51.3%)	8 (50.0%)	12 (52.2%)	
Exogastric	8 (20.5%)	3 (18.8%)	5 (21.7%)	
Transgastric	11 (28.2%)	5 (31.3%)	6 (26.1%)	
Pathological horizontal margin				
Positive	0 (0%)	0 (0%)	0 (0%)	
Negative	39 (100%)	16 (100%)	23 (100%)	

The number of patients and percentages are listed for categorical values. Means and standard deviations are listed for continuous variables. The Near group comprised patients in whom the distance between the tumor edge and the EGJ was ≤ 2 cm, and the Far group comprised patients in whom this distance was > 2 cm

EGJ esophagogastric junction, *GIST* gastrointestinal stromal tumor

*Statistically significant ($P<0.05$)

hypothesized that the rate of complications such as EGJ stenosis and gastroesophageal reflux disease caused by EGJ dysfunction would be increased in patients with tumors close to the EGJ. However, none of these issues occurred in our patients. We believe that this is because when the EGJ was close to the tumor edge, we actively selected to perform hand-sewn suturing, which minimized the extent of resection and deformation, rather than using a stapler for resection and suturing, which tends to result in excessive resection and deformation. In addition, in all cases, we routinely observed the resection with endoscopy to keep the resection range from being excessive, and the endoscope was passed through the stomach and used as an EGJ bougie during suturing. These practices helped overcome the technical difficulty of laparoscopic local resection for GISTs near the EGJ. Oral intake was started later in patients from the Near group than in those from the Far group. Surgeons' likely desire to carefully start ingestion in cases where the tumor is close to the EGJ, and complications probably did not influence this decision in the present study.

Although a total of six complications occurred in the patients in this study, we found no marked difference between groups in the incidence of complications. According to the Clavien–Dindo classification [10], five of them were grade I or II, while only one case of anastomotic leakage was grade IIIb. This anastomotic leakage occurred in a case where the tumor edge was on the EGJ. Because the oral edge of the resection line affected the esophagus, an esophagogastric anastomosis was created in that case. This may increase the risk of anastomotic leakage compared to gastrogastric anastomosis. Furthermore, suturing in the limited surgical field of the lower mediastinum is also considered to increase the risk of anastomotic leakage. Thus, laparoscopic local resection, especially for tumors located very close to the EGJ, should be performed only by highly experienced surgeons.

From an oncological perspective, the pathological horizontal margin was negative in all cases. This good result is attributed to conducting endoscopic observation when determining the resection line and during resection itself. However, a total of three tumors recurred in our study, all of which were located on the EGJ. In addition, two of them were large GISTs (diameter > 5 cm) with high malignant potential. Laparoscopic local resection of GISTs located

Table 2 A comparison of the intraoperative parameters and postoperative outcomes in the Near and Far groups

Factors	All patients ($N=39$)	Near group ($n=16$)	Far group ($n=23$)	P value
Procedure				0.57
Laparoscopic wedge resection	24 (61.5%)	9 (56.3%)	15 (65.2%)	
Laparoscopic and endoscopic cooperative surgery	15 (38.5%)	7 (43.7%)	8 (34.8%)	
Length of operation (min)	184.1 ± 73.5	187.8 ± 79.0	181.4 ± 71.1	0.79
Blood loss (mL)	27.9 ± 106.5	48.1 ± 154.6	13.9 ± 52.6	0.33
Conversion to open surgery	1 (2.6%)	1 (6.3%)	0 (0%)	0.23
Complications[a]	6 (15.4%)	4 (25.0%)	2 (8.7%)	0.17
Grade I	1 (2.6%)	1 (6.3%)	0 (0%)	
Wound infection	1 (2.6%)	1 (6.3%)	0 (0%)	
Grade II	4 (10.3%)	2 (12.5%)	2 (8.7%)	
Atelectasis	2 (5.1%)	1 (6.3%)	1 (4.3%)	
Urinary tract infection	1 (2.6%)	1 (6.3%)	0 (0%)	
Enteritis	1 (2.6%)	0 (0%)	1 (4.3%)	
Grade III	1 (2.6%)	1 (6.3%)	0 (0%)	
Anastomotic leakage	1 (2.6%)	1 (6.3%)	0 (0%)	
Resumption of oral intake (days)	3.5 ± 1.1	3.9 ± 1.4	3.2 ± 0.7	0.047*
Postoperative hospital stay (days)	11.6 ± 6.5	13.5 ± 9.3	10.3 ± 3.1	0.13
Disruption of tumor capsule	1 (2.6%)	1 (6.3%)	0 (0%)	0.23
Modified Fletcher classification				0.07
Very low	1 (2.6%)	1 (6.3%)	0 (0%)	
Low	26 (66.7%)	8 (50.0%)	18 (78.3%)	
Moderate	9 (23.1%)	4 (25.0%)	5 (21.7%)	
High	3 (7.7%)	3 (18.8%)	0 (0%)	
Postoperative adjuvant chemotherapy	2 (5.1%)	2 (12.5%)	0 (0%)	0.09
Tumor recurrence	3 (7.7%)	3 (18.8%)	0 (0%)	0.038*
Follow-up period (months)	33.1 ± 30.7	33.6 ± 28.6	33.1 ± 32.8	0.88

The number of patients and percentage are listed for categorical values. Means and standard deviations are listed for continuous variables. The Near group comprised patients in whom the distance between the tumor edge and the EGJ was ≤ 2 cm, and the Far group comprised patients in whom this distance was > 2 cm

*Statistically significant ($P<0.05$)

[a]Evaluated according to the Clavien–Dindo classification

Table 3 Clinical characteristics and outcomes of the four patients with GISTs located on the EGJ

Case	Sex	Age (years)	Tumor size (cm)	Complications	Disruption of tumor capsule	Mitotic Count/50 HPFs	Modified Fletcher Classification	Postoperative adjuvant chemotherapy	Recurrence
1	Female	78	8.5	Wound infection	Yes	32	High	Imatinib	Liver metastases
2	Female	74	7.4	None	No	20	High	Imatinib	Liver metastases
3	Male	88	4.0	None	No	10	Moderate	None	Peritoneal dissemination
4	Male	79	4.0	Anastomotic leakage	No	10	Moderate	None	None

EGJ esophagogastric junction, *GIST* gastrointestinal stromal tumor, *HPF* high-power field

on the EGJ requires operation in a limited surgical field, and if the lesions is larger than 5 cm, the surgical difficulty is even higher. Previous reports have demonstrated that large GISTs tend to have high malignant potential [11]. Therefore, especially for large GISTs, less invasive surgery without complications is a better foundation for ensuring the early start of postoperative adjuvant chemotherapy. However, peritoneal dissemination occurred in one of our

patients with a GIST located on the EGJ that was < 5 cm in diameter. The tumor capsule was not disrupted in the intraoperative findings or operative video, and the surgical margin was negative.

One reason for tumor recurrence may be accidental exposure of the tumor to the abdominal cavity during the procedure. Because laparoscopic local resection involves opening the stomach with a full-thickness incision, surgeons should remember that peritoneal or local recurrence can arise regardless of careful intraoperative management to avoid tumor disruption during surgery. Surgical techniques for removing lesions without opening the stomach, such as a combination of laparoscopic approaches to neoplasia with the non-exposure technique (CLEAN-NET) and non-exposed endoscopic wall-inversion surgery (NEWS), have been devised and implemented [12, 13]. Because these procedures do not entail opening the stomach with a full-thickness incision, surgical and oncological contamination by the gastric contents during surgery can be minimized. In most of the reports, however, CLEAN-NET has been indicated only for GISTs located > 2 cm from the EGJ, and NEWS has been indicated only for GISTs smaller than 3 cm in size [13–15]; all of our patients who experienced recurrence fell outside these indications.

Although there is no evidence-based approach for GISTs located on the EGJ, especially in tumors larger than 5 cm, surgeons should carefully select the best procedures, including open local resection and laparoscopic proximal gastrectomy as well as laparoscopic local resection, to prevent complications and tumor recurrence.

Several limitations associated with the present study warrant mention. First, because GISTs near the EGJ are rare, the sample size was small; nevertheless, it was larger than those of previous studies of GISTs near the EGJ. Second, the safety of laparoscopic local resection for GISTs near the EGJ must be confirmed by further studies, such as comparisons of laparoscopic local resection with open local resection and of laparoscopic local resection with laparoscopic proximal gastrectomy.

In conclusion, except for GISTs located on the EGJ, laparoscopic local resection of GISTs near the EGJ can be performed safely with few postoperative complications and a low risk of recurrence.

Declarations

Conflict of interest Kohei Tanigawa and other co-authors have no conflicts of interest.

References

1. Soreide K, Sandvik OM, Soreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): a systematic review of population-based cohort studies. Cancer Epidemiol. 2016;40:39–46.
2. Kong SH, Yang HK. Surgical treatment of gastric gastrointestinal stromal tumor. J Gastric Cancer. 2013;13:3–18.
3. Goh BK, Goh YC, Eng AK, Chan WH, Chow PK, Chung YF, et al. Outcome after laparoscopic versus open wedge resection for suspected gastric gastrointestinal stromal tumors: a matched-pair case-control study. Eur J Surg Oncol. 2015;41:905–10.
4. Sakamoto Y, Sakaguchi Y, Akimoto H, Chinen Y, Kojo M, Sugiyama M, et al. Safe laparoscopic resection of a gastric gastrointestinal stromal tumor close to the esophagogastric junction. Surg Today. 2012;42:708–11.
5. Xiong W, Zhu J, Zheng Y, Luo L, He Y, Li H, et al. Laparoscopic resection for gastrointestinal stromal tumors in esophagogastric junction (EGJ): how to protect the EGJ. Surg Endosc. 2018;32:983–9.
6. Kanaji S, Nakamura T, Yamamoto M, Imanishi T, Suzuki S, Tanaka K, et al. Successful laparoscopic gastric resection and safe introduction of a single-incision technique for gastric submucosal tumors located near the esophagogastric junction. Surg Today. 2015;45:209–14.
7. Matsui H, Nabeshima K, Okamoto Y, Nakamura K, Kondoh Y, Makuuchi H, et al. Fundic rotation technique: a useful procedure for laparoscopic exogastric resection of gastric submucosal tumors located on the posterior wall near the esophagogastric junction. Tokai J Exp Clin Med. 2011;36:152–8.
8. Xiong W, Xu Y, Chen T, Feng X, Zhou R, Wan J, et al. Laparoscopic vs open surgery for gastrointestinal stromal tumors of esophagogastric junction: a multicenter, retrospective cohort analysis with propensity score weighting. Chin J Cancer Res. 2021;33:42–5.
9. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol. 2006;23:70–83.
10. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–13.
11. 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;231:51–8.
12. Inoue H, Ikeda H, Hosoya T, Yoshida A, Onimaru M, Suzuki M, et al. Endoscopic mucosal resection, endoscopic submucosal dissection, and beyond: full-layer resection for gastric cancer with nonexposure technique (CLEAN-NET). Surg Oncol Clin N Am. 2012;21:129–40.
13. Mitsui T, Yamashita H, Aikou S, Niimi K, Fujishiro M, Seto Y. Non-exposed endoscopic wall-inversion surgery for gastrointestinal stromal tumor. Transl Gastroenterol Hepatol. 2018;3:17.
14. Onimaru M, Inoue H, Ikeda H, Abad MRA, Quarta Colosso BM, Shimamura Y, et al. Combination of laparoscopic and endoscopic approaches for neoplasia with non-exposure technique (CLEAN-NET) for gastric submucosal tumors: updated advantages and limitations. Ann Transl Med. 2019;7:582.
15. Aoyama J, Goto O, Kawakubo H, Mayanagi S, Fukuda K, Irino T, et al. Clinical outcomes of non-exposed endoscopic wall-inversion surgery for gastric submucosal tumors: long-term follow-up and functional results. Gastric Cancer. 2020;23:154–9.