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Laparoscopic Wedge Resection for Gastrointestinal Stromal Tumors of the Stomach: Initial Experience

Yoshinari Mochizuki[1], Yasuhiro Kodera[2], Michitaka Fujiwara[2], Seiji Ito[1], Yoshitaka Yamamura[1], Akira Sawaki[3], Kenji Yamao[3], and Tomoyuki Kato[1]

Departments of [1]Gastroenterological Surgery and [3]Gastroenterology, Aichi Cancer Center Hospital, Nagoya, Japan
[2]Department of Surgery II, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Abstract

Purpose. Surgery for gastrointestinal stromal tumors (GIST) of the stomach is now frequently performed using a laparoscopic approach. We investigated the feasibility and effectiveness of laparoscopy in the management of GIST of the stomach.

Methods. We reviewed the records of 12 consecutive patients who underwent laparoscopic surgery for GIST between April 2000 and April 2004, and compared their short-term outcomes with those of patients who underwent open surgery. All laparoscopic wedge resections were done using stapling devices and 3–4 trocars, often with the aid of intraoperative gastroscopy. We examined all patients preoperatively using various diagnostic modalities, including endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA). A laparoscopic approach was not indicated if the tumor was located near the cardia or pylorus or if it was ≧5 cm in diameter.

Results. A specific diagnosis of GIST was obtained preoperatively by EUS-FNA in 10 of the 12 patients. The median diameter of the lesion was 2.7 cm (range, 1.5–4.8 cm). Although intraoperative complications were encountered in two patients, conversion to open surgery was not required, and we were able to perform complete tumor excision with negative surgical margins in all patients. The median operative time was 100 min (range, 65–180 min), similar to that for open surgery. First flatus was passed earlier, and the interval to resuming oral intake was shorter than after open surgery. No major postoperative complications such as leakage developed, and the median postoperative hospital stay was 7 days (range, 5–12 days). All diagnoses made by EUS-FNA were confirmed by immunohistopathological evaluation of resected specimens.

Conclusion. Laparoscopic wedge resection is a feasible treatment option for GISTs of the stomach if the lesion is <5 cm in diameter.

Key words Gastrointestinal stromal tumor · Stomach · Laparoscopic surgery

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Introduction

As a result of mass screenings for gastric cancer, submucosal tumors of the stomach are being detected more frequently in Japan. About 70% of these lesions are mesenchymal tumors, such as gastrointestinal stromal tumors (GIST).[1] A preoperative pathological diagnosis of GIST cannot be made by endoscopic biopsy because of its submucosal location, but endoscopic ultrasonography with fine-needle aspiration (EUS-FNA) allows for easy diagnosis.[2] However, GISTs display a wide clinical spectrum from benign to obviously malignant,[3] and preoperative assessment of the degree of potential malignancy remains difficult.

Despite the development of a new chemotherapeutic agent, imatinib mesylate, surgery remains the only curative treatment for primary GIST. The rationale for resection is to ensure that the tumor is removed with a negative surgical margin, since GIST does not spread beyond the surrounding gastric wall and has a low incidence of lymph node metastasis.[4–8] Thus, wedge resection has long been the standard treatment for gastric GIST. Investigators have also recently begun to explore less invasive options to improve quality of life without compromising curability. Laparoscopic surgery is considered less invasive than open surgery, resulting in faster recovery and an earlier return to daily life. The benefits of laparoscopic cholecystectomy have encouraged surgeons to expand this approach to include other procedures, including herniorrhaphy[9] and surgery for

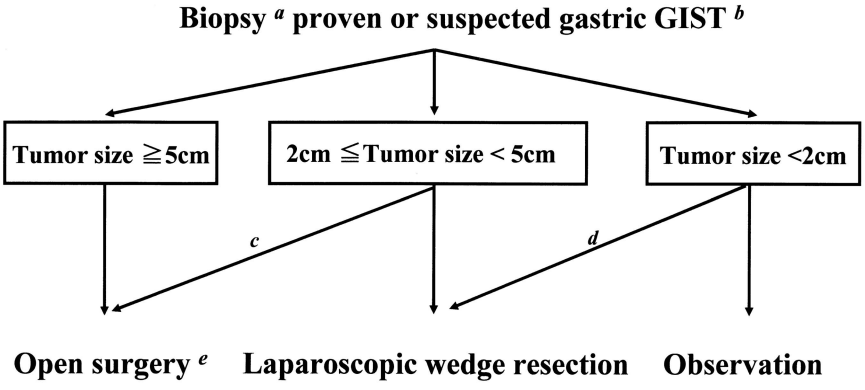

Fig. 1. Aichi Cancer Center Hospital algorithm for the surgical management of gastric gastrointestinal stromal tumors (GIST). *a*, specimen obtained by endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA); *b*, based on characteristic features on endoscopic ultrasonography (EUS), computed tomography (CT), or endoscopy; *c*, located near the cardia or pylorus; *d*, malignant pattern based on EUS findings; *e*, surgical procedures — wedge resection, proximal gastrectomy, distal gastrectomy, or total gastrectomy

gastroesophageal reflux disease.[10] Wedge resection of the stomach to remove submucosal tumors including GIST is also considered to be a relatively simple operation that can be performed laparoscopically.[11–14] We conducted this study to investigate the feasibility and effectiveness of laparoscopic surgery for GISTs of the stomach.

Patients and Methods

Patients

We reviewed the retrospective gastric surgery database at Aichi Cancer Center and found 12 consecutive patients who underwent laparoscopic wedge resection for mesenchymal tumors of the stomach between April 2000 and April 2004. The database included demographic, clinical, operative, and pathological data. The perioperative complications and patient outcomes were also recorded.

Preoperative Evaluation and Indications for Laparoscopic Treatment

Preoperative diagnoses of tumor type, size, location, and the presence of metastatic lesions were made in all patients by using a combination of gastrofiberscopy, upper gastrointestinal radiography, endoscopic ultrasonography (EUS), and computed tomography (CT). EUS-FNA was routinely performed in all patients for preoperative verification of the histopathological diagnosis by hematoxylin–eosin and immunochemical stains (c-kit, CD34, desmin, smooth-muscle actin [SMA], and S-100). If the aspirated specimen was identified as a neurogenic or myogenic tumor with features suggestive of a benign tumor, the surgical option could be ruled out. Otherwise, a surgical approach was based on the size and location of the tumor. Laparoscopic treatment was contraindicated for tumors located near the cardia or pylorus, where the gastroesophageal junction or pyloric ring might have become involved in the resection line. Moreover, if wedge resection would have resulted in gross deformity of the stomach, because of tumor involvement of the wall, a conventional laparotomy approach was selected because of the clearer operative field, to avoid the risk of the gastric stenosis. Finally, because larger tumors must be handled carefully to prevent rupture and spillage, laparoscopic surgery was indicated only for tumors <5 cm in diameter. Our institute algorithm for gastric GIST is shown in Fig. 1. Written informed consent was obtained from all patients before surgery.

Surgical Procedures

After the induction of general anesthesia, the patient was placed in the supine position with the legs abducted. A camera port was inserted in the paraumbilical lesion using an open technique. Carbon dioxide was insufflated through this port to create pneumoperitoneum, with an insufflation pressure of 10–12 mmHg. Two additional ports were inserted in the upper abdomen to help identify the tumor location. After finding the tumor, 1–2 more ports were placed to allow for manipulation of the stomach and resection of the tumor.

"Inspection and palpation" of lesions in the anterior gastric wall was done using laparoscopic grasping forceps passed along the anterior surface of the stomach. For access to posterior gastric lesions and to allow easier mobilization of the tumor, the stomach was separated from the greater omentum using ultrasonic coagulating shears (Harmonic Scalpel; Ethicon Endo-Surgery, Cincinnati, OH, USA). The tumor was mobilized, brought into the field of vision, and elevated using atraumatic grasping forceps. A linear stapler (Proximate, Ethicon Endo-Surgery) was applied and fired (Fig. 2a). Each resection required 2–3 staples.

Intraoperative gastroscopy was performed routinely to identify the precise location of the tumor and to ensure that excision was done with an adequate surgical

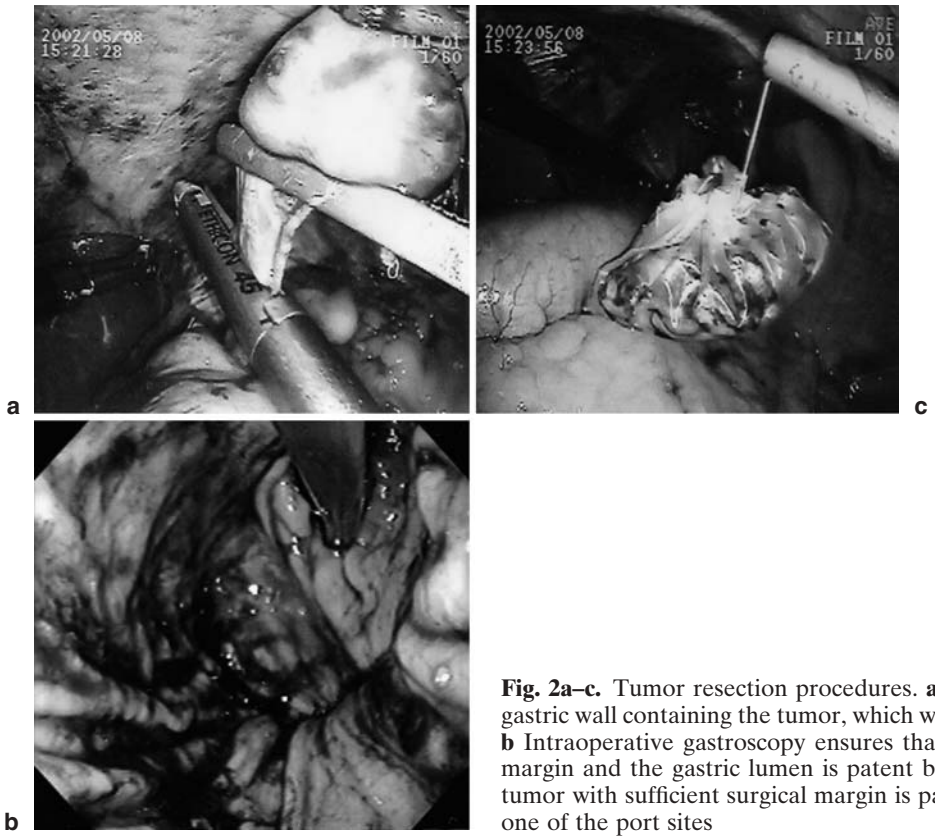

Fig. 2a–c. Tumor resection procedures. **a** An endscopic stapler is fired across the gastric wall containing the tumor, which was "tented-up" with an atraumatic clamp. **b** Intraoperative gastroscopy ensures that the tumor is excised with an adequate margin and the gastric lumen is patent before an endoscopic stapler is fired. **c** A tumor with sufficient surgical margin is packed into a plastic bag and removed via one of the port sites

margin (Fig. 2b). After resection, integrity of the staple line was tested by submerging the stomach in irrigation fluid and then insufflating air via the endoscope. Immediately after each specimen was removed in a bag via one of the port sites (Fig. 2c), it was scrutinized to ensure that a sufficient resection margin had been obtained.

Histopathology of Surgical Specimens

Surgical specimens were fixed in formalin and stained using hematoxylin–eosin. Immunohistochemical staining was performed for myogenic and neurogenic markers (desmin, SMA, and S-100) in addition to c-kit and CD34. A gastrointestinal stromal tumor was defined as a cellular spindle cell, epithelioid, or occasionally pleomorphic mesenchymal tumor expressing c-kit, CD34, or both.

Comparison with Open Wedge Resection

For comparison, results for ten consecutive patients with GIST <5 cm in diameter who underwent open wedge resection between 1995 and April 2000, before the introduction of laparoscopic surgery, were retrieved from the retrospective database at Aichi Cancer Center. Operative time, intraoperative blood loss, interval until passage of first flatus and oral intake, postoperative hospital stay, rate of postoperative complications, and recurrence were compared between this group (OS group) and the 12 patients treated with laparoscopic surgery (LS group), by using the Mann–Whitney *U*-test and Fisher's exact test.

Results

The patient demographics and tumor characteristics are summarized in Table 1. The male : female ratio was almost equal, and the mean age was 60 years (range, 42–76 years). The lesion was resected completely via laparoscopy in all 12 patients. The tumors were located in the upper third of the stomach in six patients, the middle third in five, and the lower third in one. The anterior wall was involved in two patients, the posterior wall in two, and the greater curvature in eight.

Intraoperative complications were encountered in two patients. One suffered pneumothorax caused by injury of the right diaphragm during cholecystectomy for coexisting cholelithiasis, and one suffered bowel injury during insertion of the first port. Both these incidents were restored intraoperatively without difficulty

Table 1. Patient demographics and tumor characteristics of the gastrointestinal stromal tumors resected laparoscopically

Patient no.	Age (years)	Sex	Location 1	Location 2	Tumor size (cm)	Diagnosis on EUS-FNA	Diagnosis on surgical specimen	Operative time (min)	Hospital stay (days)[a]	Complication	Recurrence
1	47	M	U	Gre	4.8	GIST	GIST	140	14		Absent
2	42	M	U	Ant	2.2	GIST	GIST	85	6		Absent
3	73	M	U	Gre	2.2	GIST	GIST	138	11	Pneumonia	Absent
4	62	M	M	Post	4	GIST	GIST	131	9		Absent
5	65	F	M	Gre	3.5	GIST	GIST	180	11	Pneumothrax[b]	Absent
6	64	F	M	Post	3	GIST	GIST	101	8		Absent
7	57	F	L	Ant	2.9	Suspected GIST	GIST	92	7		Absent
8	74	M	U	Gre	2.5	Unknown	Schwannoma	164	6		Absent
9	76	M	U	Gre	3	GIST	GIST	65	7	Bowel injury	Absent
10	63	F	M	Gre	1.6	GIST	GIST	85	5		Absent
11	54	F	U	Gre	1.5	GIST	GIST	100	6		Absent
12	47	F	M	Gre	1.5	Myogenic tumor	Leiomyoma	87	7		Absent

U, M, and L denote upper third, middle third, and lower third of the stomach, respectively
Gre, Ant, and Post denote greater curvature, anterior wall, and posterior wall of the stomach, respectively
EUS-FNA, endoscopic ultrasonography-guided fine-needle aspiration; GIST, gastrointestinal stromal tumor
[a] Postoperative hospital stay
[b] Contributed to cholecystectomy for a coexisting cholelithiasis

and no further critical complications were experienced. Moreover, no major postoperative complications such as bleeding, leakage along the suture line, obstruction, or intra-abdominal abscess occurred, and there were no deaths related to laparoscopic surgery. The median postoperative hospital stay was 7 days (range, 5–12 days).

The median tumor diameter was 2.7 cm (range, 1.5–4.8 cm). Gross observation revealed complete tumor excision with negative surgical margins in all patients. Immunoreactivity for c-kit or CD34 was noted in 10 of the 12 patients. The diagnosis of GIST had been made preoperatively by EUS-FNA in each of these ten patients. The other two lesions were stained negatively for both c-kit and CD34, with one reactive for S-100 and the other reactive for desmin and SMA, leading to diagnoses of schwannoma and leiomyoma, respectively. In one of these two patients, the specimen from EUS-FNA was insufficient for immunochemical staining, but was considered potentially malignant due to high cellularity. Although the other tumor was positive for SMA, resection was recommended for a malignant pattern based on EUS findings. After a median follow-up period of 26 months (range, 6–53 months), all patients were asymptomatic and free of local recurrence or metastases.

Comparison with Open Wedge Resection

Table 2 lists the perioperative data. There were no significant differences in tumor size between the LS and OS groups. Although the duration of surgery was similar in both groups, intraoperative blood loss was significantly less in the LS group. First flatus was passed earlier in the LS group, leading to an earlier resumption of oral intake. Frequency of complications was comparable between groups, with no operative or in-hospital mortality. Postoperative hospital stay was significantly lower in the LS group than in the OS group.

Discussion

Gastrointestinal stromal tumors of the stomach are unusual, accounting for only about 1% of all primary gastric neoplasms.[15–17] An accurate diagnosis of the submucosal tumor is essential for determining the surgical indications. Rapid innovations have been achieved in the diagnostic modalities for gastrointestinal tumors, and EUS has proven superior in diagnosing submucosal lesions of the stomach, allowing a clear view of the gastric wall and surrounding structures.[18,19] In addition, EUS-FNA through this device allows histopathological evaluation of submucosal lesions that are usually inaccessible by routine endoscopic biopsy. In the current series, 11 of the 12 specimens obtained by EUS-FNA were immunoreac-

Table 2. Comparative perioperative data between laparoscopic and open surgery for gastrointestinal stromal tumors

Variable	Laparoscopic surgery ($n = 12$)	Open surgery ($n = 10$)	P value
Age (years)	60 (42–76)	59 (41–67)	n.s.
Gender (M:F)	6:6	4:6	n.s.
Location 1	U:6M:5L:1	U:8M:2L:0	
Location 2	Gre: 8 Post: 2 Ant: 2	Gre: 3 Less: 3 Post: 3 Ant: 1	
Tumor size (cm)	2.7 (1.5–4.8)	3.15 (1.5–4.5)	n.s.
Operative time (min)	100 (65–180)	122 (55–199)	n.s.
Blood loss (g)	0 (0–100)	62 (0–230)	0.002
First flatus (days)	2 (1–3)	4 (2–5)	0.014
Oral intake (days)	2 (1–4)	5 (4–8)	0.0001
Complications	3	4	n.s.
Hospital stay (days)	7 (5–12)	17 (11–51)	0.005
Diagnosis of surgical specimen GIST/leiomyoma/schwannoma	10/1/1	10/0/0	
Recurrence	0	0	n.s.

U, M, and L, upper third, middle third, and lower third of the stomach, respectively
Gre, Less, Ant, and Post, greater curvature, lesser curvature, anterior wall, and posterior wall of the stomach, respectively
GIST, gastrointestinal stromal tumor; n.s., not significant

tive for c-kit, CD34, and SMA. A diagnosis of GIST was confirmed in ten patients by evaluating the surgically resected specimens, and a neurogenic tumor was diagnosed postoperatively in one patient. Previous reports suggest that EUS findings and the MIB-1 labeling index of the specimen might correlate with the malignant potential of GIST.[8,20] However, these results, together with histological examination of FNA aspirate, appear insufficient to accurately differentiate between benign and malignant GIST, preoperatively.[21,22]

Tumor size is another widely accepted prognostic factor, which can be evaluated preoperatively.[7,23–25] We previously reported recurrence in 3% of GISTs with a diameter <5 cm, 7% of those with a diameter between 5 and 10 cm, and 56% of those with a diameter >10 cm.[8] We think that tumors <2 cm in diameter have a low risk of metastasis, especially since these small tumors are occasionally found in stomach tissue resected for reasons unrelated to GIST, suggesting that such patients have never experienced GIST metastases.[26] Thus, we determined that surgery is always indicated for tumors ≧2 cm in diameter and diagnosed as GIST.

We also consider that GIST is a good indication for laparoscopic resection because of the low frequency of lymph node metastases.[4–8,27] The development of endoscopic stapling devices has made laparoscopic wedge resection an attractive alternative to the conventional open approach; however, attention must be paid to tumor size and location. According to Choi and Oh, proximal or distal gastrectomy should be performed for tumors located near the pylorus or gastroesophageal junction because wedge resection may compromise the gastric lumen.[28] Even if laparoscopic wedge resection is possible, this procedure cannot be justified for treating lesions in the cardia or pyloric ring, because the advantages of laparoscopic surgery do not override to risk of postoperative complications.[29] In the current series, we did not perform laparoscopic surgery for tumors located <2 cm from the gastroesophageal junction or pyloric ring, and there was no incidence of postoperative gastric stenosis.

To maximize the chance of curability and ensure that resection is carried out safely, large tumors are not operated on laparoscopically. Huge lesions are difficult to resect using endoscopic linear staplers, since access is limited and the potential for luminal compromise is increased when a spherical mass is resected linearly. Matthews et al. reported that ultrasonic coagulating shears are invaluable for resecting large tumors, because they allow for an adequately free margin without including the resected specimen.[14] However, in addition to the risk of contaminating the abdominal cavity, this method requires competence with laparoscopic suturing, which is technically demanding and stressful for the general surgeon. Moreover, the removal of a GIST requires special care to prevent tumor spillage, necessitating gentle handling of the tumor to avoiding injuring the serosa by resecting an adequate margin of surrounding normal tissue, and using a bag for removal of the tumor from the abdominal cavity. The unnecessary recurrence of advanced disease resulting from the use of laparoscopy is also a controversial issue. Aogi et al. indicated that laparoscopic resection should be avoided for larger GISTs because of the difficulties encountered when grasping the lesion.[29] At present, laparoscopic resection of suspicious malignant tumors such as large GISTs seems unwise because of the possibility of port-site recurrence and peritoneal seeding.[30] Taking these factors into account, we suggest

that only gastric GISTs <5 cm in diameter are suitable for treatment by laparoscopic surgery. In the current series, no port-site recurrence or peritoneal seeding was observed during many years of follow-up.

Advanced laparoscopic procedures are technically challenging, requiring the ability to identify and dissect tissue planes without the usual tactile clues, to control multiple blood vessels, and to manipulate and extract large specimens. Analyses of the learning curves for laparoscopic herniorrhaphy and colectomy, which require advanced skills, suggest that surgeons must perform 30–40 of these operations before attaining technical proficiency.[9,31,32] In contrast, almost all general surgeons have acquired the requisite skills to perform laparoscopic cholecystectomy, which is relatively simple and able to be performed within the same time as open surgery. Thus, laparoscopic cholecystectomy is widely accepted. It is noteworthy that the operative time in our series was reduced to that needed for open surgery after our initial experience of only five patients. The mean operative time for open surgery in our institute is 120 min; however, whereas that of our initial five operations was 134 min, that of our subsequent seven operations was only 99 min. The frequency of complications was also comparable with that in open surgery. All of these findings point to the simplicity of the laparoscopic technique for GIST resection, as long as patients are carefully selected in advance. The use of up-to-date laparoscopic instrumentation such as laparoscopic coagulating shears for dissection and the endoscopic stapler for resection may represent another prerequisite for success. Finally, intraoperative gastroscopy should be mentioned as a further aid to adequate resection. Gastroscopy can also be helpful for locating the mass, monitoring gastric lumen patency until resection is completed, and controlling the suture line. Intraoperative gastroscopy is therefore used widely in laparoscopic surgery for gastric GISTs, for identifying and marking tumors, ensuring sufficient margins, and preventing luminal stenosis.[14,28,33] In conclusion, as long as patients are carefully selected, laparoscopic surgery is feasible for resecting GISTs of the stomach, resulting in faster recovery, even when performed by surgeons with limited experience in advanced laparoscopic procedures.

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