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Excellent oncological outcomes besides short-term safety of laparoscopic and endoscopic cooperative surgery for gastric gastrointestinal stromal tumor

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ABSTRACT

Background and study aims Laparoscopic and endoscopic cooperative surgery (LECS) for gastric submucosal tumor was developed as a type of minimal local resection and is now widely used in Asian countries. However, the oncological safety of LECS for gastric gastrointestinal stromal tumor (GIST) remains unclear. LECS has potential oncology-related problems that may influence survival outcomes. Furthermore, the feasibility and safety of LECS have not yet been fully established.

Patients and methods Patients who were intended to undergo LECS for gastric GIST from 2006 to 2020 were retrospectively selected. The indication for LECS was determined according to the guidelines. The completion of LECS, complications, and survival outcomes of the patients were analyzed.

Results Two hundred fifty-nine patients were eligible in this study. According to intraoperative findings, 44 patients underwent local resection without luminal endoscopic procedures. Of the remaining 215 patients, 213 completely underwent LECS, which corresponds to a completion rate of 99.1%. Six patients (2.8%) had postoperative complications of Clavien-Dindo classification grade II or higher. Delayed gastric emptying was most commonly found in four patients (1.9%). Old age ($P=0.0349$), female sex ($P=0.0095$), tumor located in the lesser curvature ($P=0.0015$), and large tumor diameter ($P=0.0232$) were significantly more common in patients with complications. The 3-year overall and disease-specific survival rates were 99% and 100%, respectively, in 215 patients who were intended to undergo LECS.

Conclusions Despite several oncological concerns, LECS for gastric GIST is oncologically safe besides a feasible and safe procedure in the short-term.

Introduction

Gastrointestinal stromal tumor (GIST) is derived from Cajal-mediated cells scattered within the gastrointestinal tract walls, and has an annual incidence of 10 to 15 patients per million people [1–3]. The stomach is the most common organ in which GIST forms a submucosal tumor (SMT), and surgical resection is the main treatment modality [4, 5]. Gastric GIST is usually locally resected without lymph node dissection because it generally

has no lymph node metastasis. Many studies have reported favorable short- and long-term outcomes after such local treatment [6–9].

Laparoscopic and endoscopic cooperative surgery (LECS) was established by Hiki et al. in 2008 to minimize the area of gastric resection by laparoscopic local resection for gastric SMT including GIST [10]. In LECS for gastric SMT, both the mucosa and submucosa close to the root of the tumor protrusion is first dissected by luminal endoscopy, which is the technique of endoscopic submucosal dissection for cancer. This mucosal incision line becomes the cutting line along which the tumor is subsequently resected with the whole layer of the stomach. The defect in the stomach after resection is closed with an endoscopic linear stapler or is hand-sewn laparoscopically. LECS for gastric SMT has become common in Asian countries, and previous reports of initial experiences revealed that LECS for gastric SMT can be performed safely [11–16].

However, whether LECS is safe for GIST that has formed gastric SMT remains unclear. Only one small-sample-sized study has reported long-term results of gastric GIST resected by LECS [6]. Actually, LECS for gastric GIST which is a potential malignant tumor essentially has two surgical oncology-related problems. The first is direct tumor handling. LECS enables minimal resection of the stomach, and as a result, the tumor is handled nearly directly. In LECS, only a very short length of surgical margin is maintained and the tumor is grasped or sometimes retracted directly using endoscopic forceps to remove it from the stomach wall. Furthermore, LECS requires opening the stomach wall in the pneumo-abdominal cavity. Dissemination of tumor cells into the abdominal cavity is concerning, especially when the tumor has an ulceration called a delle, but so-called inverted-LECS was developed to prevent contamination of the gastric juice and contact of the tumor with the abdominal wall during a full-thickness incision [13]. Whether such issues influence long-term outcomes of gastric GIST treated by LECS have hardly been investigated. Moreover, even the feasibility and short-term safety of LECS for gastric GIST have not yet been established. As previous studies to evaluate these factors had small sample sizes and always included not only GIST but also other types of SMT, they did not present definitive outcomes. In fact, LECS for gastric GIST seems to be feasible, and few postoperative complications occur because it is a type of local resection. However, the rates of incomplete surgery, patient profiles, and factors related to postoperative complications were not sufficiently investigated because of the small sample sizes in previous studies.

In this study, to establish the long-term safety as well as the feasibility and short-term safety of LECS for gastric GIST more definitively, the completion rate, postoperative complications, and oncological outcomes of LECS for gastric GIST were analyzed by collecting a larger number of narrowly defined patients who were treated with the same intention at our institute. The results of this study are useful as a reference for determining indications, monitoring any complications, and determining methods of postoperative surveillance in LECS for gastric GIST.

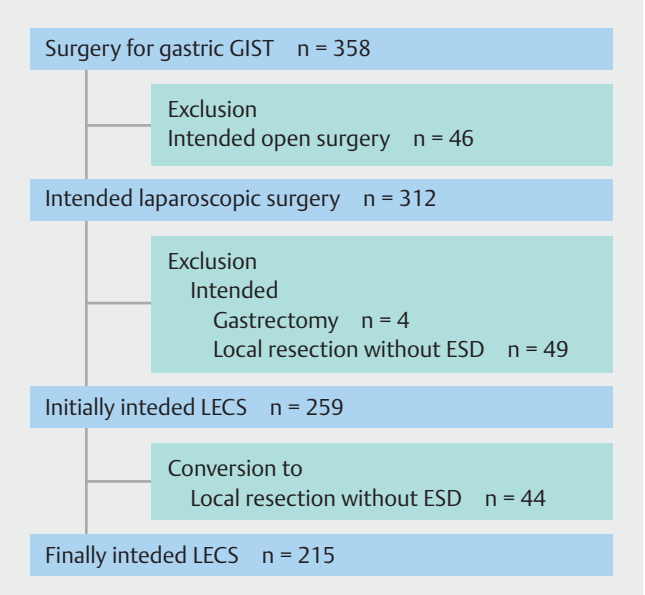
Patients and methods

Patients

This study investigated consecutive patients who underwent surgery for gastric GIST at the Department of Gastroenterological Surgery, the Cancer Institute Hospital, Tokyo, Japan, between January 2006 and December 2020. Patients who underwent planned open surgery were excluded from the analysis set according to the flowchart in ▶ **Fig. 1**. In addition, patients who underwent planned laparoscopic local resection without luminal endoscopic procedures were not included in the group intended to undergo laparoscopic surgery. Data on patients who were intended to undergo LECS were collected and patients whose procedures were converted to laparoscopic local resection without luminal endoscopy according to intraoperative endoscopic findings were finally excluded (▶ **Fig. 1**). The present study was approved by the ethics committee of the Cancer Institute Hospital (number 2021-GB-032).

Selection of surgical procedure

Selection of open or laparoscopic surgery mainly depended on tumor size (≤ 5.0 cm or > 5.0 cm) according to Japanese guidelines for GIST [17], presence or absence of combined resection of other organs, and the surgeon's choice. In addition, indications for local resection and gastrectomy depended on tumor location and size. Gastrectomy was planned if the tumor involved more than half of the cardia or pylorus, or if the tumor attached to the stomach wall was more than half of the gastric circumferential length. In local resection, the final decision about which procedure was conducted – LECS or laparoscopic local resection without luminal endoscopic procedures – depended on the findings from intraoperative luminal endoscopy.



▶ **Fig. 1** Flowchart of patient enrollment. GIST, gastrointestinal stromal tumor; ESD, endoscopic submucosal dissection; LECS, laparoscopic and endoscopic cooperative surgery.

Laparoscopic local resection without luminal endoscopic procedures was selected when intraoperative luminal endoscopy revealed that the tumor did not protrude or slightly protruded into the gastric lumen even though findings from preoperative computed tomography (CT) or luminal endoscopy indicated intraluminal growth.

Surgical procedure

LECS procedures were performed as reported previously [10]. First, a camera was inserted via a 12-mm port in the umbilicus. Under insufflation of 10 mmHg, three 5-mm ports and one 12-mm port were inserted into the upper left, lower left, upper right, and lower right quadrants. A luminal endoscope was inserted into the stomach and endoscopic dissection was performed to make a circumferential incision in both the mucosal and submucosal layers around the tumor (▶ **Fig. 2a**). Next, an incision was made through all layers from the lumen of the stomach, and the tumor was removed by making an incision in the circumferential direction with the assistance of laparoscopic and luminal endoscopic procedures (▶ **Fig. 2b**, ▶ **Fig. 2c**). The defect in the stomach wall was closed with a stapler or hand-sewn sutures (▶ **Fig. 2d**).

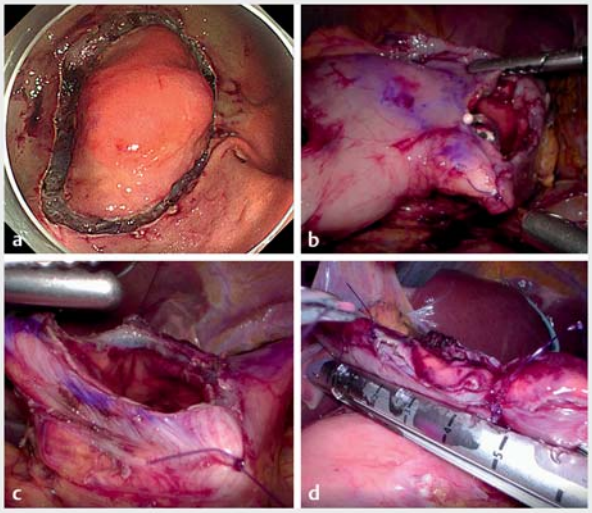
Laparoscopic local resection without luminal endoscopic procedures is performed for extraluminal GIST. Patient positioning and port settings were prepared in the same way as for LECS. After exposing the blood vessels in the excision area around the tumor using an ultrasonic coagulation device or a vessel sealing system, the intact stomach wall attaching the tumor was clamped with a linear stapler. Then, the linear stapler was fired, and the tumor was removed.

Postoperative follow-up

According to gastric GIST treatment guidelines in Japan, postoperative surveillance using CT is performed every 6 to 12 months for patients at very low risk or low risk after complete resection, and CT is performed every 4 to 6 months for patients at intermediate risk or high risk [17].

Evaluation

Patient factors included age, sex, symptoms, performance status, and body mass index. Tumor histopathological factors included tumor diameter, tumor location, presence of mucosal defects called delles, mitotic index, and risk grade. Hematological tests included prognostic nutritional index [18], and prealbumin. The feasibility of LECS was defined as completion of LECS. The percentage of completion was calculated as the number of patients who underwent LECS among those who were finally intended to undergo LECS, excluding patients who underwent laparoscopic local resection without luminal endoscopic procedures. Surgical factors included surgical procedure, surgical time, bleeding, postoperative hospital stays, and postoperative complications. Postoperative complications were assessed in patients who completely underwent LECS according to the Clavien-Dindo classification [19]. As a principle of grading in the Clavien-Dindo classification, Grade II is defined as receiving medication for some symptoms or findings. Grade II is also applied when intravenous nutritional management is unavoidable. If treatment with local anesthesia or drain replacement is required, it is defined as Grade IIIa. Grade IIIb is defined as requiring general anesthesia, such as reoperation. Grade IV is defined as requiring Intensive Care Unit management, which is classified into two grades: Grade IVa for single organ dysfunction and Grade IVb for multiple organ dysfunction.



▶ **Fig. 2** **a** Endoscopic submucosal dissection was performed to make a circumferential incision around the tumor. **b** The seromuscular layers were cut along the submucosal dissection line using a luminal endoscopic device with a laparoscopic cooperation. **c** While the tumor was removed, the gastric wall around the cutting edge was lifted up circumferentially, like a crown, by several stitches to avoid spilling the gastric contents into the abdominal cavity. **d** The defect was closed using a stapler after it was temporarily closed with hand-sewn sutures.

Follow-up data included adjuvant chemotherapy, recurrence, and 3- and 5-year overall survival (OS) and disease-specific survival (DSS) of patients who were intended to undergo LECS.

In histological evaluation, many GISTs consist of cells that exhibit a relatively single spindle-shaped morphology. GIST was defined as the presence of a positive c-kit or CD34 marker in immunohistochemistry [20]. The mitotic index was determined according to the number of mitotic images per 50 high-power fields, and the risk grade was determined according to the modified Fletcher classification [21, 22].

Statistical analysis

Continuous variables were evaluated by ANOVA or Student's t-test and categorical variables by Fisher's exact test or the chi-squared test, as appropriate. Clinicopathological characteristics and follow-up data were evaluated in terms of OS and DSS. Follow-up time was calculated from the date of surgery to death or endpoint. OS and DSS were estimated by the Kaplan-Meier method and compared using the log-rank test. $P<0.05$ was considered to indicate statistical significance. All statistical analyses were conducted using the SAS software package (JMP Pro14, SAS Institute, Cary, North Carolina, United States).

▶ **Table 1** Characteristics of patients who were intended to undergo LECS for gastric GIST

Variables	Finally intended LECS n = 215
Age at diagnosis, years, median (IQR)	64 (54, 72)
Sex	
▪ Male	112 (52.1)
▪ Female	103 (47.9)
Performance status	
▪ 0	182 (85.1)
▪ 1	29 (13.5)
▪ 2	3 (1.4)
Preoperative pathological diagnosis	
▪ GIST	74 (34.4)
▪ No diagnosis	141 (65.6)
Delle	
▪ Yes	33 (15)
▪ No	182 (85)
Tumor location	
▪ Upper	
– Fornix	50 (23.2)
– Cardia	21 (9.8)
– Body	69 (32.1)
▪ Middle	52 (24.2)
▪ Lower	23 (10.7)
Circumferential location	
▪ Greater curvature	43 (20)
▪ Lesser curvature	38 (17.7)
▪ Anterior wall	55 (25.6)
▪ Posterior wall	79 (36.7)
Tumor diameter, mm, median (IQR)	30 (23, 40)
Modified Fletcher classification	
▪ Very low	28 (13)
▪ Low	128 (59.4)
▪ Intermediate	17 (8)
▪ High	17 (8)
▪ Unknown	25 (11.6)

Results represented as n (%)
GIST, gastrointestinal stromal tumor; LECS, laparoscopic and endoscopic cooperative surgery; IQR, interquartile range.

Results

Characteristics of patients who were intended to undergo LECS

During the study period, 259 of 358 patients who underwent surgery for gastric GIST were initially intended to undergo LECS. In 44 of 259 patients, an intraoperative decision was made to perform laparoscopic local resection without luminal endoscopic procedures because intraoperative luminal endoscopy confirmed that the tumors were of an extraluminal growth type and endoscopic mucosal dissection was not required. Thus, 215 patients were finally intended to undergo LECS (▶ **Fig. 1**) and their clinicopathological characteristics are listed in ▶ **Table 1**. Nearly two-thirds of the patients had tumors located in the upper third, followed by those in the middle and lower thirds. Furthermore, more than 30 % of the patients had tumors involving the cardia or the fornix. Median tumor diameter was 30 mm (range 9 to 62 mm). Thirty-three patients (15 %) had tumors with ulceration called delle in which SMT was exposed. Regarding the recurrence risk evaluated by the modified Fletcher classification, more than 70 % of patients were classified as low or very low risk, while the remaining patients were classified as intermediate or high risk in equal proportions. Twenty-five patients (11.6 %) whose tumors were not assessed in a mitotic index were not classified.

Completion of LECS

Of the 215 patients, two patients were converted to open surgery simultaneously following LECS. For one patient, reconstructive surgery was needed because of esophageal stricture. In another patient, an area in which the blood supply was insufficient appeared, and gastrectomy incorporating the area was performed by an open procedure. The completion rate of LECS was 99.1 % (213/215).

Surgical data and postoperative complications of LECS

The 213 patients in whom LECS was completed were enrolled in this analysis. The procedure took approximately 3 hours to complete and the median blood loss was 5 g. R0 resection was achieved in all the patients. Six patients (2.8 %) had postoperative complications of Clavien-Dindo grade II or higher. Delayed gastric emptying was most commonly found in four patients (1.9 %), and anastomotic leakage and postoperative bleeding were found in one patient (0.5 %). Complications of greater than grade III were found in one patient (0.5 %) (▶ **Table 2**).

Comparing the presence or absence of postoperative complications with clinicopathological factors, old age (P = 0.0349), female sex (P = 0.0095), tumor located in the lesser curvature (P = 0.0015), and large tumor diameter (P = 0.0232) were significantly more common in patients with postoperative complications (▶ **Table 3**).

▶ **Table 2** Surgical data and postoperative complications of LECS.

Variables	Completed LECS n = 213
Surgery time, min, median (IQR)	181 (152.5, 210)
Bleeding, g, median (IQR)	5 (5, 10)
Closure of defect	
▪ Stapler	182 (85.5)
▪ Hand-sewn	31 (14.5)
Curability	
▪ R0	213 (100)
Hospital stays, days, median (IQR)	7 (6, 8)
Postoperative complications according to the Clavien-Dindo classification	
▪ Grade II	5 (2.3)
▪ ≥ Grade III	1 (0.5)
Anastomotic leakage	
▪ Grade II	0
▪ ≥ Grade III	1 (0.5)
Delayed gastric empty	
▪ Grade II	4 (1.9)
▪ ≥ Grade III	0
Bleeding	
▪ Grade II	1 (0.5)
▪ ≥ Grade III	0

Results represented as n (%)
GIST, gastrointestinal stromal tumor; LECS, laparoscopic and endoscopic cooperative surgery; IQR interquartile range.

▶ **Table 3** Relationship between postoperative complications and clinicopathological factors in patients who underwent LECS.

Variables	Without complications n = 207	With complications n = 6	*P* value
Age at diagnosis, years, median	64	74.5	0.0349
Sex			
▪ Male/female	111/96	0/6	0.0095
Performance status			
▪ 0/1 or 2	177/30	5/1	0.8817
Delle			
▪ Yes/no	31/176	1/5	0.909
Prognostic nutritional index			
▪ <47/>46	36/171	2/4	0.3147
Prealbumin			
▪ <22/>21	23/183	2/4	0.097
Surgery time, min, median	180	219	0.3574
Bleeding, g (gram), median	5	5	0.5289
Tumor location			
▪ Upper/middle or lower	136/71	3/3	0.4259
Circumferential location			
▪ Lesser curvature/others	34/173	4/2	0.0015
Tumor diameter, mm, median	30	43.5	0.0232

LECS, laparoscopic and endoscopic cooperative surgery

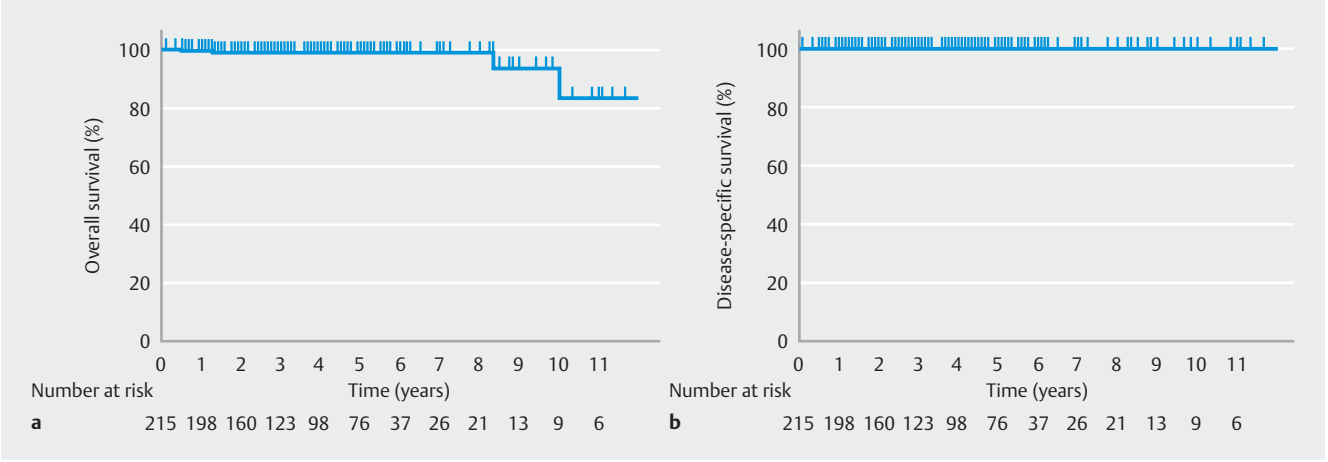
Survival outcomes

The median follow-up time in the 215 patients who were finally intended to undergo LECS was 43 months. One of the 215 patients experienced liver metastasis as recurrence. That patient underwent conversion to open surgery following LECS. The recurrence risk was pathologically classified as high risk. The 3-year and 5-year OS and DSS rates in the 215 patients were 99 % and 100 %, respectively (▶ **Fig. 3a**, ▶ **Fig. 3b**). No patient in whom LECS was completed experienced recurrence.

Discussion

At our institution, local resection using the LECS technique was performed for consecutive gastric GIST according to our own criteria based on the Japanese guidelines irrespective of tumor location. Although this was a single-institutional and retrospective study of LECS, three new findings were obtained. First, LECS for gastric GIST was a feasible procedure. We determined the surgical indication for LECS according to tumor location and size. We were able to complete LECS in more than 99 % of patients who were intended to undergo LECS. Second, LECS was a very safe procedure. Fewer than 3 % of the patients who underwent LECS experienced Clavien-Dindo grade II or higher postoperative complications. Several factors were associated with occurrence of complications, although the incidences were very low. Third, the patients who were finally intended to undergo LECS had favorable survival outcomes. Only one patient who was intended to undergo LECS experienced recurrence. The data clearly showed that LECS for gastric GIST was feasible and safe in the short term. Furthermore, it could achieve favorable long-term outcomes according to our patient selection criteria based on the Japanese guidelines.

There was a high rate of completion of LECS in this study, and the procedure is expected to be feasible because it is essentially a local resection. However, the feasibility of LECS may depend on tumor location and size. Gastric GIST is frequently located in the upper stomach, and more than 60 % of tumors were loca-



▶ **Fig. 3** **a** Overall survival and **b** disease-specific survival curves for gastric GIST patients who were finally intended to undergo LECS. GIST, gastrointestinal stromal tumor; LECS, laparoscopic and endoscopic cooperative surgery.

ted there in this series. It is sometimes difficult to remove the proximal tumor and close the defect in the stomach wall, especially when a tumor is located in the posterior wall and around the cardia or fornix. In this study, two patients in whom LECS failed had such features. These two patients successfully underwent tumor removal, but esophageal stricture or circulation failure was found after closure of the defect, although the margin and devascularization was maintained at a minimum. While the technical feasibility and safety of LECS have been reported in some studies thus far, the feasibility of intended LECS was first established in this study.

Delayed gastric emptying after LECS was common in this study. An analysis of the relationship between complications and clinicopathological factors indicated that GIST located in the lesser curvature was significantly associated with complications. It has been reported that the branches of the vagus nerve, which controls gastric peristalsis [23], reach the lesser curvature. Some reports have shown a relationship between the branches of the vagus nerve and delayed gastric emptying [24]. Therefore, in LECS for tumors located in the lesser curvature, cutting the vagus nerve branches may be associated with delayed gastric emptying. Preservation of these nerve branches may be a solution that prevents delayed gastric emptying. In this study, all the patients who experienced postoperative complications were women. Although the reasons why these complications are limited to women is unclear, surgeons should pay careful attention to patients with the other related factors identified in this analysis: age ≥75 years and tumor size ≥43.5 mm.

The present study revealed that only one of the patients with intended LECS experienced recurrence of gastric GIST. This information validated a previous report on the effectiveness of laparoscopic surgery including both laparoscopic local resection and LECS for gastric GIST [6]. Because the median follow-up time of the patients in this study was <5 years, the result may be insufficient. However, several studies showed that 3-year and 5-year survival outcomes of gastric GIST might be equivalent [8, 9, 25, 26]. Thus, the information may be based on the largest study regarding the long-term oncological aspect of LECS. Although many studies of LECS focused on surgical technique or short-term outcomes, one of the truly important issues in LECS is oncological outcome because LECS is undertaken for malignant disease. As described above, LECS has essentially unavoidable issues in oncology surgery. However, this study clearly demonstrated that LECS did not increase the risk of recurrence if our patient selection criteria were maintained. Because we selected patients for LECS, the tumor diameter was <5 cm, and more than 70% of the tumors removed by LECS were classified as very low or low risk. Furthermore, such tumors had an extremely low risk of recurrence and one patient who experienced recurrence had a tumor classified as high risk. Current guidelines for GIST recommend postoperative surveillance by CT once every 6 to 12 months for even very-low and low-risk tumors [17]. However, the favorable results of this study suggest that such uniform intensive surveillance may be unnecessary for patients clinically suitable for LECS. Patients who underwent LECS hardly experienced recurrence because LECS is an oncologically safe procedure, and gastric GIST that has indications for LECS is usually classified as lower risk. Further studies are required to determine adequate surveillance, considering medical costs, too.

This study has several limitations. First, it is a single-institutional retrospective observational study. Gastric GIST is rare and the number of complications and recurrence events was so small at our institution that risk factors could not be analyzed sufficiently. However, such a relatively large-scale and long-observational study may be valuable because evidence regarding the short- and long-term outcomes of LECS is lacking. Furthermore, there were some patients whose tumors were not examined by the mitotic index because of their different historical backgrounds. Therefore, risk classification could not be determined in more than 10% of patients. Thus, in the future, a prospective study should be conducted at multiple institutions to assess the true short- and long-term safety of LECS for gastric GIST.

Conclusions

In conclusion, LECS is a feasible and perioperatively safe procedure for gastric GIST that has appropriate indications in terms of location and size. Furthermore, patients suitable for LECS have a favorable survival outcome because LECS is an oncologically safe procedure and they have lower-risk tumors. Postoperative surveillance methods recommended in the guidelines may need to be reevaluated, considering the highly curable nature of gastric GIST removed by LECS.

Competing interests

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References

[1] Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. Arch Pathol Lab Med 2006; 130: 1466–1478

[2] Joensuu H, Hohenberger P, Corless CL. Gastrointestinal stromal tumour. Lancet 2013; 382: 973–983

[3] Mucciarini C, Rossi G, Bertolini F et al. Incidence and clinicopathologic features of gastrointestinal stromal tumors: a population-based study. BMC Cancer 2007; 20: 230

[4] Joensuu H, Fletcher C, Dimitrijevic S et al. Management of malignant gastrointestinal stromal tumors. Lancet Oncol 2002; 3: 655–664

[5] DeMatteo RP, Lewis JJ, Leung D et al. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg 2000; 231: 51–58

[6] Honda M, Hiki N, Nunobe S et al. Long-term and surgical outcomes of laparoscopic surgery for gastric gastrointestinal stromal tumors. Surg Endosc 2014; 28: 2317–2322

[7] Ye X, Kang WM, Yu JC et al. Comparison of short- and long-term outcomes of laparoscopic vs open resection for gastric gastrointestinal stromal tumors. World J Gastroenterol 2017; 23: 4595–4603

[8] Yang Z, Feng X, Zhang P et al. Clinicopathological features and prognosis of 276 cases of primary small (≤ 2 cm) gastric gastrointestinal stromal tumors: a multicenter data review. Surg Endosc 2019; 33: 2982–2990

[9] Askari A, Brittain R, Hilmi M et al. Unusual presentations, management and outcomes of gastric stromal tumors: a single-center case series. Ann Gastroenterol 2021; 34: 26–32

[10] Hiki N, Yamamoto Y, Fukunaga T et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. Surg Endosc 2008; 22: 1729–1735

[11] Matsuda T, Nunobe S, Kosuge T et al. Laparoscopic and luminal endoscopic cooperative surgery can be a standard treatment for submucosal tumors of the stomach: a retrospective multicenter study. Endoscopy 2017; 49: 476–483

[12] Matsuda T, Hiki N, Nunobe S et al. Feasibility of laparoscopic and endoscopic cooperative surgery for gastric submucosal tumors (with video). Gastrointest Endosc 2016; 84: 47–52

[13] Nunobe S, Hiki N, Gotoda T et al. Successful application of laparoscopic and endoscopic cooperative surgery (LECS) for a lateral-spreading mucosal gastric cancer. Gastric Cancer 2012; 15: 338–342

[14] Aoyama J, Kawakubo H, Matsuda S et al. Clinical outcomes of laparoscopic and endoscopic cooperative surgery for submucosal tumors on the esophagogastric junction: a retrospective single-center analysis. Gastric Cancer 2020; 23: 1084–1090

[15] Eom BW, Kim CG, Kook MC et al. Feasibility of non-exposure simple suturing endoscopic full-thickness resection in comparison with laparoscopic endoscopic cooperative surgery for gastric subepithelial tumors: results of two independent prospective trials. Cancers (Basel) 2021; 13: 1858

[16] Mahawongkajit P, Chanswangphuvana P. Laparoscopy-assisted endoscopic full-thickness resection of upper gastrointestinal subepithelial tumors: A single-center early experience. Mol Clin Oncol 2020; 12: 461–467

[17] Nishida T, Hirota S, Yanagisawa A et al. Clinical practice guidelines for gastrointestinal stromal tumor (GIST) in Japan: English version. Int J Clin Oncol 2008; 13: 416–430

[18] Kanda M, Mizuno A, Tanaka C et al. Nutritional predictors for postoperative short-term and long-term outcomes of patients with gastric cancer. Medicine 2016; 95: e3781

[19] Clavien PA, Strasberg SM. Severity grading of surgical complications. Ann Surg 2009; 250: 197–198

[20] Blay JY, Bonvalot S, Casali P et al. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20-21 March 2004, under the auspices of ESMO. Ann Oncol 2005; 16: 566–578

[21] Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. Hum Pathol 2008; 39: 1411–1419

[22] Rutkowski P, Bylina E, Wozniak A et al. Validation of the Joensuu risk criteria for primary resectable gastrointestinal stromal tumour – the impact of tumour rupture on patient outcomes. Eur J Surg Oncol 2011; 37: 890–896

[23] Yi SQ, Ru F, Ohta T et al. Surgical anatomy of the innervation of pylorus in human and Suncus murinus, in relation to surgical technique for pylorus-preserving pancreaticoduodenectomy. World J Gastroenterol 2006; 12: 2209–2216

[24] Kim DK, Hindenburg AA, Sharma SK et al. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol 2005; 12: 222–227

[25] Kramer K, Knippschild U, Mayer B et al. Impact of age and gender on tumor related prognosis in gastrointestinal stromal tumors (GIST). BMC Cancer 2015; 15: 57

[26] Park CH, Kim GH, Lee BE et al. Two staging systems for gastrointestinal stromal tumors in the stomach: which is better? BMC Gastroenterol 2017; 17: 141