Optimal minimally invasive surgical procedure for gastric submucosal tumors

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Abstract

Background Laparoscopic wedge resection (LWR) is widely performed for managing gastric submucosal tumors (SMTs). Despite the development of novel procedures such as laparoscopy–endoscopy cooperative surgery (LECS) and nonexposed endoscopic wall-inversion surgery (NEWS), the most appropriate surgical intervention for gastric SMTs remains unclear.

Methods We retrospectively reviewed patient characteristics, surgical outcomes, postoperative courses, results of histopathological examinations, and surgical costs of 71 consecutive patients who underwent LWR, LECS, or NEWS for gastric SMTs from January 2010 to June 2016 in our institute.

Results LWR, LECS, and NEWS were performed in 31, 14, and 26 cases, respectively. Patient backgrounds were comparable between groups. LWR was not performed for esophagogastric (E–G) junction tumors to avoid postoperative stricture, and LECS was not performed for ulcerated tumors to prevent tumor dissemination. NEWS was considered for tumors smaller than 3 cm for transoral extraction. Resected specimen area of the LWR group was significantly larger than that of the other groups. Further, the

LWR group had a significantly higher complication rate. Compared to the LECS group, postoperative serum C-reactive protein level was significantly lower and postoperative hospitalization was significantly shorter in the NEWS group. Also, operation costs were significantly lower in the NEWS group.

Conclusions The surgical procedure for gastric SMTs must be carefully chosen according to tumor size, location, and presence or absence of ulceration. For selected patients, NEWS is suggested to be an appropriate option for the treatment of gastric SMTs.

Keywords Gastrointestinal stromal tumors · Esophagogastric junction · Minimally invasive surgical procedures · Laparoscopic surgery

Introduction

The detection rate of gastric submucosal tumors (SMTs) is as high as 3% in Japan, which is higher than in Western countries because gastric cancer screening is often included in routine medical checkups in Japan [1]. The operative indications for gastric SMTs are tumors suspected of being gastrointestinal stromal tumors (GIST) or other malignant tumors and symptomatic tumors [1–3]. Because of the low rate of lymph node metastasis, local resection without lymph node dissection is indicated in the majority of cases [4]. To avoid the invasiveness of open laparotomy, laparoscopic wedge resection (LWR) has become established for managing tumors less than 5 cm in diameter [1].

Recently developed novel laparoscopic surgical methods have decreased the invasiveness of SMT treatment. Laparoscopy–endoscopy cooperative surgery (LECS) decreases the area of resection in a healthy stomach compared with

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conventional treatment [5]. Furthermore, nonexposed endoscopic wall-inversion surgery (NEWS), developed by Goto et al., avoids transmural communication in addition to minimizing the size of the resected specimen [6–11]. We have proven the feasibility and safety of NEWS in 20 consecutive cases in 2016 [9].

In the present study, we conducted a comparative review of patient characteristics, surgical outcomes, postoperative clinical course, histopathological manifestations, and the operative cost of LWR, LECS, and NEWS for gastric SMTs in a series of 71 consecutive patients. We hypothesized that LECS and NEWS would have wider applications, be less invasive, and offer cost advantages. To the best of our knowledge, this is the first study comparing minimally invasive laparoscopic methods for the treatment of gastric SMTs.

Methods

Patients

Between January 2010 and June 2016, 118 patients underwent surgical treatment for gastric SMTs at the Department of Surgery and Cancer Center of Keio University School of Medicine. We retrospectively analyzed patient characteristics, surgical outcomes, postoperative courses, results of the histopathological examination, and surgical costs of the 71 consecutive patients who underwent curative resection for gastric SMTs by LWR, LECS, or NEWS. The following surgical methods were excluded: open wedge resection ($n = 13$), hand-assisted laparoscopic

wedge resection ($n = 4$), open gastrectomy ($n = 2$), laparoscopy-assisted gastrectomy ($n = 5$), combination of laparoscopic and endoscopic approaches to neoplasia with nonexposure technique (CLEAN-NET; $n = 11$) [12], endoscopic submucosal dissection ($n = 3$), and other methods ($n = 9$).

The surgical approach (LWR, LECS, or NEWS) was selected by preoperative imaging studies and intraoperative findings as follows (Fig. 1). NEWS was considered for tumors smaller than approximately 3 cm in the minor axis on preoperative imaging because NEWS requires transoral extraction, as previously described [6–9]. LWR was not performed for tumors of the esophagogastric (E–G) junction or near the pylorus to prevent postoperative stricture resulting from the relatively wide extent of resection; tumors that show extraluminal growth pattern were usually adapted to LWR whereas the indications for LECS and NEWS were not restricted by tumor growth pattern. Tumors located on the lesser curvature were usually treated by LECS or NEWS to prevent excessive deformation of the stomach; tumors with ulceration were not considered suitable for LECS to prevent tumor dissemination into the abdominal space. LWR was performed by a single port at patient request according to our previously described method [13]. Gastric SMTs were defined as SMTs of the E–G junction when part of the tumor was located within 1 cm above or 2 cm below the E–G junction. For each procedure, partial mobilization of the stomach and laparotomy for specimen delivery was optional.

The same team of surgeons performed all operations. Patients were discharged when body temperature was 36.0 °–37.5 °C, and they were able to take regular diets,

Fig. 1 Surgical algorithm for gastric submucosal tumors (SMTs). ^aIndicates submucosal tumors, ^bindicates major axis of the tumor, ^cindicates tumor of the greater curvature of the gastric body, ^dindicates minor axis of the tumor, ^eindicates nonexposed endoscopic wall-inversion surgery, ^findicates laparoscopy–endoscopy cooperative surgery, ^gindicates laparoscopic gastrectomy, ^hindicates laparoscopic wedge resection, ⁱindicates open laparotomy

did not require any intravenous drip or medication other than oral analgesic agents, were ambulatory, and able to be discharged directly to their homes. All patients provided written informed consent for treatments received. The present study was approved by the Ethics Committee for Clinical Research at Keio University, Japan (approval number: 20150144).

Surgical procedures

LWR

A camera port was inserted into the umbilical lesion using an open technique. Three or four additional ports were inserted according to tumor location. Local resection was performed using laparoscopic linear stapling devices inserted via the 12-mm port.

When the patient requested, the single-incision laparoscopic surgery was performed [13]. A multiple instrument access device was inserted into the umbilical lesion by Hasson's method with a 2.5-cm skin incision. An additional 2-mm laparoscopic loop-type retractor was used in cases in which liver retraction or lifting of the stomach wall was necessary.

LECS

A camera port was inserted into the umbilical lesion using an open technique. In total, three or four additional ports were inserted according to tumor location. After vessel preparation of excision areas, tumor peripheries were marked under endoscopy. Specimens were extirpated by endoscopic submucosal incision and subsequent laparoscopic seromuscular dissection around tumor periphery markings. Incision lines were then closed using laparoscopic linear stapling devices. To avoid postoperative stricturing and stomach deformation, full-thickness suturing using a hand-sewn technique was used to close the incisions near the E–G junction, pylorus, or lesser curvature of the gastric body (Fig. 2) [5].

NEWS

A camera port and three or four additional ports were inserted using the same procedure as that for LECS. Mucosal markings were endoscopically placed around lesions. Accordingly, serosal markings were laparoscopically created on the opposite side of mucosal markings under endoscopic guidance. Circumferential seromyotomy was laparoscopically performed around serosal markings, followed by continuous seromuscular suturing.

Fig. 2 Operative procedure of laparoscopy–endoscopy cooperative surgery (LECS). **a, b** Circumferential incision of the entire layer by both endoscopic and laparoscopic methods. **c** Full-thickness suturing by hand-sewn technique. **d** Completion of operation

Fig. 3 Operative procedure of nonexposed endoscopic wall-inversion surgery (NEWS). **a** Circumferential seromyotomy by laparoscopic electrocautery. **b** Seromuscular suture by hand-sewn technique. **c** Endoscopic submucosal incision by endoscopic electrocautery. **d** Mucosal suture by endoscopic clip device

Submucosal incisions were circumferentially performed outside the mucosal markings under endoscopy. After lesion removal, mucosal suturing was performed using endoscopic clipping devices. Specimens were transorally extracted using an endoscopic retrieval device (Fig. 3) [6–11].

Cost analyses

Operative costs for each case such as costs of ports, suturing devices, cutting devices, anesthesia, and personnel expenses were calculated. Costs of ports include the cost of camera ports, 12-mm ports, 5-mm ports, multiple instrument access devices, and 2-mm laparoscopic loop-type retractors. The cost of suturing devices include the costs of laparoscopic linear stapling devices, reloads, endoscopic clipping devices, and surgical sutures. The cost of cutting devices include the costs of endoscopic and laparoscopic electrocauteries and laparoscopic energy devices. The cost of anesthesia includes costs of anesthetic maintenance. Personnel expenses included those of surgeons, endoscopists, anesthesiologists, and nursing staff. Costs of reusable equipment and anesthetic induction were excluded from the present analysis because they did not vary among procedures.

Statistical analyses

All data, including patient age, sex, tumor size, operative procedure, operative duration, intraoperative blood loss, blood tests, intraoperative and postoperative complications, postoperative hospital stay duration, histopathological diagnosis, tumor area, resected specimen area, and operative costs for each procedure, were recorded in a computer database. Tumor and resected specimen areas were calculated based on the major and minor axes, assuming an elliptical shape. Tumor and resected specimen areas were calculated as $3.14AB/4$, where A = major axis length and B = minor axis length. All data are presented as mean $\pm$ standard deviation. Data were evaluated using the chi-square test or one-way analysis of variance with the Tukey test for multiple comparisons. P values <0.05 were considered statistically significant. Analyses were performed using SPSS statistics version 22 (IBM Corporation, Armonk, NY, USA).

Results

Patient background data (Table 1)

A total of 71 patients who underwent LWR, LECS, or NEWS were reviewed. Each group was well matched in

Table 1 Patient background data

	LWR ^j	LECS ^k	NEWS ^l	<i>P</i> value
No. of patients	31	14	26	
Gender (male:female)	16:15	7:7	12:14	0.918
Age (years)	59.2 ± 11.3	55.8 ± 13.3	59.5 ± 13.8	0.636
BMI (kg/m ²) ^a	22.8 ± 3.9	23.0 ± 4.2	21.8 ± 2.5	0.473
Tumor location				0.003
E–G junction ^b	0	7	5	
Upper ^c	19	4	13	
Middle ^d	6	3	6	
Lower ^e	6	0	2	
Type of tumor growth				0.001
Intraluminal	17	12	25	
Extraluminal	14	2	1	
Tumor cross section				0.584
Ant ^f /post ^g /gre ^h /less ⁱ	8/7/10/6	6/2/5/1	8/9/5/4	

^a Body mass index^b Esophagogastric junction^c Upper third of the stomach body^d Middle third of the stomach body^e Lower third of the stomach body^f Anterior wall side of the gastric body^g Posterior wall side of the gastric body^h Greater curvature side of the gastric bodyⁱ Lesser curvature side of the gastric body^j Laparoscopic wedge resection^k Laparoscopy–endoscopy cooperative surgery^l Nonexposed endoscopic wall-inversion surgery

terms of age at surgery, sex, and body mass index (BMI). A significantly greater number of operations for SMTs of the E–G junction were performed in the LECS and NEWS groups than in the LWR group (LWR, 0; LECS, 7; NEWS, 5; *P* = 0.003). Tumors that showed an extraluminal growth

pattern were significantly more likely to be managed surgically by LWR than by LECS or NEWS (LWR, 14; LECS, 2; NEWS, 1; *P* = 0.001). There were no differences for tumor cross section among the groups.

Surgical outcome (Table 2)

Mean operative duration was significantly shorter in the LWR group compared with other groups (LWR, 112.0 min; LECS, 210.0 min; NEWS, 206.2 min; *P* < 0.001). Mean serum C-reactive protein (CRP) levels on postoperative days (POD) 1 and 3 were significantly higher in the LECS group than in other groups (POD 1: LWR, 2.7 mg/dl; LECS, 5.3 mg/dl; NEWS, 2.4 mg/dl; *P* < 0.001; POD 3: LWR, 4.1 mg/dl; LECS, 6.8 mg/dl; NEWS, 2.5 mg/dl; *P* < 0.001). Mean postoperative hospitalization duration was significantly shorter in the NEWS group than the LWR group (LWR, 8.8 days; LECS, 9.6 days; NEWS, 7.6 days; *P* = 0.007). There were seven cases of postoperative complications in the LWR group, of which five cases were the development of impermanent digestive symptoms, and one case of intraoperative capsular rupture and one of postoperative stenosis. Within the seven cases, five tumors were located at the upper or lower gastric body, and four tumors showed an intraluminal growth pattern. Tumor size ranged from 2.2 to 4.4 cm (median, 2.9 cm). Three of the cases were managed using a single port. Endoscopic balloon dilatation was required in the case of postoperative stenosis. All cases that suffered impermanent digestive symptoms recovered with conservative measures without aftereffects, classified as grade I in the Clavien–Dindo classification. All other patients were discharged following an uneventful recovery. Patients were discharged when body temperature was 36.0 °–37.5 °C, they were able to take a regular diet without requiring any intravenous drip or medication except oral analgesic agents, were ambulatory, and able to be discharged directly to their homes. No patient required rehospitalization.

Table 2 Surgical outcomes

	LWR ^b	LECS ^c	NEWS ^d	<i>P</i> value
Operative duration (min)	112.0 ± 52.0	210.0 ± 61.8	206.2 ± 43.6	<0.001
Intraoperative blood loss (g)	11.2 ± 36.8	12.9 ± 24.3	1.0 ± 4.0	0.268
CRP (mg/dl) ^a				
POD 1	2.7 ± 1.6	5.3 ± 2.7	2.4 ± 1.3	<0.001
POD 3	4.1 ± 3.1	6.8 ± 4.2	2.5 ± 1.4	<0.001
Postoperative hospital stay (days)	8.8 ± 2.2	9.6 ± 1.8	7.6 ± 1.5	0.006
Number of complications	7	0	0	0.028

^a Serum C-reactive protein levels on postoperative days (POD) 1 and 3^b Laparoscopic wedge resection^c Laparoscopy–endoscopy cooperative surgery^d Nonexposed endoscopic wall-inversion surgery

Histopathological examinations (Table 3)

Every patient underwent curative resection with negative margins, irrespective of the surgical procedure. The mean ratio of resected specimen area to tumor area (specimen area/tumor area) was significantly higher in the laparoscopy (LAP) group compared with other groups (LAP, 449.7%; LECS, 261.2%; NEWS, 191.0%; $P < 0.001$). Neither recurrence nor metastasis was observed in the present study.

Cost analysis (Table 4)

NEWS was associated with a significantly lower mean total cost than the other groups (LWR, 306,644 yen; LECS, 287,891 yen; NEWS, 226,070 yen; $P < 0.001$). The primary reason appeared to be the difference in the cost of suturing devices as laparoscopic linear staplers were used less in the NEWS group (mean cost of suturing devices: LWR, 102,968 yen; LECS, 40,721 yen; NEWS, 700 yen; $P < 0.001$).

Discussion

Complete tumor excision is the treatment of choice for gastric SMTs (including nonmetastatic GISTs) [1–3]. Because lymph node dissection is not typically required, LWR has been suggested as the most appropriate surgical treatment for tumors smaller than approximately 5 cm in diameter [1, 4]. Retrospective studies to establish the feasibility and safety of laparoscopic resection for gastric SMTs have been reported [14–19]. Novel techniques such as LECS and NEWS have recently been developed to decrease the invasiveness of surgical interventions for gastric SMTs [5–11]. Although we previously reported the lesser invasiveness of SILS and NEWS [6–9, 13], to the best of our knowledge this is the first study to provide a comparative verification of minimally invasive laparoscopic methods.

LECS and NEWS allow minimally invasive surgical interventions for gastric SMTs of the E–G junction, which have been difficult to treat with LWR because of the wide extent of resection potentially leading to postoperative structuring. After we introduced LECS in 2011 and NEWS in 2013, gastrectomy was required in only one case of

Table 3 Histopathological findings

	LWR ^h	LECS ⁱ	NEWS ^j	<i>P</i> value
Tumor size (cm) ^a	3.2 ± 0.9	3.3 ± 0.8	2.7 ± 0.9	0.043
Tumors with ulceration (<i>n</i>)	6	0	6	0.158
Pathological diagnosis (<i>n</i>)				<0.001
GIST ^b	27	6	16	
Leiomyoma	1	7	2	
Others ^c	3	1	8	
Mitotic index (/50)	3.3 ± 2.8	1.8 ± 1.6	3.2 ± 3.6	0.563
Modified Fletcher classification (<i>n</i>)				0.002
Very low	0	0	8	
Low	21	6	7	
Intermediate	6	0	0	
High	0	0	1	
Positive margins ^d	0	0	0	
Recurrence ^e	0	0	0	
Area of resected specimen ^f (cm ²)	27.6 ± 23.6	15.4 ± 6.4	8.3 ± 5.1	<0.001
Area of tumor ^g (cm ²)	7.0 ± 3.9	6.6 ± 2.5	5.1 ± 2.9	0.101
Specimen area/tumor area (%)	449.7 ± 310.1	261.2 ± 149.6	191.0 ± 142.1	<0.001

^a Major axis of the tumor

^b Gastrointestinal stromal tumor

^c Includes schwannomas, benign cysts, and heterotopic pancreatic tissues

^d Number of cases in which the resected specimen had positive margins

^e Number of cases in which recurrence was observed by December 2016

^f Calculated by the major and minor axes of the resected specimen

^g Calculated by the major and minor axes of the tumor

^h Laparoscopic wedge resection

ⁱ Laparoscopy–endoscopy cooperative surgery

^j Nonexposed endoscopic wall-inversion surgery

Table 4 Surgical costs

	LWR ^f	LECS ^g	NEWS ^h	<i>P</i> value
Ports (yen) ^a	78,032 ± 10,738	69,907 ± 5,933	74,530 ± 6,737	0.016
Suturing devices (yen) ^b	102,968 ± 49,344	40,721 ± 50,428	700 ± 177	<0.001
Cutting devices (yen) ^c	99,645 ± 20,728	128,500 ± 0	102,961 ± 39,066	0.005
Personnel (yen) ^d	24,252 ± 11,264	45,486 ± 13,384	44,661 ± 9,434	<0.001
Anesthesia (yen) ^e	1747 ± 811	3276 ± 964	3,217 ± 679	<0.001
Total (yen)	306,644 ± 60,301	287,891 ± 41,862	226,070 ± 40,494	<0.001

^a Cost of camera ports, 12-mm ports, 5-mm ports, multiple instrument access devices, and 2-mm laparoscopic loop-type retractors

^b Cost of laparoscopic stapling devices, reloads, endoscopic clipping devices, and surgical sutures

^c Cost of endoscopic and laparoscopic electrocauteries and laparoscopic energy devices

^d Expenses of surgeons, endoscopists, anesthesiologists, and nurses

^e Expenses of anesthetic maintenance

^f Laparoscopic wedge resection

^g Laparoscopy–endoscopy cooperative surgery

^h Nonexposed endoscopic wall-inversion surgery

circumferential SMT of the E–G junction. NEWS was also performed for the treatment of ulcerated SMTs because of the absence of tumor dissemination [9]. However, we limited indications for NEWS to tumors smaller than approximately 3 cm in the minor axis owing to the necessity of transoral extraction; in the present study, the minor axis of tumors was predominantly less than 3 cm (mean value of minor axis: LWR, 2.6 cm; LECS, 2.5 cm; NEWS, 2.2 cm). NEWS appears to be an appropriate surgical option for the resection of SMTs under laparoscopy.

The shorter operative duration observed in the LWR group compared to the LECS and NEWS groups appears to be attributable to the use of laparoscopic linear stapling devices and avoidance of circumferential incisions under laparoscopy and endoscopy. Linear stapling devices certainly simplify the surgical procedure and shorten operative duration; however, their use may lead to postoperative deformation or stricturing when the tumor is located at the lesser curvature side, E–G junction, or the pylorus. In the present study, the use of laparoscopic linear stapling devices in the LWR group significantly expanded the area of the resected stomach according to histopathological findings. The postoperative complications observed in the LWR group, including postoperative stenosis and digestive symptoms, may have resulted from the relatively wide extent of resection. Additionally, disturbance of excursion caused by the use of a single port may have led to stenosis and deformation of the stomach in the three cases who suffered digestive symptoms after single-incision laparoscopic surgery. The hand-sewn technique may be indispensable in such cases.

The hand-sewn technique also confers a cost benefit. However, the longer operative duration of LECS and NEWS resulted in higher personnel and anesthetic

expenses than LWR; by eliminating laparoscopic linear stapling devices, LECS and NEWS resulted in significantly lower costs than LWR. Furthermore, the operative duration of NEWS should shorten as cases accumulate. In practice, the mean operative duration of cases treated in 2013 was 269.3 min, whereas that of cases treated in 2016 was 195.2 min. Accordingly, the personnel and anesthetic costs of LECS and NEWS should continue to decrease in the future.

In the present study, serum CRP levels, an indicator of inflammation, was significantly higher in the LECS group than other groups on both postoperative days 1 and 3, possibly because LECS is the only surgical method that involves transmural communication. Preventing the leakage of the digestive fluid into the abdominal space during operations has been posited as an important factor in preventing the postoperative elevation of inflammatory markers. Because the technique is less invasive, the NEWS group demonstrated significantly shorter postoperative hospital stay durations than the LECS group.

Considering our results, the surgical algorithm shown in Fig. 1 seems suitable for the treatment of gastric SMTs. For cases unlikely to suffer postoperative stricture after resection using surgical staplers (tumors that show an extraluminal growth pattern and tumors of the greater curvature of the gastric body), LWR may be selected because of the shorter operative duration. According to patient choice, SILS may represent an alternative option. For other cases, we recommend NEWS for all tumors that can be transorally extracted (smaller than approximately 3 cm) for reasons of decreased postoperative inflammation, smaller extent of resection, shorter postoperative hospital stays, and the cost–benefit relationship. In cases where transoral extraction is difficult, LECS or laparoscopic gastrectomy (LAG)

should be selected according to the presence or absence of ulceration and tumor size. CLEAN-NET [12] and inverted LECS with CROWN method [20, 21] may also represent a feasible option [12]. For circumferential SMTs of the E–G junction, we particularly recommend laparoscopy-assisted proximal gastrectomy using the technique we previously established for early E–G junction cancers [22].

The present study was limited by being a retrospective analysis. Further accumulation of clinical cases and prospective randomized trials are required to establish the most appropriate treatment options for gastric SMTs.

Conclusions

Operative procedures for gastric SMTs must be carefully selected according to patient characteristics and tumor properties. NEWS may represent a widely applicable and less invasive technique with cost benefits for gastric SMTs smaller than 3 cm.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study.

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