

Laparoscopic-endoscopic cooperative surgery for gastric submucosal tumors

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and 58 (57.4%) women, with mean age of 51.2 ± 13.1 years (range, 14-76 years). The most common symptom was belching. Almost all ($n = 97$) patients underwent surgery with preservation of the cardia and pylorus, with the other four patients undergoing proximal or distal gastrectomy. The mean distance from the lesion to the cardia or pylorus was 3.4 ± 1.3 cm, and the minimum distance from the tumor edge to the cardia was 1.5 cm. Tumor pathology included gastrointestinal stromal tumor in 78 patients, leiomyoma in 13, carcinoid tumors in three, ectopic pancreas in three, lipoma in two, glomus tumor in one, and inflammatory pseudotumor in one. Tumor size ranged from 1 to 8.2 cm, with 65 (64.4%) lesions < 2 cm, 32 (31.7%) > 2 cm, and four > 5 cm. Sixty-six lesions (65.3%) were located in the fundus, 21 (20.8%) in the body, 10 (9.9%) in the antrum, three (3.0%) in the cardia, and one (1.0%) in the pylorus. During a median follow-up of 28 mo (range, 1-69 mo), none of these patients experienced recurrence or metastasis. The three patients who underwent proximal gastrectomy experienced symptoms of regurgitation and belching.

Abstract

AIM: To assess the feasibility, safety, and advantages of minimally invasive laparoscopic-endoscopic cooperative surgery (LECS) for gastric submucosal tumors (SMT).

METHODS: We retrospectively analyzed 101 consecutive patients, who had undergone partial, proximal, or distal gastrectomy using LECS for gastric SMT at Peking Union Medical College Hospital from June 2006 to April 2013. All patients were followed up by visit or telephone. Clinical data, surgical approach, pathological features such as the size, location, and pathological type of each tumor; and follow-up results were analyzed. The feasibility, safety and effectiveness of LECS for gastric SMT were evaluated, especially for patients with tumors located near the cardia or pylorus.

RESULTS: The 101 patients included 43 (42.6%) men

CONCLUSION: Laparoscopic-endoscopic cooperative surgery is feasible and safe for patients with gastric submucosal tumor. Endoscopic intraoperative localization and support can help preserve the cardia and pylorus during surgery.

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Key words: Laparoscopic-endoscopic cooperative surgery; Gastric submucosal tumor; Minimally invasive surgery; Laparoscopy; Endoscopy

Core tip: We retrospectively analyzed 101 consecutive patients who had undergone partial, proximal or distal gastrectomy using laparoscopic-endoscopic cooperative surgery (LECS) for gastric submucosal tumor (SMT) at Peking Union Medical College Hospital from June 2006 to April 2013. Ninety-seven patients underwent surgery with preservation of the cardia and

pylorus, with the other four patients undergoing proximal or distal gastrectomy. LECS is feasible and safe for gastric SMT, especially for patients with tumors near the cardia or pylorus. Intraoperative localization and support by endoscopy can help preserve the cardia and pylorus during surgery.

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INTRODUCTION

Since the first gastrectomy was performed in 1880, surgical methods have developed rapidly due to improvement in anastomosis techniques, surgical staplers, and gastrointestinal tube application^[1]. Moreover, since the first cholecystectomy by electronic laparoscopy was performed in 1987, minimally invasive laparoscopic surgery has become more popular for its lower postoperative morbidity rates and faster postoperative recovery^[2-5]. Minimally invasive surgery is suitable for benign gastric lesions, especially for gastrointestinal stromal tumors (GISTs). Although GISTs are potentially malignant, nodal metastasis is rare. Therefore, excision of the tumor with negative margins but without lymphadenectomy has become a standard approach, while GISTs are indicated for minimally invasive partial gastrectomy^[6-9].

Although gastric small mucosal tumors (SMT) have been resected laparoscopically, this type of surgery is associated with two potential problems. Laparoscopy may be unable to determine the location of gastric SMTs, because of their small size or intraluminal growth pattern. In addition, complications may arise during the laparoscopic removal of SMTs located near the cardia or pylorus; these complications can include stenosis or damage to the cardia or pylorus. We have therefore developed a technique, called minimally invasive laparoscopic-endoscopic cooperative surgery (LECS), for removal of SMTs. This paper represents our analysis of findings in 101 patients who successfully underwent LECS for gastric SMT at the Department of General Surgery, Peking Union Medical College Hospital, from June 2006 to April 2013.

MATERIALS AND METHODS

Clinical data

From June 2006 to April 2013, 101 patients successfully underwent LECS for gastric SMT at the Department of General Surgery, Peking Union Medical College Hospital; the cardia and pylorus were preserved in 97 of these patients. In addition to routine preoperative tests, all patients underwent upper gastrointestinal endoscopy with

endoscopic ultrasound (EUS) and a computed tomography (CT) scan with three-dimensional gastric display. Demographic and clinicopathological characteristics were analyzed retrospectively. Demographic features assessed included patient sex and age, the length of the operation, estimated blood loss, and rate of conversion to open surgery. Postoperative data included time to bowel function recovery (normal passage of gas), surgical complications (*e.g.*, leakage, stenosis, and bleeding), and length of postoperative hospital stay. The clinicopathological characteristics of the SMTs included their size, location, and pathological type.

Surgical procedures

LECS was performed with the patient under general anesthesia in the reverse Trendelenburg position. The surgeon stood between the patient's legs, the first assistant was to the right or the left of the patient's body, the laparoscopist to the right of the patient's legs, and the gastroscopist to the left of the patient's head.

Setup for laparoscopic surgery

A camera port was inserted into the inferior (1 cm) umbilical incision (10 mm port) using an open technique. Three additional ports (two 5 mm and one 12 mm in diameter) were inserted into the left upper and right upper quadrants and the inferior xiphoid process (on the right or left side according to the location of the SMT), respectively, under a pneumoperitoneum of 1.60-1.86 kPa, with a laparoscopic view (30° angle range).

Endoscopic procedures

With the patient anesthetized, the endoscope was inserted through the oropharynx. The mucosae of the esophagus and stomach were viewed, taking care not to infuse too much air into the stomach. The location of the SMT was confirmed, all liquids and gas were withdrawn, and the endoscope was withdrawn through the cardia to remain in the esophagus^[10].

Operative approaches

Tumors within the anterior wall of the stomach: The omentum was detached and a little air was allowed to fill the stomach endoscopically. Using both the laparoscope and the endoscope, the location of the SMT was confirmed by the method of touch and marked by one or two suture lines. The gastric wall, including the SMT, was elevated with two seromuscular sutures placed opposite each other and 2-4 cm from the lesion. The tumors, as well as some normal gastric tissues, were removed with a linear endoscopic gastrointestinal stapler (*e.g.*, EC60). If the tumor was located near the esophagogastric junction or pyloric ring, the endoscope was placed distally into the stomach or duodenum to protect the normal gastric tissues from stenosis or damage. After the lesion was resected, direct intraluminal visualization was performed to ensure that the tumor was totally removed and that there was no bleeding or leakage. The amount of air in

Table 1 Demographic and clinical characteristics of the 101 patients who underwent laparoscopic and endoscopic cooperative surgery for gastric submucosal tumors *n* (%)

Parameters	Statistics
No. of patients	101
Age (yr)	51.2 ± 13.1 (range 14-76)
Sex	
Male	43 (42.6)
Female	58 (57.4)
Chief complaint	
Dyspepsia (regurgitation, eructation, belching, epigastralgia, and epigastric discomfort)	69 (68.3)
Physical examination (asymptomatic)	27 (26.7)
Melena	5 (5.0)
Tumor location	
Cardia	3 (3.0)
Gastric fundus	66 (65.3)
Gastric body	21 (20.8)
Gastric antrum	10 (9.9)
Pylorus	1 (1.0)
Distance between the tumor and cardia or pylorus (cm)	3.4 ± 1.3 (minimum 1.5)

Data are presented as mean ± SD.

the stomach and peritoneum was balanced, resulting in a good visual field.

Tumors within the posterior wall of the stomach:

The proximate curvature was detached to expose the tumor, using, for example, the Ligasure vascular sealing system. The posterior wall was rotated, and the tumor was resected using a technique similar to that described for anterior lesions.

Tumors within the lesser curvature (anterior and posterior gastric wall borderline) of the stomach:

The small omentum was detached to expose the tumor, followed by tumor resection using the technique described above. For larger tumors, the left gastric vessels were cut off to prevent both operative and postoperative bleeding. Endoscopic support was especially important for tumors located near the esophagogastric junction^[11].

The resected tumor was placed in a specimen retrieval bag located outside the left upper quadrant port. The tumor was cut open along the suture lines, and any ruptures in tumor integrity were assessed. The tumor was measured, immersed in 10% formalin solution, and sectioned. The sections were routinely stained with hematoxylin and eosin, and the number of mitotic figures per 50 high powered fields (HPF) was counted. Risk classifications for GIST were those described by the National Institutes of Health (NIH) in 2008. Gastric GIST was confirmed by immunohistochemistry, using antibodies to identify CD-117 (c-kit), CD-34, and DOG-1.

Follow-up

All patients were followed up by visit or telephone after 1, 3, 6, 9, 12, 24, 36, 48, and 60 mo. Each follow-up included a medical history review of any reports of abdominal

discomfort, as well as CT scans and upper gastrointestinal endoscopy to exclude tumor recurrence or metastasis.

Statistical analysis

Data are expressed as mean ± SD. All analyses were performed using SPSS 12.0 software (SPSS, Chicago, IL, United States).

RESULTS

Surgery was successful in all 101 patients. The demographic and clinical characteristics of the 101 patients are depicted in Table 1. Three patients each had two GISTs.

Of the 101 patients, four underwent proximal or distal gastrectomy, including three with tumors located at the cardia, and one with a tumor located at the pylorus. The remaining 97 patients had preservation of the cardia and pylorus. During surgery, tumor location could not be confirmed by laparoscopy alone in 92 patients.

The mean operation time was 113 ± 36 min, and none of these patients required conversion to open surgery. Mean estimated blood loss was 36 ± 18 mL. The postoperative course of all patients was uneventful, with no anastomosis leakage. One patient who underwent proximal gastrectomy had an anastomotic stenosis because of scar physique. This patient was successfully treated by balloon dilatation under X-ray fluoroscopy. One patient experienced anastomotic bleeding and was successfully treated by conservative methods (drug hemostasis and blood transfusion). The average time to first gas passage was 2.9 ± 0.9 d, the average time for nasogastric tube placement was 1.9 ± 0.5 d, and the average postoperative hospital stay was 4.2 ± 1.1 d (Table 2). Seven patients underwent simultaneous laparoscopic cholecystectomy for gallstones, and two underwent simultaneous endoscopic polypus dissection.

All the resected tumors were cut open along the suture lines, with none showing evidence of rupture.

The clinicopathological characteristics of the submucosal stomach tumors, including their location, are shown in Table 3. Of the 101 tumors, 78 (77.2%) were GISTs, with 53 located in the gastric fundus, 14 in the gastric body, seven in the antrum, three in the cardia, and one in the pylorus. The remaining tumors included 13 (12.9%) leiomyomas, 11 in the gastric fundus and two in the gastric body; three (3.0%) ectopic pancreases, two in the gastric fundus and one in the antrum; three (3.0%) carcinoids, two in the gastric body and one in the antrum; two (2.0%) lipomas, one each in the gastric body and antrum; one (1.0%) glomus tumor in the gastric body; and one (1.0%) inflammatory pseudotumor in the gastric body. Maximum tumor size ranged from 1 to 8.2 cm, with 65 (64.4%) lesions < 2 cm in size, 32 (31.7%) > 2 cm, and four > 5 cm.

Gastric GIST was confirmed by immunohistochemistry in 78 patients, with 68 (87.2%) positive for CD117, 65 (82.9%) positive for CD34, and 65 (82.9%) positive for DOG1. Using the NIH biological risk classification for GIST^[12], we found that 54 (69.2%) tumors were of

Table 2 Operative data for laparoscopic and endoscopic cooperative surgery *n* (%)

Parameters	Statistics
Operation time (min)	113 ± 36
Conversion to open surgery	0 (0)
Intraoperative blood loss (mL)	36 ± 18
Postoperative complications	
Gastric fullness	0 (0)
Anastomotic leakage	0 (0)
Anastomotic stenosis	1 (1.0)
Anastomotic bleeding	1 (1.0)
Postoperative hospital stay (d)	4.5 ± 2.1
Time for nasal-gastric tube placement (d)	1.9 ± 0.5
Time until bowel function recovery (d)	2.9 ± 0.9

Data are presented as mean ± SD.

very low risk, including 41 in the gastric fundus, seven in the gastric body, four in the antrum, and two in the cardia; and 16 (23.5%) were of low risk, including eight in the gastric fundus, four in the gastric body, two in the antrum, one in the cardia, and one in the pylorus. Six tumors (7.7%), of mean size 5.4 ± 1.3 cm, were of moderate risk, including three in the gastric fundus, two in the gastric body, and one in the antrum. Two tumors (2.6%) were of high risk, one located in the gastric fundus was 8.2 cm in size; and the second, located in the gastric body, showed 13 mitotic figures/50 HPF. The first patient was treated with imatinib for 2 mo before the surgery, which decreased the tumor size from 8.8 to 8.2 cm in diameter. The eight patients in the moderate- and high-risk classes were treated with adjuvant imatinib for 1-2 years.

All the patients were followed up after LECS, for a mean time of 28 mo (range, 1-69 mo). The three patients who underwent proximal gastrectomy developed symptoms of regurgitation, eructation, and belching. None of the 101 patients who underwent LECS showed evidence of tumor recurrence, metastasis, nutritional disturbances (*e.g.*, weight loss, vitamin deficiency, deficiency of trace elements), or decreased quality of life. One patient developed primary liver cancer 2 years and 4 mo after LECS, but this patient remains alive. In addition, none of the patients with preserved cardia and pylorus experienced any symptoms of epigastric discomfort.

DISCUSSION

We have shown here that LECS is feasible, yielding satisfactory surgical results, in patients with gastric SMT. Usually, gastric SMTs are resected by open surgery, either distal or proximal gastrectomy^[13]. Operation time and postoperative hospital stay are longer, and many patients develop gastroesophageal reflux disease (GERD). Quality of life may decrease, and the risk of remnant gastric cancer or esophageal carcinoma may increase. In contrast, LECS requires a relatively small resection of the healthy gastric wall, with very low rates of postoperative morbidity and mortality. Of our 101 patients, only two experienced postoperative complications, one with anastomotic

Table 3 Clinicopathologic characteristics of submucosal tumors *n* (%)

Parameters	Statistics
Pathological diagnosis	
Gastrointestinal stromal tumor	78 (77.1)
Leiomyoma	13 (12.9)
Ectopic pancreas	3 (3.0)
Carcinoid	3 (3.0)
Lipoma	2 (2.0)
Glomus tumor	1 (1.0)
Inflammatory pseudotumor	1 (1.0)
Tumor size (cm)	4.9 ± 0.6

Data are presented as mean ± SD.

stenosis and one with anastomotic bleeding. Although tumors with an extragastric growth pattern can be easily treated using conventional laparoscopic wedge resection, laparoscopic methods alone have some limitations for the resection of gastric SMTs. Laparoscopy has been found to be less efficient than open surgery in removing small tumors and tumors located in the posterior gastric wall and lesser curvature of the stomach. In addition, the removal of large tumors and those located near the cardia or pylorus can result in post-operative complications, such as stenosis or damage to the cardia or pylorus.

All of our patients routinely underwent two important preoperative tests, upper gastrointestinal endoscopy with EUS and CT scan with a three-dimensional gastric display, both of which are very important for this surgery. EUS was used to assess depth of tumor invasion, lesion location, tumor size, and growth pattern^[14-18]. The diagnostic accuracy of EUS, however, may be affected by technical problems or skills or the subjective view of the operator, whereas the diagnostic accuracy of CT scanning was less subjective. CT three-dimensional imaging was helpful in assessing tumor size, the distance between the tumor and local tissues (cardia and pylorus), and the diagnosis and staging of SMTs. Use of these two tests could therefore determine whether localized gastric SMTs can be resected.

Endoscopic submucosal dissection (ESD) performed by experienced endoscopists has been used to remove gastric SMTs^[19,22]. We found that 78 of our 101 (77.2%) SMTs were GISTs. GISTs are a type of mesenchymal neoplasm, originating from Cajal cells; are located in the submucous, muscularis propria, or subserous layer; and have an intraluminal or extrinsic growth pattern. ESD resection of tumors in the muscularis propria, while preserving the integrity of the serous layer, is very difficult. ESD alone may result in high rates of resection failure, intraoperative bleeding, and perforation. In addition, this procedure cannot easily differentiate between benign and malignant tumors. Since GISTs are regarded as potentially malignant and in need of complete resection, ESD alone should not be used to remove gastric SMTs.

The development of the LECS procedure has expanded the range of minimally invasive surgery. The endoscopic assistant cut the exact edges from the gastric

lumen, followed by tumor resection aided by endoscopy. Endoscopic support could reduce complications, such as stenosis or damage to the cardia or pylorus, especially when the tumor is located in the gastric fundus or antrum. Moreover, direct intraluminal visualization can confirm that the tumor has been totally removed, that there is no bleeding from the suture lines, and that there are no perforations. When observing through the endoscope, the pneumoperitoneum should be at lower pressure and the laparoscope should be removed for a better view. All gas and liquid should be removed endoscopically for better laparoscopic procedures. Laparoscopy may be sufficient, however, for large tumors, for tumors located near the cardia and pylorus, and for tumors with an extrinsic growth pattern. Even in these situations, however, endoscopic support is important for protecting the cardia and/or pylorus from damage during resection, even if the endoscope is not need to confirm tumor location. LECS can therefore improve the success rates and outcomes of minimally invasive surgery without postoperative morbidity or mortality.

The sphincter muscles in the cardia and pylorus are important anatomical structures for preserving regurgitation. Although 59.1% of SMTs were reported located at the fundus^[11], we found that the percentage was higher, 67.9%. Resection of the cardia can cause symptoms like heartburn due to gastric acid regurgitation. These patients may have to take medicines like proton pump inhibitors for a long time, reducing patient quality of life, and may develop GERD or esophageal carcinoma. Of our 101 patients, only three underwent proximal gastrectomy, with all three developing symptoms of regurgitation, eructation, and belching. Similar findings would be observed after resection of the pylorus, since duodenal juice would regurgitate into the remnant stomach, causing inflammation at the suture lines and corresponding symptoms and ultimately leading to remnant gastric cancer^[21,22]. Therefore, it is very important to preserve these important anatomical structures. LECS can decrease the risk to resect the cardia and pylorus. We found that the minimum distance from the edge of the tumor to the cardia was 1.5 cm. The importance of endoscopic support was inversely correlated with the distance between the tumor edge and the cardia or pylorus^[23]. In addition, GISTs are supplied by many blood vessels. When resecting larger tumors within the lesser curvature, the left gastric vessels should be cut off to prevent postoperative bleeding. In this study, one 76-year-old patient experienced anastomotic bleeding, because of atherosclerosis. After 2 d of conservative therapy, consisting of blood transfusions, he got better and was discharged.

All 101 of our patients underwent minimally invasive surgery, with LECS in 97 resulting in the preservation of the cardia and pylorus. None of these patients required conversion to open surgery. Intraoperative bleeding was limited and recovery of bowel function was rapid, with a low postoperative morbidity (except for one patient each with anastomotic stenosis and bleeding), and no

postoperative mortality. Postoperative hospital stay was much shorter than in several previous studies. Except for the three patients who underwent proximal gastrectomy, none developed symptoms like GERD and their quality of life did not decrease over a relatively long-term follow-up, suggesting the importance of preserving the anatomical structure and physical function of the cardia and pylorus. None of our 78 patients with gastric GIST developed tumor recurrence or metastasis after LECS, regardless of risk classification, indicating that total resection of SMTs, including potentially malignant GISTs, by the LECS techniques yields satisfactory surgical outcomes. We found that 50% of tumors classified as moderate or high risk, and most with more than five mitoses per 50 HPFs, were located at the gastric fundus. Patients in moderate- and high-risk categories required adjuvant imatinib^[24]. We found that two patients had tumors < 5 cm, but more than 10 mitotic figures per 50 HPFs.

LECS can be used for two types of partial gastrectomy. The first consists of laparoscopic wedge resection of gastric SMTs and distal or proximal gastrectomy under endoscopic guidance; and the second consists of laparoscopic cutting of the anterior wall of the stomach, to expose SMTs in the posterior gastric wall, followed by partial resection of the posterior gastric wall. All 101 of our patients with SMTs underwent complete resection, even if the tumors were located in the posterior, the lesser curvature of the stomach or near the cardia or pylorus. The greater curvature of the stomach was detached, the stomach was turned axially, and wedge resection was performed. A good view during this procedure requires that the amount of air in the stomach and peritoneum should be balanced.

LECS is indicated for the removal of SMTs (*e.g.*, leiomyomas, lipomas, and schwannomas), polyps with broad stalks, gastric epithelial tumor degeneration (moderate or severe atypical hyperplasia), lesions with low potential for malignancy (*e.g.*, carcinoid tumors and GISTs), and early-stage, localized gastric carcinomas^[25]. Because GISTs may easily rupture during laparoscopic surgery, resulting in peritoneal seeding, the integrity of a resected GIST is regarded as a significant prognostic factor. Before 2007, the guidelines of the National Comprehensive Cancer Network did not recommend laparoscopic surgery for GIST resection, except for tumors < 2 cm in diameter and with a low risk of rupture. Although almost one-third of the tumors in this study were > 2 cm in diameter, LECS was successful for all tumors, regardless of tumor size. These findings indicate that the performance of laparoscopic and endoscopic techniques by skilled operators, non-contact with the tumor during surgery, and the use of a specimen retrieval bag are key factors for good surgical results. Tumors > 5 cm in diameter require resection of a relatively large portion of healthy stomach to ensure tumor integrity without rupture^[26].

This study had several limitations, including its retrospective design and lack of comparisons with open or laparoscopic surgery. Prospective, multicenter, compara-

tive studies are needed to evaluate the role of LECS for gastric SMT.

In conclusion, we have shown here that LECS is a safe, easy, and beneficial procedure for gastric SMTs. Endoscopy functions to locate the tumor and to support the gastric lumen. The LECS technique, therefore, provides an alternative gastric wedge resection procedure with minimal transformation of the stomach.

COMMENTS

Background

Although gastric small mucosal tumors (SMT) have been resected laparoscopically, this type of surgery is associated with two potential problems. Laparoscopy may be unable to determine the location of gastric SMTs, because of their small size or intraluminal growth pattern. In addition, complications may arise during the laparoscopic removal of SMTs located near the cardia or pylorus; these complications can include stenosis or damage to the cardia or pylorus.

Research frontiers

Laparoscopic-endoscopic cooperative surgery (LECS) is indicated for the removal of SMTs (e.g., leiomyomas, lipomas, and schwannomas), polyps with broad stalks, gastric epithelial tumor degeneration (moderate or severe atypical hyperplasia), lesions with low potential for malignancy (e.g., carcinoid tumors and gastrointestinal stromal tumors), and early-stage, localized gastric carcinomas.

Innovations and breakthroughs

The authors have developed a technique, called minimally invasive LECS, for removal of SMTs. This paper represents the analysis of findings in 101 patients who successfully underwent LECS for gastric SMT at the Department of General Surgery, Peking Union Medical College Hospital, from June 2006 to April 2013.

Applications

The study results suggest that the LECS is feasible and safe for patients with gastric SMT. Endoscopic intraoperative localization and support can help preserve the cardia and pylorus during surgery.

Terminology

LECS represents a technique, called minimally invasive laparoscopic-endoscopic cooperative surgery for removal of gastric small mucosal tumors.

Peer review

This is a very interesting paper about laparoscopic-endoscopic surgery for gastric submucosal tumor. In this manuscript, the authors analyzed 101 patients who underwent laparoscopic-endoscopic surgery for gastric submucosal tumor. The authors discussed the safety and advantages of minimally invasive laparoscopic-endoscopic cooperative surgery for gastric submucosal tumor. The clinical data was well collected, and the surgical procedures of the patients were well described. The references are updating.

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