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Original Article

Laparoscopic and Open Resection of Gastrointestinal Stromal Tumors of the Stomach

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Abstract

Introduction : Laparoscopic resection has been reported as reasonable for patients with gastrointestinal stromal tumors (GISTs). In this study, we report the feasibility of the laparoscopic approach for GIST of the stomach. We also discuss the laparoscopic approach for GIST larger than 5 cm, which is reported to be difficult to treat by laparoscopic surgery.

Materials and Methods : We retrospectively reviewed 22 patients with GIST of the stomach resected by laparoscopic or open procedures between January 2006 and February 2014.

Results : Laparoscopic resections were performed in 9 patients and open resections in 13 patients. Curative resections with negative resection margins were successfully completed for all patients. Although the size of the tumors was greater in open surgery cases than in laparoscopic patients ($P = 0.03$), the loss of blood was lower and the hospital stay was shorter in laparoscopic cases ($P = 0.01$ and 0.003 , respectively). Laparoscopic resection was performed for 2 patients with GISTs larger than 5 cm. Both were located at greater curvature, and curatively resected without any complications or recurrence.

Discussion : Our experience suggests that laparoscopic surgery for GISTs of the stomach, including those larger than 5 cm, may be feasible after careful deliberation of its indications. Laparoscopic resection for GIST was associated with lower loss of blood and shorter hospital stay in comparison with open resection.

Key words : Gastrointestinal tumor · Laparoscopy · Gastric surgery

Introduction

Gastrointestinal stromal tumors (GISTs) are mesenchymal neoplasms of the gastrointestinal tract originating from the intestinal pacemaker cells of Cajal¹⁾. These tumors are diagnosed by their expression of CD34, CD117, and a c-kit protein. GISTs can occur throughout the entire gastrointestinal tract, with approximately 70% arising in the stomach^{1)–3)}.

Although some GISTs appear benign, they are considered potentially malignant³⁾. Imatinib

mesylate has been used as molecular-targeted therapy for metastatic GISTs⁴⁾. However, surgery still remains the only curative treatment for the management of resectable GISTs. Minimally invasive resection with a negative surgical margin was reported as sufficient for the treatment of GISTs⁵⁾. Wide resection or extensive lymphadenectomy was not required⁵⁾. Therefore, wedge gastrectomy has been traditionally performed for GISTs of the stomach. Recently, laparoscopic resection has been reported as feasible, and comparable to open resection^{6)–9)}.

The 2007 National Comprehensive Cancer Network (NCCN) guideline recommended that laparoscopic resection be limited to tumors smaller than 5 cm⁴⁾. Much controversy exists about the maximum diameter of a GIST for laparoscopic resection. Some investigators have reported successful resection of GISTs of the stomach larger than 5 cm using a laparoscopic approach¹⁰⁻¹²⁾. It is suggested that factors other than tumor diameter, such as the location of the tumor, the surgeon's skill, or technological advancements in devices, may guarantee a safe laparoscopic approach.

The aims of this study were to evaluate the feasibility of laparoscopic resection of GISTs of the stomach and to examine the laparoscopic strategy for large GISTs.

Materials and methods

Patients and indications

We performed curative resection in 22 consecutive patients with primary GIST of the stomach between January 2006 and February 2014 in a single institution (Matsuyama Red Cross Hospital, Ehime, Japan). All patients were diagnosed as having GIST by postoperative immunohistochemistry evaluation. The surgical approach was selected by preoperative conference, considering the size and the location of the tumor, although the laparoscopic approach was mainly considered for tumors smaller than 5 cm on preoperative imaging such as computed tomography or magnetic resonance imaging.

Surgical procedures

For the laparoscopic procedure, the patient was placed in the supine position with the legs open. The surgeon stood on the right side of the patient. The assistant and the scopist stood on the left side of the patient and between the patient's legs, respectively. In general, five port sites, including the camera port, were used. First, we mobilized the stomach enough to observe the margin of the tumor. When the tumor originated from the

posterior wall or lesser curvature of the stomach, we opened the omental bursa or lesser omentum. The wedge resection was performed with an endoscopic stapler. The tumors were removed via a mini-laparotomy to an endoscopic retrieval bag (EZ purse ; Hakko Medical, Nagano, Japan).

For the open procedure, the patient was placed in the supine position and a similar procedure was performed via an upper midline laparotomy.

Adjuvant therapy and follow-up

Adjuvant chemotherapy was standard for the patients with high-risk GIST in accordance with Fletcher's classification¹³⁾. We administered adjuvant chemotherapy for the patients with high-risk GIST except for those who were not willing to receive chemotherapy or whose general condition was not suitable for chemotherapy.

Follow-up examinations comprising clinical examination and radiological investigations, including computed tomography, took place every 6 months for 5 years.

Results

Laparoscopic resections were performed in 9 patients and open resections in 13 patients. The patients' baseline characteristics are shown in Table 1. The mean age was 55.0 years for the laparoscopic group and 72.9 years for the open group. The patients who underwent laparoscopic surgery were significantly younger and had a higher body mass index than those undergoing open surgery ($P = 0.01$ and $P = 0.02$, respectively). Fifty-five percent of the patients exhibited symptoms, the most common being melena (23 %), anemia (14 %), and abdominal pain (9 %). Forty-five percent of the patients were diagnosed with GIST incidentally. The tumors were located at the upper third of the stomach in half of the patients. In the laparoscopic group, the GIST tended to originate from the greater curvature. By contrast, patients in the open group tended to have a GIST arising from the lesser curvature. There were no significant differences in sex,

Table 1 Patients' background

Variables	Total group (n = 22)	Laparoscopic group (n = 9)	Open group (n = 13)	<i>P</i> value
Gender				
Male (%)	15(68)	7(78)	8(62)	0.41
Female (%)	7(32)	2(22)	5(38)	
Age at operation (years)*	65.6 ± 3.2	55.0 ± 5.3	72.9 ± 2.4	0.01
Body mass index (kg/m ²)*	22.2 ± 3.7	24.5 ± 1.2	20.6 ± 0.8	0.02
Symptom				0.12
free (%)	10(45)	4(44)	6(46)	
melena (%)	5(23)	4(44)	1(8)	
hematemesis (%)	1(5)	0(0)	1(8)	
abdominal pain (%)	2(9)	1(11)	1(8)	
anemia (%)	3(14)	0(0)	3(23)	
abdominal mass (%)	1(5)	0(0)	1(8)	
Site 1				0.31
upper third of stomach (%)	11(50)	6(67)	5(38)	
middle of stomach (%)	9(41)	2(22)	7(54)	
lower third of stomach (%)	2(9)	1(11)	1(8)	
Site 2				
lesser curvature (%)	7(32)	1(11)	6(46)	
greater curvature (%)	5(23)	3(33)	2(15)	
anterior wall (%)	2(9)	1(11)	1(8)	
posterior wall (%)	8(36)	4(44)	4(31)	

*; mean ± standard error

symptoms, and tumor site between the 2 groups.

Surgical outcomes are shown in Table 2. Partial gastrectomy was performed for all patients in laparoscopic group, while 2 patients were treated by distal gastrectomy or total gastrectomy in open group. There was no conversion to open surgery in laparoscopic group. The mean operating time was 117 min in both groups. Mean loss of blood was 26 g in the laparoscopic group and 297 g in the open group. The hospital stay was 8.8 days for laparoscopic patients and 17.7 days for open surgery patients. The loss of blood was significantly lower and the hospital stay was significantly shorter for the laparoscopic group ($P = 0.01$ and $P = 0.003$, respectively). There were no postoperative complications in the laparoscopic group, but one patient in the open group experienced postoperative acalculous cholecystitis.

Pathological variables are shown in Table 3. The mean tumor size was 3.8 cm in the laparoscopic group and 7.2 cm in the open group, hence significantly smaller in laparoscopic patients ($P =$

0.03). There were no significant differences in mitotic rate, Fletcher classification, and histology. Seven of the total 22 patients had high-risk GIST. In the laparoscopic group, three patients had high-risk GIST, 2 of whom had a GIST larger than 5 cm. The size of the 2 tumors was 6 cm and 7 cm, respectively. Both patients were preoperatively diagnosed with gastric submucosal tumor larger than 5cm. We selected the laparoscopic approach because both of these tumors were located in the greater curvature. We successfully performed curative resections with negative resection margins in all patients.

Clinical outcomes are shown in Table 4. The mean follow-up period for all cases was 44.1 months. Although the duration of follow-up was short for the laparoscopic group, all patients in this group remain alive without recurrence. In the open group, 2 patients had recurrence of GIST and 1 patient died of recurrence.

Table 2 Surgical outcomes

Variables	Total group (n = 22)	Laparoscopic group (n = 9)	Open group (n = 13)	P value
Surgical Procedure				0.13
Partial gastrectomy (%)	20(91)	9(100)	11(85)	
Distal gastrectomy (%)	1(5)	0(0)	1(8)	
Total gastrectomy (%)	1(5)	0(0)	1(8)	
Operating time (min)*	117 ± 11	117 ± 12	117 ± 16	0.52
Loss of blood (g)*	186 ± 74	26 ± 18	297 ± 118	0.01
Hospital stay (day)*	14.0 ± 2.1	8.8 ± 0.9	17.7 ± 3.1	0.003
Complications				0.30
- (%)	21(95)	9(100)	12(92)	
+ (%)	1(5)	0(0)	1(8)**	

*; mean ± standard error, **; acalculous cholecystitis

Table 3 Pathological variables

Variables	Total group (n = 22)	Laparoscopic group (n = 9)	Open group (n = 13)	P value
Tumor size (cm) *	5.8 ± 0.8	3.8 ± 0.6	7.2 ± 1.1	0.03
Mitotic count (per 50HPF)				0.17
< 5(%)	10(45)	3(33)	7(54)	
6-10 (%)	6(27)	4(44)	2(15)	
> 10 (%)	6(27)	2(22)	4(31)	
Negative margin (%)	22(100)	9(100)	13(100)	-
Fletcher classification				0.51
very low risk (%)	1(5)	1(11)	0(0)	
low risk (%)	6(27)	2(22)	4(31)	
intermediate risk (%)	8(36)	3(33)	5(38)	
high risk (%)	7(32)	3(33)	4(31)	
Histology				0.30
Spindle (%)	11(50)	6(67)	5(38)	
Epithelioid (%)	2(9)	1(11)	1(8)	
Mixed (%)	7(32)	2(22)	5(38)	

*; mean ± standard error

Table 4 Clinical outcomes

Variables	Total group (n = 22)	Laparoscopic group (n = 9)	Open group (n = 13)	P value
Duration of follow up (months)*	44.1 ± 5.2	27.5 ± 5.9	55.4 ± 6.1	0.02
Recurrence (%)	2(9)	0(0)	2(15)	0.13
Disease related death (%)	1(5)	0(0)	1(8)	0.30

*; mean ± standard error

Discussion

In this report, we demonstrate the feasibility of laparoscopic resection of GISTs of the stomach. Laparoscopic surgery was associated with lower loss of blood and shorter hospital stay in comparison with open resection. Moreover, we

successfully performed curative resection using the laparoscopic approach in 2 patients with GISTs larger than 5 cm.

Several investigators have reported that laparoscopic resection for GISTs is compatible with open surgery in terms of morbidity, mortality, and long-term outcome⁽⁶⁻⁹⁾. However, these reports

are retrospective, with a small sample size or short duration of follow-up. There are no large prospective randomized trials comparing laparoscopic with open resection of GISTs of the stomach. Some authors have reported that laparoscopic resection of GISTs is associated with a shorter operation time, a shorter hospital stay, or a lower recurrence rate⁶⁾⁷⁾. In contrast, Nishimura et al⁸⁾ reported that there was no difference in operating time and blood loss between laparoscopic and open resection for GISTs. In our study, laparoscopic resection was associated with a smaller loss of blood and a shorter hospital stay. This relationship was also apparent in patients with GISTs smaller than 5 cm. In these patients, laparoscopic resection ($n = 7$) was associated with less blood loss and a shorter hospital stay when compared with open resection ($n = 5$) ($P = 0.05$ and $P = 0.02$, respectively). In our study, there was no correlation between operation time or short-term outcomes and the surgical approach. More prospective randomized trials are needed in the drive towards better evidence-based recommendations.

NCCN guidelines recommended that laparoscopic resection is limited to tumors smaller than 5 cm⁴⁾. Recently, there have been some reports on curative resection by laparoscopy for GISTs of the stomach larger than 5 cm¹⁰⁾⁻¹²⁾. The investigators recommended that the hand-assisted procedure could be used to facilitate gentle tumor handling, and that the fibrous tissue or normal gastric wall should be used to handle the mass. However, it has been reported that intraoperative rupture is associated with a high recurrence rate⁵⁾. It is also reported that the tumor rupture confers increased risk of recurrence, so the tumor ruptures are proposed to be included in high-risk category¹⁴⁾. In this report, there was no patient with tumor rupture. We determined the surgical approach based on the location and size of the tumor. In the cases of large GIST, we did not select laparoscopic resection when tumors were located near the cardia or pylorus, to keep a

negative surgical margin. We believe it is also feasible to resect and repair using laparotomy through a small incision after laparoscopic mobilization of the tumor. We also chose open surgery in cases of large GISTs originating in the posterior wall and supplied from the posterior gastric artery. Such tumors may be difficult to mobilize, and carry the risk of a large amount of hemorrhage from the splenic artery. By the same reason, tumors at the lesser curvature of the antrum should not be treated with laparoscopic surgery. In this study, 2 patients with GISTs larger than 5 cm underwent laparoscopic surgery. One of which was located at the greater curvature of the fundus and the other at the greater curvature of the upper stomach. A GIST located at the greater curvature seems to be the best indication for laparoscopic resection, although the surgeon's experience and skill would also be necessary. Careful preoperative examination and a skillful surgeon undoubtedly contribute to successful and curative surgery.

Laparoscopic resection for GISTs of the stomach is a safe and less invasive procedure than open surgery when the indication is fully examined. We also support the idea that when the tumor is located mainly at the greater curvature, the laparoscopic strategy is also feasible for GISTs of the stomach larger than 5 cm.

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胃 GIST に対する腹腔鏡下胃切除術の有用性の検討

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目的: 消化管間葉系腫瘍 (GIST) に対する腹腔鏡下切除術は, 症例を限定すれば有用な手法であると報告されている. 我々は胃の GIST に対する腹腔鏡下胃切除術の有用性について検証し, さらに腹腔鏡下手術が困難とされている 5 cm 以上の胃 GIST に対する腹腔鏡下手術の有用性についても考察した.

方法: 2006 年 1 月から 2014 年 2 月までに腹腔鏡下または開腹による胃切除術を受けた, 胃 GIST の 22 症例について後ろ向きに検討した.

結果: 9 症例は腹腔鏡下胃切除術を施行されており, 13 症例は開腹手術を受けていた. すべての症例で断端陰性であり, 治癒切除が施行されていた. 腹腔鏡下手術症例では開腹症例と比較して有意に腫瘍径が小さかったが ($P=0.03$), 出血量は少なく ($P=0.01$), 術後在院期間も短かった ($P=0.003$). 胃大弯側に存在する 5 cm 以上の胃 GIST の 2 症例に対しても腹腔鏡下手術が施行されていたが, いずれの症例も治癒切除が施行されており, 術後合併症や再発は認めなかった.

考察: 胃 GIST 症例に対する腹腔鏡下手術は有用であると考えられた. 腫瘍径が 5 cm 以上の胃 GIST に対しても, 腫瘍の位置や周囲組織との位置関係を考慮し慎重に適応を考慮することで, 腹腔鏡下手術は有用と考えられた. 胃 GIST 症例に対する腹腔鏡下手術は開腹手術と比較して手術時間が短く, 在院日数も短縮していた.