

Effect of Minimally Invasive Surgical Training Center on Laparoscopic Surgery: Observation from Preliminary Results for Primary Stomach Gastrointestinal Stromal Tumor in a Health Care System

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Abstract: Gastrointestinal stromal tumors (GISTs), are different from other mesenchymal tumors by immunohistochemistic biomarkers and are often encountered in the alimentary tract and less commonly originating from omentum, mesentery and peritoneum. They usually present as subepithelial tumors in the gastrointestinal tract or intraabdominal masses with malignant potential. The tumors might cause symptoms such as pain, intraluminal or extraluminal GI tract bleeding and obstruction but might also present as incidental findings. Gastroscopy, Ultrasonography and CT scan are employed for preoperative evaluation. The surgical principles are to excise the tumor with safe margin microscopically.

Minimally invasive procedures are revolutionary innovation in surgery. Asian Institute of TeleSurgery training center is established in mid Taiwan in 2008 with the cooperation between Show Chwan Health Care System and European Institute of TeleSurgery in Strasbourg, France. We retrospectively reviewed 24 primary stomach GISTs operated at our institution in the past four years. The patients were divided into laparoscopy group (18 patients) and laparotomy group (6 patients) depending on the main surgical methods. The patients' age, gender, hospital stay, operative time, blood loss, tumor size and complication rate were used for statistical analysis. There were significant differences in tumor size and blood loss between the two groups with a *p* value of less than 0.05. In the past 4 years, 75% of primary gastric GISTs in our hospital were managed by laparoscopic surgery. Our experience showed that laparoscopic surgery is feasible for primary stomach GISTs in selective cases.

Keywords: Minimally invasive surgery, laparoscopy, gastrointestinal stromal tumor, GIST, AITS, EITS.

INTRODUCTION

The incidence of gastrointestinal stromal tumor (GIST) is increasing [1]. In Taiwan, the annual incidence of GISTs is 13.7 cases per million populations [2]. GISTs, originating from interstitial cells of Cajal, belong to the stromal or mesenchymal neoplasms and present as subepithelial masses of the alimentary tract typically [1, 3]. Mostly, GISTs are located in the stomach, duodenum and proximal small intestine, but can arise from lower gastrointestinal tract, omentum, mesentery, and peritoneum [1, 3]. GISTs are neoplasms with malignant potential and gastric GISTs consist of five percent of gastric neoplasms [1, 3, 4]. Subepithelial stomach tumors are common findings

during upper gastrointestinal endoscopy, ultrasonography or computerized tomography and resection of such lesions are often undertaken by minimally invasive surgery [1, 4-9].

Show-Chwan Asian Institute of TeleSurgery (AITS) training center cooperating with IRCAD (The Research Institute against Cancer of the Digestive Tract) was established in 2008. We investigate the preliminary results of laparoscopic surgery on primary stomach GISTs in our institution (Chang-Hua and Chang-Bing Show Chwan Memorial Hospitals).

MATERIAL AND METHODS

From January 2009 to December 2012, there were fifty patients with pathological diagnosis of GIST at our institution (Chang-Bing and Chang-Hua Show Chwan Memorial Hospitals). We reviewed the medical charts

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retrospectively and enrolled the patients with primary stomach GISTs. Patients with recurrent or metastatic lesions at presentation were excluded. The patients receiving induction therapy for unresectable or borderline resectable tumor was also excluded. In total, twenty four patients were enrolled in the study. The patients were divided into two groups, the laparoscopy group and the laparotomy group according to the main surgical methods. The laparotomy group is defined as performing laparotomy to excise the tumor. The patients undergoing laparoscopic surgery initially but being converted to laparotomy method for resecting the main lesions due to technical problems or bleeding belonged to the laparotomy group. The patients receiving laparoscopic surgery totally or hybrid of laparoscopy and mini-laparotomy method were classified as laparoscopy group. The patients who underwent abdominal surgery with incidental findings of GISTs were classified according to the management of the GISTs. The blood loss and surgical time were recorded only for the management of GISTs.

All the pathologic specimens were reviewed for the negative margin microscopically. Adjuvant therapy, the inhibitor of c-kit kinase was prescribed according to the tumor size, mitosis and presence of the molecular marker. Gender, age, tumor size, hospital stay, operative time, bleeding amount and complication rate were factors used for statistical analysis.

RESULTS

Twenty four patients, 8 male and 16 female, with primary stomach GISTs were enrolled in the study. The patients were divided into two groups. The laparoscopy group was consisted of 18 patients (5 male, 13 female) and the laparotomy group was consisted of 6 patients (3 male, 3 female). The patients' mean age was 64.3 years old (range: 43~91 years old). The mean hospital stay was 13.0 days (range: 5~41 days). The resected mean tumor size was 5.1 cm (range: 1.0~12.0 cm). In laparoscopy group, the mean tumor size was 3.9 cm (range: 1~8.5 cm). The mean tumor size was 8.7cm (range: 4.5~12 cm) in laparotomy group. The mean blood loss was 90.8 ml (range: 50~380 ml). The mean operative time was 103.5 minutes (range: 30~240 minutes). The patient's characteristics were shown in Table 1.

In laparoscopy group, all eighteen patients underwent wedge resection of stomach, including one patient with incidental finding of GIST in the high body while undergoing laparoscopic hemigastrectomy for antral adenocarcinoma. The incidental GIST was found during laparoscopic surgery for stomach cancer because the 2-cm GIST was located on the anterior wall of high body which could not be examined by gastroscopy for the extraluminal lesion. In laparotomy group, two out of six patients underwent wedge resection, 3 patients received hemigastrectomy (a first

Table 1: The Clinical Characteristics of GIST Patients for Surgery

| Variable | Laparotomy | | laparoscopy | | p |
|------------------|------------|--------|-------------|--------|-------|
| | n | % | n | % | |
| Patient No. | 6 | (25) | 18 | (75) | |
| Gender | | | | | |
| M | 3 | (50) | 5 | (27.8) | 0.362 |
| F | 3 | (50) | 13 | (72.2) | |
| Complication | | | | | |
| Yes | 2 | (33.3) | 2 | (11.1) | 0.251 |
| No | 4 | (66.7) | 16 | (88.9) | |
| Operation Histry | | | | | |
| Yes | 1 | (16.7) | 1 | (5.6) | 0.45 |
| No | 5 | (83.3) | 17 | (94.4) | |
| Tumor location | | | | | |
| U | 3 | (50) | 14 | (77.8) | 0.18 |
| M | 1 | (16.7) | 3 | (16.7) | |
| L | 2 | (33.3) | 1 | (5.6) | |

Chi-square test.

Abbreviation: No; n: number, M (Gender): male, F: female, p: statistical p value, U: upper, M (tumor location): middle, L: lower.
p < 0.05 for significance.

Table 2: The Surgical Results for the GIST Patients

| Variable | laparotomy (n:6) M±SD | Laparoscopy (n:18) M±SD | t | p |
|---------------|--------------------------|----------------------------|-------|---------|
| Age | 63.33±20.69 | 64.61±14.41 | -0.33 | 0.77 |
| Hospital days | 19.00±3.11 | 10.94±7.18 | -1.44 | 0.16 |
| Tumor size | 8.65±3.11 | 3.91±2.28 | -2.94 | 0.002** |
| Bleeding | 196.67±146.52 | 55.56±16.17 | -2.90 | 0.03* |
| op time | 124.17±61.76 | 96.67±61.60 | -1.04 | 0.31 |

Chi-square test.

Mann-Whitney test.

Abbreviation: M: mean, SD: standard deviation, t: t value and p: p value in statistics.

p < 0.05 for significance.

patient with an 11.5-cm tumor in gastric body causing internal bleeding, a second patient with a 5.5-cm tumor in the antrum with obstruction and GI tract bleeding, and a third patient with a 4.5-cm tumor in antrum causing obstruction) and one patient with a 10-cm tumor in the cardia underwent total gastrectomy. There were two patients with postoperative complication in both groups respectively. In laparoscopy group, one 89-year-old female with a large tumor (8 cm) in the upper lesser curvature undergoing laparoscopic wedge resection was re-admitted due to delayed gastric emptying after a 13-day hospitalization. The other 81-year-old female with old CVA and diabetes mellitus suffered from duodenal stump bleeding after laparoscopic hemigastrectomy for adenocarcinoma with incidental finding of a 1.5-cm GIST in high body managed by wedge resection at the operation. She recovered after supportive treatment and had a longer hospital stay (28 days). In laparotomy group, one 41-year-old male received total gastrectomy with Roux-en-Y esophagojejunostomy for a 10-cm tumor in cardia and suffered from dyspepsia and diarrhea with a 28-day hospital stay. The other 87-year-old male suffered from post-operative pneumonia after hemigastrectomy for a 5.5-cm GIST. He stayed at hospital for 41 days. There was no surgical mortality in the series. There were three incidental findings at operation for other indications. Two patients was found to have small GISTs while receiving hemigastrectomy for gastric cancer (both patients receiving laparoscopic surgery) and one 57-year-old male undergoing laparoscopic gastric tube reconstruction for esophageal squamous cell carcinoma was found to have a 1-cm GIST at the gastric body. All the incidental GISTs were found during operations. These lesions were smaller tumors which could not be diagnosed by imaging studies or scopes before surgeries. There was no converted case in laparoscopy group. Two patients died during follow-up period. Both patients died of medical problems. One

died of cardiovascular accident at 91 years of age and the other died of diabetes related complication at 81 years of age. All of the patients' specimens were free of tumor invasion in the surgical margin.

The patients' characteristics such as age, gender, hospital stay, tumor size, blood loss, surgical time and complication rate were recorded. There were no statistical difference for the patients' gender and complication rate (Chi-square test, *p* value of 0.362 and 0.251 respectively). By independent T test, there were no statistical difference in age, hospital stay and operative time. However, operative blood loss and the tumor size differed between the two groups significantly (*p* value of 0.03 and 0.002, independent T test). The statistical data was shown in Table 2.

DISCUSSION

Gastrointestinal stromal tumors (GISTs) are neoplasms with malignant potential and possess specific pathological characters different to other mesenchymal tumors [1, 3]. The special molecular hallmark, c-kit (CD-117) presents a 91.4% of positive rate in Taiwanese [10]. GISTs occur most commonly in the alimentary tract, especial in the stomach (60-70%), duodenum (20-25%), proximal intestine and might arise from omentum, mesentery and peritoneum [3, 4]. Because of their originating from gastrointestinal tract, GISTs are amenable to laparoscopic resection [4-9]. Since preoperative diagnosis is difficult, excision of submucosal tumor in the stomach is recommended [1, 7, 9, 11]. Our previous reports have demonstrated that laparoscopic surgery is feasible for such kind of submucosal tumors in stomach [12, 13].

To dates, many documents have highlighted laparoscopic surgery for the disease [4-9, 11, 14, 15]. For the tumors located in the stomach, we should

consider the tumor size, safe margin, intraluminal or extraluminal growth, physiologic effect after reconstruction and the possible postoperative complication [4, 5]. The tumors on the anterior wall of the great curvature side of stomach (Figure 1) might be excised by wedge resection using either laparoscopic excision of the tumors and closure of the defect by staplers (Figure 2) or suture techniques. To avoid the spillage of tumor cells on the great curvature side of stomach while managing the larger neoplasm, laparoscopic sleeve gastrectomy is an alternative [16]. For the neoplasms located in the lesser curvature (Figure 3), it might be difficult to use laparoscopic staplers to divide the tissue and we could perform

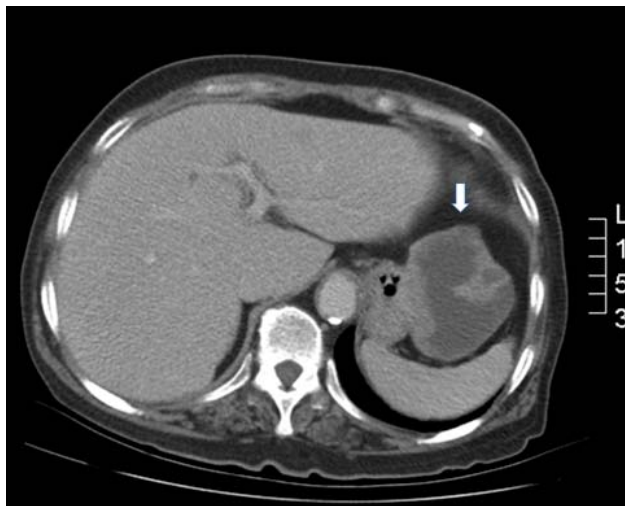


Figure 1: GIST in the greater curvature of stomach. The pedunculated tumor (arrow) locates in the great curvature of the gastric fundus composed of heterodense content.

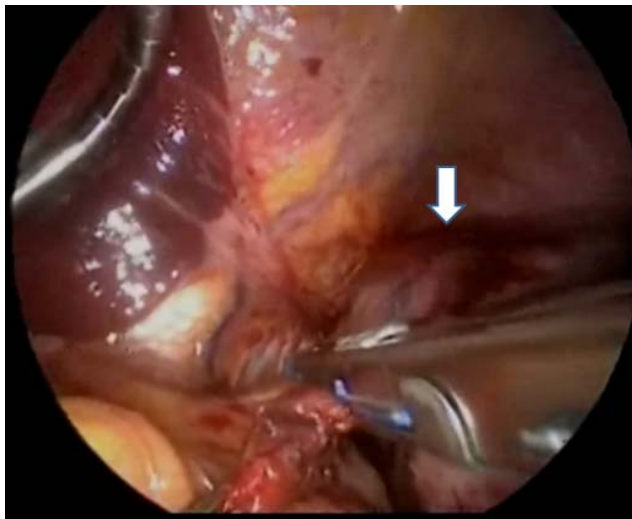


Figure 2: Resection and closure of the stomach. The neoplasm could be divided by GIA linear staplers and the stapler could seal the surgical defect in the stomach.

wedge resection and repair the stomach defect by laparoscopic suture techniques (Figure 4) or hand-assisted laparoscopic surgery [17]. For the tumors in the posterior wall of stomach, we could excise the lesion either by laparoscopic gastrotomy with excision of the tumors or overturn the stomach to excise as the anterior ones, so called eversion method [12, 18]. Furthermore, if the tumors are located in the lesser curvature or great curvature of the stomach, postoperative stricture, reflux symptoms or delayed gastric emptying should be taken into account before surgery [1, 4]. Some surgeons recommended hybrid of endoscopic and laparoscopic surgery, especially for smaller tumor [9, 14].



Figure 3: GIST in the lesser curvature of stomach. The extraluminal neoplasm (arrow) locates in the lesser curvature of the gastric cardia.

In our series, most of the patients were symptomatic and some of them presented as incidental findings while undergoing abdominal surgeries. Even for the smaller lesion, we could find the lesion by anatomic location or perform gastrotomy with intragastric excision. Recently, single incision laparoscopy surgery (SILS) is popular and gastric submucosal lesion, especially on the anterior wall or the great curvature can be excised [19]. In our series, no SILS was done and we might consider the procedures for feasible cases in the future. Most documents emphasize on negative margin on surgical specimens microscopically though current recommendation highlights at least a 10-mm margin free of tumor and to avoid tumor spillage or rupture during manipulation [11]. Although our follow-up period is short, no recurrent or metastatic case is found up to publication of this report.

Attendance of Minimal invasive training program could change the surgeons' preference in surgical



Figure 4: Laparoscopic resection and sutures for the stomach defect.

The liver (arrow head) was retracted by the laparoscopic instrument and wedge resection of the stomach containing the tumor (arrow) was performed. (left).

The stomach defect could be closed by laparoscopic suturing techniques. (right).

decision making [20]. In our system, the digestive surgeons all possess ability of laparoscopic techniques but the training center indeed push us going straightforwardly [20]. For example, a 60-year-old male suffered from gastric ulcer perforation and peritonitis with an 8.5-cm stomach GIST in the great curvature at presentation (Figure 5). Both situations were managed by laparoscopic surgery and the patient was discharged uneventfully. In the past, the patient might be managed with transitional laparotomy. Tumor size is



Figure 5: a stomach GIST patient with perforated peptic ulcer and peritonitis.

On the computed tomography, pneumoperitoneum (free air on imaging) (arrow) hint perforation in gastrointestinal tract and a large heterodense mass (arrow head) presented in the greater curvature of stomach.

always concerned for laparoscopic surgery and earlier recommendation is for tumor smaller than 5 cm [5, 6]. For the larger neoplasm, hand-assisted laparoscopic surgery is an alternative [17]. However, the surgeons might be used to performing intracorporeal sutures.

In our series, parameters such as gender, age, hospital stay and complication rate were similar in the two groups. Tumor size and surgical blood loss were significantly different between the two groups. Before surgery, our surgeons all reviewed the endoscopic and imaging studies. We also did some laparoscopic surgery for larger tumor with protruding appearance. However, smaller tumors might make the surgeons choose laparoscopic surgery and we could find that no case was converted to laparotomy method in laparoscopic surgery group. The conversion rate was recognized according the updated consensus or guidelines [21, 22]. In earlier reports, the conversion rates ranged from 9.1 to 23.3% with the samples similar to ours [4, 8]. It was reasonable to encounter more blood loss for the larger tumor or difficult case performed by laparotomy method. In the past four years, 75% of primary gastric GISTs at our institution were managed by laparoscopy. Some review articles showed that the oncologic outcomes in laparoscopic surgery would not be inferior to laparotomy method with shorter hospital stay [4, 7, 15, 17]. In our study, since the follow-up period is short, longer follow-up period is needed to monitor the oncological outcomes.

Recently, there are some minimally invasive training curriculum constructed for skills training, evaluation,

and certification [23-25]. Our previous reports have shown the training effect on surgeons' choice and patients' results [20, 26]. The training courses have promoted us in advanced techniques and provided us opportunity communicating with local and foreign experts. By reviewing the preliminary results for laparoscopic surgery on stomach GISTs, we have demonstrated the benefit of the training curriculum. We should keep going on the way.

CONCLUSION

Laparoscopic surgery for primary stomach gastrointestinal stromal tumor is feasible and safe in selective patients. Complete resection with negative tumor margin and avoidance of tumor spillage during manipulation are recommended. Furthermore, according our reviews, we believe the minimally invasive training center makes us forge ahead vigorously in the way.

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