

# Expanding the Indications for Laparoscopic Gastric Resection for Gastrointestinal Stromal Tumors

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## ABSTRACT

**Objective:** Laparoscopic resection of large gastric gastrointestinal stromal tumors (GIST) has been controversial. This generally has been limited to small lesions. We hypothesize that laparoscopic mobilization and resection using, in some cases, extracorporeal anastomosis of the gastrointestinal (GI) tract is an oncologically safe alternative to open surgery even when tumors are large.

**Methods:** Four patients underwent a laparoscopic approach for gastric GIST tumors >2 cm at Methodist Dallas Medical Center over a 6-month period. Patient demographics, operative findings, postoperative course, and pathologic characteristics were examined.

**Results:** The mean age in this patient group was 58 years (range, 36 to 77). Gastrointestinal bleeding and dyspepsia were the most common symptoms. Seventy-five percent of the patients were females. Mean tumor size was 10 cm (range, 2.5 to 20) with distribution in the stomach as follows: 75% greater curvature and 25% antrum. Tumors were removed by wedge, sleeve, and partial gastrectomies. Two of these tumors showed a high grade and the other 2 a moderate grade of differentiation. The number of mitoses was <5/50 HPF in all the tumors. No intraoperative spillage occurred in any patients, even with the largest tumor (20 cm). Importantly, all tumors were excised with a negative gross and microscopic margin. Average length of stay was 4 days. No patients required reoperation, and there were no complications postoperatively.

**Conclusion:** Minimally invasive assisted approaches may be an option to treat large GIST tumors. Obeying principles of minimal touch, no spillage, and obtaining a neg-

ative margin, a safe operation with a laparoscopic approach is feasible, even in giant tumors. The large size of diagnosed GIST tumors should not preclude a minimally invasive approach.

**Key Words:** GIST, Laparoscopic surgery, Minimally invasive, Tumor.

## INTRODUCTION

Gastrointestinal stromal tumors (GIST) are the most common nonepithelial, mesenchymal neoplasms of the gastrointestinal tract. The tumor originates from the interstitial pacemaker cells of Cajal accounting for less than 3% of all gastrointestinal neoplasms.<sup>1,3,10</sup> These tumors were reported for the first time in 1983 as a separate entity from gastrointestinal smooth muscle and nerve sheath tumors.<sup>2</sup> Immunohistochemical studies have shown that up to 94% of GIST tumors express CD117, a *c-kit* protein, and 60% to 70% of GIST tumors stain for CD34. Therefore, GIST is now considered a completely separate entity from leiomyoma and leiomyosarcoma.<sup>2,4,5,6,15</sup>

Gastrointestinal stromal tumors occur mainly in the stomach (40% to 70%) followed by 15% each within the small and large bowel.<sup>6,7</sup> These tumors spread by the hematogenous route, with the liver being the most common site of metastasis.

Endoscopic ultrasound (EUS) can be used to diagnose and biopsy these lesions.<sup>5,12</sup> Tumor size >5 cm and >10 mitoses/50 high-power field have previously been correlated with a poor outcome.<sup>5,8,9,15</sup> However, the presence of metastatic disease is the only definitive sign of malignancy.

Targeted therapies have been developed for GIST tumors, but surgical resection remains the optimal first-line therapy.<sup>3,6,8,10</sup> Achieving a microscopically free margin appears to be the key element in surgical therapy, and due to the pattern of spread, extensive nodal dissection is not warranted.<sup>11</sup> Adjuvant therapy with imatinib (Gleevec), an agent that targets *c-kit*, is used in patients with aggressive

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tumor characteristics, based on the Fletcher grade classification for malignant potential.<sup>3,9,11,12,13</sup>

More recently, minimally invasive approaches have been shown to be oncologically feasible and safe in other tumor sites, for example colon cancer as reported by Jacob and Salky.<sup>14</sup> Prior reports have suggested limiting the minimally invasive approach to those gastric GIST tumors that are <2 cm in size.<sup>1,7,15</sup>

The purpose of this study was to examine the efficacy of minimally invasive resection of GIST tumors that are >2 cm. The specific oncologic factors that were examined in this study were the ability to make the diagnosis of these gastric tumors by EUS preoperatively, ability to achieve no spillage during surgery, ability to achieve complete tumor resection with negative margins, and the ability to perform safe intestinal anastomosis, if needed.

## MATERIALS AND METHODS

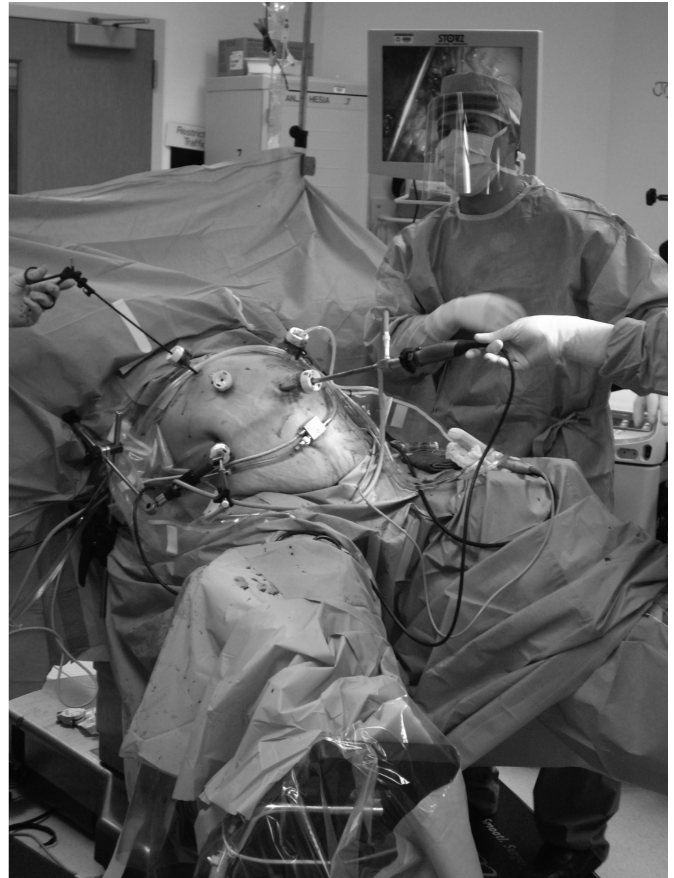
A retrospective analysis of 4 patients who underwent laparoscopic resection of a suspected gastric GIST at Methodist Dallas Medical Center in 2007 was performed after receiving Institutional Review Board approval for the study. All 4 patients had a GIST tumor >2 cm.

Patient demographics, clinical presentation, and anatomical location of the tumors were analyzed. Perioperative parameters measured included postoperative recovery including morbidity, mortality, and length of hospitalization. Tumor histopathologic characteristics including size, mitotic activity, and violation of the pseudocapsule were also reviewed.

An initial EUS-guided fine-needle aspiration was performed as part of the staging. Suspicion for GIST was based on endoscopic features, such as an intact mucosa, a predominantly submucosal location, and in some cases, a pedunculated appearance.

These patients also underwent a preoperative abdominal computed tomography (CT) scan as part of their diagnostic workup for assessment of the presence of distant metastases or local tumor invasion. The position of the patients in the operating room and location of the trocars for the laparoscopic resection of these tumors are shown in **Figure 1**.

Tumors >5 cm and close to the esophagogastric junction were excluded from laparoscopic wedge resection but included in indications for laparoscopic operation with a small laparotomy (so-called laparoscopic-assisted operation). Distal gastrectomy was used for bulky tumors lo-



**Figure 1.** Demonstrating position of the patient and location of the trocars.

cated in the middle or distal third of the stomach and wedge resection for peripheral gastric tumors (**Table 1**).

The general principle used during the surgical approach is described as follows: The lesser sac was opened preserving the gastroepiploic vessels bilaterally extending up to the short gastric vessels and distally towards the duodenum by using a 5-mm Harmonic scalpel. The stomach was then elevated out of the way by using a self-retaining retractor through a 5-mm port that was placed in the right lower quadrant.

These tumors have massive collateral vessels that were ligated and divided with clips. Once the tumor was released from the area of the lateral, inferior, and medial aspect of these collateral vessels, attention was then paid to the stomach. A window was created underneath the stomach all the way to the splenic flexure that was mobilized, and the splenic flexure was taken down to mobilize the colon away from this tumor. We used an Endo GIA stapler (63.5mm) that was inserted through the umbilical

**Table 1.**  
Endoscopic Ultrasound (EUS) With Preoperative Workup Characteristics and Type of Surgery Performed

EUS Characteristics	EUS Suspicious for Gastrointestinal Stromal Tumors	EUS Biopsy	Operation Performed
10-cm mass in the body of stomach, no vascular invasion	None	Negative	Distal Gastrectomy
2.5-cm submucosal mass anterior wall stomach	Yes	Positive	Wedge Resection
3.6-cm submucosal mass in antrum of stomach, no invasive patterns	Yes	Negative	Distal Gastrectomy
14-cm submucosal mass in greater curvature of stomach	Yes	Positive	Sleeve Gastrectomy

port and fired across the greater curvature of the stomach, allowing the tumor to be freed from the stomach. The only attachments left on the tumor at this time were in the posterior aspect.

The pneumoperitoneum was released, and the supraumbilical incision was extended for a length of approximately 6 cm to 7 cm, allowing us to gently deliver this tumor through the anterior abdominal wall. We ligated the posterior attachments and some small collateral vessels by using 5-mm ligature clips and 2–0 silk sutures. At this point, the tumor was freed and sent to pathology for frozen section. There was no rupture or spillage of the tumor or bleeding from the tumor.

**RESULTS**

Four patients underwent gastric GIST resection in a 6-month period. The mean age in this patient group was 58 (range, 36 to 77). Gastrointestinal bleeding and dyspepsia were the most common symptoms. Seventy-five percent of the patients were females. All patients were accurately diagnosed preoperatively as having nonmetastatic GIST by using EUS and CT scan.

Seventy-five percent of tumors were considered to be GIST by classic ultrasound appearance, and 50% were biopsy proven gastric GIST tumors at the time of EUS. Mean tumor size was 10 cm (range, 2.5 to 20) with distribution in the stomach as follows: 75% greater curvature and 25% antrum. None of these patients received neoadjuvant therapy.

Two of the 4 gastric GIST tumors were removed by wedge resection by using a laparoscopic stapler surrounding the tumor with a margin of normal tissue. The tumor was removed from the abdominal cavity by using a laparoscopic retrieval bag. In the other 2 cases, a partial gastrec-

tomy with extracorporeal anastomosis was performed. We used the Harmonic scalpel to mobilize the greater curvature of the stomach to the duodenum. The distal stomach and proximal duodenum were divided to include the entire tumor. The midline port wound was extended to remove this specimen with the help of a laparoscopic retrieval bag. An extracorporeal side-to-side stapled gastrojejunostomy was performed. Two of these tumors showed a high-grade and the other 2 showed a moderate-grade of differentiation. Lack of violation of the pseudocapsule and margin negativity was confirmed in all cases. The number of mitoses was <5/50 HPF in all the tumors. There was no intraoperative spillage in any patient, even with the largest tumor at 20 cm.

Average length of stay was 4 days. No patients required reoperation, and no postoperative complications occurred. Patients were discharged tolerating a regular diet.

**DISCUSSION**

We report herein on the efficacy of the minimally invasive assisted approach for the treatment of large gastric GIST >2 cm. This report suggests that preoperative selection by EUS followed by a meticulous oncologic operative technique can result in complete resection of large GIST with negative margins and no spillage. The guidelines for minimally invasive gastrectomy for GIST should be modified to include large lesions.

Patients with gastric GIST have better survival than those with small intestinal GIST as reported by Emory et al.<sup>4</sup> Surgical management has been shown to be a critical factor in their treatment, even in the era of imatinib. Achieving a negative margin resection with no spillage at the time of surgery is essential.<sup>3,16</sup> The ability to achieve this status is paramount in choosing patients who might

be candidates for a minimally invasive approach. The utility of EUS has been found to be very helpful in making this determination, and, in fact, the diagnosis was made by EUS in 75% of this population. It is the belief of our group that minimally invasive techniques should not be used for gastric resections that require nodal dissections (ie, adenocarcinoma). Therefore, preoperative diagnosis is essential in patient selection. The question of which surgeons are qualified to perform these minimally invasive resections is controversial. In fact, a team approach is often the best approach, because technical laparoscopic skills are required, as is excellent knowledge of upper gastrointestinal anatomy. Intraoperative endoscopy can be beneficial for tumors that are close to the esophagus. A detailed knowledge of tumor biology and the potential role of neoadjuvant therapy are essential. It is unclear whether any surgeon could possess all of these skills, and the alignment of a team might be the best approach.

Surgery is the preferred management for GIST when feasible. There is still debate regarding the most appropriate operative approach and the extent of resection required.<sup>5,15</sup> The aim of surgery is complete removal of the tumor with negative resection margins and preservation of anatomical function.<sup>17</sup> However, even microscopically positive margins may not change overall prognosis, as demonstrated by DeMatteo et al.<sup>16</sup> Unlike adenocarcinoma, in which submucosal and subserosal lymphatic spread requires a 5 cm to 6 cm surgical margin, gastric GIST tends to grow out of the primary organ instead of infiltrating the submucosal tissue. Lymph node metastases are very rare, and routine lymphadenectomy is not required. Wedge resection of gastric GIST tumors has been widely reported to be successful.<sup>7,13</sup> Also evidence exists that laparoscopic resection of gastric GIST tumors is effective with minimal morbidity, and no reported mortality. With this report, we corroborate the experience of Novitsky et al<sup>15</sup> who demonstrated that the laparoscopic approach appears to offer excellent therapeutic outcomes, with a 92% long-term disease-free survival for gastric GIST tumors of various sizes (1.0 cm to 8.5 cm).<sup>16,17</sup> We would like to expand the laparoscopic indications for resection of these large tumors to a size ranging from 2.5 cm to 20 cm. Yano et al<sup>18</sup> have reported the removal of 2 gastric GIST tumors in the 7 cm to 8 cm diameter range by using hand-assisted laparoscopic surgery (HALS).

If a laparoscopic approach is contemplated, several factors including patient characteristics, tumor features (size, location, invasion), as well as the surgeon's experience and expertise, need to be considered. Tumor rupture during laparoscopy should be avoided, as peritoneal

seeding affects the disease-free period and overall survival. Resection margins need to be clear in all cases, confirming the oncological safety of the laparoscopic approach.

The role of neoadjuvant and adjuvant therapy in GIST has evolved over the past several years, and imatinib is now used in patients who display poor prognostic features, such as large size or mitotic activity.<sup>2,8</sup> A neoadjuvant approach is used selectively in difficult to access surgical sites.<sup>8</sup>

The main purpose of this report is to question the size limits on minimally invasive resection of gastric GIST. This study has shown that large GIST can be resected safely, while obeying the cancer principles that are paramount to treating this disease.

GIST tumors have an unpredictable behavior. Even with risk stratification, careful follow-up is required. Even though the majority of GIST tumors are likely to recur within 2 years after surgery, follow-up beyond this period would seem sensible.

## CONCLUSION

Although more definitive results will require a large-scale, prospective, randomized trial with longer postoperative follow-up evaluation, we conclude from this study that minimally invasive assisted approaches may be an option to treat large gastric GIST tumors. Obeying principles of minimal touch, no spill, obtaining a negative margin, and a safe operation with a laparoscopic approach is feasible, even in giant tumors. Large size, nonmetastatic gastric GIST tumors should not preclude a minimally invasive approach. Long-term follow-up with abdominal tomography is necessary.

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