Laparoscopic Gastric Gastrointestinal Stromal Tumor Resection

*The Mayo Clinic Experience*

Kevin L. Huguet, MD; Robert M. Rush Jr, MD; Deron J. Tessier, MD; Richard T. Schlinkert, MD; Ronald A. Hinder, MD, PhD; Gary G. Grinberg, MD; Michael L. Kendrick, MD; Kristi L. Harold, MD

**Hypothesis:** Laparoscopic resection of gastric gastrointestinal stromal tumors (GISTs) is safe and effective.

**Design:** Retrospective medical record review.

**Setting:** Tertiary referral center.

**Patients:** Patients undergoing laparoscopic resection of gastric GISTs from April 1, 2000, to April 1, 2006.

**Main Outcome Measures:** Demographic data, diagnostic workup, operative technique, tumor characteristics, morbidity, mortality, and follow-up.

**Results:** Thirty-three patients underwent attempted laparoscopic resection of gastric GISTs, with 31 operations completed laparoscopically. The mean patient age was 68 years (age range, 35-86 years). The female to male ratio was 18:15. Sixteen patients (49%) were asymptomatic, and their tumors were found incidentally. Of 24 patients (73%) who underwent preoperative endoscopic ultrasonography, the results of fine-needle aspiration verified the diagnosis in 13 patients (54%). The mean operative time was 124 minutes (range, 30-253 minutes). A combined endoscopic-laparoscopic approach was used in 11 patients (33%). The mean tumor size was 3.9 cm (range, 0.5-10.5 cm). Two patients (6%) underwent conversion to an open procedure. The median hospital stay duration was 3 days. The mean follow-up was 13 months (range, 3-64 months). There were no local recurrences. Three patients (9%) experienced complications, including 1 wound infection and 2 episodes of upper gastrointestinal tract bleeding. There were no mortalities.

**Conclusion:** Although technically demanding, the laparoscopic approach to gastric GISTs is safe and effective, resulting in a short hospital stay duration and low morbidity.


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**The Characterization and Treatment of Gastrointestinal Stromal Tumors (GISTs) have undergone marked change in the past decade.** The evolution has been rapid from open procedures on tumors supposedly arising from smooth muscle to combined endoscopic-laparoscopic approaches on masses that arise from the interstitial cell of Cajal. These pluripotential intestinal pacemaker cells are of myogenic and neurogenic origin and are found in the muscular layers of the intestinal wall. The advent of immunohistochemical identification of cell markers such as CD117, an identifier for the c-kit protooncogene found in the interstitial cell of Cajal and in GISTs, has allowed for more specific diagnoses of a conundrum of intestinal mural tumors with varying malignant potential now called GISTs. GISTs can be differentiated from other myogenic, neurogenic, and mesenchymal tumors such as neurofibromas, schwannomas, and smooth muscle sarcomas of the intestinal tract.

Although tumor size and degree of mitotic activity most accurately predict malignant or benign behavior, other predictors of more aggressive biologic behavior include high cellularity, high nuclear grade, and the presence of mucosal ulceration or invasion. This can be found anywhere in the gastrointestinal tract; however, more than 50% of cases have been reported in the stomach. Surgical resection is the mainstay of therapy, and the advent of advanced laparoscopic and endoscopic-endoluminal techniques has allowed for minimally invasive resection of these uncommon tumors. In this study, we sought to characterize our experience with laparoscopic management of GISTs.
Thirty-three consecutive patients underwent laparoscopic resections of gastric GISTs at the 3 Mayo Clinic sites from April 1, 2000, to April 1, 2006. After institutional review board approval, medical records were reviewed retrospectively for demographic data, symptoms, diagnostic modality, surgical treatment, pathologic findings, and follow-up. Operative time, specific tumor location in the stomach, blood loss, number of ports, and conversion to an open procedure were also recorded. Tumors were classified as having low (measuring <5 cm and having <5 mitoses per high-power field), intermediate (measuring 5-10 cm or having 5-10 mitoses per high-power field), or high (measuring >10 cm or having >10 mitoses per high-power field) malignant potential based on the number of mitoses and the tumor size.

Operative technique involved placement of 3 to 6 laparoscopic ports. Most lesions were resected using a wedge technique facilitated by an endoscopic linear stapling device. For lesions located near the gastroesophageal junction or the antrum, the staple line was oriented longitudinally against the axis of the stomach to avoid luminal narrowing. Otherwise, the staple line was oriented whatever way facilitated tumor removal with adequate margins. Several gastric GISTs located on the posterior aspect of the stomach were removed via a transgastric method that involved an anterior gastroscopy. A transgastric su- rface was placed on the mucosal surface of the posterior gastric wall to mark the tumor and to retract the specimen ventrally into the gastroscopy. The tumor was resected with a linear stapler by enveloping the mucosa around the tumor (Figure A, B, and C). The anterior gastroscopy was closed using a linear stapler. Specimens were routinely removed within a specimen retrieval bag. Intraoperative endoscopic assistance was used at the surgeon's discretion. Frozen-section analysis was performed to ensure a negative microscopic margin.

Statistical analysis was performed using the t test for comparing means of continuous data. The Fisher exact test was used for analyzing differences between small groups, and univariate analysis was used for assessing symptom correlation to the disease.

**RESULTS**

Thirty-three patients underwent attempted laparoscopic resection of 33 gastric GISTs from April 1, 2000, to April 1, 2006; 31 operations were completed laparo- scopically. There were approximately equal numbers of men (n = 15) and women (n = 18). The mean patient age was 68 years (age range, 35-86 years). Most patients (16 [49%]) were asymptomatic, with the tumors found incidentally. Initial symptoms included pain in 7 patients (21%), gastroesophageal reflux in 6 patients (18%), dyspepsia in 2 patients (6%), dysphagia in 1 patient (3%), and gastrointestinal tract bleeding in 1 patient (3%). Among the asymptomatic patients, computed tomography (CT) (performed for other reasons) demonstrated tumors in 12 of 16 patients, and endoscopic ultrasonography–guided fine-needle aspiration (FNA) was performed in each of those patients. Two tumors were discovered incidentally during laparoscopic paraesophageal hernia repairs and were resected.

The diagnostic modality used most often to characterize the tumor before surgery was CT. Of 33 patients in our series, 28 underwent CT. The smallest tumor seen on CT was 1.6 cm. Esophagogastroduodenoscopy was performed in 28 patients, and no tumor was seen in 4 patients. Esophagogastroduodenoscopy with biopsy was performed in 15 patients, with a positive diagnosis of gastric GIST obtained in 3 patients (20%). Preoperative esoph- endoscopic ultrasonography (EUS) was performed in 24 patients (73%), and a mass localized to the gastric wall was found in all 24. Endoscopic ultrasonography–guided fine-needle aspiration (FNA) was performed in each of those patients.
Table 1. Comparison of Operative Data Based on Tumor Size

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\geq 5$ (n=8)</th>
<th>$&lt;5$ (n=25)</th>
<th>$P$ Value</th>
</tr>
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<tbody>
<tr>
<td>Transgastric resection, No. (%)</td>
<td>1 (13)</td>
<td>4 (16)</td>
<td>NS*</td>
</tr>
<tr>
<td>Conversion to open procedure, No. (%)</td>
<td>0</td>
<td>2 (8)</td>
<td>NS*</td>
</tr>
<tr>
<td>Hand port use, No. (%)</td>
<td>1 (13)</td>
<td>3 (12)</td>
<td>NS*</td>
</tr>
<tr>
<td>Previous operations, No. (%)</td>
<td>5 (63)</td>
<td>17 (68)</td>
<td>NS*</td>
</tr>
<tr>
<td>Ports used, No.</td>
<td>4</td>
<td>4</td>
<td>.63</td>
</tr>
<tr>
<td>Operative time, min</td>
<td>143</td>
<td>119</td>
<td>.32</td>
</tr>
<tr>
<td>Hospital stay duration, d</td>
<td>4</td>
<td>5</td>
<td>.54</td>
</tr>
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Abbreviation: NS, not significant.

a Two tumors were not tested.
b t-Test.

c-h2 Analyzis.

d Based on criteria described by Fletcher et al.*

Table 2. Characteristics of 33 Tumors

| Characteristic Value
<table>
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<tr>
<td>Tumor size, mean (range), cm</td>
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<tr>
<td>c-kit Positive, No. (%)</td>
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<tr>
<td>Malignant potential of tumor, No. (%)b</td>
</tr>
<tr>
<td>Low (&lt;5 cm and &lt;5 mitoses/HPF)</td>
</tr>
<tr>
<td>High (&gt;10 cm and &gt;10 mitoses/HPF)</td>
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Abbreviation: HPF, high-power field.

24 patients and provided a positive diagnosis in 13 (34%). Magnetic resonance imaging was performed in 3 patients and was useful in 2 of them to further delineate that the tumors were of gastric origin.

During surgery, 5 tumors were located proximally to the gastroesophageal junction or cardia, 24 tumors on the body of the stomach, and 4 tumors in the distal stomach or antrum. Of 24 gastric GISTs located on the body of the stomach, 5 were localized to the posterior wall and were removed using a transgastric approach. Overall, the mean operative time was 124 minutes (range, 30-253 minutes), and there was no significant difference in the mean operative times of those patients who had previous abdominal surgery and those who did not (115 vs 149 minutes, $P=.08$). The mean operative times of patients with gastric GISTs 5 cm or larger were not significantly longer than those with smaller tumors (143 vs 118 minutes, $P=.30$) (Table 1).

A combined endoscopic-laparoscopic approach was used in 11 patients. Two of the 33 patients (6%) underwent conversion to an open procedure. In 1 patient, the resection narrowed the gastric lumen, and open reconstruction was required. In the other patient, the lesion could not be found laparoscopically, despite the use of intraoperative EGD and a hand port before conversion to laparotomy.

There were no mortalities in our series. The median hospital stay duration was 3 days (range, 1-40 days). Three patients (9%) experienced complications, including 1 wound infection and 2 episodes of upper gastrointestinal tract bleeding. One patient experienced upper gastrointestinal tract bleeding due to a gastric ulcer. The other patient experienced complications from gastrointestinal tract bleeding and gastric outlet obstruction after resection of an antral tumor. This required laparoscopic gastrojueunostomy and resulted in a prolonged hospital stay duration of 40 days. There were no local recurrences in this series during a mean follow-up of 13 months (range, 3-64 months); 5 patients were lost to follow-up.

The mean tumor size was 3.9 cm (range, 0.5-10.5 cm), 25 tumors (76%) had fewer than 5 mitoses per high-power field, and 25 tumors (76%) were less than 5 cm in size. Thirty of 33 patients had tumors that were c-kit positive (Table 2). Two patients had positive margins on final pathologic examination. One patient had a tumor located on the posterior wall of the antrum, and the other patient had a 10.5-cm tumor located high on the anterior surface of the greater curvature. Intraoperative gross and frozen section analyses revealed negative margins; however, the final pathologic reports showed microscopically positive margins. Treatment with imatinib was started for both patients after surgery, and these patients have been disease free for longer than 1 year of follow-up.

**COMMENT**

Gastric GISTs remain elusive tumors, and in most cases the diagnosis is made incidentally. Although EGD is somewhat accurate in identifying the lesions, obtaining a tissue sample with routine intraluminal endoscopic biopsy forceps rarely acquires enough tissue to make a microscopic diagnosis. Gastric GISTs usually appear as a well-circumscribed extraluminal mass arising from the gastric wall on CT. Although not specific, by combining CT with EUS (and EUS-guided FNA), most of these tumors can be classified and the anatomy defined before performing an operation for resection. Endoscopic ultrasonography can define the anatomic layer that gives rise to the tumor, and FNA can determine the presence of the c-kit mutation in most cases, which is crucial to the classification of stromal tumors.

Simultaneous endoscopy and laparoscopy allow precise localization of intraluminal and submucosal lesions and are sometimes necessary during operative localization of gastric GISTs. Although we did not remove any lesions via a totally endoluminal approach, we were able to remove 5 tumors through a transgastric approach, minimizing the use of large gastric resections and their associated morbidity. Formal gastrectomies have been shown to be more invasive and unnecessary for the removal of most gastric GISTs.

Criteria for differentiating benign from malignant gastric GISTs have been debated for several years. The most reliable prognostic indicators are size and mitotic index. Most tumors in our series were found to be of low malignant potential. This determination was based on tumor size and mitotic count, as described previously by Fletcher et al.* Gastric GISTs that are smaller than 5 cm and have fewer than 5 mitoses per high-power field are
considered to have low malignant potential. Tumors measuring 5 to 10 cm or having 5 to 10 mitoses per high-power field are considered intermediate risk, and those measuring greater than 10 cm or having more than 10 mitoses per high-power field are considering high risk. Using this stratification system, the distributions of our patients into low, intermediate, and high risk for malignant neoplasms are 79% (n = 26), 15% (n = 5), and 6% (n = 2), respectively.

When comparing tumors 5 cm or larger with tumors smaller than 5 cm, we found no difference in conversion rates, operative time, or morbidity. The advent and improvement of endoscopic linear stapling devices have facilitated the laparoscopic approach to gastric surgery. However, one should be aware that the microscopic margin of these tumors can approximate the specimen size of the staple line; therefore, frozen section analysis may not accurately depict the true margin of resection. The pathologist must examine the outside staple line, if possible, for confirmation of a negative microscopic margin. In addition, wedge resections using stapling devices must be performed with care for lesions in proximity to the pylorus and the gastroesophageal junction. A good adjunct to avoid narrowing at the gastroesophageal junction is to perform the resection with a dilator or flexible gastroscope in place.

Gastric GISTs are uncommon growths that can arise in any location in the stomach. Computed tomography and EUS-guided FNA are the diagnostic modalities of choice. Almost all of these tumors are amenable to laparoscopic resection without compromising oncologic principles. Careful follow-up of these patients is necessary to ensure that local and distant recurrences are identified early.

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Correspondence: Kristi L. Harold, MD, Department of Surgery, Mayo Clinic Scottsdale/Phoenix, 5777 E Mayo Blvd, Phoenix, AZ 85054 (Harold.Kristi@mayo.edu).
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REFERENCES