### **Original Research Article**

DOI: http://dx.doi.org/10.18203/2349-2902.isj20164054

# Outcome of surgical resection for localized gastrointestinal stromal tumors

Ashraf M. El-Badry<sup>1</sup>\*, Medhat I. M. Ahmad<sup>2</sup>, Hitham M. Ali<sup>3</sup>

<sup>1</sup>Department of General Surgery, <sup>2</sup>Department of Radiology, <sup>3</sup>Departement of Anesthesia and Intensive care, Sohag University Hospital, Faculty of Medicine, Sohag University, Sohag, Egypt

**Received:** 03 November 2016 **Accepted:** 07 November 2016

### \*Correspondence:

Dr. Ashraf Mohammad El-Badry,

E-mail: ashraf.elbadry@med.sohag.edu.eg

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### **ABSTRACT**

**Background:** Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract. The clinical outcome and the factors which are potentially related to tumor recurrence and survival after surgical intervention for GISTs has not been adequately addressed in the Southern part of Egypt.

**Methods:** Medical records of adult patients who underwent surgical resection of localized GISTs (February 2007 - December 2013) in Sohag University Hospital were reviewed. Data on the clinical presentation, treatment strategies, tumor characteristics including the risk for aggressive behavior and survival rate were analyzed.

**Results:** Fifteen patients with 7 gastric (47%), 5 small bowel (33%), 2 duodenal (13%) and 1 colonic (7%) GISTs and median age of 56 (range: 32-73) years were eligible. Nine patients (60%) were males. Non-specific abdominal pain was the most common presenting symptoms (40%). Emergency presentation occurred only in two patients (13%). Complete resection was achieved in thirteen patients (87%). There was no major operative morbidity or mortality. The risk for aggressive behaviour was low in 7 (47%), intermediate in 5 (33%) and high in 3 (20%) patients. Two patients died 7 and 10 months after surgery, one with histopathological criteria of high risk for aggressive tumor behaviour and the other with incomplete tumor resection. During a median follow up of 21 (range: 8 - 48) months, overall and recurrence-free survival were 87% and 67%, respectively.

**Conclusions:** Adequate resection of GISTs is associated with high rate of survival. Increased risk for aggressive tumor behaviour and incomplete resection are associated with tumor recurrence and decreased survival.

Keywords: Fletcher classification, GIST, Gastrointestinal stromal tumor

### INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are potentially malignant mesenchymal neoplasms which were firstly described. GISTs occur in 10-13/million annually and represent the predominant type of gastrointestinal sarcoma (85 %) and the most common single subtype (18 %) of all sarcomas. GISTs derive from or exhibits differentiation to the interstitial cells of Cajal which are located in the gut wall. These cells are consider the pacemaker of the gastrointestinal tract as they organize

the interaction between the gut's autonomic nervous system and smooth muscle cells to regulate the motility and peristaltic movement. <sup>8</sup> GISTs may arise anywhere in the entire digestive tract but most commonly in the stomach (50-60%) and the small bowel (30-35%). A minority (<5%) of all GISTs occur in locations outside the gastrointestinal tract such as the omentum, mesentery and the retro peritoneum and referred to as E-GISTs. <sup>9</sup> There are three distinctive histological categories of GISTs including spindle cell (70%) epithelioid, and the mixed types. <sup>10</sup> Most of GISTs show a mutation c-KIT

and PDGFRA genes.<sup>8,11</sup> The definitive diagnosis of GISTs is based on confirmation of the morphological characteristics of the tumor supported by immunohistochemical studies on KIT and discovered on GIST-1 (DOG-1) which are the most sensitive and specific GISTs biomarkers.<sup>10</sup>

The location of GISTs in the submucosa and lacking local invasion has substantial impact on the intitial clinical presentation. Symptoms may be ambiguous such as nonspecific abdominal pain and fatigue until GISTs reach an adequately large size to provoke GIST's-related sypmtoms such as bleeding, bowel obstruction or palpable mass. <sup>9,12</sup> Likewise, almost one fourth of the GISTs are discovered incidentally during imaging studies due to unrelated disorder. <sup>13</sup>

In sharp contrast with carcinomas of the digestive tract which exhibit local invasion and lymphatic and vascular dissemination, GISTs show neither local invasiveness nor lymphatic spread. Thus, similar to soft tissues sarcomas, TNM criteria (T, tumor size; N and M, lymphatic and vascular dissimination) are not practical to reflect GIST behavior. As a substitute, histological parameters such as tumor size and location, the rate of mitosis, the status of resection margin and occurrence of tumor rupture are the most accepted prognostic factors.

Before the era of KIT and PDGFRA gene mutations, surgical resection was the only standard option of potentially curative treatment.<sup>13</sup> Currently, multidisciplinary team including surgeon, radiologist, pathologist and medical oncologist is essential for diagnosis and precise decision regarding surgical resection, tumor characterization and adjuvant treatment.<sup>13</sup>

GISTs were not adequately studied in the Southern part of Egypt, especially in Sohag governorate with almost 5 million populations. We carried out this study to review the clinical presentation, types of surgical intervention, histopathological characteristics an factors associated with recurrence and survival after resection of GISTs in this region.

### **METHODS**

This retrospective study was carried out in the Department of General Surgery, Sohag University Hospital (February 2007 - December 2013).

Inclusion criteria comprised adult patients underwent surgical resection of localized GISTs with proven postoperative histopathological examination of the resected specimen. Relevant data of eligible patients studies, presentation, imaging including clinical procedures, surgical laboratory investigations, postoperative complications, histopathological assessment and survival were reviewed and analyzed.

All patients were evaluated by abdominal ultrasonography. Preoperative computed tomography (CT) was performed before elective surgical interventions. Upper and/or lower gastrointestinal endoscopy were undertaken when indicated.

The status of resection margin was used to designate the resection as complete (R0, indicating absence of both macroscopic and microscopic residual tumor) or incomplete (R1 and R2, signifying presence of microscopic or macroscopic residual neoplastic tissues, respectively).<sup>15</sup>

"Risk of aggressive behavior of GISTs" was defined according to 16 Fletcher et al's classification as follows: very low risk: tumor size < 2 cm with mitotic count < 5/50 high power field (HPF); low risk: tumor size 2-5 cm with mitotic count < 5/50 HPF; intermediate risk: tumor size < 5 cm with mitotic count 6-10/50 HPF or tumor size 5-10 cm with mitotic count < 5/50 HPF; high risk: tumor size >5 cm with mitotic count > 5/50 HPF or tumor size > 10 cm with any mitotic count or mitotic count > 10/50 HPF with any tumor size. 16

Postoperatively, some patients were assigned to receive adjuvant therapy based on multidisclipenary team decision for each patient.<sup>17</sup> All patients were followed up in the outpatient clinic regularly every 3 month during the first year and each 6 months thereafter.

### **RESULTS**

## Demographic data, clinical presentation and surgical intervention

Fifteen patients were enrolled among them 9 were males. The median age was 56 (range 32-73) years. Seven GISTs (47%) were found in the stomach, 5 in the small bowel (33%), 2 in the duodenum (14%) and 1 in the colon (7%).

Gastric mass was identified during computed tomography (CT) examination of all patients with gastric GISTs. Definitive diagnosis was established histopathologically only in three patients with gastric GISTs by upper GI endoscopic biopsy.

Non-specific abdominal pain was the most common presenting symptom (40%), followed by hematemesis (33%), fatigue (33%), anemia (27%); intestinal obstruction (20%) and acute abdomen (13%) were the main presenting symptoms. In patients with non-gastric GISTs, histopathological diagnosis was not obtained preoperatively. However, the tumors were found during preoperative CT imaging studies in 6 patients, including both cases of duodenal and the only one case of colonic GISTs. In the remaining 2 patients (13%), GISTs were discovered during emergency exploratory laparotomy for intestinal obstruction (Figure 1 A, B, C and D) and acute abdomen in the other. The predominant symptom in all

small bowels, duodenal and colonic GISTs was nonspecific abdominal pain. Accompanying obstructive symptoms were recorded in three (20%) patients.









Figure 1: (A) Small bowel GIST (black arrow) presented as intestinal obstruction (intussusception); (B) Tumor resected; (C) Small bowel anastomosis; (D) Resected specimen.

Surgical resection was done on selective basis in 13 patients (87%). All patients were treated with conventional open surgery. No tumor rupture was reported among all cases. Patients with gastric GISTs underwent subtotal gastrectomy (1), partial gastrectomy (2) and wedge resection (4) patients. Segmental resection with safety margin and primary re-anastomosis was carried out in all five patients with small bowel GISTs. Both patients with duodenal GIST were treated with local duodenal resection (sparing the pancreatic head) followed by end-to-en duodenojejunostomy. Colonic GIST patient underwent right hemicolectomy. These data are summarized in Table 1.

Table 1: Demographic and clinical data.

	Number	(%)					
Demographic data							
Male	9/15	60					
Female	6/15	40					
Gist location							
Stomach	7/15	47					
Small bowel	5/15	33					
Duodenum	2/15	13					
Colonic	1/15	7					
Clinical presentation							
Abdominal pain	6/15	40					
Hematemesis	5/15	33					
Fatigue	5/15	33					
Anemia	4/15	27					
Intestinal obstruction	3/15	20					
Acute abdomen	2/15	13					
Surgical procedure							
Subtotal gastrectomy	1/15	7					
Partial gastrectomy	2/15	13					
Gastric wedge resection	4/15	27					
Segmental small bowel resection	5/15	33					
Local duodenal resection	2/15	13					
Right hemicolectomy	1/15	7					

### Histopathological data

Surgical resection was complete (R0) in 13 patients. One patient with gastric GIST had suboptimal resection which was confirmed by microscopically positive (R1) resection margin. R2 resection occured in one patient with duodenal GIST in whom local duodenal resection was done since pancreaticodudenectomy was deemd risky.

The mitotite index was < 5/50 HPF in 10 patients (5 gastric, 4 small bowel and 1 duodenal tumor), 6-10/50 HPF in 3 (1 in each gastric, small bowl and duodenal groups) and > 10/50 HPF in two patient with (1 gastric and 1 colonic) tumor.

The diameter of the resected specimen was larger in gastric GISTs with a median of 6 (range: 3.5-11) cm compared with the median diameter in small bowel

tumors which was 4.5 (range: 3-9) cm and also duodenal tumors (3 cm in both patients). Of note, the largest tumor diameter was found in the only case of colonic GIST (14 cm). Regarding the risk for aggressive tumor behavior,

seven patients (47%) exhibited low risk, five (33%) showed intermediate risk 5 and two (30%) had high risk. Tumor categories according to the risk for aggressive behavior are summarized in Table 2.

Table 2: Histopathological data.

	Gastric	Small bowel	Duodenal	Colonic	Total (%)
Tumor diameter					
< 2 cm	0/7	0/5	0/2	0/1	0/15 (0)
2 - 5 cm	3/7	4/5	2/2	0/1	9/15 (60)
6 - 10 cm	3/7	1/5	0/2	0/1	4/15 (27)
> 10 cm	1/7	0/5	0/2	1/1	2/15 (13)
Mitotic count /50 high pov	wer field (HPF)				
< 5	5/7	4/5	1/2	0/1	10/15 (67)
5-10	1/7	1/5	1/2	0/1	3/15 (20)
> 10	1/7	0/5	0/2	1/1	2/15 (13)
Fletcher classification					
Very low risk	0/7	0/5	0/2	0/1	0/15 (0)
Low risk	3/7	3/5	1/2	0/1	7/15 (47)
Intermediate risk	2/7	2/5	1/2	0/1	5/15 (33)
High risk	2/7	0/5	0/2	1/1	3/15 (20)
Surgical margin					
R0	6/7	5/5	1/2	1/1	13/15 (86)
R1	1/7	0/5	0/2	0/1	1/15 (6)
R2	0/7	0/5	1/2	0/1	1/15 (6)

### Adjuvant therapy and survival

Five patients (33%) received adjuvant therapy with imitinib as decided by the multidisciplinary team. Regular follow up was maintained for a median of 21 (range: 8-48) months.

Two patients with duodenal and gastric GISTs died during the seventh and tenth months postoperatively, respectively, despite the regular treatment with adjuvant imitinib. One patient who underwent resection of the gastric GIST had local recurrence, liver metastasis, incomplete (R1) resection and high risk for aggressive behavior (size 11 cm and mitotic count > 10/50 HPF). The other patient with duodenal GIST who underwent R2 resection suffered from local recurrence and peritoneal deposits despite low risk for aggressive behavior (size 3 cm and mitotic count < 5/50 HPF) of the tumor.

Among the study cohort, 13 patients were alive during the follow up period (87%) while 10 (67%) exhibited no tumor recurrence. Three patients (20%) with small bowel and duodenal GISTs developed tumor recurrence after 9, 20 and 31 months, respectively. All had undergone complete tumor resection; nonetheless the risk for aggressive behavior was intermediate in the small bowel and low in the duodenal GISTs.

### **DISCUSSION**

In this study we present a single center experience with the clinical outcome of surgical treatment of GISTs. We provided data on the clinical presentation, location, surgical intervention, histopathological evaluation, adjuvant therapy and survival after resection of GISTs.

The median age of patients enrolled in this study was 56 years old with higher incidence of GISTs in males. The stomach harbored the tumor in 47% of cases followed by the small bowel (33%), duodenum (13%) and colon (7%). These results are comparable with the previous studies which indicated that the majority of GISTs occur in patients older than 50 years with roughly comparable incidence in both genders or may be higher in males with the stomach being the most common location for GIST predilection. 9.18-20 Likewise, in agreement with many other studies abdominal pain, gastrointestinal bleeding, fatigue and anemia were the predominant presenting symptoms in our series. 9.21

A previous report documented that a confident histopathological diagnosis through endoscopic biopsy can be accomplished in 46% of patients with gastric GISTs.<sup>21</sup> In this series, we showed successful histopathological diagnosis in 3 (43%) out of seven biopsies obtained from patients who had gastric GISTs.

Of note, we have not used percutaneous biopsy for fear of tumor rupture and dissemination. About 25% of GISTs are reported to be discovered incidentally during imaging or emergency lapatotomy. In this study, GISTs were incidental finding in 6 out of 15 patients (40%). Among those patients, four were found during imaging studies for abdominal pain. The remaining two included two patients who underwent emergency laparotomy for intestinal obstruction and acute abdomen (small bowel GISTs).

During regular follow up visits two patients died due to disease recurrence and progression. The first patient had undergone subtotal gastrectomy for removal of large gastric tumor suffered from local recurrence and hepatic metastasis. The large tumor size (>10 cm) was associated with increased mitotic count (> 10/50 HPF), both factors are likely to contribute to grave prognosis. Incomplete tumor resection in the second patient who had local resection for duodenal GIST appears to be the detrimental factor, the small tumor size and low mitotic count strongly support this impression. In contrast to Caterino and his co-workers who demonstrated an association between diminished survival and emergency presentation of GISTs, both patients who received emergency resection survived during entire follow up period. Is

An analysis of data from ten population-based studies revealed that the 5-year recurrence-free survival rates for GISTs treated with surgery alone was approximately 70%. The median postoperative follow up period was 21 (range: 8-48) months. Overall, 13 patients (87%) among the study cohort while 10 patients (67%) had recurrence-free survival. These rates should be interpreted with caution due to the low number of tumors with high risk for aggressive behavior and relatively short follow up period.

### **CONCLUSION**

Surgical resection of GISTs remains as the only potentially curative treatment option. Increased risk for aggressive tumor behavior and incomplete resection are associated with recurrence and poor survival.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

### REFERENCES

- 1. Nishida T, Goto O, Raut CP, Yahagi N. Diagnostic and treatment strategy for small gastrointestinal stromal tumors. Cancer. 2016;122:3110-8.
- 2. Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol. 1983;7:507-19.
- 3. Maki RG, Blay JY, Demetri GD, Fletcher JA, Joensuu H, Martín-Broto J, et al. Key issues in the clinical management of gastrointestinal stromal

- tumors: an expert discussion. The Oncologist. 2015;20:823-30.
- Shenoy S. Small bowel sarcoma: tumor biology and advances in therapeutics. Surg Oncol. 2015;24:136-44
- Ducimetière F, Lurkin A, Ranchère-Vince D, Decouvelaere AV, Péoc'h M, et al. Incidence of sarcoma histotypes and molecular subtypes in a prospective epidemiological study with central pathology review and molecular testing. PloS One. 2011;6(8):e20294.
- 6. Kindblom LG, Remotti HE, Aldenborg F, Meis-Kindblom JM. Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal. Am J Pathol. 1998;152:1259-69.
- 7. Wada R, Arai H, Kure S, Peng WX, Naito Z. Wild type GIST: clinicopathological features and clinical practice. Pathol Int. 2016;66:431-7.
- 8. Ud Din N, Ahmad Z, Arshad H, Idrees R, Kayani N. Gastrointestinal stromal tumors: a clinicopathologic and risk stratification study of 255 cases from Pakistan and review of literature. Asian Pac J Cancer Prev APJCP. 2015;16:4873-80.
- 9. Joensuu H, Hohenberger P, Corless CL. Gastrointestinal stromal tumour. Lancet Lond Engl. 2013;382:973-83.
- 10. Jakhetiya A, Garg PK, Prakash G, Sharma J, Pandey R, Pandey D. Targeted therapy of gastrointestinal stromal tumours. World J Gastrointest. Surg. 2016;8:345-52.
- 11. Gheorghe M, Predescu D, Iosif C, Ardeleanu C, Băcanu F, Constantinoiu S. Clinical and therapeutic considerations of GIST. J Med Life. 2014;7:139-49.
- 12. Poort H, van der Graaf WT, Tielen R, Vlenterie M, Custers JA, Prins JB, et al. Prevalence, impact, and correlates of severe fatigue in patients with gastrointestinal stromal tumors. J Pain Symptom Manage. 2016;52:265-71.
- 13. Valsangkar N, Sehdev A, Misra S, Zimmers TA, O'Neil BH, Koniaris LG. Current management of gastrointestinal stromal tumors: surgery, current biomarkers, mutations, and therapy. Surgery. 2015;158:1149-64.
- 14. Agaimy A. Gastrointestinal stromal tumors (GIST) from risk stratification systems to the new TNM proposal: more questions than answers? A review emphasizing the need for a standardized GIST reporting. Int J Clin Exp Pathol. 2010;3:461-71.
- 15. Caterino S, Lorenzon L, Petrucciani N, Iannicelli E, Pilozzi E, Romiti A, et al. Gastrointestinal stromal tumors: correlation between symptoms at presentation, tumor location and prognostic factors in 47 consecutive patients. World J Surg Oncol. 2011;9:13.
- 16. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol. 2002;33:459-65.

- 17. Mathoulin-Pélissier S, Chevreau C, Bellera C, Bauvin E, Savès M, Grosclaude P, et al. Adherence to consensus-based diagnosis and treatment guidelines in adult soft-tissue sarcoma patients: a French prospective population-based study. Ann Oncol. 2014;25(1):225-31.
- 18. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg. 2000;231:51-8.
- 19. Arolfo S, Teggia PM, Nano M. Gastrointestinal stromal tumors: thirty years' experience of an institution. World J Gastroenterol. 2011;17:1836-9.
- 20. Joensuu H, Eriksson M, Sundby Hall K, Hartmann JT, Pink D, Schütte J, et al. One versuss three years of adjuvant imatinib for operable gastrointestinal stromal tumor: a randomized trial. JAMA. 2012;307:1265-72.
- 21. Kassem M, Elzeiny M, Elhaddad H. Management of gastrointestinal stromal tumors: a prospective and retrospective study. Egypt J Surg. 2016;35:11.

**Cite this article as:** El-Badry AM, Ahmad MIM, Ali HM. Outcome of surgical resection for localized gastrointestinal stromal tumors. Int Surg J 2017;4:9-14.