

# Gastrointestinal Stromal Tumors: A Surgical Experience

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## Abstract

**Background:** Gastrointestinal stromal tumor (GIST) is a rare tumor of the gastrointestinal tract presenting with a varied presentation based on the site of tumor, biological behavior of the tumor, and response to chemotherapy; here, we report a total of 21 cases to report present surgical experience in the treatment of GIST patients and to evaluate the prognostic factors.

**Materials and Methods:** Data of all cases of GIST managed at M. S Ramaiah Medical College from April 2010 to June 2015, were noted, and the clinical and pathological features of patients were collected. 21 patients underwent curative surgery; the median follow-up period was 20 months (range 14-24 months). Furthermore, data about treatment variables, patterns, and factors that predict survival were collected and analyzed. Resection of metastases was performed in selected patients in whom the primary tumor is controlled. Patient and tumor characteristics were evaluated as well as treatment variables with special emphasis to study patterns of failure and prognostic factors that predict patient survival.

**Results:** The tumor originated most frequently from the stomach (45%); the small intestine was the second most frequent tumor origin. All patients were symptomatic at presentation. This could be explained by the large size of tumors ranging from 5 cm to 42 cm with a median size of 18 cm. Surgical resection remained the treatment of choice for all resectable tumors since it is the only chance for cure. A 1-2 cm margin was advocated to achieve adequate resection. The goal of surgery is complete resection of gross disease avoiding tumor rupture and achieving negative margins.

**Conclusion:** Surgical resection is the mainstay of treatment of GIST.

**Key words:** Gastrointestinal stromal tumor, Gastrointestinal stromal tumor treatment, Imatinib

## INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract (GIT) and are believed to originate from the interstitial cell of Cajal.<sup>1-3</sup> Management of GIST has evolved very rapidly in the last decade. The advent of effective newer drugs for GIST has altered but not diminished the role of surgery, which remains the standard therapy, and only an adjunct to control the disease and decrease recurrence.<sup>4-8</sup>

## MATERIALS AND METHODS

### Patients and Methods

All cases of GIST managed at our center from April 2010 to June 2015, were included in the study. The clinical and pathological features of patients were collected. Furthermore, data about treatment variables, patterns, and factors that predict survival were collected and analyzed.

All patients had full laboratory workup, chest radiogram, and computed tomography of the abdomen and the pelvis for surgical planning. Upper or lower GIT endoscopies were performed when indicated with biopsy (if feasible).

Resections are classified as

- I. Complete gross removal of the tumor (R0)
- II. Incomplete (R2) when the tumor is unresectable at exploration or when gross residual disease is present after resection and

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III. Complete (R1) when all gross diseases are excised regardless of microscopic margins.<sup>9</sup>

Resection of metastases was performed on selected patients in whom the primary tumor was controlled. Histological confirmation of diagnosis was performed followed by evaluation of morphological and immunohistochemical characteristics including expression of CD117 and CD34. Patient and tumor characteristics were evaluated as well as treatment variables with special emphasis to study patterns of failure and prognostic factors that predict survival. Risk factors including tumor size, mitotic count/50 high power field (HPF), and resection margin were assessed.<sup>10</sup>

### Statistical Analysis

Data were analyzed using SPSS with statistical package version 15. Quantitative data were presented as median and range. Qualitative data were expressed as frequency and percentage. Survival was calculated by the Kaplan–Meier method. Overall survival (OS) was calculated from the date of pathological diagnosis to date of death or last follow-up. Disease free survival (DFS) was calculated from date of surgical intervention to date of recurrence or death or last follow-up.

### Patient Characteristics

Patients included 16 males (76.19%) and 5 females (23.8%), median age being 58 years (range 20-68 years).

## RESULTS

Among the patients included in the study, there were no post-operative mortalities and morbidities (Tables 1-5, Figures 1 and 2, Graph 1).

**Table 1: Mode of presentation in the studied group**

Presentation	Number (%)
Primary disease	20 (95)
Primary disease with metastases	01 (5)
Hepatic	01 (5)
Hepatic+Pulmonary	00
Recurrence	01 (5)
Isolated	01 (5)
Metastasis	00

**Table 2: Tumor site in 21 cases of GIST**

Anatomic site	Number (%)	Historical data (%)
Stomach	09 (45)	60
Small intestine	07 (35)	30
Gastroesophageal junction	01 (5)	
Colon	01 (5)	
Rectum	01 (5)	
Small bowel resection with involved mesentery	01 (5)	

GIST: Gastrointestinal stromal tumor

### Recurrence

There was 1 case of recurrence.

### Survival

For the 21 patients who underwent curative surgery, the median follow-up period was 20 months (range 14-24 months).

In present series, tumor originated most frequently from the stomach (45%); the small intestine was the second most frequent tumor origin. These findings are similar to other reports.<sup>11-15</sup>

All patients were symptomatic at presentation. This could be explained by the large size of tumors ranging from 5 cm to 42 cm with a median size of 18 cm. In contrast, a Western study reported that only 50-70% of patients are symptomatic.<sup>13</sup>

Among 20 patients who underwent complete resection (CR), those with tumor size <5 cm had a median DFS of 22 months compared to 16 months in those with tumor size 5-10 cm. The median DFS dropped significantly to 5 months when tumors were larger than 10 cm ( $P = 0.015$ ). Yao *et al.*<sup>16</sup> demonstrated that tumor size has a significant impact on OS.

## DISCUSSION

In present series, tumor originated most frequently from the stomach (45%); the small intestine was the second

**Table 3: Histopathological and immunopathological features of tumors in 20 cases of GIST**

Features	Number (%)
Histopathology	
Spindle cell	13 (65)
Epithelioid	4 (20)
Mixed	3 (15)
Mitotic count per 50 hpf	
<5	4 (20)
5-10	11 (55)
>10	06 (30)
Tumor kit immunoreactivity	
+ve	19 (95)
-ve	01 (5)

**Table 4: Surgical treatment in the 21 cases of GIST**

Operation	Number
Partial gastrectomy	7
Subtotal gastrectomy	2
Resection anastomosis of small bowel	7
Esophagogastric resection	1
Colectomy	1
Hepatic resection+ resection of recurrent masses	1
Omentectomy	1

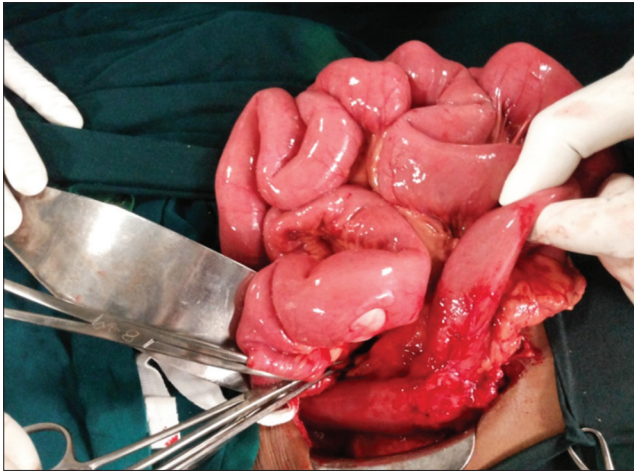


Figure 1: Jejunal GIST

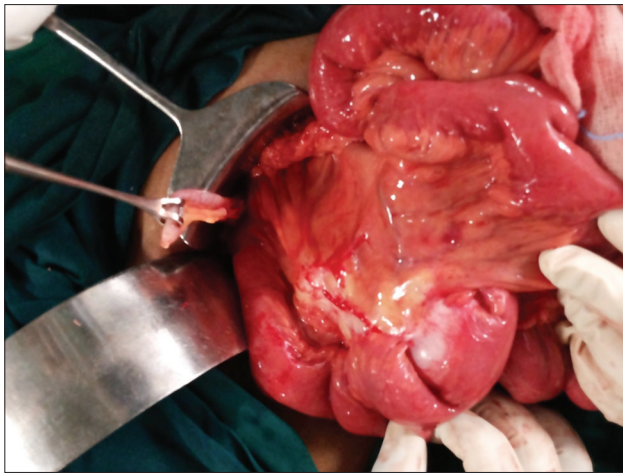
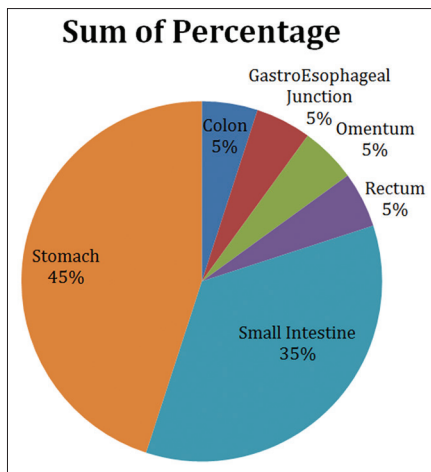


Figure 2: Jejunal GIST, (appendix cited)



Graph 1: Different sites of Presentation

most frequent tumor origin. These findings are similar to other reports.<sup>12</sup> All patients were symptomatic at presentation. This could be explained by the large size

of tumors ranging from 5 cm to 42 cm with a median size of 18 cm. In contrast, a Western study reported that only 50-70% of patients are symptomatic.<sup>13</sup> Among 20 patients who underwent CR, those with tumor size <5 cm had a median DFS of 22 months compared to 16 months in those with tumor size 5–10 cm. The median DFS dropped significantly to 5 months when tumors were larger than 10 cm ( $P = 0.015$ ). Yao *et al.*<sup>16</sup> demonstrated that tumor size has a significant impact on OS. However, the majority of tumors >5 cm in present series and none having local recurrences worth minimum follow-up of 18 months. Histological examination revealed spindle cell tumors in 65% of specimens, whereas 20% were epithelioid and 15% were mixed. This is comparable with the described incidence in other studies.<sup>17</sup> Surgical resection remains the treatment of choice for all resectable tumors since it is the only chance for cure.<sup>1,12</sup> A 1-2 cm margin was advocated to achieve adequate resection.<sup>18</sup> However, more recently, Dematteo *et al.*<sup>19</sup> demonstrated that tumor size (and not a wide negative microscopic margin) was more important in determining survival. The goal of surgery is CR of gross disease avoiding tumor rupture and achieving negative margins. Metastasis the liver in 65%, the peritoneal surface in 50%, and in both in about 20%.<sup>12</sup> In the present study, one patient had liver metastasis (5%). Different risk categories have been compiled by Fletcher *et al.*<sup>11</sup> based on primary tumor diameter and mitotic counts per 50 HPF which determine the risk of local recurrence and survival. In our study, primary tumor presentation, gastric origin, tumor size, and mitotic count had a significant influence on DFS. Kit/PDGFR tyrosine kinase inhibitors such as imatinib (Gleevec) have been applied in the treatment of unresectable or recurrent GISTs. This oral therapy has demonstrated good response in the majority of patients and has emerged as the gold standard treatment for patients with metastatic GISTs.<sup>20</sup> One patient operated for mesenteric GIST in jejunum was on imatinib for 14 months, came back to us with metachronous lesion in ileum despite patient continuing on imatinib, which was resected later. However, long-term success is limited due to the development of imatinib resistance via secondary mutations or clonal selection. In the present study, 1 patient with metastatic disease and 1 patient with recurrent disease received neoadjuvant Gleevec for 4 years and 6 months, respectively.

## CONCLUSION

GIST is a rare tumor of the GIT presenting with a varied presentation based on the site of the tumor, biological behavior of the tumor, and response to chemotherapy.

**Table 5: Disease free survival of the patients with GIST who underwent complete resection in relation to the risk factors**

Item	Number	DFS in months	P value
Age			
<40	3	16	Insignificant
>40	18	18	
Gender			
Male	16	20	Significant
Female	05	23	
Presentation			
Primary	19	19	Significant
Recurrent	2	8	
Site			
Gastric	9	18	Significant
Others	12	13	
Size			
<5	3	20	Significant
5-10	12	12	
>10	6	04	
Surgical margin			
Negative	15	16	Significant
Positive	06	18	
Mitosis per 50 hpf			
<5	3	22	Significant
5-10	13	16	
>10	05	05	

DFS: Disease free survival

With advancement in radiological diagnosis and confirmation with immunohistochemistry (IHC), management of the disease has been standardized.

Tumor size, mitotic index, gastric origin, and primary presentation are important predictors for disease-specific survival in patients presenting with primary disease. IHC should be done in all, and those who are in high-risk, metastatic, and unresectable groups require imatinib mesylate. Patients, who are CD117 positive, show good response to imatinib mesylate. Surgical resection remains the main modality of treatment followed by chemotherapy in the form of tyrosine kinase inhibitor such as imatinib.

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