

Gastrointestinal Stromal Tumor (GIST)'s Surgical Treatment, NCI Experience

MOHAMAD EL-ZOHAIRY, M.D.*; EL-SAYED ASHRAF KHALIL, M.D.*; IBRAHIM FAKHR, M.D.*; MAGDY EL-SHAHAWY, M.D.* and IMAN GOUDA, M.D.**

The Departments of Surgical Oncology and Pathology**, National Cancer Institute, Cairo University.*

ABSTRACT

Purpose: To review the clinical presentation, surgical management, and prognostic factors for gastrointestinal stromal tumors.

Patients and Methods: A prospective study which was carried out between January 2002 and March 2004 on thirty-three patients with gastrointestinal stromal tumor (GIST) at the National Cancer Institute, Cairo University. All patients were evaluated preoperatively and underwent exploratory laparotomy with a curative intent, they were followed up for period ranging between 14-35 months.

Results: Among the 33 patients there were 17 males and 16 females. The mean age of patients was 52.8 years. Clinical findings included gastrointestinal bleeding (42.4%), palpable mass (33.3%) and abdominal pain (24.3%). The stomach was the most common site of origin of the disease (39.4%), followed by the colorectal region (24.2%). Tumors were high grade in 63.6% of patients and low-grade in 36.4% of patients. Complete resection of all gross disease was accomplished in 26 patients (78.7%), among whom, multiple adjacent organ resection was required in 6 patients (22.2 %) and metastatic disease was identified in the liver in 3 patients at the time of exploratory surgery of these one could be resected. Immunohistochemical staining for CD117 was positive in 88.9% of patients. The median follow-up period was 20 months (range, 14-35 months). The overall median survival in this study was 25 months, and the cumulative survival at 30 months was 46.9%. Unfavorable prognostic factors were incomplete resection and, high-grade histological features ($p < 0.05$). None of the patients received adjuvant or palliative chemotherapy. Twenty six patients (78.8%) are alive free of disease. Of the 7 patients with incomplete resections or biopsy only; 4 patients (12.1%) are alive with disease and 3 patients died.

Conclusion: Surgical resection, including en bloc resection of locally advanced tumors, remains the only curative treatment. Overall survival is significantly affected by high-grade tumors and positive resection margin.

Key Words: Gastrointestinal stromal tumor - GIST - Sarcoma - STI-571, c-kit proto-oncogene - CD 117 - CD 34 - Therapy - Surgery.

INTRODUCTION

Until 20 years ago most gastrointestinal (GI) mesenchymal tumors were considered to be of smooth muscle origin. However, GI sarcomas had been observed to be relatively resistant to standard doxorubicin-based chemotherapy regimens compared with leiomyosarcomas of the uterus or trunk. Mazur and Clark in 1984 reported that many supposed smooth muscle tumors lacked immunohistochemical or electron microscopic evidence of smooth muscle or neural immunoreactivity, and they suggested that the neutral term 'gastric stromal tumor' would be more appropriate [1]. It has since become clear that the tumor cells comprising GISTs are closely related to the interstitial cells of Cajal (ICC) being positive for c-kit (CD 117) and CD-34, and negative for desmin and S-100. Not all GISTs arise from the interstitial cells of Cajal, however, as some come from the mesentery or omentum which lacks interstitial cells of Cajal, suggesting an origin from multipotential mesenchymal stem cells [2,3]. GISTs are reported to constitute about 5 per cent of all sarcomas [4] and occur predominantly in the age between 40-60 years.

No significant sex difference has been noted [2,5]. They most commonly occur in the stomach (40% to 70%), but also commonly arise in the small bowel and associated mesentery (20% to 40%), esophagus (<5%) or colon and rectum (5% to 15%) [6]. Most patients with GISTs are asymptomatic, although patients with advanced disease may present with symptoms of a mass lesion, abdominal pain, or bleeding. At least 10% to 30% are discovered incidentally during

laparotomy, endoscopy, or other imaging studies, while between 15% and 50% of GISTs presents with overtly metastatic disease. Occasionally the diagnosis is made during a celiotomy for peritonitis, small bowel obstruction, or bleeding [7]. Different risk categories have been compiled by Fletcher et al. [8] and are outlined in Table (1).

Table (1): Proposed approach for assigning risk to gastrointestinal stromal tumors (Fletcher et al. [8]).

	Size (cm)	Mitotic count (per 50 HPF*)
Very low risk	<2	<5
Low risk	2–5	<5
Intermediate risk	<5	6–10
	5–10	<5
High risk	>5	>5
	>10	Any
	Any	>10

*HPF: High-power field.

Endoscopy occasionally identifies submucosal lesions, with or without ulceration, from which only 50% are preoperatively histopathologically diagnosed [6]. Recent studies suggest that endoscopic ultrasonography can help to differentiate between GISTs and other gastrointestinal lesions. Characteristics associated with malignancy include tumor size greater than 4cm, an irregular extraluminal border, echogenic foci, and cystic spaces [9].

Computed tomography scans are critical to determine the anatomic extent of a GIST lesion during evaluation before operation. Radiographic signs corresponding to aggressive malignant GIST include calcification, ulceration, necrosis, cystic areas, fistula, metastasis, ascites and signs of infiltration. PET imaging can be useful in staging the initial disease, in planning the operative approach, and in helping to identify the extent of malignant lesions and the presence of metastases and the responsiveness or resistance of the tumor to therapy [10].

Surgical resection is the main treatment for GISTs. Preoperative percutaneous biopsy carries the theoretical risk of peritoneal seeding or tumor rupture, and is indicated only for clearly irresectable disease or when treatment would be altered, as would be the case if the mass proved to be lymphoma. All tumors should be approached with the intention of performing

complete en bloc removal of the tumor (R0 resection) and surrounding normal tissue, including the adjacent organs if they are involved [6,11,12,13]. Unlike intestinal adenocarcinoma, GIST rarely metastasizes to lymph nodes, and thus lymphadenectomy is seldom warranted [4,11]. Achieving negative pathologic margins of resection generally is not difficult because GIST tends to hang from, not diffusely infiltrate, the organ of origin. Consequently, wedge resection of the stomach [13] or segmental resection of the intestine provides adequate therapy, and more extensive surgery has no better benefit [14].

GISTs are notoriously unresponsive to ordinary chemotherapy and, until the recent introduction of the KIT inhibitor imatinib (STI-571), there has been no effective therapy for the locally advanced or metastatic disease. This agent selectively inhibits the tyrosine kinases. STI-571 is a targeted therapy directed against the apparent fundamental and critical pathogenetic defect in GIST [15].

GISTs are generally thought to be malignant, but they have different degrees of aggressiveness, resulting in varying times to the development of metastases. However, the prediction of malignant potential may be difficult; small tumors with low mitotic activity may still metastasize. Anatomic location is also important; a small GIST from the small intestine may have a worse prognosis than a large tumor from the stomach [13]. To date, proposed prognostic features indicative of malignancy or high risk for aggressive clinical behavior include tumor size 5cm or larger, mitotic rate 2/10 HPF or greater, and proliferation index 10% or more [4]. Further criteria correlating with poor prognosis are site (distal as opposed to gastric), increasing histological grade, and DNA aneuploidy as determined by DNA-flowcytometry [15]. Nevertheless, predicting biological potential often remains difficult, and complementary approaches in the critical assessment of GISTs, such as cytogenetic and molecular cytogenetic techniques, are increasingly being considered [20].

After operation, recurrences typically develop at the local site of resection, peritoneum and in the liver. Tumor recurs in 40–90%, despite histopathologically complete resection [16]. Fifty percent of recurrences involve the liver

[17]. GIST is four times more likely to recur if the primary site is intestine compared with stomach (40% versus 9%, respectively) [18]. Complete resection in patients with a primary GIST is associated with a 5-year survival rate of 48-65% [3,16]. The median duration of survival for patients with a metastatic GIST is approximately 20 months, and 9-12 months for patients with local recurrence [9].

The aims of this work were to study the disease presentation, to determine the utility of endoscopic and radiographic studies in diagnosing this disease, and to examine the impact of surgical treatment, clinical and pathologic features on survival.

MATERIAL AND METHODS

From January 2002 to March 2004, 33 patients with GIST were operated upon at the surgical department NCI, Cairo University. Twenty-seven patients presented with primary disease while 5 patients presented with recurrent disease. All patients underwent full laboratory work up, chest radiography and computed tomography (CT) of the abdomen and pelvis for surgical planning and to exclude distant metastasis. Abdominal ultrasonography was done to those patients suspected to have liver involvement. Upper and lower GI endoscopy were performed when indicated with an endoscopic biopsy when the latter was feasible. FNAC was not routinely done due to its little yield. Our protocol was to do preoperative evaluation, perform surgery in the form of complete wide resection with a safety margin about 4cm if bowel is to be resected, evaluation of postoperative complications and to do follow up for a minimum of 14 months. All specimens were examined in relation to the risk factors, namely size and histopathological grade. Specimens were also subjected to immunohistochemistry staining including CD 34 and CD 117 (Fig. 1-A,B).

RESULTS

Among the 33 patients there were 17 men and 16 women with a mean age at diagnosis of 52.8 (range: 16-71) years and most (60.6%) of cases occurred between 41-60 years (Table 2). All patients were symptomatic on presentation. The most common symptom was gastrointestinal bleeding, which occurred in 14 patients (42.4%)

(Table 3). Other clinical manifestations were: Palpable mass in 11 patients (33.3%), abdominal pain in 8 patients (24.3%), constipation was found in 5 patients (15.2%), nausea with or without vomiting in 4 patients (12.1%) and lastly, recent significant weight loss in 3 patients (9%). Moderate anemia was found in only 3 patients (9%). Almost 35% of patients manifested more than a single complaint or a physical finding. The mean duration of symptoms before presentation was 5 months (range: 1-14 months).

Table (2): Clinical characteristics.

	No.	%
Age:		
0-40	7	21.2
41-60	20	60.6
61-80	6	18.2
Sex:		
Male	17	51.5
Female	16	48.5
Total	33	100.0

Table (3): Clinical picture.

Signs and symptoms	No.	%
Gastrointestinal bleeding	14	42.4
Palpable mass	11	33.3
Pain (colic)	8	24.2
Constipation	5	15.2
Nausea / vomiting	4	12.1
Anemia	3	9.0
Weight loss	3	9.0

Computed tomography (CT) of the abdomen and pelvis was the most commonly used investigation tool, being done for 32 patients out of 33 (96.3%), Fig. (2A, 2B). In those 32 patients for whom the CT were obtained, radiographic findings suggested the presence of GIST in only 16 cases (48.5%). The other investigative tools used included: Upper GI endoscopy used in 13 patients (39.4%) (Fig. 3), lower GI endoscopy used in 11 patients (33.3%) and abdominal ultrasound used for 11 patients (33.0%). Endoscopic abnormalities were demonstrated in 10 of the 13 patients who underwent upper GI endoscopy (77.0%). Those abnormalities were: Extra-gastric mass in 7 patients (70.0%) and ulcerating mass in 3 patients (30.0%). However, a preoperative endoscopic pathological diagnosis

was confirmed in only 1 patient (10.0%). As for lower GI endoscopy, abnormalities were detected in 9 of the 12 patients in whom it was performed (75.0%). Detected abnormalities were: Ulcerating and extra luminal mass in 7 and 2 patients respectively (77.7%, 22.2%). An endoscopic pathological diagnosis was reached in 3 only patients (33.3%). Upper gastrointestinal radiography was done in 3 patients and was abnormal in 2 of the 3 (66.7%) (Fig. 4). Superior mesenteric angiography was done in one patient with obscure GIT bleeding and revealed tumor blushes, indicating small intestinal tumor (Fig. 5). FNAC was done in 2 patients and revealed spindle cell tumor.

Anatomic distribution and pathologic features of the tumors are listed in table (4). The most common anatomic origin was the stomach (13 cases; 39.4%) (Figs. 6,7), followed by the colon and the rectum (8 patients; 24.2%) (Fig. 8), the small intestine (7 patients; 21.2%) and least frequently, the intestinal mesentery (3 cases; 9.1%) (Fig. 9). In two patients (6.1%), a definite anatomical origin could not be specified. Tumors exhibited high histopathological grade in 21 patients (63.6%) and low histopathological grade in 12 patients (36.4%). Most patients had lesions that measured 5 cm or more in their greatest dimension (75.8%); leaving only 8 of the lesions measuring less than 5cm in their greater dimension (24.2%). The median size of the tumors was 14cm (range: 2-55cm).

Table (4): Anatomic and pathologic characteristics.

	No.	%
Tumor size:		
<5cm	8	24.2
>5cm	25	75.8
Grade:		
High grade	21	63.6
Low grade	12	36.4
Surgical margins:		
Negative	26	78.7
Positive	7	21.3
Origin:		
Stomach	13	39.4
Colon/rectum	8	24.2
Small Bowel	7	21.2
Mesentery	3	9.1
Undetermined	2	6.1
Total	33	100.0

The different operative procedures performed during this study are listed in table (5). Complete resection of all gross disease with final negative pathologic margins was accomplished in 26 patients (78.7%). Resections in this group included subtotal or wedge gastric resection in 10 patients (30.3%), segmental small bowel resection in 5 patients (15.2%), abdomino-perineal resection in 4 patients (12.1%), segmental colon resection in a single patient (3.0%) and small bowel resection with en bloc resection in 2 patients (6.1%). Extended resections for locally advanced disease were done in 4 of these 26 patients. Adjacent organs resected in those late patients included the spleen, tail of pancreas, transverse colon and portions of the diaphragm and the liver. Four patients (12.1%) had incomplete resections; two of them had gross residual disease (6.0%), one had margin-positive resections (3.0%) and another one had irresectable liver deposit (3.0%). Three patients (9.1%) underwent exploratory procedures with biopsy only due to the irresectability of the disease (Fig. 10).

Table (5): Operative procedures performed in 33 patients with GIST.

Type of resection	No.	%
Complete resections (en bloc resection of all gross disease local organ resection):	26	78.8
1- Subtotal or wedge gastric resections	10	30.3
2- Small bowel segmental resections	5	15.2
3- Abdomino-perineal resections	4	12.1
4- En bloc resections of mesenteric mass	2	6.1
5- Segmental colon resections	1	3.0
6- Extended en bloc resections (multiple organs):	4	12.1
• Gastric sarcomas + spleen + distal pancreas	1	3.0
• Gastric sarcomas + transverse colon	1	3.0
• Recurrent gastric sarcomas + transverse colon + diaphragm	1	3.0
• Small bowel sarcomas + liver	1	3.0
Incomplete resections (margin positive, gross residual disease left):	4	12.1
• Incomplete resections	2	6.1
• Abdomino-perineal resections with positive margins	1	3.0
• Small bowel segmental resections, leaving liver deposit	1	3.0
Biopsy only (locally advanced):	3	9.1
• Biopsy + transverse colostomy	1	3.0
• Biopsy	2	6.1
Total	33	100.0

During the previous procedures we had 3 intraoperative complications (9%): Two cases of minor bladder injury due to extensive adhesions (6%), repaired primarily in 2 layers and a single case of major vascular injury (aorta) (3%) in one of the recurrent cases and was repaired primarily. There was no intraoperative mortality. During the post operative period 4 patients developed complications (12%); 3 morbidities and a single mortality. Two of the patients developed wound sepsis (6%) and a third patient developed a cysto-cutaneous urinary fistula (3%); all cases were managed conservatively. There was a single postoperative death (3%) in a patient with an irresectable locally advanced disease, who underwent a simple biopsy. Death was due to massive myocardial infarction.

The overall median survival in this study

was 25 months, and the cumulative survival at 30 months was 46.9% (Fig. 11). The 3 prognostic factors analyzed for effect on overall survival included grade, size, and resection status (Table 6). Prognostic factors that significantly influenced survival were tumor grade, and the completeness of resection. Twelve patients had low-grade tumors, with cumulative survival of 74.1%, as opposed to 21 patients with high-grade tumors whose cumulative survival was 22.9% ($p=0.038$) (Fig. 12). Patients who underwent complete resection had a cumulative survival of 71.0%, whereas patients who underwent incomplete resection had a cumulative survival of only 28.6% ($p=0.048$) (Fig. 13). Eight patients had tumors measuring less than 5cm, with a cumulative survival of 78.8% compared with 35.4% for patients with tumor of 5cm or more in size ($p=0.191$) (Fig. 14).

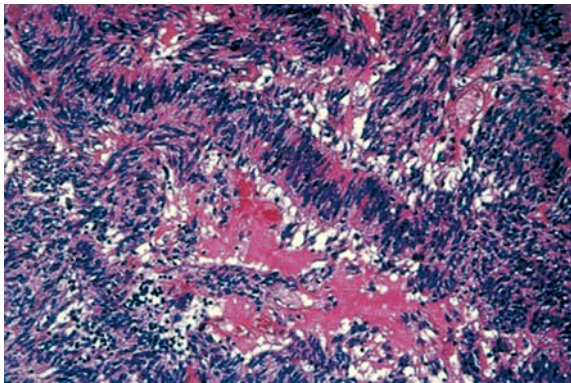


Fig. (1-A): GIST showing prominent palisading arrangement of cells.

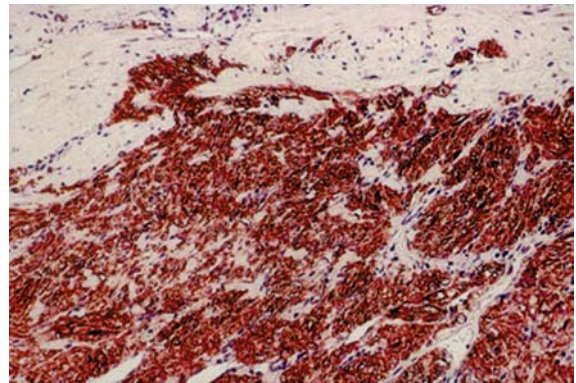


Fig. (1-B): Strong positive immunostaining in GIST.

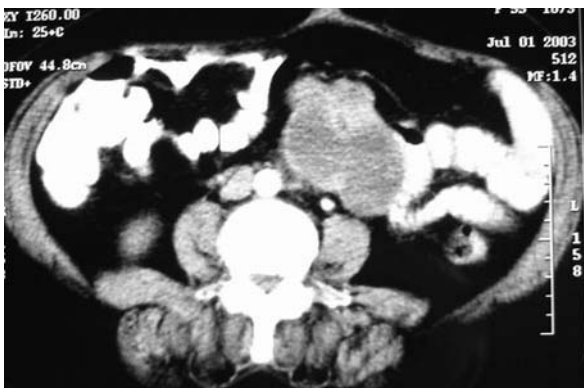


Fig. (2-A): CT scan showing an exophytic jejeunal tumor with central areas of low attenuation.



Fig. (2-B): CT scan showing a liver metastasis with peripheral enhancing portion and a necrotic center.



Fig. (3): Upper GI endoscopy of a 47-year-old woman with an endophytic GIST.

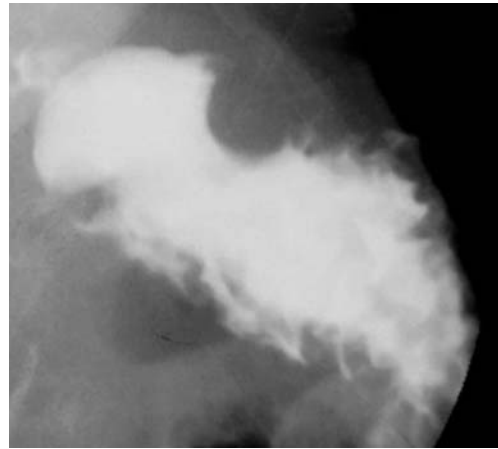


Fig. (4): A Barium meal showing a smooth filling defect at the greater curvature.



Fig. (5): Selective superior mesenteric angiography for a patient with an obscure GI hemorrhage showing tumor blush, indicating a small intestinal tumor.

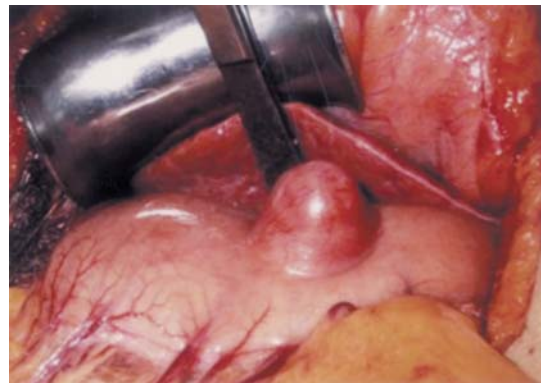


Fig. (6): A 43-year-old man with an exophytic GIST of the stomach.



(A)



(B)

Fig. (7): Representative morphological findings in a gastric GIST. A: Preoperative CT scan detecting tumor next to the liver. B: The same tumor after partial gastric resection, typically covered by intact mucosa and a central ulceration.



(A)



(B)

Fig. (8): A 52-year-old man with a GIST of the rectum. A: CT scan showing a well-defined heterogeneous mass posterior to the bladder. B: Photograph of the open gross specimen showing extra luminal tumor with small ulcer.



Fig. (9): Huge mesenteric tumor.



Fig. (10): Sleeve resection of stomach using GIA-90 stapler.

Table (6): Analysis of factors that influence overall survival.

	n	Median Surv. (mths)	Estimated Surv. (%)	p value
Overall Survival	33	25	46.9	
<i>Grade:</i>				
Low	12	–	74.1	0.038
High	21	24	22.9	
<i>Size:</i>				
<5cm	8	–	78.8	0.191
>5cm	25	24	35.4	
<i>Resection status:</i>				
Complete	26	–	71.0	0.048
Incomplete	7	20	28.6	

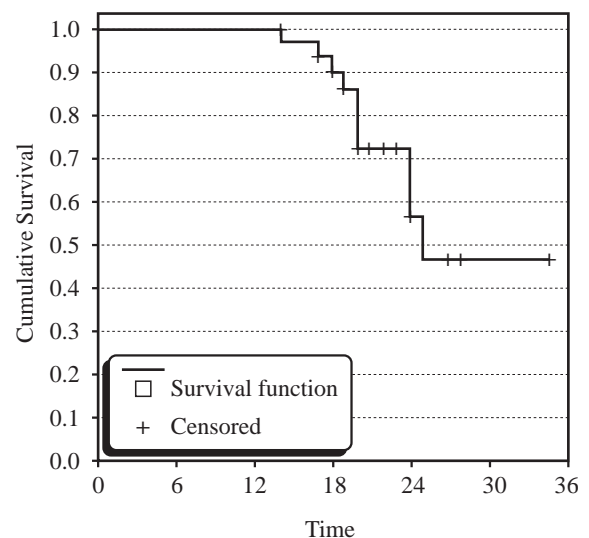


Fig. (11): Overall survival for the whole group.

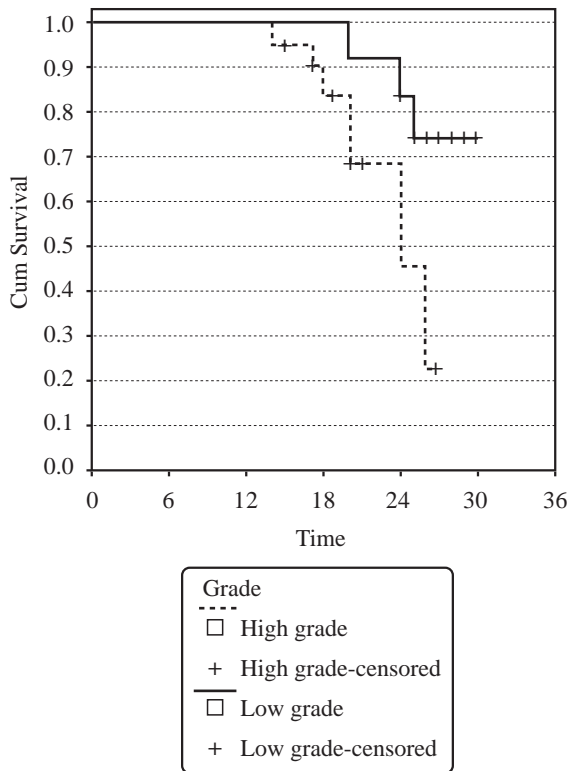


Fig. (12): Overall survival by tumor grade.

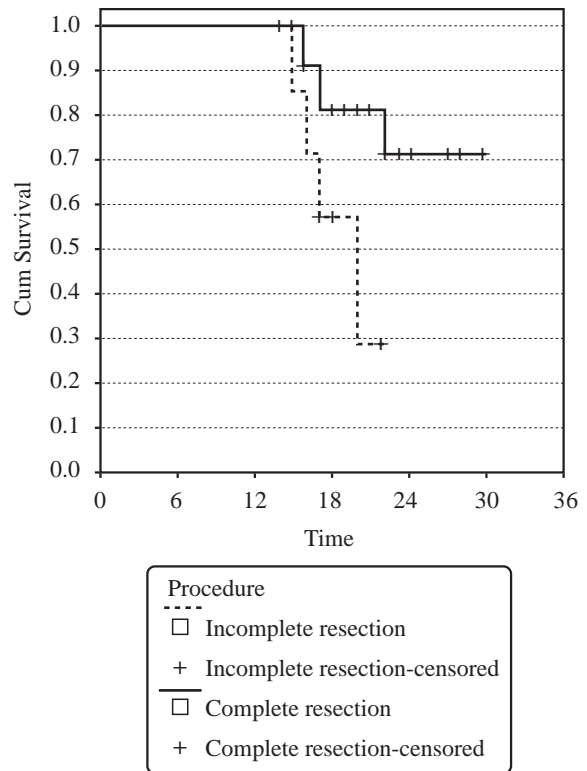


Fig. (13): Overall survival by completeness of tumor resection.

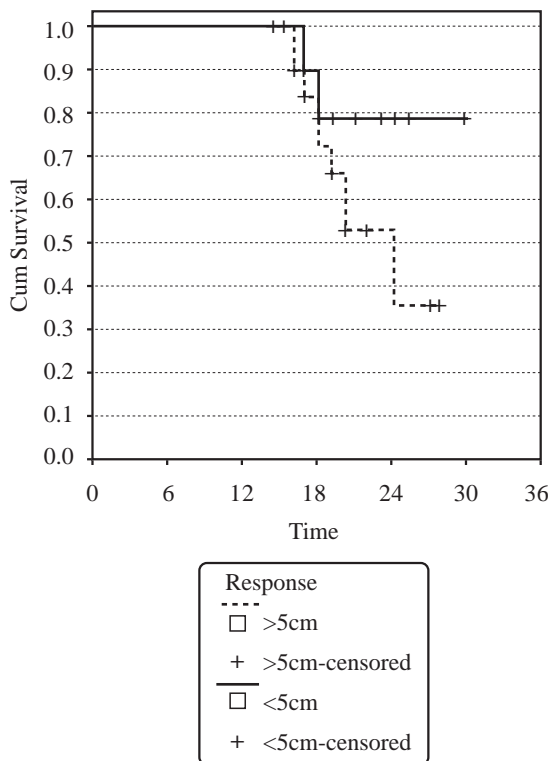


Fig. (14): Overall survival by tumor size.

None of the patients received adjuvant or palliative chemotherapy. Twenty four patients (72.7%) out of the 26 patients who had complete resections are alive, 18 of them are free of disease (69.3%). The remaining 6 patients developed recurrence during the period of the study (23.6%); of these last, 4 could be salvaged (66.7%). Most of the recurrences (5 cases; 83.3%) were due to tumors at the intestinal mesentery or in the small intestine and only one was of gastric origin (16.6%). Among the 7 patients who underwent incomplete resections or just biopsy; 4 patients (12.1%) are still alive with disease and 3 patients died (0.9%).

DISCUSSION

GIST represents the most common mesenchymal tumors of the gastrointestinal tract. GIST characteristically stain positive for CD117 and CD34, but less commonly for SMA and S100 (neural cell marker), which are expressed typically by leiomyosarcomas and schwannomas, respectively [8,20]. In our series of patients, 88.9% of tumors that were available for testing showed positive staining for CD117 and 69%

for CD34 which is consistent with other reports who described a CD117 which is positive in (85-94%) of cases [21] and a CD34 which is only positive in 52-72% of cases [3].

The symptoms associated with primary gastrointestinal sarcomas are usually vague and nonspecific. The non-specificity of the symptoms associated with this disease has been considered as a contributing factor in the delayed diagnosis associated with GIST [22]. Despite the fact that most patients in our series were symptomatic and most patients had some combination of bleeding, pain, and abdominal mass, the mean duration of symptoms before referral to the surgical service was 5 months. Patients in this study most frequently experienced gastrointestinal bleeding. This finding is consistent with other reports in which gastrointestinal bleeding was the most frequent clinical manifestation [22,23]. The second most frequent manifestation was a palpable mass, and the third most frequent manifestation was mild abdominal pain.

By analysis of the utility of the frequently ordered diagnostic studies that were performed before surgical exploration, the most frequently ordered diagnostic test in our series was the CT scan (96.3%). The CT was most useful in terms of demonstrating a mass lesion, determining its size and its relation to the contiguous organs as well as confirming the present or absence of distant metastases; however it was conclusive in only 48.5% of the cases. In our study, although 9 underwent endoscopic biopsy, only 3 (33.3%) of the patients had a confirmed pathologic diagnosis after these tests. Upper GI endoscopy to evaluate a patient with upper gastrointestinal bleeding seems a reasonable first test to detect a benign source but it was our general impression that these studies added little in terms of planning the extent and the type of the operation. This is due to the fact that most of the endoscopically detected lesions were extra-luminal with an intact mucosa. Needle biopsy was performed infrequently and, when performed, was not helpful in the establishment of a definitive diagnosis. No other imaging test that was evaluated (including upper gastrointestinal contrast study or abdominal ultrasound scanning) was found to be more sensitive than CT for the detection and staging of a primary gastrointestinal sarcoma. As for angiography,

being used in only one patient, its efficiency could not be evaluated.

In our series, tumors originated most frequently from the stomach (39.4%), these findings are similar to other reports in which the stomach was involved in 38% to 65% of cases [4,22,24]. The colorectal origin was the second most common tumor origin in our series, this is in contrast to other reports in which small intestine tumors are the second most common tumors [4,22,24].

In our study, 75.8% of the patients had tumors greater than or equal to 5cm (median size 14cm) and 24.2% had tumors less than 5cm. Cases with tumor size <5cm (8 cases) had a cumulative survival of 78.8% and those with a tumor >5cm had a cumulative survival of 35.4%. This difference was not statistically significant owing to the small number of cases with tumors <5cm and due to the lower frequency of deaths in this group. Similarly, several studies have demonstrated that the tumor size, whether less than 5cm or greater than 10cm, does not significantly affect survival [16,22,25].

Katharine et al. [26] has found that tumor size have a significant impact on overall survival. Independent of tumor grade, tumors of 5cm or larger had a 28-month median survival as opposed to those that were less than 5cm, which had a 42-month median survival. Other studies have shown impact on survival with a different tumor size cut off point. McGrath et al. [24] found a significantly better 5-year survival rate in patients whose tumors were less than 10cm as compared to those with 10cm or more.

As with sarcomas elsewhere, histological grade is a powerful prognostic characteristic. Twelve patients had low-grade tumors with a cumulative survival of 74.1% compared with 21 patients with high-grade tumors whose cumulative survival was 22.9% ($p=0.038$). Previous reports have shown that low-grade lesions are associated with improved overall 5-year survival in the 40% to 80% range compared with high-grade lesions with overall survival rates between 16% and 28% [27,28].

Complete surgical resection emerged as the most important prognostic variable in this study. A complete resection removed all gross disease with negative pathological margins, including

en bloc resection of contiguous organs when necessary. The cumulative survival for patients who underwent a complete resection was 71.0% compared with 28.6% for those patients who underwent an incomplete resection ($p=0.048$).

In a recent report, Langer et al., in 2003 they described the outcome of 39 patients following surgery. Complete R0 resection was achieved in 35 of the 39 patients and of these only five died from recurrent disease, compared with 3 of the 4 patients with involved margins. Incomplete resection should only be performed for the palliation of pain, bleeding or the symptoms of mass effect [12].

Tumor rupture before or during resection is another predictor of poor outcome [16,30]. Meticulous surgical dissection is imperative to avoid tumor rupture and intraperitoneal dissemination during the resection of these often soft and fragile tumors. Univariate analysis of different studies of GIST found that tumor size of less than 5cm, low histological grade, presence of localized disease, and complete surgical resection without tumor spillage were all favorable prognostic factors [16,27,29].

A number of other pathologic features have also been correlated with survival as reported by many authors, including mitotic index, aneuploidy, cellular morphometry, proliferative index, and percent S-phase fraction [3,16,31].

The incidence of lymph node involvement in our series was 0%, which is consistent with a low incidence of lymph node metastases seen in other reports (less than 2%) [16,25,32,33].

Previously, the only proven treatment for GIST was surgical resection; radiation therapy and chemotherapy have been ineffective. However, the drug imatinib mesylate (Gleevec), is currently being studied in clinical trials at several institutions. The drug has proven effective in early- and late-stage disease. Imatinib mesylate initially helps control disease in 80% or more of patients, with an objective response observed in 50-60% of cases [3]. As this drug is very expensive, it is not routinely used at NCI.

Conclusion:

Complete resection with an aggressive attempt to remove all gross disease and achieve negative margins remains the fundamental sur-

gical principle in the management of GIST. Extensive preoperative testing and biopsy do little to alter this recommendation. For localized gastric tumors, wedge resection with negative margins appears adequate. More extensive gastric lesions may require total gastrectomy or en bloc resection of adjacent organs. Small bowel and colon lesions are removed with segmental resections and, when indicated, may require the removal of involved contiguous organs. As the incidence of lymph node involvement is low, extended lymph node dissections are not warranted. A larger patient series with a longer follow up is needed for better evaluation of all possible prognostic factors affecting survival and recurrence of GIST cases. Imatinib mesylate should be included in the future studies in an attempt to improve our results.

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