Management of gastrointestinal stromal tumors: a prospective and retrospective study

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Received 05 July 2015
Accepted 05 August 2015

The Egyptian Journal of Surgery
2016, 35:11–19

Background
Gastrointestinal stromal tumors (GISTs) are a group of unusual neoplasms arising from the interstitial cells of Cajal. GISTs are the most common mesenchymal tumors of the gastrointestinal (GI) tract. Diagnosis always requires immunohistochemical staining for the expression of c-KIT protein (CD-117).

Purpose
The aim of this study was to present the prospective and retrospective experience of the Gastrointestinal Surgery Department, Alexandria Faculty of Medicine, in the management of GISTs.

Materials and methods
This study was carried out on 102 patients: a prospective study on 22 patients from April 2013 to April 2015 and a retrospective study on 80 patients between January 2009 and March 2013. All patient data, the different clinical presentations, the impact of surgical treatment, complications, follow-up, and survival data were collected and analyzed.

Results
This study included 102 patients (63 men and 39 women) who presented with GISTs on clinical, radiological, and/or endoscopic aspects. Their mean age at diagnosis was 49.18 ± 14.58 years. The most frequent presenting symptom was GI bleeding, seen in 42 patients (41.18%). Twenty-five patients (24.51%) presented with abdominal swelling and pain. Twenty-four patients (23.53%) presented with anemia for investigation. Eight patients (7.84%) presented with repeated attacks of abdominal pain only. The tumors were located in the stomach in 54 patients (52.9%). Upper gastrointestinal endoscopy was performed in 64 patients (62.75%). Upper gastrointestinal endoscopy revealed the presence of a gastric lesion in 46 patients and a duodenal lesion in six patients and was completely free in 12 patients. Complete resection was achieved in 92 patients (92%), whereas eight patients (8%) had incomplete resection.

Conclusion
This study concludes that GISTs can occur anywhere in the GI tract but most commonly in the stomach. The prognosis is strictly related to the size of the tumor, number of mitoses, and completeness of surgical resection.

Keywords:
c-KIT protein (CD-117), gastrointestinal stromal tumors, imatinib (Gleevec), surgical resection

Egyptian J Surgery 35:11–19

1110-1121

Introduction

Gastrointestinal stromal tumors (GISTs) are a group of neoplasms of mesenchymal origin that develop in the gastrointestinal (GI) system. GISTs are the most common (~80%) mesenchymal tumors of the GI tract, accounting for 1–3% of all GI malignancies [1–4]. These tumors are believed to arise from the interstitial cells of Cajal, a complex cellular network thought to act as pacemaker cells that regulate peristalsis [3–5]. Morphologically, GISTs can be classified into spindle cell type (70%), epithelioid type (20%), and mixed type (10%) [6,7]. Grossly, GISTs are submucosal lesions that appear to arise from the muscularis propria of the bowel wall; intramural in origin, they are often exophytic extraluminal and/or endophytic intraluminal and may have overlying mucosal ulceration. Their size can be extremely variable, from tiny incidental cases to huge masses [8]. Large GISTs nearly always outgrow their vascular supply, leading to extensive areas of necrosis and hemorrhage [9,10].

With the advent of immunohistochemical staining techniques [11–16], Mazur and Clark [11] in 1983 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 ‘stromal tumor’ would be more

appropriate. The discovery of CD-117 expression in many GISTs suggested that they were a specific entity, distinct from smooth muscle tumors [10,13]. This has led to the widely accepted classification of mesenchymal tumors of the GI tract into GISTs, true smooth muscle tumors, and far less frequently into true Schwann cell tumors. However, not all GISTs arise from the interstitial cells of Cajal, as some come from the mesentery or omentum, which lacks interstitial cells of Cajal, suggesting an origin from multipotential mesenchymal stem cells [16].

Most GISTs express the CD-34 antigen (70–78%) and the CD-117 (72–94%) antigen [15]. Other markers that have been used in the evaluation of GISTs include desmin, actin, and S100 (about 20–30% of GISTs express smooth muscle actin, around 10% of GISTs may have positive results for S100, and very rarely about 1–2% express desmin [14,15]).

GISTs can occur anywhere in the GI tract. Approximately 50–70% of GISTs originate in the stomach. The small intestine is the second most common location, with 20–30% of GISTs arising from the jejunum and ileum [7]. They can arise at any age, with a peak around 60 years, and they affect the male and female population equally.

According to guidelines, no GIST can be considered truly benign (about 10–30% of GISTs have malignant behavior) [8], but according to several features they are stratified for risk of malignant behavior. Tumor size, mitotic index, and aneuploidy are negative prognostic factors, as is tumor location (gastric tumors have a better prognosis than those of the small bowel and the rectum). Malignancy is characterized by local invasion and metastases.

The clinical presentations of these tumors are highly variable according to the site and size of the tumor. The most frequent symptoms are iron deficiency anemia, weight loss, GI bleeding, abdominal pain, and mass-related symptoms. Other presentations include nausea, vomiting, and abdominal distension. Other rare presentations include biliary obstruction, dysphagia, intussusception, and hypoglycemia. Patients may present with acute abdomen, obstruction, perforation or rupture, and peritonitis [10–13].

DeMatteo *et al.* [7] reported that metastatic disease is found in nearly half of the patients. The liver is the most common site (65%), followed by the peritoneum (20%), whereas lymph nodes, bone, and lung metastases are rare.

Surgical resection is the 'gold standard' for therapy of GISTs. The primary goal of surgery is complete resection of the disease [8]. However, locally recurrent tumors are usually not amenable to complete resection because of peritoneal implantation, and hence the results of secondary surgery, in the case of recurrent disease, are generally poor [8]. Survival after complete surgical resection ranges from 48 to 80% at 5 years. If resection is not complete, only 9% of patients survive for an average of 12 months [13–15]. The molecular pathogenesis of GISTs is linked to deregulated KIT tyrosine-kinase activity, which has resulted in the successful application of tyrosine-kinase inhibitor [16], imatinib (Gleevec), in the treatment of GIST patients with malignant metastatic or unresectable disease. New evidence-based treatment guidelines recommend imatinib as first-line therapy in cases of marginally resectable GISTs, and postoperative imatinib administration is advised if imatinib response improves resectability [17,18].

The aim of this study was to present the prospective and retrospective experience of the Gastrointestinal Surgery Department, Alexandria Faculty of Medicine, in the management of GISTs.

Materials and methods

This study was carried out on 102 patients:

(1) A prospective study on 22 patients from April 2013 to April 2015.
(2) A retrospective study on 80 patients between January 2009 and March 2013.

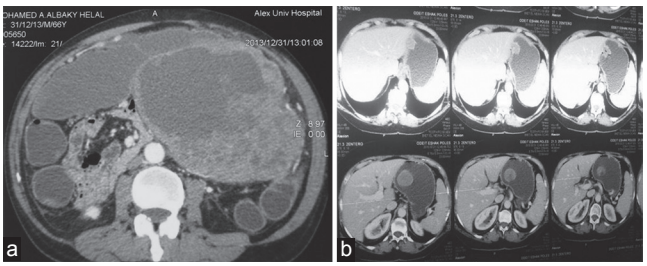
All patient data, the different clinical presentations, value of different investigative tools, histopathological examination and immunohistochemical analysis for c-KIT (CD-117), the impact of surgical treatment, intraoperative and postoperative complications, as well as follow-up and survival data were collected, reviewed, and analyzed.

Computed tomography (CT) scan of the abdomen and pelvis was performed for all patients (Fig. 1). Upper gastrointestinal endoscopy (UGIE) or colonoscopy was done when indicated.

Using the 'risk of aggressive behavior classification' proposed by Fletcher *et al.* [3] (Table 1) we classified GISTs as low, intermediate, and high risk.

Ethical approval was given by Ethical Committee of Alexandria Faculty of Medicine. Informed consent from all patients was taken. In the retrospective study confidentiality of the patients was preserved.

Figure 1



Different computed tomography (CT) images of gastric gastrointestinal stromal tumor (GIST). (a) Large exophytic heterogeneous tumor at the greater curvature of the stomach. (b) Small GIST along the lesser curvature.

Table 1 Proposed approach for defining risk of aggressive behavior in gastrointestinal stromal tumors [3]

Characteristics	Size[a]	Mitotic count
Very low risk	<2 cm	<5/50 HPF
Low risk	2–5 cm	<5/50 HPF
Intermediate risk	<5 cm	6–10/50 HPF
	5–10 cm	<5/50 HPF
High risk	>5 cm	>5/50 HPF
	>10 cm	Any mitotic rate
	Any size	>10/50 HPF

[a]The single largest dimension.

Table 2 Patient characteristics

Characteristics	Number of patients [*n* (%)]
Sex	
Male	63 (61.76)
Female	39 (38.20)
Age (years)	
Mean ± SD	49.18 ± 14.85
Range	23–78
Clinical presentations[a]	
GIT bleeding	42 (41.18)
Abdominal pain and swelling	25 (25)
Anemia	24 (24.51)
Intestinal obstruction	5 (4.90)
Acute abdomen (peritonitis)	8 (7.84)

GIT, gastrointestinal tract; [a]Two patients had more than one presentation.

Data were presented as numbers, percentages, arithmetic mean (*X*), and SD and were analyzed with SPSS (version 10, Chicago: SPSS Inc.) and statistical tests were performed with MedCalc (Version 7.3.0.1, MedCalc Software, Mariakerke, Belgium). Disease-free survival (DFS) curve and overall survival (OS) curve were calculated from the date of trial entry until disease progression, relapse, or death. They were estimated using the Kaplan–Meier method. [19].

Results

This study included 102 patients who presented with GISTs on clinical, radiological, and/or endoscopic aspects. Table 2 summarizes the demographic data and presenting symptoms of cases. The most frequent presenting symptom was GI bleeding in 42 patients (41.18%), of whom 24 patients had hematemesis and melena, 15 patients had melena only, and three patients had severe fresh bleeding per rectum. The tumors were located in the stomach in 54 patients (52.9%), in the duodenum in eight patients (7.8%), in the small intestine in 28 patients (27.5%), in the small intestinal mesentery in five patients (4.9%), in the colon in four patients (3.9%), and in the rectum in three patients (2.9%).

Ninety-one patients (89.22%) presented with primary disease, whereas 11 patients (11%) presented with recurrent disease. Patients with recurrent tumors had their initial tumor located in the small intestine in seven patients and in the stomach in four patients.

UGIE was performed in 64 patients (62.75%). These patients presented with GI bleeding (hematemesis and/or melena), anemia, or abdominal mass, which was suspected to be within the reach of the endoscope. UGIE revealed the presence of a gastric lesion in 46 patients and a duodenal lesion in six patients; no lesion was seen in 12 patients. UGIE located the lesion in the stomach and duodenum correctly but did not show the lesion in the distal third part of the duodenum in two patients, in the small intestine in seven patients, and in the colon in three patients. The three cases of colonic lesion were detected by colonoscopy.

Colonoscopy was performed in six patients: three patients presented with melena (two cases at the ascending colon and one case at the transverse colon); the other three patients presented with severe fresh bleeding per rectum (two cases at the rectum and the other at the sigmoid).

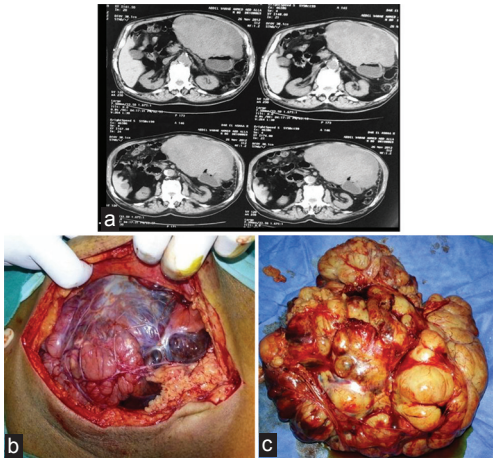
Endoscopic biopsy was performed in 52 patients who showed a lesion on UGIE, and the true pathological nature of the lesions was diagnosed in only 24 of them (46.15%). The pathology report of the other 28 patients showed different forms of chronic gastritis or duodenitis, or was normal as the biopsy was probably taken from the overlying mucosa and the lesions were usually deeply seated.

CT scan was the most commonly performed imaging tool in this study, having been performed on 101 patients (99.02%). CT was able to detect the lesion in all cases, and to locate its site of origin (Figs. 2–6). CT findings were able to suggest the diagnosis of GIST in 78 patients (77.23%) out of 101. It was not possible to perform a

CT scan for a morbidly obese patient who presented with a huge abdominal swelling. He had an abdominal ultrasound examination that showed the presence of a large cystic abdominal swelling (30 cm in diameter), and this was followed by an ultrasound-guided biopsy that was inconclusive, bringing only necrotic tissue. This patient was then operated upon to explore this undefined abdominal swelling.

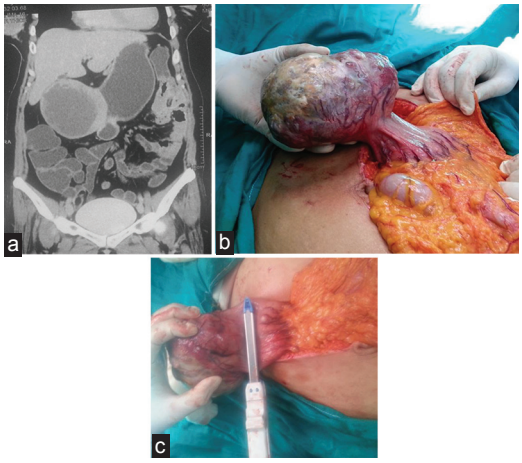
In all, 100 patients were operated upon. All operated patients underwent surgical resection. Table 3 describes the surgical procedures performed in relation to the site of the tumor. Two patients presented with advanced invasive gastric GIST and metastatic invasive duodenal GIST; they did not undergo surgical treatment. These two patients underwent ultrasound-guided biopsies that were conclusive in the two

Figure 2



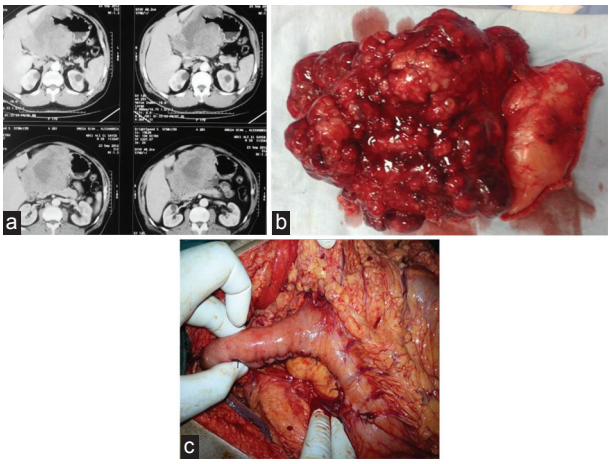
An image of a giant gastric gastrointestinal stromal tumor (GIST). (a) Computed tomography (CT) showing a heterogeneous mass extending to the epigastrium and left hypochondrium. (b) Intraoperative image of the huge mass. (c) The specimen after excision showing hypervascularity and friability.

Figure 4



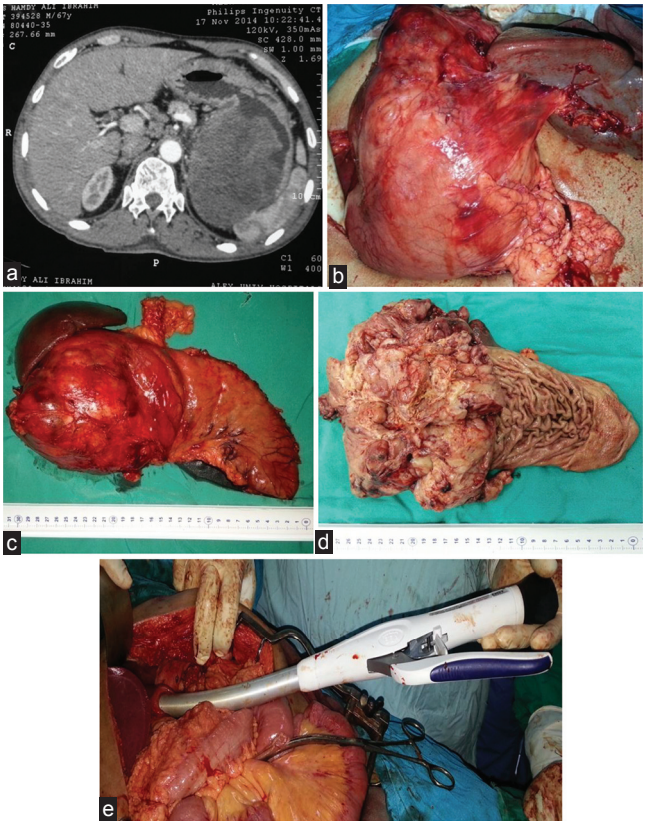
(a) Computed tomography (CT) with IV contrast, an exophytic cystic tumor at the gastric antrum. (b) A huge pedicled tumor at the antrum. (c) Resection using a linear stapler.

Figure 3



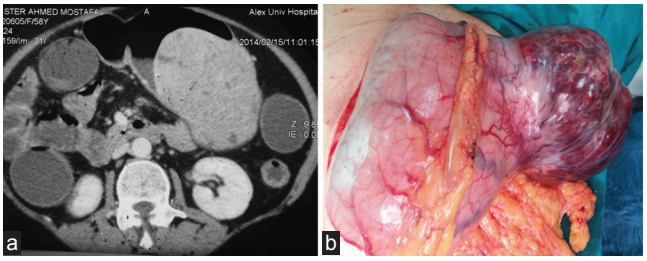
A case of gastric gastrointestinal stromal tumor (GIST). (a) Computed tomography (CT) revealing a large exophytic mass occupying the lesser curvature and distal stomach with marked encroachment on the gastric lumen with central necrosis. (b) The specimen after excision. (c) The lesser curvature was closed after removal with a linear stapler followed by interrupted sutures to invert the staple line.

Figure 5



(a) Computed tomography (CT) images of a giant heterogeneous gastric gastrointestinal stromal tumor (GIST). (b) Intraoperative view of the mass tumor situated in the upper two-third of the stomach. (c) Total gastrectomy specimen. (d) Cut section through the specimen showing friable tissue and central necrosis. (e) Reconstruction by Roux-en Y esophagojejunostomy.

Figure 6



(a) Computed tomography (CT) image of a gastric gastrointestinal stromal tumor (GIST). A sizable exophytic gastric GIST with areas of necrosis. (b) A highly vascular exophytic tumor with a nodular surface (operative view).

Table 3 Different surgical procedures according to tumor anatomical location

Site (*n*)	Surgical procedure	Completeness of resection
Stomach (53)	Localized wedge resection (45)	Complete (53)
	Total gastrectomy (4)	
	Partial gastrectomy (2)	
	Partial gastrectomy+splenectomy and distal pancreatectomy (2)	
Duodenum (6)	Localized wedge resection (5)	Complete (6)
	Partial duodenectomy (1)	
Small intestine (28)	Segmental resection (23)	Complete (23)
	Segmental resection+peritoneal toilet (3)	Incomplete (3)
	Segmental resection + metastasectomy (2)	Incomplete (2)
Small intestinal mesentery (7)	Segmental intestinal resection + tumor excision	Complete (4)
		Incomplete (3)
Colon (4)	Segmental resection (2)	Complete (4)
	Hemicolectomy (2)	
Rectum (2)	Anterior resection (1)	Complete (2)
	Total colectomy and abdominoperineal resection with terminal ileostomy (1)	

cases and allowed for the administration of imatinib (Gleevec) [the standard dosage for the treatment of GISTs is 400–600 mg once daily for 12 weeks (may be extended for another 12 weeks)]. One patient improved dramatically after 6 months of treatment with disappearance of the associated ascites. Surgery was proposed to the patient but he refused and did not attend further follow-up. The other patient was followed up with a CT scan after 1 year of treatment, which showed that the duodenal and hepatic lesions had become less dense. CT-guided biopsy from the hepatic lesions showed evidence of myxomatous degeneration without active tumor cells.

Complete resection was achieved in 92 patients (92%), whereas eight patients (8%) had incomplete resection (Figs. 2–6).

Of the eight patients who underwent incomplete resection, three patients presented with a picture of perforated acute appendicitis, which on exploration was proved to be ruptured tumors with acute peritonitis. The patients presented later with peritoneal deposits and liver metastases. At each surgery, all of the peritoneal deposits were removed. Another two patients presented with recurrent disease. The initial tumors were located in the stomach in one case and in the small intestine in another. Both presented with recurrent tumors in the small intestine and had a history of having undergone two operations for the initial lesion. They also presented with extensive peritoneal and omental deposits, which were removed as much as possible. Anastomotic leakage occurred and the general condition of the patients worsened and they died from multiorgan failure caused by sepsis. The last three patients had huge mesenteric GISTs that underwent incomplete resection as they were fixed to the pancreas and retroperitoneal tissue. All eight patients received postoperative Gleevec therapy.

Histopathological examination of the 100 resected specimens confirmed the diagnosis of GIST in 98 patients only. In the other two patients the diagnosis was a paraganglioma of the small intestinal mesentery in one patient and a duodenal carcinoid tumor in the second. These two patients were subsequently excluded from further analysis. Hence, this study included only 98 patients with the definite diagnosis of GISTs. The GIST originated from the stomach in 53 cases (54%), from the duodenum in seven cases (7%), from the small intestine in 28 cases (28.5%), from the small intestinal mesentery in four cases (4%), from the colon in four cases (4%), and from the rectum in two cases (2%). C-KIT analysis was performed in all patients and proved positive in 91 patients (89.22%).

The mean tumor size was 9.26±5.91 cm (ranged from 2.6 to 30 cm). It was less than 5 cm in 36/98 cases (36.7%), 5–10 cm in 41/98 cases (41.8%), and more than 10 cm in 21/98 cases (21.4%).

The mitotic count was low (2–5/50 HPF) in 60/98 cases (61.3%) and high (>5/50 HPF) in the remaining 38/98 cases (38.7%). None of the patients with low mitotic counts (<5/50 HPF) had recurrence, nor did they die during the 5-year follow-up period, whereas the 5-year OS and the 5-year DFS of patients with high mitotic counts (>5/50 HPF) were 67% (SE = 0.22) and 20% (SE = 0.13), respectively. This difference was statistically significant between the two groups of patients.

Using the 'risk of aggressive behavior' classification, tumors were classified as low risk [53/98 patients (54%)], intermediate risk [5/98 patients (5.1%)],

and high risk [40/98 patients (40.8%)]. Using the 'risk of aggressive behavior classification' for our patients, we found that the 5-year DFS was 100 and 20% for patients with low risk and high risk, respectively. This difference was statistically significant (P = 0.0007). The 5-year OS was 100 and 67% for patients with low risk and high risk, respectively, and this difference was also statistically significant (P = 0.0086). Table 4 shows the anatomic and pathologic GISTs' characteristics.

The perioperative follow-up was smooth in 96 patients, with few minimal complications that were in the form of chest infection (13/98 = 13.2%) and wound infection (12/98, 12.2%), which were treated conservatively. One patient died in the perioperative period from multiorgan failure related to sepsis.

Only 92 patients attended the follow-up visits. The mean duration of follow-up was 56.79 ± 33.46 months (ranged from 6 to 77 months) in the retrospective group and from 2 to 20 months in the prospective group.

Overall, 10 patients (10/98 = 10.2%) developed metastases, or recurrence. One patient who presented initially with a primary large gastric GIST developed liver metastases 13 months after the operative procedure and was subsequently managed by Gleevec therapy. In two patients who presented initially with recurrent gastric GIST, recurrence occurred at 6 and 11 months, respectively, after the operative procedure. Of the remaining seven patients GIST of the small intestine was seen in six cases and mesenteric GIST in one case. Four of the remaining six cases of intestinal GIST presented initially with recurrent disease. Their recurrences occurred at 6, 7, 13, and 15 months respectively. Two presented initially with a primary intestinal GIST and in them recurrence occurred at 12 and 18 months, respectively. All recurrences in these six patients were located in the peritoneum, intestinal mesentery, and serosal surface of the small intestine. One of them died during the follow-up period at 36 months. The last patient with mesenteric GIST underwent incomplete resection initially, with recurrence after 1 month, and received Gleevec therapy.

Table 4 Anatomic and pathologic gastrointestinal stromal tumor characteristics (in the 98 patients with a definite diagnosis of gastrointestinal stromal tumor)

Characteristics	n = 98 [n (%)]
Tumor origin	
Stomach	53 (54)
Duodenum	7 (7)
Small intestine	28 (28.5)
Mesentery	4 (4)
Colon	4 (4)
Rectum	2 (2)
Tumor size (cm)	
<5	36 (36.7)
5–10	41 (41.8)
>10	21 (21.4)
Mitotic count	
Low (2–5/50 HPF)	60 (61.3)
High (>5/50 HPF)	38 (38.7)
Risk class	
Low	53 (54)
Intermediate	5 (5.1)
High	40 (40.8)

The 3- and 5-year OS rates for all patients, using the Kaplan–Meier actuarial curve, were 92.1 and 81.4%, respectively. The 3- and 5-year DFS rates for all patients were 73.2 and 64.5%, respectively.

Discussion

This study included 102 patients (63 men and 39 women) who presented with GISTs. Their mean age at diagnosis was 49.18 ± 14.58 years (ranged from 23 to 78 years).

Cavaliere *et al.* [8] stated that GISTs can arise at any age, with a peak around 60 years, and that they affect the male and female populations equally. Miettinen *et al.* [16,20] stated that GISTs are rare before the age of 40 years and very rare in children. Miettinen *et al.* [20] and DeMatteo [21] reported a slight male predominance; however, other reports showed no sex difference [5]. The results in this study were consistent with most of the series reported in the literature.

In this study, analysis for CD-117 was performed in all patients and was positive in 91 patients (89.22%). Lin *et al.* [9] and El-Zohairy *et al.* [22] reported that CD-117 was positive in 89 and 88.9% of their patients, respectively.

The symptoms associated with primary GISTs are usually vague and nonspecific and depend on the size and location of the lesion [22,23]. Incidental discovery accounts for approximately one-third of cases [23]. The most common symptoms are GI bleeding in 41.1% of patients, abdominal pain in 20–50%, and GI obstruction in 10–30%; 20% of patients may be asymptomatic[18]. The results in this study were consistent with those of other series reported in the literature [1,23,24].

Cavaliere *et al.* [8] and El-Zohairy *et al.* [22] reported that the endoscopic biopsy was diagnostic in 57.14 and 33.3% of their patients, respectively. This was in accordance with the findings in our study. This can be

attributed to the fact that the biopsy was taken from the overlying mucosa and that the lesions are usually more deeply seated.

El-Zohairy *et al.* [22] noted that CT was most useful in terms of demonstrating a mass lesion, determining its size and its relation to the contiguous organs. Daldoul S *et al.* [12] stated that CT is the most common imaging technique used to assess distant metastases from GIST.

In the present study, the stomach was the most common organ from which tumors originated (54%), followed by the small intestine (28.5%). This is in accordance with most of the findings reported by the different series in the literature [3,25].

DeMatteo *et al.* [7] found no correlation between the tumor's site of origin and survival in 200 patients. Contrary results have been reported by Lillemoe and Efron [26] in 133 patients with resected GISTs, in whom survival was related to the tumor's site. In our series, patients with gastric lesions had better prognosis than did patients with lesions in other sites.

Fletcher *et al.* [3] stated that there were more data suggesting that anatomic location was a prognostic factor independent of tumor size, mitotic rate, and patient's age, with a trend for small bowel tumors to have the worst prognosis and esophageal tumors the best, but the basis for these differences remain uncertain [27,28]. Our results coincide with those of Lin *et al.* [9] who found that most of their patients with small intestinal GISTs had lesions larger than 5 cm and a poorer outcome than those with gastric tumors. In our study, three patients who developed recurrence and metastases had their initial tumor originating from the small intestine, and two of them died. Yan *et al.* [28] found that GISTs were four times more likely to recur if the primary site was the intestine compared with the stomach.

The primary goal of surgery was complete en-bloc resection of the disease, with avoidance of tumor rupture as this was considered a poor prognostic factor [13]. This study agreed with the findings of El-Zohairy *et al.* [22] that achieving negative pathologic margins of resection was generally not difficult because GISTs tended to hang from, and not diffusely infiltrate, the organ of origin. Several reviews had reported that small GISTs can be treated adequately by wedge (gastric) or segmental (bowel) resection [29] and more extensive surgery had no better benefit [22]. However, larger GISTs might require more extensive en-bloc resection including adjacent structures or organs if involved [29,30]. GISTs, even with high malignant potential, rarely metastasized to lymph nodes to warrant lymph node dissection [22,31,32]. In our series, the incidence of lymph node involvement was 0%, and no extended lymph node dissection was performed. In this study, complete resection was possible in 92 patients (92%), and resection was considered incomplete in eight cases (8%). Boni *et al.* [33] reported that macroscopically complete resection was possible in 84% of their cases and found that the presence of residual tumor was significantly related to early recurrence and short survival.

The mean tumor size in our series was 9.26 ± 5.91 cm (ranged from 2.6 to 30 cm). Lin *et al.* [9] reported a mean tumor size of 7.5 ± 5.7 cm, whereas Bucher *et al.* [30] reported a median tumor size of 5 cm (ranged from 0.5 to 26). An overall 36.7% of our patients had tumors less than 5 cm and 63.3% had tumors more than 5 cm in diameter.

Boni *et al.* [33] found that patients with GISTs less than 5 cm had a significantly longer survival compared with patients with bigger tumors. In our series, all patients with tumors less than 5 cm were disease free and alive at 5-year follow-up, whereas the 5-year DFS and OS for patients with tumors larger than 5 cm were 33% (SE = 0.16) and 75% (SE = 0.19), respectively. These differences between the two groups of patients were statistically significant. Katharine *et al.* [34] found that tumor size had a significant impact on OS as tumors 5 cm or larger in size had a 28-month median survival, whereas those that were less than 5 cm had a 42-month median survival.

Lin *et al.* [9] reported a 5-year survival of 76% for patients with mitotic counts less than 5/50 HPF, 73% for those with counts between 5 and 10/50 HPF, and 31% for those with counts greater than 10/50 HPF. Boni *et al.* [33] confirmed that low number of mitoses at HPF is related to prognosis with significantly longer survival in the very low-risk and low-risk group compared with the high-risk group.

Bucher *et al.* [30] stated that patient survival after primary surgical resection of GISTs ranges from 48 to 80% at 5 years [7,32]. The overall 5-year survival in our patients was 91.7%, and the overall 5-year DFS was 73.3%, which coincided with the previous findings. For low-risk GIST, the 5-year survival rate (~95%) was similar to the normal population, whereas for high-risk GIST the 5-year survival rate ranged from 0 to 30% [30]. Our results were in accordance with these findings.

In this study Gleevec was used in the incomplete resection cases and in the 10 patients with recurrent metastatic disease to the liver, with locally advanced gastric lesion, small intestine, and its mesentery. We obtained satisfactory results with control of the primary tumor. Some of the liver metastases showed regression in size, whereas some others disappeared. Van den Abbeele *et al.* [35] noted that tumor liquefaction (cystic degeneration) can occur, which may give the appearance of progressive disease, although the tumor is in reality responding.

Conclusion

This study concludes that GISTs can occur anywhere in the GI tract but most commonly in the stomach. GISTs are uncommon and aggressive tumors; their incidence is probably increasing nowadays. The presentation varies according to tumor site with abdominal pain and GI bleeding being most common. The prognosis is strictly related to the size of the tumor, number of mitoses, and completeness of surgical resection. Surgery is still the standard treatment in localized GIST and recurrence of the tumor can occur even after radical surgery. As regards GIST, imatinib therapy (Gleevec) is more effective and considered the first-line therapy for advanced primary GIST, as well as those with recurrent or metastatic GIST. Endoscopy with biopsy is used to identify the tumor, with definitive diagnosis depending on histological and immunohistochemical analysis (CD-117). It is critical that patients be evaluated by a multidisciplinary team with expertise in GISTs to coordinate surgery and therapy and to ensure maximal benefits over the course of the disease. We recommend that all patients with a GIST be regularly followed up and continually evaluated by the surgical team for a possible resectability because we believe that the best strategy is 'surgery when possible' aimed at obtaining an R0 resection when possible.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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