

Outcomes and Prognostic Factors of Primary Gastric GIST Following Complete Surgical Resection: A Single Surgeon Experience

Chakrapan Euanorasetr MD*

*Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Objective: To examine the surgical outcomes and to identify prognostic factors influencing tumor recurrence and survival after curative resection of primary gastric GIST as performed by one surgeon.

Material and Method: The medical records of patients with primary gastric GIST (c-kit or CD117-positive) who underwent curative resection by one surgeon between January 2001 and March 2009. The clinicopathological features, tumor recurrence, and recurrence-free survival were assessed.

Results: Twenty-two patients (10 males and 12 females) with a median age of 66 years (range, 39-98 yrs) were reviewed. According to the NIH risk criteria, high-risk, intermediate-risk and low-risk GISTS were found in 12 (54.5%), one (4.5%), and nine (41%) patients, respectively. After a median follow-up of 42 months (range, 19-96 months), three patients (13.6%) developed tumor recurrence, all of whom had high-risk GIST. No patient died during this follow-up period. The recurrence-free probability at 5 years was 88% (95% CI; 59%-97%). Univariable analysis showed that high mitotic count (> 5/50 HPF) was a significant predictor of tumor recurrence.

Conclusion: Low and intermediate-risk gastric GIST have an excellent prognosis after complete surgical resection alone, while high-risk group are associated with increased disease recurrence despite complete surgical resection. Adjuvant therapy should be advocated for patients with high-risk gastric GISTS. High mitotic count is an important prognostic factor for recurrence after surgery.

Keywords: Curative resection, Tumor recurrence, Recurrence-free survival, NIH risk criteria, Gastrointestinal stromal tumor (GIST), Gastric GIST

J Med Assoc Thai 2011; 94 (1): 55-64

Full text. e-Journal: <http://www.mat.or.th/journal>

In the past, most mesenchymal tumors of the GI tract were diagnosed as leiomyomas, leiomyosarcomas, leiomyoblastomas and Schwannoma⁽¹⁻⁶⁾. In 1983, Mazur and Clark⁽⁷⁾ introduced the term “gastrointestinal stromal tumor” or GIST to indicate a distinctive entity of GI mesenchymal tumor. Subsequently, Kindblom et al⁽⁸⁾ identified the interstitial cells of Cajal, an intestinal pacemaker cells, as the origin of GIST, further characterizing them as separate from smooth muscle and neural tumors of the GI tract. The proposed change of the name from stromal tumor to the formally more logical term gastrointestinal pacemaker cell tumors, or GIPACT⁽⁸⁾, however could not replace the widely accepted term GIST.

Correspondence to:

Euanorasetr C, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Phone: 0-2201-1315, Fax: 0-2201-1316

E-mail: racen@mahidol.ac.th

The management of GIST has evolved considerably over the last decade. Before 2001, the only proven therapy was surgery. GIST was known to be refractory to conventional chemotherapy and radiation therapy⁽⁹⁻¹¹⁾. The development of tyrosine kinase inhibitor (TKI) changed the management of advanced/metastatic GIST. To date, two TKI have been approved by the US FDA for the treatment of GIST: imatinib mesylate (first-line) for metastatic/unresectable GIST approved in 2002, and sunitinib malate (second-line) for refractory/intolerant GIST approved in 2006^(3,10). However, surgery remains the mainstay and only curative treatment for localized, resectable primary disease.

The exact incidence of GIST is unknown. The reported annual incidence from population-based studies is 11-14.5 cases per million population, which includes incidentally discovered GIST and those found at autopsy^(12,13). Although GIST is the most common, representing about 80%, mesenchymal tumor of the GI

tract, they are relatively rare tumors accounting for only 0.1% to 3% of all GI tumors^(14,15). GIST most frequently occurs in the stomach, around 70%^(3,16-19). Gastric GIST accounts for about 1% of gastric malignancies^(10,20).

GISTs have a wide spectrum of clinical behavior, from benign to frankly malignant. Due to the great success of targeted therapy, determining the prognosis of GISTs is becoming more important. The determination of risk may be useful for planning postoperative strategies and assessing the need for adjuvant therapy.

There has been no study of gastric GISTs based on long-term follow-up data after surgery in the Thai population. The purpose of the present study was to examine the surgical outcomes of localized, primary gastric GIST after complete surgical resection, and to identify risk factors of recurrent disease in a sample of Thai patients operated on by a single surgeon.

Material and Method

Twenty-two consecutive patients with localized primary gastric GIST operated by one surgeon (CE) at the Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University between January 2001 and March 2009 were retrospectively reviewed. The author excluded (a) previously treated gastric GIST (b) patients with GIST of other organs (c) advanced metastatic/unresectable gastric GIST.

Immunophenotypic analysis for KIT (CD117), CD 34, α -smooth muscle actin (α -SMA), S-100 protein, and desmin was performed as necessary. The diagnosis of GIST in this retrospective study was made from compatible histological pathology on light microscopy and the positivity of CD117 (KIT expression)⁽²¹⁾.

The author defined extent of resection by using the presence or absence of macroscopic disease following surgery and microscopic margins from pathologic report. R0 (complete surgical resection) and R1 resection were defined as the resection of all clinically evident disease with negative or positive microscopic margins, respectively. R2 resection was defined as the presence of gross residual disease.

Recurrence-free survival time was defined as the time from surgery to the time of clinical or radiological evidence of relapse. Based on follow-up data, the author determined the prognostic impact of age, gender, tumor size, mitotic count, necrosis, mucosal ulceration, location of tumors, and type of operation.

Each tumor was categorized according to the National Institute of Health (NIH) risk criteria, based on tumor size and mitotic index as shown in Table 1. Tumor size was defined as the largest diameter in any dimension from pathological reports. Mitotic index was determined by counting mitoses per 50 high power field (HPF). The present study was conducted with the approval of the Research Ethics Committee of our hospital.

Continuous variables were summarized as mean (SD) or median (range) as appropriate. Categorizable variables were summarized as counts and percentages. Risk factors for recurrence were tested for statistical significance using the log-rank test. Estimates for the hazard ratio were done using the COX proportional hazard model. The Kaplan-Meier estimates were used to construct the recurrence-free probability curves. A p-value of less than 0.05 was considered statistically significant.

Results

The clinicopathological features of 22 patients are summarized in Table 2. The age ranged from 39 to 98 years (median, 66 years). Most of the patients were older than 50 years of age (19/22 = 86.4%). The male-to-female ratio was 1:1.2, a slight female predominance.

Gastric GIST tended to be located in the upper-third of the stomach, with 11 (50%), eight (36.4%) and three (13.6%) tumors in the upper-, middle- and lower-third, respectively. Most of the tumors (15/22 = 68.2%) presented at the greater curvature of the stomach. The tumor size ranged from 2 to 20 cm (median 5.5 cm). The mitotic index varied from 0 to more than 100 mitoses per 50 HPF (median 5/50 HPF). Necrosis and mucosal ulceration was demonstrated in nine (40.9%) patients each. The most commonly used diagnostic and investigational tools were upper GI endoscopy and

Table 1. NIH risk criteria⁽²¹⁾

Risk category	Tumor size (cm)	Mitotic count (per 50 HPF)
Very low risk	<2	<5
Low risk	2-5	<5
Intermediate risk	<5 or 5-10	6-10 <5
High risk	>5 or >10 or any	>5 any >10

Table 2. Clinicopathological characteristics of patients with gastric GIST (n = 22)

Factors	Number of patients (%)
Location of gastric GIST	
Upper third	11 (50%)
Middle third	8 (36.4%)
Lower third	3 (13.6%)
Invasion to adjacent structures	
Presence	0
Absence	22 (100%)
Extent of resection	
Local (wedge resection)	16 (72.7%)
Formal resection	6 (27.3%)
Proximal gastrectomy	1 (4.5%)
Distal or subtotal gastrectomy	4 (18.3%)
Total gastrectomy	1 (4.5%)
Adjacent organs resection	
No	18 (81.8%)
Yes	4 (18.2%)
Associated neoplasm	
Presence	2 (9.1%)
Absence	20 (90.9%)
Tumor size (cm)	
≤ 10	13 (59.1%)
> 10	9 (40.9%)
Mitotic count (per 50 HPF)	
≤ 5	15 (68.2%)
> 5	7 (31.8%)
Necrosis	
Presence	9 (40.9%)
Absence	13 (59.1%)
Lymph node metastasis	
Yes	0/9
No	9/9 (100%)
Positive immunohistochemical staining	
CD117	22/22 (100%)
CD34	10/10 (100%)
α-SMA	2/17 (11.8%)
S-100 protein	0/16 (0)
Desmin	0/4 (0)
Recurrent disease	
Yes	3 (13.6%)
No	19 (86.4%)
Median follow-up time	42 months (range; 12-96 months)

CT scan in 18 (81.8%) and 16 (72.7%) respectively. Endoscopy identified a submucosal mass in 13 cases (72.2%) and external compression in five cases (27.8%). CT scan detected a gastric mass in all 16 cases (100%).

In only two cases (9.1%), the diagnosis of GIST was confirmed preoperatively with tissue biopsy. Three patients (13.6%) with gastric GIST in the present study were asymptomatic. These included one detected incidentally during gastroscopy for GERD, one during ultrasonography for a urological complaint and one during a CT scan for sigmoid carcinoma. In symptomatic cases (19/22 = 86.4%), the most common presenting symptoms were upper GI bleeding (8/19 = 42.1%) and dyspepsia (8/19 = 42.1%), followed by abdominal mass (7/19 = 36.8%). Two cases (9.1%) were associated with a second neoplasm. One had sigmoid carcinoma and the other had Brunner's gland adenoma of the duodenum.

A complete surgical resection with negative margin was achieved in all 22 cases. No patients received adjuvant or neoadjuvant therapy. The majority of procedures (16/22 = 72.7%) were local excision (wedge resection). Formal gastrectomy was performed in six patients (27.3%). En bloc multi-organ resection was performed in four patients (18.2%). Two patients underwent combined wedge resection of stomach + splenectomy + distal pancreatectomy, one patient underwent combined total gastrectomy + splenectomy + distal pancreatectomy and one patient underwent combined wedge resection of stomach + splenectomy. However, pathological examination showed no direct invasion of adjacent structures in all these four cases. Nine patients underwent lymph node dissection and no lymph nodes metastasis was observed. There was no postoperative mortality in our series.

All specimens were immunohistochemical positive for CD 117. A positive reaction for CD 34 was obtained in all ten patients that were tested (100%), and α-SMA (α-smooth muscle actin) was positive in two of 17 patients (11.8%). There was no positive reaction for S-100 protein and desmin in all tested specimens.

With a median follow-up of 42 months (range, 12-96 months), recurrence occurred in three patients (13.6%). All patients were still alive at the time of the last follow-up. The median time to detection of recurrence was 20 months (range, 13-96 months). Two of the three recurrences (66.6%) occurred within two years of primary surgery. The characteristics of patients who developed recurrences are summarized in Table 3. All had intra-abdominal recurrence. The site of recurrence was the peritoneum alone in one patient, the liver alone in one, and locoregional + peritoneum in the remaining patient.

Of the three patients with recurrence, two underwent complete resection of recurrent disease

Table 3. Characteristics of patients with recurrence after complete surgical resection of gastric GIST

Age	Gender	Location of primary tumor	Size (cm)	Mitotic count (per 50 HPF)	NIH risk categories	Type of recurrence	Time to recurrence	Results
44	M	Proximal	6	10	High	Liver	1 yr 1 month	Still alive after IM therapy for 1 yr 6 months
74	M	Proximal	19.5	8	High	Peritoneum	1 yr 8 months	Still alive after complete tumor removal and IM therapy for 3 months
39	F	Proximal	20	40	High	Locoregional + peritoneum	7 yrs 9 months	Still alive after total gastrectomy and subtotal pancreatectomy with small bowel resection for 1 months (waiting for IM therapy)

IM = imatinib mesylate

combined with postoperative imatinib therapy. In one patient, liver recurrence occurred 13 months after the initial operation for gastric GIST and the patient is now undergoing imatinib therapy without surgery. The recurrence-free survival probability curve is shown in Fig. 1. The recurrence-free probability at 5-year is 87.7% (95% CI; 58.8% to 96.8%).

According to the NIH risk criteria, the majority of the tumors (12/22 = 54.5%) were classified as high-risk (Table 4). All recurrences occurred in high-risk group. The relationship between the clinicopathological findings and recurrence, by univariable analysis, are shown in Table 5. Univariable analysis demonstrated that mitotic count had a significant impact on tumor recurrence. Multivariate analysis was not performed because the sample size was too small and number of recurrences too few.

Discussion

A larger proportion of women characterized the patients in the present study and the average age of the presented patients was a few years older than those of the published literature^(22,23). A positive reaction for α -SMA has been reported in 19%-67% of patients, while desmin reactivity has been observed in 7%-50% and 0-22% were positive for the S-100 protein^(2,24-27). The present series showed a positive reaction for α -SMA in 11.8% of patients and no positive reaction for S-100 protein and desmin in all patients that were tested. The incidence of immunopositivity in the present study differed somewhat from those in previous studies, which included both intestinal and gastric GIST.

In the present study, 3/22 patients (13.6%) were asymptomatic. In one Japanese series⁽¹⁰⁾, asymptomatic

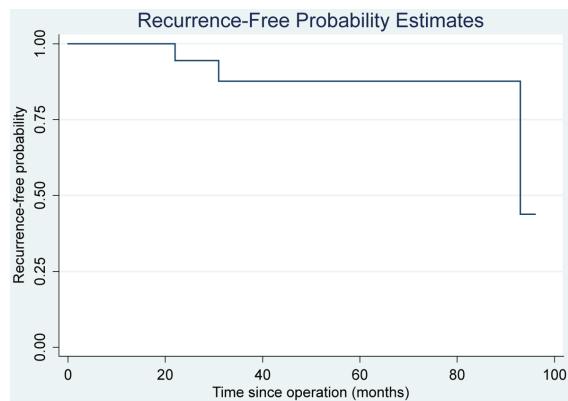


Fig. 1 Recurrence-free probability curve

Table 4. Comparison of NIH risk criteria (n = 22)

Risk criteria	Number (% of sample)	Recurrence (% of category)	5-year recurrence free survival, percent (95% CI)
Very low risk	0	-	-
Low risk	9 (41%)	0	100
Intermediate risk	1 (4.5%)	0	100
High risk	12 (54.5%)	3 (25%)	78.8 (38.1 to 94.3)

Table 5. Mean recurrence-free survival time and univariable hazard ratio

Factors	Recurrence (%)	Mean recurrence-free survival time, months (95% CI)	Hazard ratio (95% CI)	p-value*
Gender				
Men (n = 10)	2 (20)	62.1 (44.5-79.7)	Not estimable	0.083
Women (n = 12)	1 (8)	94.5 (92.4-96.6)		
Age				
> 50 years (n = 19)	1 (5)	91.1 (81.7-100.4)	0.17 (0.01-2.12)	0.134
≤ 50 years (n = 3)	2 (67)	72.3 (39.3-105.4)	1	
Tumor size				
> 10 cm (n = 9)	2 (22)	82.9 (64.5-101.3)	2.86 (0.26-32.0)	0.373
≤ 10 cm (n = 13)	1 (8)	88.8 (75.4-102.1)	1	
Mitotic count				
> 5/50 HPF (n = 7)	3 (43)	69.2 (41.0-97.3)	Not estimable	0.034
≤ 5/50 HPF (n = 15)	0	87.0 (not estimable)		
Necrosis				
Yes (n = 9)	2 (22)	82.7 (64.2-101.2)	2.81 (0.25-31.7)	0.383
No (n = 13)	1 (8)	89.8 (78.3-101.4)	1	
Mucosal ulceration				
Yes (n = 9)	1 (11)	73.0 (60.3-85.7)	1.12 (0.07-18.0)	0.937
No (n = 13)	2 (15)	87.3 (73.6-100.9)	1	
Location of tumor				
Distal (n = 3)	0	40.0 (not estimable)	Not estimable	0.653
Middle & Proximal (n = 19)	3 (16)	85.4 (73.5-97.3)		
Operation				
Wedge resection (n = 16)	3 (19)	84.0 (70.4-97.5)	Not estimable	0.455
Gastrectomy (n = 6)	0	62.0 (not estimable)		

* p-value by log-rank test

gastric GIST comprised 48% (29/60) of all cases. The high frequency of asymptomatic cases in Japan was probably due to mass screening for gastric cancer in that country. A preoperative histological diagnosis of GIST was made in only 9.1% in the present study. Preoperative diagnosis is highly uncertain and a positive endoscopic biopsy is rare due to the submucosal location of the tumor. A preoperative diagnosis of GIST therefore depends on clinical suspicion⁽²⁸⁾. A preoperative tissue diagnosis of a

resectable primary gastric GIST is not necessary, since the surgical strategy will rarely be changed by the biopsy result. Only if neoadjuvant therapy is under consideration, or if there is metastatic disease is tissue diagnosis essential⁽¹¹⁾.

The frequency of second tumors (diagnosed before, after, or at the same time as GIST) in the present series was 9.1%. DeMatteo et al⁽¹⁸⁾ observed a history of a prior malignancy in only 5% of their 200 patients with GIST. On the other hand, two large series reported

23%-26% non-GIST tumors in GIST patients^(15,29). Definite evidence regarding an association between GIST and other malignancies is still lacking.

Most of the author's procedures (72.7%) were wedge resection. Formal gastrectomy was performed in only 27.3% including total gastrectomy (4.5%). This was similar to a large series of 140 gastric GIST from Japan⁽²⁾, in which 68% of patients underwent wedge resection and only 28% underwent partial gastrectomy and 4% needed total gastrectomy.

In the present series, en bloc multi-organ resection was required to achieve circumferential tumor-free margin without disrupting the pseudocapsule in four patients (18.2%). Pathological examination did not show direct tumor invasion to adjacent organs. It is important to avoid accidental rupture of the tumor during operation that may lead to tumor spillage and peritoneal metastases^(1,10,30). In general, primary gastric GIST tended to displace or adhere to adjacent structures without direct invasion despite CT appearance⁽¹⁾.

The goal of surgery is to achieve a R-0 resection with an intact pseudocapsule of the primary tumors. The extent of resection is therefore dependent on the location and size of the primary gastric GIST. Limited resection in the form of wedge resection is usually appropriate and oncologically adequate⁽³¹⁾. Extended resection has no advantage over local excision for gastric GIST^(10,26). There are no data to support wide margin of resection typically recommended for adenocarcinoma or other sarcoma reduce the risk of recurrence in gastric GIST^(11,32). Gastric GISTs not amenable to wedge resection, because of either large size or location near the pylorus or esophagogastric junction, require more radical resection, such as distal, proximal, subtotal, or total gastrectomy. Complete surgical resection was possible in all of the present cases. The present results showed that the type of surgery had no impact on the prognosis.

Systematic lymphadenectomy is not necessary because GIST does not metastasize through the lymphatics^(1,11,31). Among nine patients who also had regional lymphadenectomy, the pathological examination revealed no lymph node involvement. Lymph node metastases rarely occur (0%-3.4%) in patients with GIST from other reports^(1,18,20,30). The possible role for lymphadenectomy in some patients is when the lymph nodes are grossly involved^(11,20).

In two of three cases of recurrent disease in the present series, surgical re-resection was undertaken with curative intent. Resection of the recurrent tumor should be considered if all recurrent disease can be

removed and it may contribute to improvement in survival. The role for debulking surgery in the era of targeted therapy has not been defined.

In the present series, recurrence after complete surgical resection of gastric GIST was 13.6% within a median follow-up period of 42 months. This compares favorably with the results of An et al⁽³³⁾ and Richter et al⁽¹⁵⁾, who found a recurrence rate of 36% and 21% after R0 resection, respectively. Other centers reported recurrence rates of around 50% (range, 17%-70%)^(1,9,11,20,26).

The large variation in the recurrence rates may have been due to the differences in the follow-up time and/or the inclusion of GISTs of other parts of the GI tract. Gastric GISTs have a more favorable outcome compared with GIST of the intestine^(1,4-6,11,24,31). However, the duration of follow-up in the present study is longer than the follow-up times of previous reports^(1,26).

The overall recurrence-free or disease-free probability at 5-year in the present study, 87.7% (95% CI; 58.8% to 96.8), was higher than in most of the published studies^(2,15,18,33). In one study, by Fujimoto et al⁽²⁾, the 5-year disease-specific survival of 129 patients with gastric GIST was 93%, whereas in most studies the disease-free survival ranged from 42% to 54%^(2,15,18,30). Possible reasons included the higher number of R0 resections and the fact that the surgery was performed by one surgeon.

Previous studies have shown that recurrences are usually intra-abdominal and occurred in the peritoneum or liver^(2,3,5,10,27). In the present series, all recurrent disease occurred in the abdomen. Two of the three recurrences (66.6%) in the present series occurred within two years of initial surgery. Previous studies have demonstrated that 60%-100% of recurrent GIST also occurred within two years^(2-3,5,10,17). One of the presented recurrence occurred 93 months after initial surgery. Proven recurrent GISTs many years (e.g. 17 years) after the resection of the primary tumor have been reported⁽²⁵⁾. This fact suggests that follow-up surveillance after surgery for gastric GIST may differ from the follow-up after surgery for gastric carcinoma, in that a long-term follow-up of more than five years is necessary for patients operated on for gastric GIST.

Identification of risk factors for recurrent disease would be useful for planning follow-up schedules and may determine the need for adjuvant therapy. A variety of factors associated with disease recurrence after complete resection have been reported previously^(3,18). Tumor size and mitotic count have

consistently been major factors associated with disease recurrence for GISTs at all sites^(2-4,11,21).

The NIH risk classification for the prognostication of GIST was published in 2002 initially without firm clinical data. To date, five large series have supported this classification^(12,31,34-36). The risk criteria do not attempt to separate benign from malignant tumors, but assign a risk for aggressive behavior. The proportion of patients within the high-risk group was the highest in our study (54.6%). Most institutional surgical series^(18,31) have reported similar findings. However, the findings of population-based studies from Sweden⁽¹²⁾ and Iceland⁽¹³⁾ found that only 25% of patients were in the high-risk category according to the NIH risk classification. All of the recurrent cases in the present study were classified as high-risk. Three of the twelve high-risk patients (25%) experienced a relapse. No patients in the low, or intermediate risk categories developed recurrence. Therefore, risk assessment can be considered to be useful for predicting disease recurrence. In the present series, the disease-free survival was not different between patients with low or intermediate-risk GIST. Hassan et al from Mayo Clinic, USA⁽³¹⁾, reported similar findings.

In the present series, a mitotic count of greater than 5/50 HPF was a significant adverse factor associated with the recurrence-free survival by univariable analysis ($p = 0.034$). Tumor size was not an independent risk factor ($p = 0.373$). This may reflect the lack of death in the present series at last follow-up. A difference in recurrence-free survival according to tumor size may become evident with longer follow-up. The impact of other factors on recurrence-free survival is less well established. Tumor location in the fundus, coagulation necrosis, male sex, ulceration, local invasion, and tumor rupture has been reported to be unfavorable prognostic factors^(2-4,11,21).

It is not well established which patients will benefit from adjuvant imatinib and the duration of treatment after complete surgical resection of primary GIST. There is growing evidence of improved recurrence-free survival with adjuvant imatinib therapy in patients with high-risk GIST after surgical resection^(37,38). Four phase III ongoing trials are evaluating imatinib in the adjuvant setting.

The present data provided support for the implementation of a two-tier risk classification, low and high-risk, which would be more appropriate and practical for identifying patients at risk for poor outcomes who might be candidates for adjuvant TKI therapy. The present data also suggested that

patients with intermediate risk might not be suitable for adjuvant therapy.

Conclusion

This is the first report of the outcomes of primary gastric GIST following complete surgical resection by a single surgeon from Thailand. Surgery remains the mainstay of treatment in localized resectable primary gastric GIST. Complete surgical resection is a safe treatment. Despite the overall favorable prognosis, some of the patients with R0 resection subsequently developed recurrent disease. Risk stratification and mitotic index are predictors of recurrence-free survival for completely resected primary gastric GIST. This is essential for the appropriate selection of patients for adjuvant imatinib therapy and close postoperative surveillance.

Acknowledgement

The author wishes to thank Mrs. Woraporn Sriyodwieng for her assistance in preparing the manuscript and Dr. Panuwat Lertsithichai for statistical advice.

Potential conflict of interest

None.

References

1. Silberhumer GR, Hufschmid M, Wrba F, Gyoeri G, Schoppmann S, Tribl B, et al. Surgery for gastrointestinal stromal tumors of the stomach. *J Gastrointest Surg* 2009; 13: 1213-9.
2. Fujimoto Y, Nakanishi Y, Yoshimura K, Shimoda T. Clinicopathologic study of primary malignant gastrointestinal stromal tumor of the stomach, with special reference to prognostic factors: analysis of results in 140 surgically resected patients. *Gastric Cancer* 2003; 6: 39-48.
3. Nikfarjam M, Kimchi E, Shereef S, Gusani NJ, Jiang Y, Liang J, et al. Surgical outcomes of patients with gastrointestinal stromal tumors in the era of targeted drug therapy. *J Gastrointest Surg* 2008; 12: 2023-31.
4. Keun PC, Lee EJ, Kim M, Lim HY, Choi DI, Noh JH, et al. Prognostic stratification of high-risk gastrointestinal stromal tumors in the era of targeted therapy. *Ann Surg* 2008; 247: 1011-8.
5. Goh BK, Chow PK, Yap WM, Kesavan SM, Song IC, Paul PG, et al. Which is the optimal risk stratification system for surgically treated localized primary GIST? Comparison of three

- contemporary prognostic criteria in 171 tumors and a proposal for a modified Armed Forces Institute of Pathology risk criteria. *Ann Surg Oncol* 2008; 15: 2153-63.
6. Liang YM, Li XH, Lu YY, Lu YL, Zhong M, Pu XL, et al. Prognostic significance of clinicopathologic parameters in gastrointestinal stromal tumor: a study of 156 cases. *Zhonghua Bing Li Xue Za Zhi* 2007; 36: 233-8.
 7. Mazur MT, Clark HB. Gastric stromal tumors. Reappraisal of histogenesis. *Am J Surg Pathol* 1983; 7: 507-19.
 8. 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.
 9. Orosz Z, Tornoczky T, Sapi Z. Gastrointestinal stromal tumors: a clinicopathologic and immunohistochemical study of 136 cases. *Pathol Oncol Res* 2005; 11: 11-21.
 10. Mochizuki Y, Kodera Y, Ito S, Yamamura Y, Kanemitsu Y, Shimizu Y, et al. Treatment and risk factors for recurrence after curative resection of gastrointestinal stromal tumors of the stomach. *World J Surg* 2004; 28: 870-5.
 11. Raut CP, Ashley SW. How I do it: surgical management of gastrointestinal stromal tumors. *J Gastrointest Surg* 2008; 12: 1592-9.
 12. Nilsson B, Bunning P, Meis-Kindblom JM, Oden A, Drotok A, Gustavsson B, et al. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era-a population-based study in western Sweden. *Cancer* 2005; 103: 821-9.
 13. Tryggvason G, Gislason HG, Magnusson MK, Jonasson JG. Gastrointestinal stromal tumors in Iceland, 1990-2003: the icelandic GIST study, a population-based incidence and pathologic risk stratification study. *Int J Cancer* 2005; 117: 289-93.
 14. Casali PG, Jost L, Reichardt P, Schlemmer M, Blay JY. Gastrointestinal stromal tumors: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Ann Oncol* 2008; 19(Suppl 2): ii35-8.
 15. Richter KK, Schmid C, Thompson-Fawcett M, Settmacher U, Altendorf-Hofmann A. Long-term follow-up in 54 surgically treated patients with gastrointestinal stromal tumours. *Langenbecks Arch Surg* 2008; 393: 949-55.
 16. Wu TJ, Lee LY, Yeh CN, Wu PY, Chao TC, Hwang TL, et al. Surgical treatment and prognostic analysis for gastrointestinal stromal tumors (GISTS) of the small intestine: before the era of imatinib mesylate. *BMC Gastroenterol* 2006; 6: 29.
 17. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol* 2006; 23: 70-83.
 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. Miettinen M, Lasota J. Gastrointestinal stromal tumors-definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. *Virchows Arch* 2001; 438: 1-12.
 20. Canda AE, Ozsoy Y, Nalbant OA, Sagol O. Gastrointestinal stromal tumor of the stomach with lymph node metastasis. *World J Surg Oncol* 2008; 6: 97.
 21. 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.
 22. Emory TS, Sabin LH, Lukes L, Lee DH, O'Leary TJ. Prognosis of gastrointestinal smooth-muscle (stromal) tumors: dependence on anatomic site. *Am J Surg Pathol* 1999; 23: 82-7.
 23. Miettinen M, Sabin LH, Lasota J. Gastrointestinal stromal tumors of the stomach: a clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up. *Am J Surg Pathol* 2005; 29: 52-68.
 24. Dematteo RP, Gold JS, Saran L, Gonan M, Liau KH, Maki RG, et al. Tumor mitotic rate, size, and location independently predict recurrence after resection of primary gastrointestinal stromal tumor (GIST). *Cancer* 2008; 112: 608-15.
 25. Tsukuda K, Hirai R, Miyake T, Takagi S, Ikeda E, Kunitomo T, et al. The outcome of gastrointestinal stromal tumors (GISTS) after a surgical resection in our institute. *Surg Today* 2007; 37: 953-7.
 26. Iwahashi M, Takifushi K, Ojima T, Nakamura M, Nakamori M, Nakatani Y, et al. Surgical management of small gastrointestinal stromal tumors of the stomach. *World J Surg* 2006; 30: 28-35.
 27. Gupta M, Sheppard BC, Corless CL, MacDonell KR, Blanke CD, Billingsley KG. Outcome following surgical therapy for gastrointestinal stromal tumors. *J Gastrointest Surg* 2006; 10: 1099-105.
 28. Knoop M, St Friedrichs K, Dierschke J. Surgical

- management of gastrointestinal stromal tumors of the stomach. *Langenbecks Arch Surg* 2000; 385: 194-8.
29. Agaimy A, Wunsch PH, Sabin LH, Lasota J, Miettinen M. Occurrence of other malignancies in patients with gastrointestinal stromal tumors. *Semin Diagn Pathol* 2006; 23: 120-9.
 30. Gold JS, Dematteo RP. Combined surgical and molecular therapy: the gastrointestinal stromal tumor model. *Ann Surg* 2006; 244: 176-84.
 31. Hassan I, You YN, Shyyan R, Dozois EJ, Smyrk TC, Okuno SH, et al. Surgically managed gastrointestinal stromal tumors: a comparative and prognostic analysis. *Ann Surg Oncol* 2008; 15: 52-9.
 32. Heinrich MC, Corless CL. Gastric GI stromal tumors (GISTs): the role of surgery in the era of targeted therapy. *J Surg Oncol* 2005; 90: 195-207.
 33. An JY, Choi MG, Noh JH, Sohn TS, Kang WK, Park CK, et al. Gastric GIST: a single institutional retrospective experience with surgical treatment for primary disease. *Eur J Surg Oncol* 2007; 33: 1030-5.
 34. Huang HY, Li CF, Huang WW, Hu TH, Lin CN, Uen YH, et al. A modification of NIH consensus criteria to better distinguish the highly lethal subset of primary localized gastrointestinal stromal tumors: a subdivision of the original high-risk group on the basis of outcome. *Surgery* 2007; 141: 748-56.
 35. Rutkowski P, Nowecki ZI, Michej W, Debiec-Rychter M, Wozniak A, Limon J, et al. Risk criteria and prognostic factors for predicting recurrences after resection of primary gastrointestinal stromal tumor. *Ann Surg Oncol* 2007; 14: 2018-27.
 36. Ahmed I, Welch NT, Parsons SL. Gastrointestinal stromal tumours (GIST) - 17 years experience from Mid Trent Region (United Kingdom). *Eur J Surg Oncol* 2008; 34: 445-9.
 37. DeMatteo RP, Maki R. Adjuvant imatinib mesylate increases recurrence free survival (RFS) in patients with completely resected localized primary gastrointestinal stromal tumor (GIST): North American Intergroup Phase III trial ACOSOG Z900 [abstract]. *J Clin Oncol* 2007; 25: 10079.
 38. Nilsson B, Sjolund K, Kindblom LG, Meis-Kindblom JM, Bunning P, Nilsson O, et al. Adjuvant imatinib treatment improves recurrence-free survival in patients with high-risk gastrointestinal stromal tumours (GIST). *Br J Cancer* 2007; 96: 1656-8.

ผลลัพธ์และปัจจัยพยากรณ์โรคของเนื้องอก GIST ปฐมภูมิที่กระเพาะอาหารหลังการผ่าตัดออกหงด: ประสบการณ์ของศัลยแพทย์หนึ่งคน

จักรพันธ์ เอื้อนเศรษฐี^{*}

วัตถุประสงค์: เพื่อศึกษาผลลัพธ์ทางศัลยกรรมและปัจจัยที่มีผลกระทำต่อการกลับเป็นช้ำของเนื้องอก GIST ที่กระเพาะอาหารหลังการผ่าตัดเพื่อรักษาให้หายขาดโดยศัลยแพทย์ 1 คน

วัสดุและวิธีการ: ทบทวนเวชระเบียนผู้ป่วย GIST ที่เกิดที่กระเพาะอาหาร (c-kit หรือ CD117 เป็นบวก) ที่ได้รับการผ่าตัดโดยศัลยแพทย์ 1 คน ระหว่างเดือน มกราคม พ.ศ. 2544 ถึงเดือนมีนาคม พ.ศ. 2552 เก็บข้อมูลเพื่อประเมินลักษณะทางคลินิกและพยาธิวิทยาของเนื้องอก การกลับเป็นช้ำของเนื้องอก และอัตราการอยู่รอดของผู้ป่วยโดยปราศจากโรค

ผลการศึกษา: ทบทวนประวัติผู้ป่วย 22 คน (ชาย 10 คน หญิง 12 คน) อายุมัธยฐาน 66 ปี (พิสัยระหว่าง 39 ถึง 98 ปี) พบร้าญูป่วยมีเนื้องอกประเทกความเสี่ยงสูง ความเสี่ยงปานกลาง และความเสี่ยงต่ำ 12 คน (54.5%), 1 คน (4.5%), และ 9 คน (41%) ตามลำดับ ตามระบบประเมินความเสี่ยงของ NIH หลังการติดตามเป็นเวลามัธยฐาน 42 เดือน (พิสัยระหว่าง 19 ถึง 96 เดือน) เกิดเนื้องอกกลับเป็นช้ำในผู้ป่วย 3 ราย (13.6%) โดยทั้งหมดอยู่ในกลุ่มความเสี่ยงสูง ไม่มีผู้ป่วยเสียชีวิตระหว่างการศึกษา อัตราการอยู่รอดโดยปราศจากโรคที่เวลา 5 ปี เท่ากับ 87.7% (95% CI, 58.8% ถึง 96.8%) การวิเคราะห์ปัจจัยเสี่ยงพบว่า จำนวนนับ mitotic figure ที่มากกว่า 5 ต่อ 50 HPF เป็นปัจจัยพยากรณ์การกลับเป็นช้ำของเนื้องอกที่มีนัยสำคัญเพียงอย่างเดียว ($p = 0.034$)

สรุป: ผู้ป่วย GIST ของกระเพาะอาหารที่มีความเสี่ยงต่ำหรือปานกลางมีการพยากรณ์โรคที่ดีเยี่ยมหลังการผ่าตัดเพื่อให้หายขาด ในขณะที่ผู้ป่วยที่มีความเสี่ยงสูงมีโอกาสที่โรคจะกลับเป็นช้ำสูงกว่า จึงควรได้รับการรักษาเสริมเมื่อหลังการผ่าตัดที่อาจเนื้องอกออกอีกได้อีก จำนวนนับ mitotic figure ที่สูงในเนื้องอก เป็นปัจจัยพยากรณ์การกลับเป็นช้ำของโรค
