Gastric GIST and prognostic models. Which is the best to predict survival after surgery?

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BACKGROUND: *Gastrointestinal Stromal Tumours (GIST) are the most frequent mesenchymal tumour of the alimentary tract. Their prognosis is largely variable as are their size, mitotic rate and site, the stomach being mostly affected. Several risk classifications have been proposed: two developed by the NIH, one proposed by the AFIP and one presented by the AJCC in 2010. The objective of this study is to compare the accuracy of the three prognostic models (AJCC, NIH and AFIP) with regard to survival after surgery, also based on the different surgical approaches.*
METHODS: *A retrospective review of all cases of gastric GIST's performed at the General and Breast Surgery Unit of the Department of General Surgery the University of Catania and at the "Gemelli" General Surgery Unit of Taormina Hospital, Italy between 2001 and 2016 was conducted. The cases were reviewed and re- classified according to the three prognostic models. Analysis of data, including Kaplan-Meyer survival curves, was performed using SPSS version 21.0.*
RESULTS: *Among a total of 1,625 gastrectomies and gastric resections were found 25 primary GIST's patients, 13 females, and 12 males, with a mean age 63 years. Cancer size varied between 1.5 cm and 37 cm and number of mitosis between 2 and 50/50 HPF. A total of 12 (48%) underwent sub-total gastrectomy (STG), seven (28%) underwent a wedge resection (WR), and 6 (12%) total Gastrectomy (TG). Twenty-three patients (92%) are currently alive at a follow up of 18 months to 17 years, and only two patients died during the long term follow-up. Both patients were AFIP high risk (6b), AJCC stage IV, already metastatic at the time of surgery. Both patients underwent total extended gastrectomy and therapy with imatinib, but died 8 and 9 years after surgery. Recurrences have been observed in 2 patients (8%), with high risk according to AFIP (6a) with AJCC stage IIIa disease.*
CONCLUSIONS: *In localized GISTs R0 surgical resection is the standard therapy as it leads to excellent outcomes. Our findings suggest that all the three classifications considered are adequate to achieve a correct prognostic evaluation.*

KEY WORDS: GIST, Prognostic factors, Prognostic models

Introduction

Gastrointestinal Stromal Tumours (GIST) are the most frequent mesenchymal tumour of the alimentary tract[1]. Up to 2% of all the malignant neoplasms of the gastrointestinal tract are GISTs [2].

In the past they were classified as gastrointestinal smooth muscle tumours. Benign neoplasms were classified as leiomyomas and malignant neoplasms as leiomyosarcomas and leiomyoblastomas [3].
With the advent of electron microscopes and immunohistochemistry, however, it was noted how these tumors lack smooth muscle-specific ultrastructure [4] and smooth muscle antigens such as desmin. Hence, this finding demonstrated that these were different kind of tumours, and the term GIST was proposed.
Since GISTs originate from the muscularis propriae of the alimentary tract, in particular from interstitial Cajal cells. Both GISTs and interstitial Cajal cells express the

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same KIT receptor tyrosine kinase [5,6,7,8]. KIT mutation can be considered a driving force of GISTs [3].
Approximately 95% of all GISTs are positive for KIT by immunohistochemistry and 10% of all GIST are positive for platelet derived growth factor receptor (PDGFRA) mutation [9].
Since GIST originate from the interstitial Cajal cells in the myenteric plexus of the gastrointestinal tract, they can occur virtually anywhere in the alimentary tract. The most common site is the stomach (50-60%), followed by the small intestine (30-35%). The colon and rectum (<6%) and oesophagus (<1%) are less frequently involved. GIST can occur also elsewhere in the abdominal cavity, such as in the omentum, the retroperitoneum or the mesentery. These extragastrointestinal GIST (E-GIST) occur in less than 5% of all cases and it is believed that they are metastases from an undetected primary tumour [3,10,11]. The main prognostic factors of the GIST tumours are the size, site, and the mitotic rate.
Gastric GISTs are usually considered as having better prognosis than small bowel GISTs and rectal GISTs. The risk of recurrence after resection of localized disease can be useful in deciding the role of adjuvant imatinib therapy. Several risk classifications have been proposed. Initially two prognostic classifications were developed, one at a consensus meeting of the National Institute of Health (NIH) and the other one, widely used, proposed by the Armed Force Institute of Pathology (AFIP) [10,12,13].
Subsequently, another classification was proposed by the American Joint Committee on Cancer (AJCC) in 2010. The initial NIH risk classification includes only the tumour size and the mitotic index. Based on these two characteristics, the NIH classification stratifies the risk in four categories: very low, low, intermediate and high. Patients in the 'very low' and 'low' category had low risk of relapse and patients with 'high' risk had unfavourable prognosis. Unfortunately the 'intermediate risk' category did not reliably identify patients with an unfavourable prognosis. Accordingly, a modification of this classification was proposed and tumour site and tumour rupture were included [12].
The AFIP risk classification stratifies the risk based on primary tumour site, with extra-gastric location having worse outcome, mitotic count, and primary tumour size [3]. This classification is widely used. When the AFIP criteria are applied, more patients have intermediate risk than with the modified NIH criteria, the latter having more patients with high risk[10]. It has to be pointed out that all mentioned risk assessment tools have in com-mon one problem. Tumour size and mitotic count are non-linear continuous variables, so that the risk thresh-olds need to be interpreted with care. Prognostic con-tour maps and heat maps have been generated through a number of series of GIST patient not treated with imatinib. They have later been validated against reference series. Several nomograms and applications for personal computer or mobile phone are available to enable rapid risk assessment and planning patient management and, among them, very effective has shown to be the MSKCC' nomogram [10,12,13,14].

Gastric Gist

GISTs occurring in the stomach have some distinctive features.
First, malignancies in this organ are the most common GIST making almost half of all cases[11].
This incidence has been steadily increasing overtime. This increase is partially due to two progressively more common practices. In fact, endoscopic gastric cancer screening and bariatric surgery are able to find smaller lesions lacking symptoms and that would have gone otherwise unnoticed. Thus, in Asian countries, like Japan or South Korea, where screening for gastric cancer is routine, the incidence of gastric GIST is higher. Also incidental findings of GISTs and other mesenchymal tumours are common during bariatric surgery, and these procedures have become more common in western countries due to increased obesity [11,15-18].

Aims

The aim of the present paper is to compare the efficacy of the three prognostic models (AJCC, NIH and AFIP, the first not taking into account tumour localization) on predicting survival after surgery. We also took into consideration the different surgical approaches used in our patients with gastric GIST.

Materials and Methods

We retrospectively reviewed all gastrectomies and gastric resections performed at the General and Breast Surgery Unit of the Department of General Surgery of Catania University Hospital and in the "Gemelli" General Surgery Unit of Taormina Hospital between 2001 and 2016. We then selected all cases of GISTs. A database was created for further analysis. Collected data included patient demographics, symptoms and modality of diagnosis, indication to surgery, type of surgery, comorbidities, surgical morbidity and mortality, histopathological findings and immunohistochemistry, neoadjuvant and adjuvant treatment and survival data. As for modality of diagnosis, history, physical examination and instrumental diagnosis, such as Endoscopy, CT scan, EUS and MRI scan were considered. Survival, recurrence and therapies were reported by consultation of outpatient database. All tumours have been also reclassified according with AJCC Cancer Staging [19,20] and NIH and AFIP Classifications [3,10].

Statistical Analysis

Analysis of data, including Kaplan-Meyer survival curves, were performed using SPSS version 21.0 (Statistical Package for Social Sciences). Assessment of possible associations between age, gender, surgical treatment and risk classifications (both AFIP and NIH) 2 test was performed, with a statistical significance level settled at $p < 0.05$.

Results

A total of 1.625 gastric resections were identified during the study period. 30 Gastric GIST have been observed in 29 patients, 14 women and 15 men. In 4 of them, 3 men and a woman, other malignancies coexisted, (2 male and a female patient with gastric cancer and a myeloma in a male patient), so they have been excluded from the study, to remove a possible survival bias by the other malignancies. One more female patient was excluded from the beginning because she underwent surgery for omental metastases from a previous gastric GIST, but there were no recorded characteristics of the primary neoplasm. At the end we evaluated 25 patients, of which 13 females, with a mean age 64 years (range 41 to 81 years), and 12 males, mean age 60 years (range 47 to 72 years). The median age was 63 years. The follow up varied between 16 years and 14 months. One of the patients had two gastric GISTs and previous lung chondromas, however the evaluation for Carney's triad was negative. The cancer size varied between 1.5 cm and 37 cm, and number of mitosis between 2 and 50/50 HPF. In particular only 4% had tumours <2 cm in diameter, whereas 28% of the patients had malignancies 2 to 5 cm in size, and 68% above 5 cm (36% having a mass of 5 – 10 cm and 32% > 10 cm).

Most of our patients had their malignancies discovered due to symptoms. Only one 68 years old patient had his tumour discovered after an altered liver test and further investigations. In the case of a 76 years old female data is unfortunately missing. The most common symptoms were bleeding (reported as hematemesis in 2 and melena in 4 patients) and anaemia. One of those patients had both symptoms. A total of 4 patients presented with anaemia although only 2 of them had anaemisation as main symptom. An additional 4 patients complained of nausea and vomiting or other dyspeptic symptoms (gastroesophageal reflux, sense of fullness after meals, abdominal distension), 8 patients sought their physician for abdominal pain, 6 epigastric and 2 colicky pain and 3 suffered from obstruction (Table I). Based on the analysis of the symptom distribution by gender and age, hematemesis and melena were more common in males (4 below median age of 63 and 1 above medina age versus only 2 female cases with equal age distribution), and that abdominal pain and obstruction did not occur below median age. Symptoms seem to be more common in female over age of 63 than in male, but this could also be due to a higher number of female patients in this group than there were male above 63 (Table II)

All our patients underwent surgical treatment. In almost half of cases 12 (48%) sub-total gastrectomy (STG) (4/5) was performed. In one case splenectomy and distal pancreatectomy was added to STG. Seven (28%) of our patients underwent a wedge resection (WR). This was decided independently from tumour size. Finally, 24% of cases were treated with total gastrectomy (TG). Four of these patients underwent also splenectomy or splenectomy and pancreatectomy, and one patient had a liver resection.

Table I - *Symptoms distribution according to age and gender*

Symptoms	F ≤63	F>63	M≤65	M> 63
Hematemesis/melena	1	1	4	1
Anaemia	1	2		1
Dyspeptic symptoms	1	1	1	1
Epigastric pain	2	2	2	
Abdominal pain		1		1
Obstruction		2		1
No symptoms				1
Missing data		1		
Total	6	9	8	5

Table II - *Distribution of surgical technique by AFIP Risk Group*

Group	Total Gastrectomy	Sub-Total Gastrectomy	Wedge Resection
1		1	
2		2	2
3a	1	3	2
3b	1	1	2
4			
5		3	
6a	1	2	1
6b	3		
Total	6 (24%)	12 (48%)	7 (28%)

Table III - *Distribution of surgical technique by NIH Risk Assessment*

Group	Total Gastrectomy	Sub-Total Gastrectomy	Wedge Resection
Very low		1	
Low		2	2
Intermediate	1	5	2
High	5	4	3
Total	6 (24%)	12 (48%)	7 (28%)

Emergency surgery was needed in only 2 patients, for unresponsive bleeding and for obstruction, and surgery was STG for the first and TG for the second. All the procedures were performed with open laparotomy No complications have been recorded.
The distribution of surgical technique based on AFIP Risk Group is reported in Table II. The distribution of surgical technique based on the NIH Risk Assessment is reported in Table III.

Risk assessment

All the patients were stratified for risk based on the three classifications (NIH, AFIP, AJCC).
According to the more commonly used AFIP classification, one male patient had no risk (0), 16% of patients very low (VL, group 2) risk (a woman and 3 men), 24% had low (L, group 3a) risk (4 female and 2 male), 28% of patients (4 female and 3 male) had moderate (M) risk (16% in group 3b and 12% in group 5) and the remaining 28% (4 female and 3 male) had high risk (H, 16% of patients in group 6a and 12% in group 6b). Distribution of patients in Risk groups and Grade of risk according to AFIP criteria as follows in Table IV.
According to NIH criteria, one male patient had very low risk, 16% of our cases were low risk (a female and 3 male), 32% patient had intermediate risk (equal distribution between women and men) and 48% had high risk (8 female patients and 4 male patients). The following table (Table V) reports AFIP and NIH criteria risk distribution by gender showing how patients with moderate risk according to Miettinen Lasota Classification are split into intermediate and high risk group in NIH Classification.

Classification

When we take into account the AFIP Risk Classification and divide the patients in low risk (0,VL and L) and moderate-high risk (M and H), patient age, using the median age as cut off value, the majority of low risk patients (54.5%) were younger than 63, whereas the majority of moderate-high risk patients (57.1%) were older than 63 (Table V).
According to the NIH Classification, patients were divided in low risk (VL, L) and intermediate-high risk (I, H). A total of 80% of patients with low risk were under median age of 63, whereas 60% of patients with intermediate-high risk were above median age of 63, however both results were not statistically significant ($p > 0.05$). (Table VII)

Table IV - *Risk assessment according to AFIP Classification*

Group	Grade of Risk	N. of cases (%)
1	0	1 (4%)
2	Very low	4 (16%)
3a	Low	6 (24%)
3b	Moderate	4 (16%)
4	?	0
5	Moderate	3 (12%)
6a	High	4 (16%)
6b	High	3 (12%)

Table V - *Risk assessment due to gender and risk according to AFIP and NIH*

Case number	Gender	AFIP risk	NIH risk
13	Male	None	Very low
17	Male	Very low	Low
14	Male	Very low	Low
19	Male	Very low	Low
22	Female	Very low	Low
15	Female	Low	Intermediate
20	Female	Low	Intermediate
10	Male	Low	Intermediate
21	Male	Low	Intermediate
24	Female	Low	Intermediate
27	Female	Low	Intermediate
16	Male	Moderate	Intermediate
11	Male	Moderate	Intermediate
3	Female	Moderate	High
2	Male	Moderate	High
5	Female	Moderate	High
26	Female	Moderate	High
12	Female	Moderate	High
18	Female	High	High
1	Male	High	High
8	Female	High	High
7	Male	High	High
6	Male	High	High
4	Female	High	High
9	Female	High	High

Table VI - *Risk by AFIP Criteria distribution according to age*

Risk	<63 years	≥63 years
0-VL-L	54.50%	45,50%
M-H	42.90%	57,10%

Table VII - *Risk by NIH Criteria distribution according to age*

Risk	<63years	≥63years
VL-L	80%	20%
I-H	40%	60%

TABLE VIII - *Distribution of tumours by stage and tumour size*

Stage	N.	Cases	T1	T2	T3	T4
Ia	5	(20%)	1	4		
Ib	6	(24%)	6			
II	8	(32%)	1	2	1	4
IIIa	3	(12%)	3			
IIIb	1	(4%)	1			
IV	2	(8%)	2			
Total	25	(100%)	2	6	10	7

TABLE IX - *Distribution by AJCC stage and risk according to AFIP*

Stage	N. cases	No risk	VL	L	M	H
Ia	5	1	4			
Ib	6			6		
II	8			3	4	1
IIIa	3					3
IIIb	1					1
IV	2					2
Total	25	1	4	9	4	7

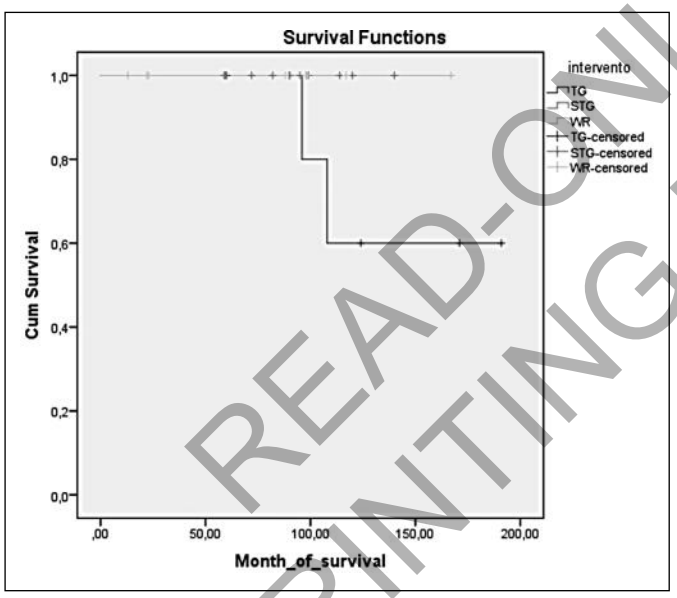

Fig. 1: Survival curve according to surgical technique.

All tumours have been also reclassified according with the AJCC Cancer Staging (2010) and the distributions were as following: 20% of patients staged Ia, 24% stage Ib, 32% stage II, 12% stage IIIa, 4 % stage IIIb, 8% stage IV (Table VIII).

The vast majority of our patients (92%) is still alive (data updated January 1st 2018) after 18 months to 17 years from surgery, and only two patients died during the long term follow-up. Both patients were AFIP high risk (6b), AJCC stage IV, already metastatic at the time of surgery, even after extended gastrectomy and therapy with imatinib dead 8 and 9 years after surgery (Table IX).

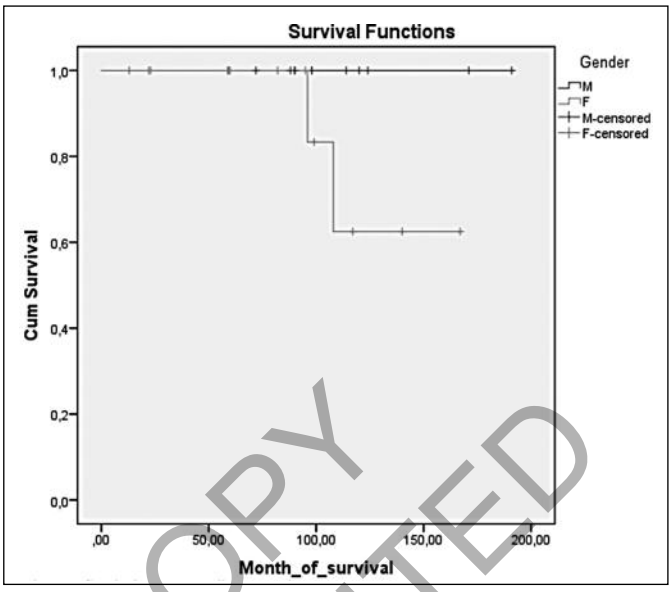

Fig. 2: Survival curve according to gender.

Recurrences have been observed in 2 patients (8%): these 2 patients had high risk according to AFIP (6a) with AJCC stage IIIa disease. Recurrence occurred after 7 and 10 years from surgery. Both are living, under treatment with Imatinib, with good control of disease. One more patient, operated on after 27 months primary therapy with Imatinib is still living with no evidence of recurrence but under continuous treatment, after 4 years.

Analysis of Kaplan-Meier curve was performed to assess the survival of patients after surgery at 1, 2, 5 and 10 years (12, 24, 60 and 120 months), taking into account surgical technique, gender and both AFIP and NIH Risk Classifications.

In particular, survival curve related to type of surgery showed that patients treated with less invasive surgery like WR or STG had better outcome than patients that underwent TG. The latter had stable survival throughout year 1, 2 and 5 of 100%, dropping then to 60% at 10 years, whereas all patients treated with STG and WR are still alive today, thus having a survival rate of 100% at 1, 2, 5 and 10 years (Fig. 1).

Taking into account patients' gender, males had better outcome than females. All men are alive with resulting survivals of 100% at 1, 2, 5 and 10 years, whereas, being our deceased patients females, survival rate of women is stable at I, II and 5 years at 100% and drops at 10 years down to 62% (Fig. 2).

For easier comparing of patients according to different risk assessments, cases were divided in low risk and moderate-high risk. AFIP risk groups 0, VL and L as well as NIH risk groups VL and L were considered low risk, whereas AFIP groups I and H and NIH groups I and H were considerate having moderate-high risk.

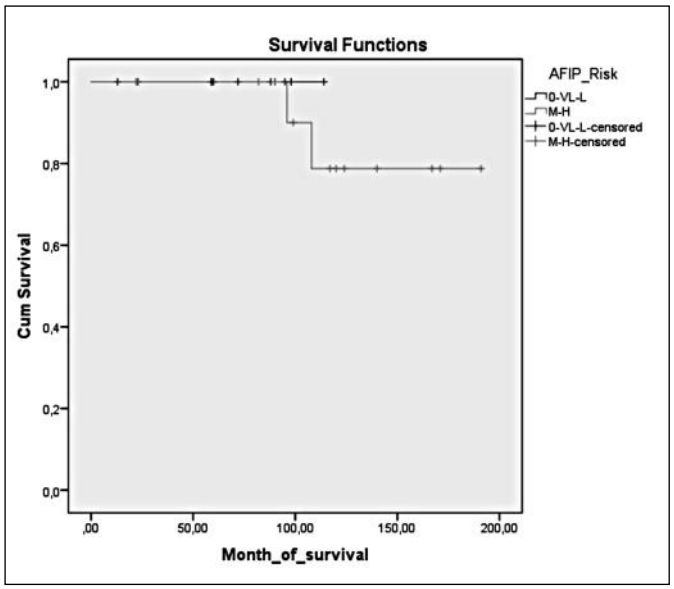

Fig. 3: Survival curve according to AFIP Risk Assessment

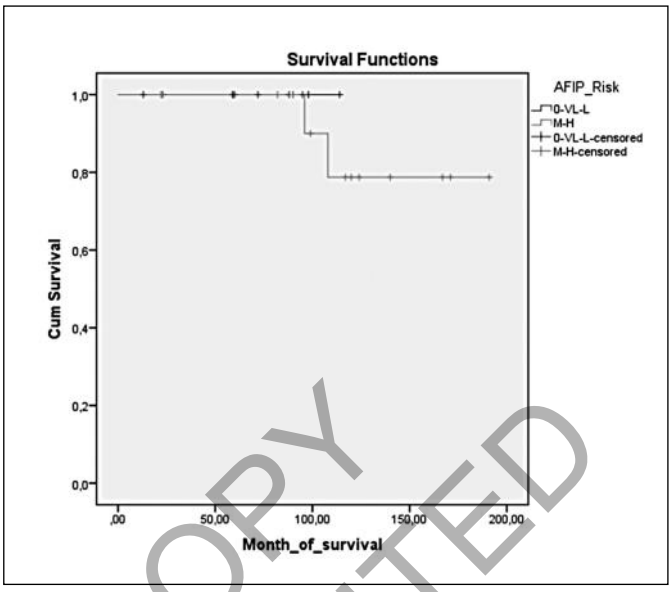

Fig. 4: Survival curve according to NIH Risk Assessment.

Table X - *Survival rates at 12, 24, 60, 120 months*

	Survival rate at 12months	Survival rate at 24 months	Survival rate at 60 months	Survival rate at 120 months	P value
Surgery					
WR	100%	100%	100%	100%	0,242
STG	100%	100%	100%	100%	
TG	100%	100%	100%	60%	
Gender					
F	100%	100%	100%	62%	0,12
M	100%	100%	100%	100%	
AFIP Risk					
VL-L	100%	100%	100%	79%	0,515
M-H	100%	100%	100%	100%	
NIH Risk					
VL-L	100%	100%	100%	100%	0,67
I-H	100%	100%	100%	81%	

Calculating survival rates according to AFIP Risk Assessment in low risk (0- VL – L) and moderate-high risk (M – H) highlighted that patients with moderate-high risk had worse outcome than patients with low risk. All low risk patients are alive today resulting in a survival of 100% throughout all setpoints (1, 2, 5 and 10 years). Patients assessed with moderate-high risk had survival of 100% at year 1, 2 and 5 and later on a survival rate of 79% (Fig. 3).

According to NIH Risk Classification survival rates for patients with low risk (VL – L) were excellent and stable at 100% throughout all years while survival dropped down to 81% for moderate-high risk patients (I – M) after being at 100% at years 1, 2 and 5 (Fig. 4).

However, all Kaplan-Meier survival curves had no statistical significance (p > 0,05) (Table X).

Discussion

Gastrointestinal stromal tumours are the most common mesenchimal tumors of the alimentary tract. Only with the advent of immunohistochemistry these malignancies became an independent pathological entity, thus its diagnosis relies on CD 117 (KIT) and DOG-1 positivity. Global incidences vary from 10 to 15 cases per million and the median age of occurrence is 63 years with diagnosis usually between age 60 and 65. The median age of GIST patients treated at Catania University Hospital and Taormina Hospital exactly matched the value reported in literature (63 years) [21,] although some study has showed an higher mean age (69) [22,23].

Gender distribution was fairly even (0.92) with 12 male and 13 female patients. This matches also with the lit-

erature. The evaluated data, with a male female ratio of 0.92, is nearer to studies from France [21] and the United Kingdom [24] but almost matches the global ratio where GIST occurs equally in women and men [11]. Other studies from the United States[25], Taiwan[26] and Korea [27] show higher incidences in male patients with a male female ratio up to 1.7[27]. Nonetheless these ratios are not the average values but only the higher end of the reported range.

It has to be pointed out that enrolled patients, although median age of 63 and almost equal gender ratio, had different distribution within these groups. In fact, males were younger on average than women (60 years versus 64 years). Although the literature shows a slightly better outcome for female patients after 5 years since surgery [27,28], our study population shows an equal survival ratio between the two genders at the same set point. However, in our study survival rates drop down at 10 years from surgery in female patients and this could be due to a more advanced age of the women in our population. Anyway, data coming from literature regarding gender distribution is discording and some do not consider tumour site [24].

Common symptoms occurring in GISTs are bleeding, both insidious chronic and acute life threatening, dyspepsia or discomfort, nausea and even palpable mass. Most patients are symptomatic. In fact, 92% of our patients suffered from at least one of the above mentioned disorders. However data from literature can vary from 8% [28] to 43,3% [21,23] of incidental diagnosis. A recent study has shown even higher rate of asymptomatic cases up to 60% [22].

Tumour size is important to assess the risk, as shown by the AFIP and NIH Criteria. In particular 68% of our patients had malignancies with a diameter > 5 cm, a distribution similar to the one described by Brabec and colleagues [29]. However, tumour size distribution varies widely in the literature [11].

As mentioned above, tumour size together with mitotic rate, is a criteria to define risk due to NIH Classification. Risk is assessed in VL, L, I and H whose percentages in our studied population are 4%, 16%, 32% and 48% respectively. Bokhary and collaborators had similar distribution with slightly more patients assessed in the I class [30]. However, literature shows a variety of distributions of risk according to NIH Criteria [27].

In this context, survival according to NIH Classification should be evaluated. As shown in Figure 4 low risk patients have excellent outcome, being all alive. Patients with moderate high risk of recurrence have 81% chance of survival. Our curves match with data by Cho and collaborators[27]. However precise comparison can only be made for the low risk patients, having the authors split their data for I and H risk. Anyway data retrieved from our AFIP Classification survival curve (Fig. 3) shows similar distribution. Between the two classifications, outcome varies only slightly for moderate-high risk patients with a difference of only 2% of survival at 10 years. Overall survival of our patients was excellent being only two patients deceased after 10 years. Data from literature shows also good overall survival in GISTs occurring in the stomach, ranging from 89,3% [28]to 69,4% [26] at 5 years.

Surgical excision is standard treatment for localized GISTs, without dissection of clinically negative lymph nodes. In our series, no nodal metastases have been found though a D2 lymphadenectomy had been performed in all total gastrectomy and gastric resections. Different surgical techniques can be performed, ranging from WR to TG, both laparotomic and laparoscopic. Despite endoscopic excision for lesions ≥ 2 cm is often described in literature there is also a wide range of studies regarding laparoscopic approach [30,31-33].

Choice of technique depends on tumour size, location and implant on gastric wall as well as performance status of the patient and possible morbidity after surgery. In fact, laparoscopic excision is not recommended in large malignancies. The excision should always follow the rules of oncological surgery with R0 excision (i.e. an excision whose margin are clear of malignant cells) as main goal [34]. A macroscopic disease free margin of 1 or 2 cm should be enough to achieve a microscopically free margin [10,12,13,35,36].

Tumour rupture, before or during surgery, causes spillage of malignant cells into the peritoneal cavity. Thus, it should be recorded and considered a negative prognostic factor. Occult peritoneal lesions can be assumed to exist. Therefore patients should be treated with imatinib. The duration of the treatment is unknown as it is still unclear if tumour rupture patient should be considered metastatic or not, but should be at least three years [12,13,37].

Our patients were all treated with a laparotomic approach, 48% with STG, 28% with WR and 24% with TG, the latter having worse outcome with only 62% of patients alive. (Fig. 1).

Undoubtedly most of TG patients had high risk of recurrence, both according to AFIP Criteria (60%) and NIH Criteria (80%), but also among the groups treated with less invasive techniques there were patients assessed with high risk. All our patients treated with WR and STG are alive. Even though all our treatments were performed in open surgery, due to decreased pain, early recovery of bowel function and hospital discharge, also a laparoscopic approach should be considered [23,38-40].

Regarding distribution according to AFIP Criteria and NIH Criteria as shown in Table V it is clear that classification not taking into account tumour site, leads to overestimation of risk. This is crucial for appropriate scheduling of follow-up. In fact VLR patients do not seem to need periodical checks. On the contrary patients with low and moderate risks should be followed up to 5 years after surgery. High risk patients even need a lifelong follow-up. For the latter class of patients CT-scans

or MRI- scans should be performed, and no limits to the number of examinations can be found in literature. If CT-scans are performed, this can result in a significant radiation exposure. Although high risk patients usually are over median age (Table VI-VII) and radiation exposure is less an issue than in younger patients, it still should be avoided. MRI could reduce radiation dose, however both methods are resources requiring qualified staff and high costs. Thus, overestimation of risk can impact not only on Public Health resources but also on patients well being. For this reason, it should be recommended to correctly assess risk according to tumour site, avoiding risk overestimation. Mutational status has not been included in any risk classification, although some genotypes such as wild type GISTs have a distinct natural history, being usually less aggressive [12,13,41] while the rare homozygous KIT mutation is associated with a particular aggressive disease [3]. Furthermore, a vast majority of PDGFRA D842V mutants and most SDH deficient GISTs occur in the stomach. Although they are not the most common, this has to be pointed out due to their primary resistance to imatinib therapy [9,42,43].

Conclusions

The population described in this work presents most of the features described in literature.
Specifically, gender and age distribution, as well as clinical presentation and symptoms match the ones of populations described by several authors. Overall prognosis is good in gastric GISTs and it depends mostly on risk of recurrence regardless of which risk assessment method is used as long as tumour localization is considered. Survival rates increase with adjuvant tyrosine kinase inhibitor therapy. In localized GISTs surgical treatment is standard therapy in fact less morbid techniques such as WR and STG have excellent outcome as long as the principles of oncological surgery are followed and R0 excision can be performed.
Accounting for the small number of patients, our findings suggest that all the three classifications considered are adequate to a correct prognostic evaluation of Gastric GIST.

Riassunto

Introduzione: I tumori stromali gastrointestinali (GIST) sono i tumori mesenchimali più frequenti del tubo digerente. La loro prognosi è estremamente variabile così come le loro dimensioni, il tasso mitotico e la sede anche se lo stomaco è l'organo interessato più frequentemente.
Sono state proposte diverse classificazioni del rischio: due sviluppate dal National Institute of Health (NIH), una proposta dall' Armed Forces Institute of Pathology (AFIP), ed una classificazione aggiuntiva presentata dall'AJCC nel 2010.
L'obiettivo di questo studio è confrontare l'accuratezza dei tre modelli prognostici (AJCC, NIH e AFIP) per quanto riguarda la sopravvivenza dopo l'intervento chirurgico, anche in base ai diversi approcci chirurgici.
Metodi: È stata eseguita una revisione retrospettiva di tutti i casi di GIST gastrico trattati presso l'Unità Operativa di Chirurgia generale e Senologia del Dipartimento di Chirurgia Generale dell'Ospedale dell'Università di Catania e presso l'Unità di Chirurgia Generale "Gemelli" dell'Ospedale di Taormina, Italia, tra il 2001 e il 2016. I casi sono stati rivisti e ri-classificati in base ai tre modelli prognostici.
L'analisi dei dati, incluse le curve di sopravvivenza di Kaplan-Meyer, è stata eseguita utilizzando la versione 21.0 di SPSS (Pacchetto statistico per le scienze sociali).
Risultati: Tra il 2001 e il 2016 sono state eseguite in totale 1.625 gastrectomie e resezioni gastriche. Fra questi sono stati identificati 25 pazienti portatori di GIST, 13 femmine e 12 maschi, con un'età media di 63 anni. Sono stati esclusi i pazienti portatori di altre neoplasie che potevano condizionarne la prognosi o già operati per GIST e venuti a all'osservazione per metastasi da GIST. Le dimensioni del tumore variavano tra 1,5 cm e 37 cm e il numero di mitosi tra 2 e 50/50 HPF.
In totale 12 (48%) pazienti sono stati sottoposti a gastrectomia sub-totale (STG), uno dei quali con splenectomia e pancreatectomia distale. Sette pazienti (28%) sono stati sottoposti a resezione a cuneo (WR) e 6 (12%) a Gastrectomia totale (TG). Ventitre pazienti (92%) sono attualmente vivi ad un follow up da 18 mesi a 17 anni e solo due pazienti sono morti durante il follow-up a lungo termine. Entrambi i pazienti erano AFIP alto rischio (6b), stadio IV AJCC, già metastatico al momento dell'intervento. Entrambi questi pazienti hanno subito una gastrectomia totale estesa e terapia con imatinib, ma sono deceduti rispettivamente 8 e 9 anni dopo la chirurgia. Le recidive sono state osservate in 2 pazienti (8%), ad alto rischio secondo AFIP (6a) con malattia in stadio IIIa AJCC.
Conclusioni: Nei GIST localizzati la resezione chirurgica è la terapia standard in quanto conduce ai migliori risultati in termini di sopravvivenza totale e libera da malattia. I nostri risultati suggeriscono che tutte e tre le classificazioni considerate sono adeguate per raggiungere una corretta valutazione prognostica.

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