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Gastrointestinal stromal tumors: Clinicopathological correlations

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Abstract
Background: Histological, genetic, and anatomical characteristics distinguish gastrointestinal stromal tumours (GISTs) from other neoplasms. GISTs, the most common gastrointestinal (GI) mesenchymal tumours, occur 7 to 19 times per million annually. This study discusses GIST clinicopathological relationships and how they might be used to optimize risk stratification and adjuvant treatment.
Method: Cross-sectional research of 99 gastrointestinal stromal tumour patients from January 2019 to January 2023 at Medical city/GIT and hepatology teaching hospital and Medical city teaching complex/teaching laboratories/histopathology department. All patients were queried about age (years), gender, tumour location and size, mitotic rate (high or low), and cancer risk group (high, moderate, low, and very low).
Results: Mean patient age 52.5 ± 13 years old. 32.3% of patients over 60, 24.3% 51-60. Males 54.5%, females 45.5%. Patients 52.5% had lower Mitotic rate 550 HPF, 49.5% are high risk. 58.59% of patients have stomach tumours, 22.22% have large bowel tumours, and 19.19% have small intestine tumours. Mitotic rate is associated with risk; 97.9% of high Mitotic rates are high risk. Site and danger are also associated: 24.1% of stomach tumours are high risk while 72.7% of small intestinal tumours are extremely low risk. No substantial connection exists between age and gender and risk. Risk category affects tumour size: high risk has large tumours, whereas low risk has small tumours.
Conclusion: Our analysis confirms key GIST prognostic correlations. We confirmed that high mitotic rate, tumour location, and size influence risk category, validating previous research. Age and gender affected GIST prevalence, but not risk category in our group. These results emphasise the need for extensive risk classification in GISTs for effective patient care and need additional study of population-specific demographics and features.

Keywords: Gastrointestinal, stromal, tumors, Clinicopathological, correlations

Introduction

Gastrointestinal stromal tumors (GISTs) represent a unique class of neoplasms, notable for their histological and genetic profiles, as well as their distinct anatomical locations. As the most frequently occurring mesenchymal tumors of the gastrointestinal (GI) tract, GISTs exhibit an annual incidence of approximately 7 to 19 cases per million [1-3]. An intriguing characteristic of GISTs is their ubiquitous potential to develop anywhere along the gastrointestinal tract, although they primarily occur within the stomach and small intestine. In rare instances, GISTs have been reported in extra gastrointestinal sites such as the omentum or mesentery [4]. The pathogenesis of GISTs is intricately linked to certain key genetic factors. The primary genetic abnormalities implicated in these tumors are activating mutations in the KIT and PDGFRA genes, which encode the stem-cell factor receptor (KIT) and platelet-derived growth factor receptor α (PDGFRα) tyrosine kinases, respectively [4]. These mutations result in a constitutive activation of the tyrosine kinase activity of these receptors, which then leads to the activation of various downstream signaling pathways. Consequently, the cell proliferation control mechanisms are compromised, resulting in the formation of GISTs. GISTs exhibit a wide array of malignancy potential, from near-benign tumors to aggressive sarcomas. Furthermore, the risk of tumor recurrence and progression to metastatic disease persists in certain patients even following the complete excision of the primary tumors [4]. The classification system developed by the National Institutes of Health (NIH) has traditionally been employed to stratify patient prognosis based on tumor size and mitotic count [5]. However, emerging literature suggests the potential utility of additional prognostic factors, which may further refine risk stratification [5]. In the clinical management

of GISTs, the introduction of imatinib, a low-molecular-weight tyrosine kinase inhibitor, has markedly transformed the therapeutic landscape. Imatinib is designed to inhibit the kinase activity of both KIT and PDGFRα, thereby directly targeting the core pathogenic mechanisms of GISTs [6]. Clinical trials have demonstrated the substantial survival benefits that imatinib offers for patients with unresectable or metastatic GISTs, as well as its overall tolerability [7,8]. The evidence thus underscores the need for accurate risk stratification to identify patients most likely to derive benefit from adjuvant imatinib therapy. This paper aims to discuss the clinicopathological correlations of GISTs, with a particular focus on how these insights could be harnessed to optimize risk stratification and guide adjuvant therapy decisions.

Method

Cross sectional study of 99 patients with gastrointestinal stromal tumor, the data collected in Medical city/GIT and hepatology teaching hospital and Medical city teaching complex/teaching laboratories/histopathology department from January 2019 to January 2023. All patients asked about age (years), gender, the site and the size of tumor, Mitotic rate (either high or low), Risk category of cancer (high, moderate, low and very low).

Statistical analysis done by SPSS 22, frequency and percentage used for categorical data, mean, median and SD for continuous data. Chi-square used for assessed association between categorical variables. T test used for evaluation differences between mean and median of continues variables. P-value less or equal to 0.05 is consider significant.

Results

Cross sectional study of 99 patients with gastrointestinal stromal tumor, mean age of patients 52.5 ± 13 years old. 32.3% of patients at age group more than 60 years, 24.3% at age group 51-60 years old. Males 54.5% and 45.5% of them are females. Patients 52.5% have less Mitotic rate 550 HPF, 49.5% of patients have high risk category. As shown in table 1.

Table 1: Distribution of patients according to the variables of study

Variables		Frequency	Percentage
Age groups (years)	21-30	6	6.0
	31-40	19	19.2
	41-50	17	17.2
	51-60	25	25.3
	>60	32	32.3
Gender	Female	45	45.5
	Male	54	54.5
Mitotic rate 550 HPF	Less	52	52.5
	More	47	47.5
Risk category	Very low	14	14.1
	Low	25	25.3
	Moderate	11	11.1
	High	49	49.5

As shown in fig 1; 58.59% of patients have tumor in stomach, 22.22% of them the tumor is large bowel involvement and 19.19% of patients occur at small intestine.

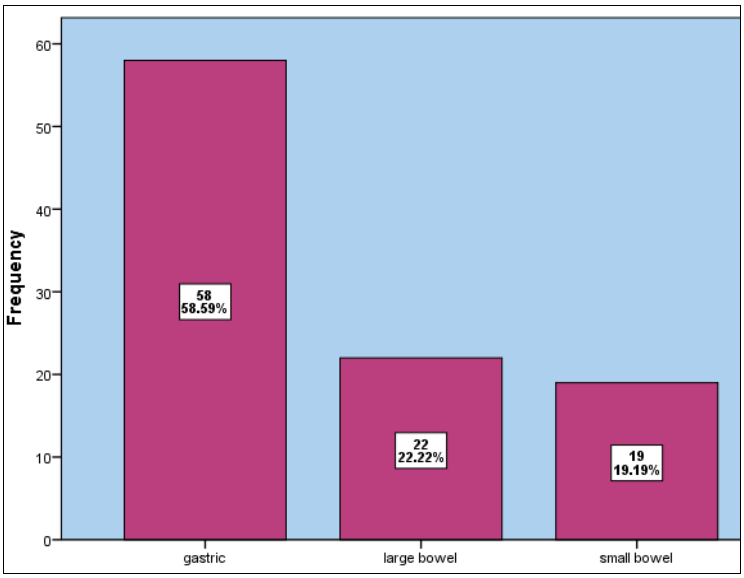

Fig 1: Distribution of patients according to site of tumor

As shown in table 2; there is significant association between Mitotic rate and risk, 97.9% of high Mitotic rate are at high risk. Also there is significant association between site and risk, 24.1% of gastric tumor are high risk category and 72.7% of small intestine tumor are very low risk. There is no significant association between (age groups, gender) and risk.

Table 2: Association between (age groups, gender, Mitotic rate, site) and risk

Variables		Risk category				Total	P-value
		Very low	Low	Moderate	High		
Age groups	21-30	1	2	0	3	6	
(years)		16.7%	33.3%	0.0%	50.0%	100.0%	
	31-40	2	5	5	7	19	
		10.5%	26.3%	26.3%	36.8%	100.0%	0.64
	41-50	4	3	1	9	17	

		23.5%	17.6%	5.9%	52.9%	100.0%	
	51-60	3	8	3	11	25	
		12.0%	32.0%	12.0%	44.0%	100.0%	
	>60	4	7	2	19	32	
		12.5%	21.9%	6.3%	59.4%	100.0%	
	Females	6	12	5	22	45	
Gender		13.3%	26.7%	11.1%	48.9%	100.0%	0.99
	Males	8	13	6	27	54	
		14.8%	24.1%	11.1%	50.0%	100.0%	
	Gastric	22	12	10	14	58	
		37.9%	20.7%	17.2%	24.1%	100.0%	
Site	Large bowel	16	6	0	0	22	0.002
		72.7%	27.3%	0.0%	0.0%	100.0%	
	Small bowel	11	7	1	0	19	
		57.9%	36.8%	5.3%	0.0%	100.0%	
Mitotic rate	Less	14	25	10	3	52	
		26.9%	48.1%	19.2%	5.8%	100.0%	0.0001
550 HPF	More	0	0	1	46	47	
		0.0%	0.0%	2.1%	97.9%	100.0%	

There is significant difference in mean of size of tumor according to Risk category, high risk category has high size than very low risk has less size tumor. As shown in table 3.

Table 3: Difference in mean of size of tumor according to Risk category

Risk category	No.	Mean of size (cm)	Std. Deviation	P-value
Very low	14	3.78	0.69	
Low	25	5.04	1.48	0.0001
Moderate	11	10.36	3.20	
High	49	11.44	3.40	

P-value ≤ 0.05 (significant).

Discussion

The age distribution of the patients in this study aligns with several other studies that confirm GISTs typically arise in middle-aged and older adults. The mean age of patients in our study was 52.5 ± 13 years, with a significant proportion (32.3%) over 60 years of age. This is consistent with findings from other studies, which suggest that the incidence of GISTs increases with age, peaking around the 6th and 7th decades of life [9, 10]. It's noteworthy that a quarter of our patients fall in the 51-60 years' age bracket, implying the potential for early onset of this tumor type in some populations. The gender distribution in our study showed a slight male predominance with 54.5% male and 45.5% female. This is in alignment with some studies that indicate a marginal male predominance [11], while other reports suggest an even distribution amongst genders [12]. This variability across studies could be attributable to population-specific genetic or environmental factors, warranting further research to delineate gender influences on GISTs' prevalence and progression. Our analysis also revealed that 52.5% of patients had a low mitotic rate (<550 HPF), which is a positive indicator as high mitotic rates are usually associated with an increased risk of aggressive behavior and poor prognosis in GISTs [13]. However, in contrast, we found a high risk category predominance, with 49.5% of patients falling into this group, suggesting a need for comprehensive patient management and monitoring. Regarding tumor location, 58.59% of GISTs were found in the stomach, aligning with existing literature that identifies the stomach as the most common site for GISTs [14]. In our study, the incidence rate of GISTs in the large bowel (22.22%) and small intestine (19.19%) was notably lower. This is consistent with several studies reporting that GISTs are less common in these parts of the GI tract [15, 16]. The association between mitotic rate and risk category observed in our study, where 97.9% of patients with high mitotic rates are classified as high-risk, supports previous research findings. Numerous studies have demonstrated that a higher mitotic rate is a potent prognostic factor for adverse outcomes in GISTs, including increased risk of tumor recurrence and metastasis [17, 18]. In fact, the mitotic index is a critical component of the risk stratification systems for GISTs, such as the National Institutes of Health (NIH) consensus classification and the modified NIH criteria [19, 20]. The relationship between tumor site and risk category in our study also aligns with previous research. We found that 24.1% of gastric tumors are high risk, while a large proportion (72.7%) of small intestine tumors are very low risk. This could be related to the inherent biological differences between GISTs arising from different parts of the gastrointestinal tract. For instance, some studies have reported that GISTs in the small intestine tend to have worse prognoses than those in the stomach, potentially because they are often detected at a later stage and are more likely to exhibit malignant behavior [21, 22]. However, it is important to note that our finding of a significant proportion of very low-risk small intestine tumors suggests possible geographical or population-based variations in tumor biology, underscoring the need for further studies in diverse populations. In our study, no significant association was found between risk and age groups or gender. This is in line with some literature suggesting that while age and gender may influence the incidence and prevalence of GISTs, their impact on the risk or prognosis of these tumors is less clear [23, 24]. However, contradictory findings exist, with a few studies suggesting a worse prognosis for older patients or a particular gender [25, 26]. This discrepancy calls for further investigation to better understand the influence of these demographic factors on the risk and outcomes of GISTs. Our study found a significant difference in the mean size of the tumor according to the risk category, with high-risk category tumors being larger than those in the very low-risk category. This finding is in accordance with previous studies, reinforcing the notion that tumor size is a fundamental prognostic factor in gastrointestinal stromal tumors (GISTs). The size of the tumor has been consistently recognized as a critical determinant of GIST behavior. According to the risk stratification criteria developed by the National Institutes of Health (NIH), the larger the tumor, the

greater the risk of recurrence after complete resection, and therefore, the higher the risk category [27, 28]. This is likely due to the fact that larger tumors tend to be more advanced, have more genetic instability, and are more likely to invade surrounding tissues or metastasize [29]. Several large-scale studies have echoed this association. A retrospective analysis of more than a thousand GIST cases found that tumor size was a significant predictor of overall and recurrence-free survival, with larger tumors carrying a worse prognosis [30]. Similarly, a population-based study concluded that size was a strong predictor of GIST recurrence after surgery [31]. While our study confirms the known association between tumor size and risk, it is essential to remember that size is just one component of risk assessment in GISTs. Other factors, such as mitotic rate and tumor location, also play a critical role in determining the behavior of the tumor and guiding treatment decisions. This multi-factorial approach to risk stratification allows for a more precise assessment and helps tailor the therapeutic approach to the individual patient's needs [32].

Conclusion

Our study reaffirms critical associations in gastrointestinal stromal tumors (GISTs) prognosis. We confirmed that a high mitotic rate, tumor site, and size are significant predictors of risk category, supporting existing literature. Despite age and gender's influence on GIST prevalence, their impact on risk category was inconclusive in our cohort. These findings highlight the importance of comprehensive risk stratification in GISTs for optimal patient management and further necessitate investigation into population-specific characteristics and demographic factors.

Conflict of Interest

Not available

Financial Support

Not available

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