International Journal of Research in Medical Sciences
Parai S et al. Int J Res Med Sci. 2024 Dec;12(12):4594-4604
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20243713

Original Research Article

Exploratory analysis of epidemiological and clinicopathological characteristics of soft tissue sarcomas: a single institutional study in Chennai

Shaoni Parai*, B. Ramkumar, G. Raja, Atul J. G., Manish Kumar Sharma, Vasanth Rooban Narasimman

Department of Medical Oncology, Government Royapettah Hospital, Chennai, Tamil Nadu, India

Received: 01 October 2024
Accepted: 19 November 2024

***Correspondence:**
Dr. Shaoni Parai,
E-mail: s.parai1990@gmail.com

ABSTRACT

Background: Soft tissue sarcomas (STS) from mesenchymal origin form diverse and complex group. Gastrointestinal stromal tumors (GIST)s are most common mesenchymal neoplasm of gastrointestinal system. Better comprehension of clinicopathological profile needed to improve overall prognosis. The objective is to study the epidemiological, clinicopathological characteristics, treatment outcome and other prognostic factors predicting overall survival (OS) and progression free survival (PFS) in STS.
Methods: This study was conducted in Medical Oncology Department, Govt Royapettah Hospital, Chennai. It is a retrospective study, data retrieved from recorded files of patients with soft tissue sarcomas presented from Jan 2017-Dec 2021, and two years follow up data collected till Dec 2023.
Results: In this study 92 patients with soft tissue sarcoma were analysed. Most commonly found histological subtype was GIST (29.3 %). In our study OS rate at 2 years (years) was 0.80. PFS rate at 2 years was 0.70. Surgical status, staging showed correlation with PFS in GIST in cox regression analysis and both PFS, OS in non-GIST sarcomas. In non-GIST sarcomas grade had correlation with PFS and Staging found as an independent factor associated with PFS. Site of primary in GIST and histopathology in non-GIST STS also showed correlation.
Conclusions: In this study median OS and PFS not reached till the last date of follow up. Surgical status and staging found to be significant prognostic factors for both GIST and non-GIST sarcomas and grade in non-GIST sarcomas.

Keywords: GIST, Overall survival, Progression free survival, Prognostic factors, Soft tissue sarcoma, Treatment outcomes

INTRODUCTION

Soft tissue sarcomas (STS) are a rare and heterogeneous group of solid tumors of mesenchymal origin, forming diverse and complex group. Incidence rate of STS are approximately 1.4-5 of 100,000 per year.[1,2] Sarcomas of soft tissues include fat, muscle, nerve and nerve sheath, blood vessels, and other connective tissues. The anatomic sites of the primary disease, histopathological (HPE) differences between sarcoma subtypes have shown a significant impact on optimal management.[3,4] The clinical presentation of STS patients may have various symptoms. Though the management of resectable STS primarily is surgery. The multimodality approach with radiotherapy (RT) and chemo is required, depending on stage, grade, site, HPE subtypes.[5] Despite these advances, the overall 5-year survival probability is around 50%. GISTs are most common mesenchymal neoplasm of gastrointestinal system. Their incidence is suggested to be approximately 1.5 of 100,000 per year.[6,7] Most GISTs originate from interstitial cells of Cajal, resulting primarily from KIT or PDGFRA activating mutations.[8] GISTs can arise anywhere along the GI tract, in rare occasions, can occur in extraintestinal sites. Patients with GISTs may present

with a variety of symptoms.[9] With the invent of successful targeted therapy in GIST, prognosis has improved much than before the era of tyrosine kinase inhibitors (TKI). This has shown hope in management of other subtypes of soft tissue sarcomas. Comprehension of STS patients' profile is essential in improving management for sarcoma patients, further research. To the best of our knowledge, there is lack of these types of studies from our region. There are very less studies comparing the clinicopathological profiles and survival data between GIST and non-GIST subtypes of STS. So, this study has been undertaken to comprehend the real word scenario in better way, to gain insight into the disease patterns and outcomes of STS in a resource limited setting.

METHODS

This study conducted in Medical Oncology Department, Govt Royapettah Hospital, Chennai. It was a retrospective study, data retrieved from recorded files of patients with soft tissue sarcomas who presented over 5 years (January 2017- December 2021), including details of demographics, clinical presentation, examination findings, radiological details, per operative findings, histopathological report, tumor characteristics, staging, treatment records and follow up details for two years (till December 2023).

Inclusion criteria

Inclusion criteria were the patients diagnosed with soft tissue sarcoma (both non-GIST soft tissue sarcoma and patients with GIST).

Exclusion criteria

Patients who lost data or follow up and patients with multiple malignancies were excluded.

OS and PFS had been calculated from records. The prognostic factors predicting OS and PFS were analyzed. PFS determined by calculating the interval from the time of start of primary treatment to the first evidence of recurrence, progression of disease, death, or last follow-up, whichever occurred first. OS defined as the interval from the time of start of primary treatment until death from all causes or last follow-up since completion of treatment for patients who are still alive, whichever occurred first.

Statistical analysis

Data analysis performed using R software and descriptive statistics computed for all patients' baseline characteristics. Characteristics of patients described using mean and standard deviation (if normally distributed) or median and interquartile range (if skewed) for continuous variables and by frequencies and percentages for categorical variables. Kaplan-Meier estimated PFS and OS, time stratified by the various predictive factor categories calculated and compared by employing the log-rank test statistics. Multivariate Cox proportional hazard models used to assess the association between participants' clinicopathologic characteristics and survival outcomes while adjusting for other covariates. Associations regarded as significant if $p<0.05$. All p values are two-sided.

RESULTS

Clinical characteristics and epidemiology

In this study we had analyzed 92 patients with STS. Median age at presentation was 49 years. Lowest age presented was 10-year, highest age 80 year. In our study males were 55.4% (n=51), 1.2 times more affected than females 44.5% (n=41).68.4% of patients had no previous comorbidity.

Patients were evaluated with clinical examination, imaging, diagnosis confirmed with HPE and immunohistochemistry (IHC). In view of resource limited setting chromosomal translocation study or molecular analysis could not be done.

Gastro Intestinal stromal tumors (GIST) were most common sarcoma subtype we came across in our study, 29% (n= 27). Among GIST spindle cell type most commonly seen (62.9%). Among Other non-GIST soft tissue sarcomas [70.6 % (n=65)], most common sarcomas were of adipocytic origin (23%), among them most common was well differentiated liposarcoma, followed by (f/b) myxoid and pleomorphic variant. Other histologies found were synovial sarcomas (SS) (16.9%), various fibroblastic sarcoma (15.3%), undifferentiated sarcomas (15.3%), peripheral nerve sheath tumors (pnstt) (10.7%), poorly differentiated pleomorphic sarcoma (9.2%), smooth or skeletal muscle tumors (9.2%).

STS (NON-GIST)

The median duration of symptoms before presentation was 7 months. The most common presentation was swelling, seen in 75% (n = 49) of the non-GIST sarcoma patients; the swelling was painless in 58% (n=*38*) and painful in 42% (n = 27) of the patients. Most common site of non-GIST STS was trunk and extremity (90.7%) followed by retroperitoneal (6.1%). Among trunk and extremity most common involvement was in extremity (76.9%). Lower limb was more common than upper limb and thigh was the most commonly involved site (32.3%). No patient had given old history of malignancy or old treatment like radiation. Two patients (3%) with known history of neurofibromatosis, diagnosed to have malignant peripheral nerve sheath tumor (MPNST).

Staging and grading

Among non-GIST STS patients presented in localized stage were 72.3% (n=47), and 27.6% (n=18) patients presented with metastases. Among them 61.1% (n=11) patients presented with lung metastases, followed by liver

metastases (22.2%), bone (16.6%). Only 2 patients (3%) presented with lymph nodal metastases, one had HPE of SS, one had high grade MPNST. In our study patients mostly presented with advanced tumor staging (T3/T4) were 60% (n=39). Most of the patients presented in stage III, III A (23%), III B (26 %). FNLCC grading used for non-GIST STS. It was available in 86.1% of the patients,51.7% (n=29) of the patients had grade 3, followed by grade 2 was seen in 33.9% (n=19), and grade 1 seen in 14.2% (n =8) of the patients.

Treatment and response

Among non-GIST STS 81.5% (n=53) patients underwent surgery. 64.1% (34) among them underwent upfront surgery. Mostly patients underwent wide resection, 10.7% of non-GIST STS patients underwent amputation.

15.3% (n=10) patients received neo adjuvant chemo (NAC). 12.3% (n=8) patients received neo adjuvant radio therapy (NA RT). Two patients (3%) had received both neo adjuvant chemo and RT (sequential).

Patients who received NAC, mostly were T4 (70%) or T3/ G3/ unresectable. Patients who received NA RT either were T4 (50%) or T3/G3/ unresectable/ based on site.

40% (n=26) received adjuvant Chemo. 61.2% (n=41) of patients had received adjuvant RT. While 29.2% (n=19) received both adjuvant chemo RT (sequential). All patients with large tumor size/high grade / high risk subtypes/close or positive margin received adjuvant therapy.

20% (n=13) did not receive any chemo. 18.4% did not receive any RT. 10.7% has received palliative RT. 24.6% (n=16) received palliative chemo. Mostly (66.1%) (43) received Doxorubicin, Ifosfamide based chemo. VAC (vincristine, adriamycin, cyclophosphamide) based regimen used in rhabdomyosarcoma. Doxorubicin, dacarbazine or gemcitabine, docetaxel used for leiomyosarcoma.

32.3% (n=21) patients had a recurrence. Among patients with initial localized disease (mostly had advanced stage, stage III presentation), 36.1 % patients recurred. Among metastatic 22.2% patients recurred. 12.3% had local recurrence, 20% developed distant mets. 66.6% of metastatic patients progressed on treatment.

Patients who received neo adjuvant therapy among them 68.7% could undergo R0 resection. In our study most commonly used 2nd line chemo regimens were gemcitabine, docetaxel/ pazopanib/ eribulin. Among metastatic non-GIST STS, followed by systemic therapy, 33.3% of patients underwent resection surgery.

Side effect

Most common side effect due to chemo was mild to moderate GI complaints (70.7%), while most common grade 3 side effect was neutropenia (32.3%). Most common surgical complication seen was post op pain and chronic swelling. Most common side effect with RT we came across was edema and fibrosis.

GIST

Most of the GIST patients in our study (88 %) had CD 117 positive on IHC. Most of the GIST patients 52% (n=14) presented with mass like effects like abdominal pain, swelling, early satiety f/b symptoms of GI bleeding (29.6%) (n=8). Two patients (7.4%) got diagnosed incidentally. Most common site of GIST presentation in our study was stomach (59.2%) f/b small bowel (jejunal 18.5 %, ileal 11.1 %) and rectal (7.4%).

Staging and grading

GIST patients presented in localized stage were 77.7% (n=21), 22.2% (n=6) patients presented with metastases, 4 had peritoneal metastases, 2 liver metastases.

GIST patients presented with advanced tumor (T3/T4) staging were 66.6%(n=18). Mostly patients presented in stage III (37%), IIIA (14.8%), IIIB (22.2%). GIST grading based on mitotic rate, available in 92.5% of patients, low grade was seen in 36% (n=9), high grade seen in 64% (n=16).

Treatment and response

81.4% (n=22) of GIST underwent surgery, 2 patients with locally advanced GIST received imatinib as neoadjuvant, all patients had received adjuvant imatinib.18.5% (5) patients who could not undergo surgery had received imatinib as palliative. 14.8% (4) patients had recurred till the last day of follow up. Among them one patient was found to have non-adherence with imatinib, he was re counselled for drug adherence and imatinib restarted, while others were treated with increased dose, two of them showed response and tolerated, one patient received sunitinib. Among metastatic GIST, 16.6 % of patients underwent resection surgery.

Side effect

Most common side effect due to Imatinib in our study was fatigue (33.3%) followed by thrombocytopenia. Grade 3 thrombocytopenia was seen only in one patient, most common side effect due to surgery found was adhesion, seen in 11.1%.

Survival analysis

Median OS, PFS not reached at 24 months in all STS subgroups. For all STS subgroups OS at 24 months was 80.4%, PFS at 24 months was 70.6%. Kaplan Meier survival curves showed: Surgery significantly associated with improved OS and PFS ($p<0.0001$) for both GIST and NON-GIST ST.

Table 1: Clinical characteristics with percentage.

Clinical characteristics	No.	Percentage
Sex ratio		
Male	51	55.4
Female	41	44.5
Epidemiology		
Histopathology		
Gist	27	29.3
Non-gist	65	70.6
Adipocytic	15	23
SS	11	16.9
FS	10	15.3
US	10	15.3
PNSTT	7	10.7
PD,PS	6	9.2
SKMT	4	6.1
SMT	2	3

Table 2: Clinical characteristics among GIST and NON GIST along with percentage.

Clinical characteristics	GIST	No.	Percentage	Non-GIST STS	No.	Percentage
M.C. symptoms	Mass like effect	14	52	Swelling	49	75
M.C. site	Gastric	16	59.2	T N E	59	90.7
	Jejunal	5	18.5	RP	4	6.1
	Ileal	3	11.1			
	Rectal	2	7.4			
Subsite				LL	37	56.9
				UL	13	20
				Trunk	9	13.8
Staging	Localized	21	77.7	Localized	47	72.3
	Metastatic	6	22.2	Metastatic	18	27.6
Staging						
	I	2	7.4			
	IA	4	14.8	IA	2	3.0
	IB	4	14.8	IB	13	20
	II	1	3.7			
	IIIA	4	14.8	IIIA	15	23.0
	IIIB	6	22.2	IIIB	17	26.1
	IV	6	22.2	IV	18	27.6
Site of METS	Peritoneal	4	66.6	Lungs	11	61.1
	Liver	2	33.3	Lymphnodal	2	3
Tumor				T1	3	4.6
	T2	9	37.5	T2	23	35.3
	T3	13	48.1	T3	21	32.3
	T4	5	18.5	T4	18	27.6
Grading	LG	9	36	G1	8	14.2
	HG	16	64	G2	19	33.9
				G3	29	51.7
	NA	2	7.4	NA	9	13.8
Treatment						
Surgery		22	81.4		50	76.9
NEO ADJ	Imatinib	2	7.4	Chemo	10	15.3
				RT	8	12.3
ADJ	Imatinib	22	81.4	Chemo	26	40

Continued.

Clinical characteristics	GIST	No.	Percentage	Non-GIST STS	No.	Percentage
				RT	38	58.4
PAL	Imatinib	5	18.5	Chemo	16	24.6
				RT	7	10.7
NO				Chemo	13	20
				RT	12	18.4
Recurrence		4	14.8		21	32.3

STS (NON-GIST)

OS rate at 2 yrs for non-GIST STS of all staging was 76.9%, OS rate at 2 yrs for localized non-GIST STS was 91.4%, metastatic was 38.8%.

Kaplan Meier survival curves showed: Site of non-GIST STS had not shown any significant association with survival analysis. HPE of non-GIST STS showed significant association with PFS (0.03), but no statistically significant association with OS (0.054). Liposarcoma had better PFS than other HPs of non-GIST STS. Stage of non-GIST STS had significant association with OS, PFS (p <0.0001) and grade had significant association with OS(p=0.0002), PFS (p =0.001). Patients who received neo adjuvant/adjuvant therapy, had not shown any statistically significant impact on OS, PFS. Though patients who received RT showed improvement in PFS but without any statistical significance. Univariate analysis showed surgical status (p<0.0001) and staging (p<0.0001) had significant correlation with OS and PFS of non-GIST sarcoma. Grade had significant relation with PFS (p=0.003). Both univariate and multivariate analysis showed staging to be an independent factor associated with PFS (p=0.01). Kaplan-Meier curves showing correlation of factors with OS at 2 years and PFS till 2 years.

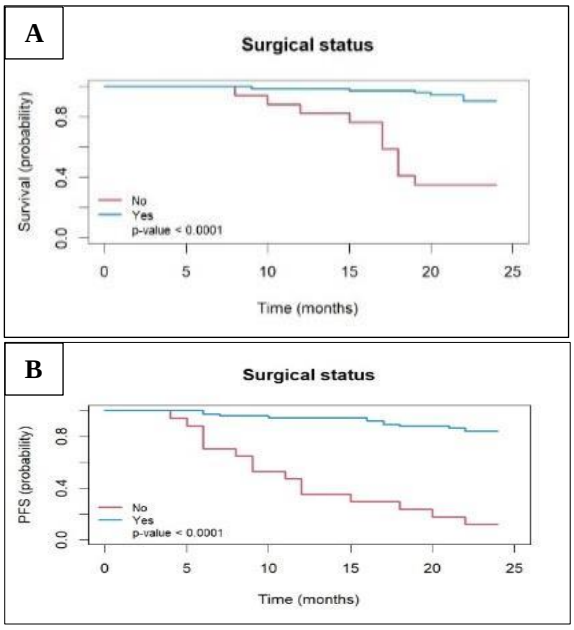

Figure 1: Surgical status (GIST and non-GIST). A) OS); B) PFS).

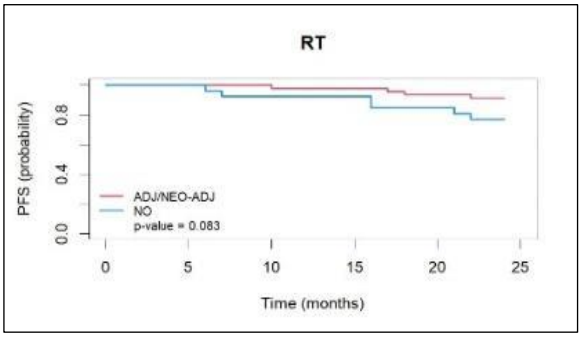

Figure 2: RT (non-GIST) (PFS).

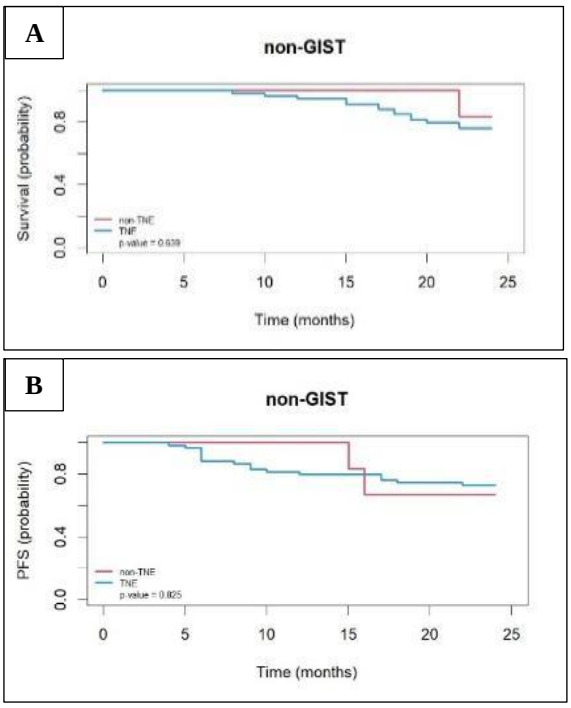

Figure 3: Site (non-GIST). A) OS; B) PFS.

GIST

OS rate for GIST of all stages was 88.8%. OS rate at 2 yrs for localized GIST was 95.2%, metastatic was 66.6%.

Kaplan Meier survival curves showed: Site of GIST (gastric vs non gastric) had significantly better OS(p=0.02), though no significant association found with PFS. Grade and staging had significant association with PFS of GIST (p=0.04) and (p<0.0001) respectively.

Though no statistically significant association found with OS.

Univariate analysis showed surgical status (p=0.0004) and staging (p=0.0003) had significant correlation with PFS of GIST. Univariate analysis showed surgical status had relation with OS of GIST but could not achieve any statistical significance (p=0.07).

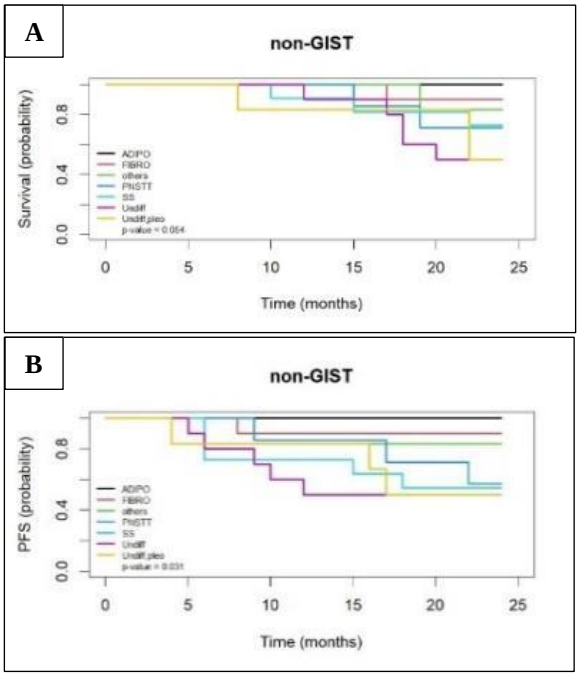

Figure 4: HPE (non-GIST). A) OS; B). PFS.

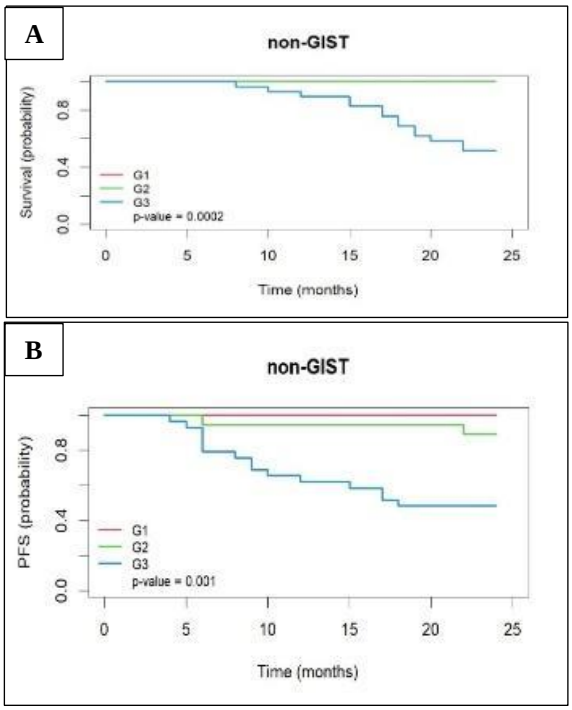

Figure 5: Grade (non-GIST). A) OS; B) PFS.

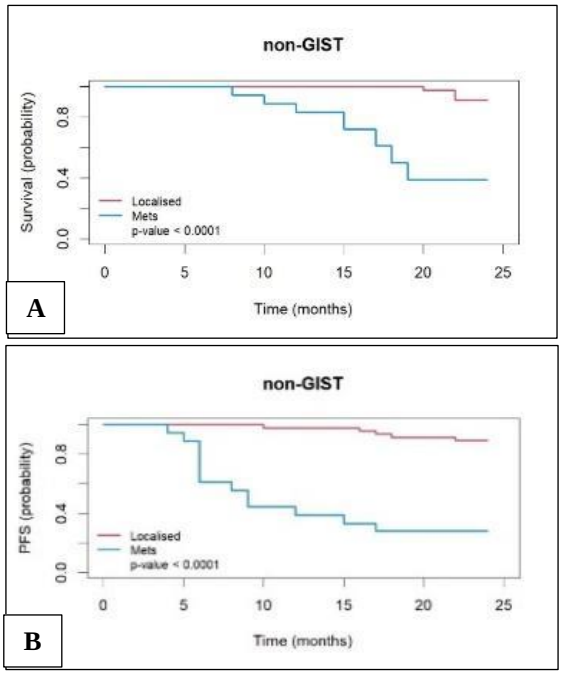

Figure 6: Stage (non-GIST). A) OS; B) PFS.

Table 3: Uni and multi variate analysis of OS at 2 years - non-GIST.

Variable	Univariate analysis	Multivariate analysis	
	P value	HR (95% CI)	P value
Age (in years)			
≤49	0.86		
>49			
Gender			
Male	0.68		
Female			
Surgical status			
No	<0.0001	Reference	0.081
Yes		0.25 (0.05-1.19)	
Site			
non-TNE	0.65		
TNE			
Grade			
G1 + G2	0.9		
G3			
Stage			
Localized	<0.0001	Reference	0.068
Mets		4.86 (0.89-26.6)	

Kaplan-Meier Curves showing correlation of factors with Survival at 2 years and Progression free survival (PFS) till 2 years.

Table 4: Uni and multi variate analysis of PFS at 2 years-non-GIST.

Variable	Univariate analysis	Multivariate analysis	
	P value	HR (95% CI)	P value
Age (in years)			
≤49	0.7		
>49			
Gender			
Male	0.28		
Female			
Surgical status			
No	<0.0001	Reference	0.49
Yes		0.63 (0.17-2.38)	
Site			
non-TNE	0.84		
TNE			
Grade			
G1 + G2	0.003	Reference	0.18
G3		3.14 (0.58-17.0)	
Stage			
Localised	<0.0001	Reference	0.014
Mets		6.91 (1.47-32.4)	

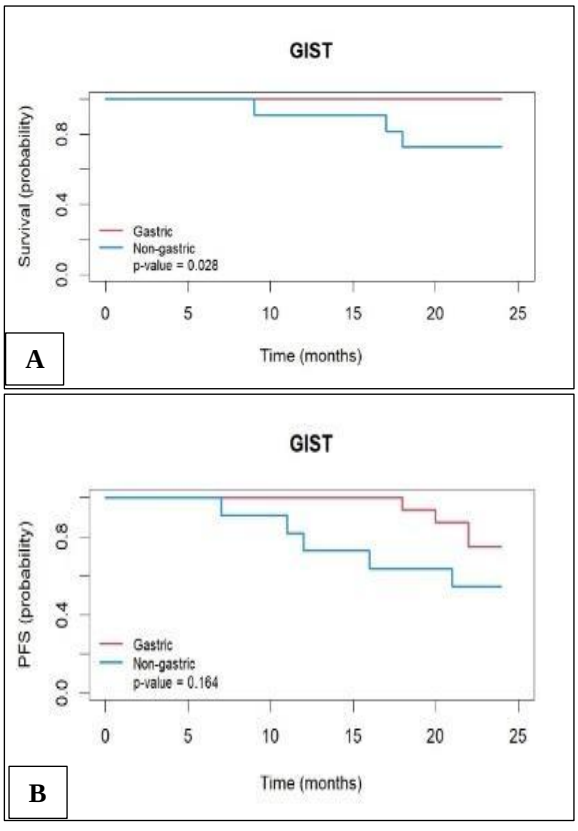

Figure 7: Site (GIST). A) OS; B) PFS.

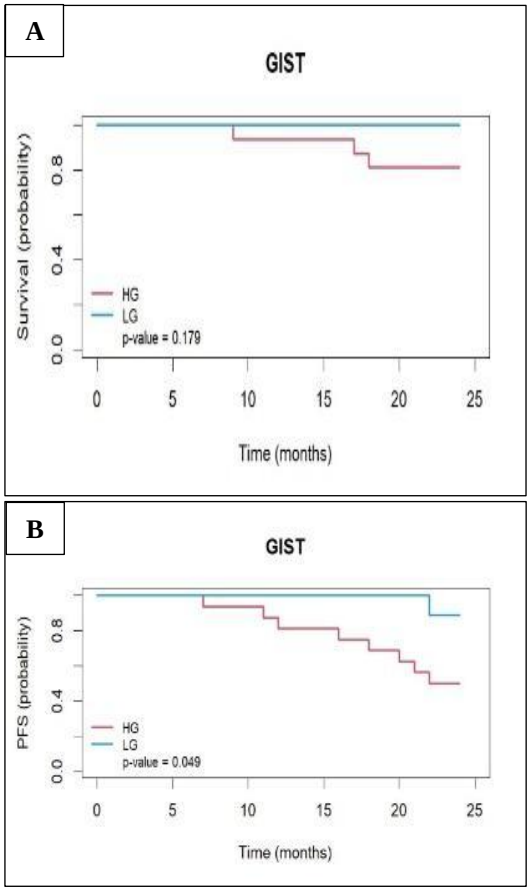

Figure 8: Grade (GIST). A) OS; B) PFS.

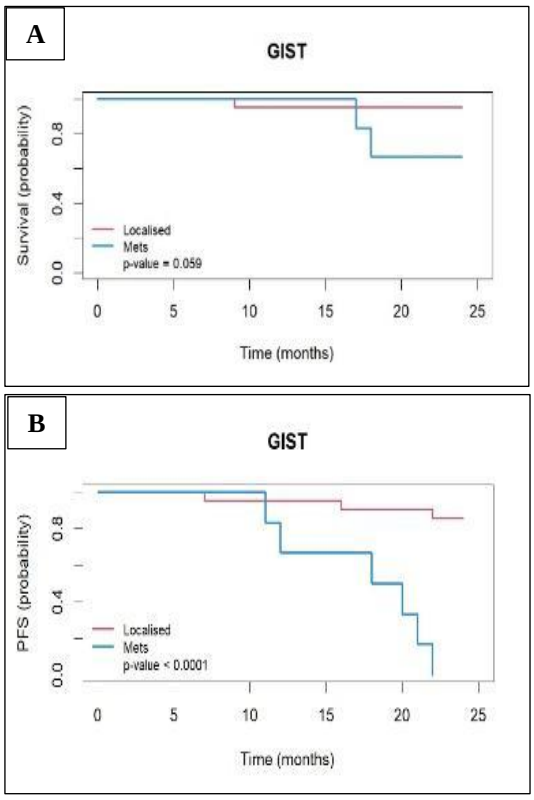

Figure 9: Stage (GIST). A) OS; B) PFS.

Table 5: Univariate analysis of OS at 2 years-GIST.

Variable	Univariate analysis
	P value
Age (in years)	
≤49	0.8
>49	
Gender	
Male	0.41
Female	
Surgical status	
No	0.07
Yes	
Site	
Gastric	0.9
Non-gastric	
Grade	
HG	0.9
LG	
Stage	
Localized	0.107
Mets	

Table 6: Uni and multi variate analysis of PFS at 2 years-GIST.

Variable	Univariate analysis	Multivariate analysis	
	P value	HR (95% CI)	P value
Age (in years)			
≤49	0.768		
>49			
Gender			
Male	0.485		
Female			
Surgical status			
No	0.0004	Reference	0.2102
Yes		0.18 (0.01-2.62)	
Site			
Gastric	0.184	Reference	0.0887
Non-gastric		4.85 (0.79-29.84)	
Grade			
HG	0.087	Reference	0.8083
LG		0.74 (0.06-8.48)	
Stage			
Localized	0.0003	Reference	0.2354
Mets		4.63 (0.37-58.14)	

DISCUSSION

STS are rare in frequency, incidence rate increases with age, with median age in Western literature is in sixth decade.[10,11] In our study, the median age was 49 years, comparable to other Indian studies.[12,13] In our study males were slightly more affected than females with ratio of 1.2:1, similar to other studies.[14]

In our study most common histological subtype found was GIST, among non-GIST STS liposarcomas were most common, other Indian studies had showed synovial sarcomas to be more common among non-GIST STS.[12-14]

In our study, patients of all STS subtypes had OS rate at 24 months of 80.43%, PFS rate at 24 months of 70.65%. OS rate at 2 yrs for all stages of non-GIST STS was 76.9%, for GIST was 88.8%.

Non-GIST STS

OS rate at 2 yrs for localized non-GIST STS was 91.4%, metastatic 38.8%. A large retrospective German study reported median survival as 5.83 years and 1-year survival rate 77%. For localized STS patients, median disease free survival (DFS) was 20.93 months, with 1-year DFS and OS rates 87.6 and 95.3%, respectively.[15] Bajpai et al reported that 3-year PFS and OS were 48 and 64%, respectively.[12] The variation in survival outcomes reflects the study population's heterogeneity, such as stage, histological subtypes, grades, and use of different treatment options.

In this study fifty percent of the patients with non-GIST STS had symptoms for more than 7 months before diagnosis. Painless nature of swelling with lack of health awareness and limited access to health care results in delayed diagnosis of these tumors, resulting worse outcomes and survival.[15,16] Most of our patients presented in metastatic (27.6%) or locally advanced stage (49.2%). In our study, extremity was most common site, followed by trunk and retroperitoneum. Shukla and Deo also reported extremity as most common site f/b chest and trunk.[15] Rastogi et al reported extremity f/b retroperitoneum as most frequent sites.[13]

Liposarcoma had better PFS compared to other histopathologies of non-GIST STS and undifferentiated pleomorphic sarcomas had shown worst PFS in KM survival curves. HPE had shown association with OS, but without any statistical significance (0.054). Most of the tumors showed high grade morphology with grade 3 in 51.7% of our study group.

Advanced staging and higher grading had shown significantly worse OS and PFS in non-GIST STS in KM curves like Casas et al study.[17] Univariate analysis showed advanced staging correlated with worse OS and PFS and higher grading with worse PFS of non-GIST sarcoma. Multivariate analysis showed staging to be an independent factor associated with PFS.

In this study all patients who could undergo complete surgical resection irrespective of GIST or non -GIST STSs had shown significantly improved OS and PFS in KM

survival curves. Univariate analysis showed significantly better OS and PFS in non-GIST STS patients who underwent surgery.

Management of localized STSs involves a multidisciplinary approach, with surgery being the important modality of therapy. Radiotherapy or chemotherapy in a perioperative setting improves outcomes in tumors of size ≥5 cm, deep seated, or high grade, though data regarding OS advantage are conflicting.[18] SMAC study showed similar results with post op chemo. Adjuvant chemo preferred to delay/prevent distant mets.[19] Preoperative therapy is associated with increased ease of resection, decreased local recurrence, reduced late toxicity, and a trend toward improved survival outcomes.[20-22] In this study neoadjuvant therapies were considered in advanced, borderline resectable tumors after tumor board discussions. We observed 68.7% complete resection rates in the neoadjuvant cohort. Study had shown limb-sparing surgery with RT as an effective treatment in patients with high-grade STS of the extremities, with no difference in OS and DFS as compared to amputation.[23] Data analysis from 16 studies indicated that RT reduced local recurrence in all subsites and improved OS for retroperitoneal STS.[24] Though in our study, patients who received neo adjuvant/adjuvant therapy failed to show any statistical significant impact on OS, PFS, but could achieve more R0 resection and limb salvage with functionality preservation was possible in most patients. Patients who received RT though showed improvement in PFS but did not achieve any statistical significance.

In the METASARC observational study, 48.6% of metastatic patients received definitive therapy for locoregional disease and metastases.[25] In this study among metastatic STS patients, the majority received only systemic chemotherapy therapy. 33.3% of the metastatic non-GIST STS patients and 16.6% of metastatic GIST underwent resection. The median PFS and OS of metastatic STS patients in our study were 9 months and 18.5 months, respectively. The median PFS and OS of metastatic STS patients in Shivarudraiah et al study were 9.83 months and 23.90 months respectively.[26]

GIST

OS rate at 2 yrs for localized GIST was 95.2%, metastatic 66.6%. According to National Cancer Institute, the 5-Year OS rate of all stages of GISTs including all sites were 83%.[27]

In this study GIST had shown better survival compared to non-GIST STS, Gastric GIST had shown better survival than non-gastric GIST in KM survival curves like Akgul et al study.[28] In this study, the 2-year median overall survival rate of patients with non-gastric and gastric GISTs were 81.8% and 93.7% respectively. Lopez Gordo et al reported that in patients with small intestine GISTs, 5-year DFS was 65.7%, and 90.8% in gastric GISTs.[9] The two most predictive independent risk factors in studies for disease recurrence were tumor size and mitotic rate.[29-31] In this study, higher staging and grading had shown significantly worse PFS in GIST, while advanced staging was associated with worse OS but did not show statistical significance (p=0.059). Univariate analysis showed advanced staging was significantly associated with worse PFS in GIST.

Miettinen and colleagues also reported high metastatic rate with larger tumor size, higher grade and non-gastric site.[29,31]

Surgery was the initial treatment for GIST. Imatinib combined with surgery as 1st line treatment had significantly improved the survival benefit of GIST.[32] Patrikidou et al found that the median progression-free survival (mPFS) and median overall survival (mOS) was 33 months and 99 months, respectively, and the 8-year OS rate reached 50%.[33]

RTOG 0132 study showed efficacy of preoperative imatinib in patients with potentially resectable disease.[34] With surgery alone 50% of patients will develop recurrence or metastasis even after complete resection and the 5-year survival rate is about 50%.[35-37] Scandinavian Sarcoma Group suggests a longer duration of postoperative imatinib improves PFS and OS for patients with a high risk of recurrence.[38] The highest risk for recurrence was observed among patients with non-gastric GIST and tumors with high mitotic count.[39] As per these studies in our study high risk patients had received minimum 3 years of Imatinib. In this study all patients who could undergo complete surgical resection had shown significantly improved OS and PFS in KM survival curves. Univariate analysis showed significantly better PFS in GIST who underwent surgery. All our GIST patients had received imatinib (as preop, adjuvant or palliative). Though statistical significance not achieved, but our study group had shown better OS (88.8% at 2 years) compared to studies where surgery alone was done.

This study has few limitations. It is a retrospective, single institutional study, done on small sample size, follow up data taken for lesser duration. In view of resources limited setting mutation analysis or translocation study could not be done.

CONCLUSION

In this study median OS and PFS not reached till the last date of follow up. OS rate at 2 years was 0.80, PFS rate at 2 years was 0.70. Most common subtype found was GIST.GIST performed better than other non-GIST STS. KM survival curves had shown gastric GIST had better OS and PFS than non-gastric GISTs. Liposarcomas showed better PFS than other non-GIST sarcomas. Univariate cox regression analysis had shown patients who could undergo surgery had better PFS in GIST and better PFS and OS in non-GIST sarcomas, while metastatic patients had worse PFS in GIST and worse PFS, OS in non-GIST STS.

Tumors with higher grade had significantly worse PFS in non-GIST sarcomas.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Toro JR, Travis LB, Wu HJ, Zhu K, Fletcher CD, Devesa SS. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978-2001: An analysis of 26,758 cases. Int J Cancer. 2006;119(12):2922-30.
2. Mastrangelo G, Coindre JM, Ducimetière F, Dei Tos AP, Fadda E, Blay JY, et al. Incidence of soft tissue sarcoma and beyond: A population-based prospective study in 3 European regions. Cancer. 2012;118(21):5339-48.
3. ErikssonM. Histology-driven chemotherapy of soft-tissue sarcoma. Ann Oncol. 2010;21(Suppl 7):vii270-vii276.
4. Reichardt P. Soft tissue sarcomas, a look into the future: different treatments for different subtypes. Future Oncol. 2014;10(8Suppl):s19-27.
5. Dangoor A, Seddon B, Gerrand C, Grimer R, Whelan J, Judson I. UK guidelines for the management of soft tissue sarcomas. Clin Sarcoma Res. 2016;6:20.
6. Nilsson B, Bümming P, Meis-Kindblom JM, Odén A, Dortok A, Gustavsson B, et al. Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the pre imatinib mesylate era-a population-based study in western Sweden. Cancer. 2005;103(4):821-9.
7. Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastro intestinal stromal tumours (GIST): a systematic review of population-based cohort studies. Cancer Epidemiol. 2016;40:39-46.
8. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, Ishiguro S, et al. Gain-of-function mutations of c kit in human gastrointestinal stromal tumors. Science. 1998;279(5350):577-80.
9. Lopez Gordo S, Bettonica C, Miró M, Estremiana F, Aranda H, Farran L. Gastric and small intestine GIST: results of 156 cases in 20 years. J Gastrointest Cancer. 2022;53(2):451-9.
10. Burningham Z, Hashibe M, Spector L, Schiffman JD. The epidemiology of sarcoma. Clin Sarcoma Res. 2012;2(1):14.
11. Chen C, Borker R, Ewing J, Tseng WY, Hackshaw MD, Saravanan S, et al. Epidemiology, treatment patterns, and outcomes of metastatic soft tissue sarcoma in a community-based oncology network. Sarcoma. 2014;2014(1):145764.
12. Bajpai J, Khanna N, Vora T, Gulia A, Laskar S, Puri A, et al. Analysis of bone and soft-tissue sarcomas registered during the year 2012 at Tata Memorial Hospital, Mumbai, with clinical outcomes. Ind J Cancer. 2018;55(1):37-44.
13. Rastogi S, Sharma A, Aggarwal A, Barwad A, Dhamija E, Panday R. Outcomes of advanced soft tissue sarcoma from dedicated medical oncology sarcoma clinic in North India and evaluation of the respective model. JCO. 2018;36(suppl_15):e23561.
14. Shukla NK, Deo SV. Soft tissue sarcoma-review of experience at a tertiary care cancer centre. Ind J Surg Oncol. 2011;2(4):309-12.
15. Saltus CW, Calingaert B, Candrilli S, Lorenzo M, D'yachkova Y, Otto T, et al. Epidemiology of adult soft-tissue sarcomas in Germany. Sarcoma. 2018;2018(1):5671926.
16. George A, Grimer R. Early symptoms of bone and soft tissue sarcomas: could they be diagnosed earlier.? Ann R Coll Surg Engl. 2012;94(4):261-6.
17. Díaz Casas SE, Villacrés JM, Lehmann Mosquera C, García Mora M, Mariño Lozano I, Ángel Aristizábal J, et al. Prognostic factors associated with tumor recurrence and overall survival in soft tissue sarcomas of the extremities in a Colombian Reference Cancer Center. Curr Oncol. 2024;31(4):1725-38.
18. ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(Suppl 3):iii102-12.
19. Sarcoma Meta-analysis Collaboration. Adjuvant chemotherapy for localised resectable soft-tissue sarcoma of adults: meta-analysis of individual data. Sarcoma Meta-analysis Collaboration. Lancet. 1997;350(9092):1647-54.
20. Grobmyer SR, Maki RG, Demetri GD, Mazumdar M, Riedel E, Brennan MF, et al. Neo-adjuvant chemotherapy for primary high-grade extremity soft tissue sarcoma. Ann Oncol. 2004;15(11):1667-72.
21. Albertsmeier M, Rauch A, Roeder F, Hasenhütl S, Pratschke S, Kirschneck M, et al. External beam radiation therapy for resectable soft tissue sarcoma: a systematic review and meta-analysis. Ann Surg Oncol. 2018;25(3):754-67.
22. Kraybill WG, Harris J, Spiro IJ, Ettinger DS, DeLaney TF, Blum RH, et al. Long-term results of a phase 2 study of neoadjuvant chemotherapy and radiotherapy in the management of high-risk, high-grade, soft tissue sarcomas of the extremities and body wall: Radiation Therapy Oncology Group Trial 9514. Cancer. 2010;116(19):4613-21.
23. Rosenberg SA, Tepper JO, Glatstein EL, Costa JO, Baker AL, Brennam M, et al. The treatment of soft tissue sarcomas of the extremities: prospective randomized evaluations of (1) limb-sparing surgery plus radiation therapy compared with amputation and (2) the role of adjuvant chemotherapy. Ann Surg. 1982;196(3):305-15.
24. Albertsmeier M, Rauch A, Roeder F, Hasenhütl S, Pratschke S, Kirschneck M, et al. External beam radiation therapy for resectable soft tissue sarcoma: a systematic review and meta-analysis. Ann Surg Oncol. 2018;25:754-67.

25. Savina M, Le Cesne A, Blay JY, Ray-Coquard I, Mir O, Toulmonde M, et al. Patterns of care and outcomes of patients with METAstatic soft tissue SARComa in a real-life setting: the METASARC observational study. BMC Med. 2017;15(1):78.
26. Shivarudraiah SM, Viswanath S, Pandalanghat S, Soneji D, Kumar M, Patel A, et al. Adult soft tissue sarcoma: a prospective observational real-world data. Ind J Medi Paed Oncol. 2021;42(04):339-45.
27. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review, 1975-2017. Bethesda, MD: National Cancer Institute; 2020.
28. Colapkulu-Akgul N, Gunel H, Beyazadam D, Ozsoy MS, Alimoglu O. Gastrointestinal stromal tumors: recurrence and survival analysis of 49 patients. Middle East J Dig Dis. 2023;15(1):19.
29. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol. 2006;23(2):70-83.
30. Joensuu H, Vehtari A, Riihimäki J, Nishida T, Steigen SE, Brabec P, et al. Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. Lancet Oncol. 2012;13(3):265-74.
31. Miettinen M, Makhlouf H, Sobin LH, Lasota J. Gastrointestinal stromal tumors of the jejunum and ileum: a clinicopathologic, immunohistochemical, and molecular genetic study of 906 cases before imatinib with long-term follow-up. Am J Surg Pathol. 2006;30(4):477-89.
32. Casali PG, Blay JY, Abecassis N, Bajpai J, Bauer S, Biagini R, et al. Gastrointestinal stromal tumours: ESMO-EURACAN-GENTURIS clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2022;33(1):20-33.
33. Patrikidou A, Domont J, Chabaud S, Ray-Coquard I, Coindre JM, Bui-Nguyen B, et al. Long-term outcome of molecular subgroups of GIST patients treated with standard-dose imatinib in the BFR14 trial of the French Sarcoma Group. Eur J Cancer. 2016;52:173-80.
34. Eisenberg BL, Harris J, Blanke CD, Demetri GD, Heinrich MC, Watson JC, et al. Phase II trial of neoadjuvant/adjuvant imatinib mesylate (IM) for advanced primary and metastatic/recurrent operable gastrointestinal stromal tumor (GIST): early results of RTOG 0132/ACRIN 6665. J Surg Oncol. 2009;99(1):42-7.
35. Eisenberg BL, Judson I. Surgery and imatinib in the management of GIST: emerging approaches to adjuvant and neoadjuvant therapy. Ann Surg Oncol. 2004;11:465-75.
36. Gold JS, Dematteo RP. Combined surgical and molecular therapy: the gastrointestinal stromal tumor model. Ann Surg. 2006;244(2):176-84.
37. 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(1):51-8.
38. Joensuu H, Eriksson M, Sundby Hall K, Reichardt A, Hartmann JT, Pink, et al. Adjuvant imatinib for high-risk GI stromal tumor: analysis of a randomized trial. J Clin Oncol. 2016;34(3):244-250.
39. Joensuu H, Eriksson M, Hall KS, Hartmann JT, Pink D, Schütte J, et al. Risk factors for gastrointestinal stromal tumor recurrence in patients treated with adjuvant imatinib. Cancer. 2014;120(15):2325-33.

Cite this article as: Parai S, Ramkumar B, Raja G, Atul JG, Sharma MK, Narasimman VR. Exploratory analysis of epidemiological and clinicopathological characteristics of soft tissue sarcomas: a single institutional study in Chennai. Int J Res Med Sci 2024;12:4594-604.