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ORIGINAL RESEARCH

Characteristics and Outcomes of Soft Tissue Sarcoma in Saudi Arabia: A 10-Year Experience

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Purpose: Soft tissue sarcomas (STS) are rare, heterogeneous malignancies representing less than 1% of solid cancers. Given the diversity of subtypes and the complexity of management, understanding regional epidemiological patterns is essential. This study aimed to evaluate the clinical characteristics, treatment strategies, and prognostic factors in STS patients in Saudi Arabia at a sarcoma center.

Patients and Methods: This retrospective study included 214 patients with STS treated between 2010 and 2020. Patient demographics, tumor characteristics, clinical stage, and treatment modalities were collected using REDCap. Overall survival (OS) was estimated using Kaplan–Meier curves, and prognostic factors were analyzed using Cox regression. Statistical significance was set at $p < 0.05$.

Results: The median age at diagnosis was 37 years (IQR: 25–49.5), and the median symptom duration before diagnosis was 8 months. Synovial sarcoma (20%) was the most common subtype, followed by liposarcoma (13.6%) and undifferentiated pleomorphic sarcoma (12%). Metastatic disease at diagnosis was reported in 39% of patients, with the lower limb being the most affected site (62.1%). Local treatment included surgery alone (45.3%), radiation alone (7.5%), and combined surgery and radiation (41.6%). Median OS was not reached in localized disease, whereas it was 26 months in metastatic cases ($p< 0.01$). Age ≥65 years (hazard ratio[HR]: 6.05, p=0.002), larger tumor size (HR: 9.12, p=0.04), and metastasis (HR: 8.77, p<0.001) were associated with worse survival. Tumors in extremities (HR: 0.38, p=0.04) and combined local therapy (HR: 0.13, p=0.009) were associated with better OS. Multimodal therapy improved OS in metastatic cases (p=0.004).

Conclusion: STS in Saudi Arabia presents at a younger age, with prolonged symptom duration, and a high burden of metastatic disease. Despite these challenges, outcomes are comparable to global trends, particularly multimodal approaches. Future research should identify barriers to early diagnosis, improve healthcare access, and explore novel systemic therapies.

Keywords: soft tissue sarcoma, survival outcome, prognostic factors, synovial sarcoma, liposarcoma, undifferentiated pleomorphic sarcoma, Saudi Arabia

Introduction

Soft tissue sarcomas (STS) represent a rare and heterogeneous group of neoplasms with more than 100 distinct histological subtypes.[1,2] STS originates from mesenchymal tissues and accounts for less than one percent of all adult solid cancers.[3] The Age-standardized incidence rates (ASR) globally range from 1.5–3.0 per 100,000 individuals[4,5] while in Saudi Arabia (SA), it is notably lower, ranging from 1.5–1.9 per 100,000.[6] The diagnosis and clinical management of STS are challenging due to their rarity and nonspecific clinical presentation. As a result, patients often experience significant delays in diagnosis, increasing the likelihood of presenting with advanced disease at the time of confirmation.[7–9] Multidisciplinary teams are essential for managing STS because of their complexity, and treatment in high-volume cancer centers improves patient outcomes.[10]

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Although extensive research has been conducted on STS in Western populations, data from the Middle East, particularly SA, are limited, highlighting the need for region-specific studies to better understand the disease patterns and treatment outcomes. The epidemiology and outcomes of STS in SA patients remain poorly characterized. STS represents a small fraction of all malignancies; however, its burden on the healthcare system is significant owing to the complexity of management and the need for multidisciplinary care. Understanding clinical characteristics, prognostic factors, and treatment outcomes is essential for optimizing treatment strategies and improving patient care. This retrospective study aimed to evaluate the clinical characteristics, treatment outcomes, and prognostic factors of STS in SA. We sought to identify the key determinants of survival and disease progression by analyzing a cohort of patients treated at a tertiary referral center. The findings of this study will contribute valuable region-specific insights to the growing body of global STS literature, ultimately informing future clinical management guidelines tailored for this population.

Material and Methods

Patients and Methods

Electronic Medical Records of all STS patients managed between January 2010 and December 2020 at the King Faisal Specialist Hospital and Research Center (KFSH&RC), Riyadh, were reviewed. The study was approved by the institutional board review committee of KFSH&RC, which granted a waiver of informed consent, ensuring adherence to ethical standards and protection of patient confidentiality throughout the research process. Study data were collected and managed using REDCap electronic data capture tools hosted at the KFSH&RC.[11,12] Two independent physicians reviewed each chart; if there was a concern in either one, the chart was reviewed by a third investigator. The data obtained included age, sex, clinical presentation, including duration of symptoms, tumor site, tumor subtype (classified according to the World Health Organization [WHO] classification), and clinical stage at diagnosis (using the American Joint Committee on Cancer [AJCC] staging system). Information on the treatment approach was recorded, including surgical interventions, radiation therapy, and systemic therapy with response assessment using the Revised Response Evaluation Criteria in Solid Tumors (RECIST version 1.1). The outcome measure for this study was overall survival (OS), defined as the duration from diagnosis to death from any cause. The secondary outcomes included the pattern of presentation and duration of symptoms, distribution of STS subtypes, and treatment modalities for STS. Prognostic factors analyzed for their association with OS included age, sex, tumor size, facial involvement, Nodal metastasis, distant metastasis, and treatment modality. Because tumor size and T stage are closely related, we assessed them for collinearity before performing the multivariate analysis. Given the strong correlation observed, only the T stage was included in the final model to avoid redundancy and to ensure the stability of the estimates.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics and clinical characteristics, providing a clear overview of the study population, which involved assessing categorical values through frequency and continuous values through median with interquartile range (IQR). The Kaplan–Meier estimator was employed to calculate OS, and survival curves were compared using Log rank tests to assess statistical significance. Analyses were conducted using Cox proportional hazards regression to identify the independent prognostic factors affecting survival outcomes. Statistical significance was set at $p < 0.05$. Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS) for Mac, Version 30 (IBM Corp, Armonk, NY, USA).

Results

Patients and Disease Characteristics

The investigation included 214 eligible Saudi participants diagnosed with STS, with a median age of 37 years (IQR: 25–49.5), and a male representation of 120 individuals (56.1%). On examination of clinical presentation, 105 patients (49.1%) exhibited painless swelling, whereas 77 (36%) experienced painful swelling. The median duration of symptoms was 8 months (IQR: 4–13 months). Among the 141 cases with available data regarding familial cancer history, only two patients reported a positive family history of cancer.

Analysis of the distribution of the primary anatomical sites revealed that the lower limb was the most prevalent location, comprising 62.1% of the cases (n=133), whereas the upper limb accounted for 19.2% (n=41). Trunk involvement was recorded in 15.4% of cases (n=33), and 3.3% (n=7) were classified as having other or indeterminate primary sites. The median tumor size was 10 cm (IQR: 6.8–15). The tumors were found to be deep in the fascia in 144 patients (67.3%), whereas 37 cases (17.3%) were superficial. Concerning clinical staging, 131 cases (61.2%) presented with localized disease, while 83 cases (38.8%) exhibited metastatic characteristics. An overview of the patients and disease characteristics is presented in Table 1. The predominant histological subtype was synovial sarcoma, which constituted 42 cases (20%), followed by liposarcoma (29 cases, 13.6%), and undifferentiated pleomorphic sarcoma (25 cases, 12%). Additional information regarding the histological subtypes is shown in Figure 1.

Local Therapy

In total, 202 patients underwent locoregional treatment: surgery in 97 cases (45.3%), a combination of surgery and radiation in 89 cases (41.6%), or radiation therapy only in 16 cases (7.5%). Conversely, 12 patients (5.6%) did not undergo local treatment. Among the patients undergoing surgery, 107 achieved R0 resection, and six were classified as R1. At the first follow-up after therapy completion, 79 (36.9%) patients had no evidence of disease recurrence, 56 (26.2%) developed distant metastasis, and 11 (5.1%) experienced local relapses.

Systemic Therapy

Of the total population, 85 patients (39.7%) received systemic therapy, whereas 129 (60.3%) did not. Among those who received systemic treatment, the median age was 33 years, and the median primary tumor size was 10 cm (interquartile range [IQR], 8–17 cm). Fifty-three patients (62.4%) in this group had metastatic disease at diagnosis, while 32 (37.6%) had localized disease. Treatment regimens are as follows: 44 patients (51.7%) were treated with a combination anthracycline-based regimen, 24 patients (28.2%) received anthracycline alone, four patients (4.7%) were treated with gemcitabine, five patients (5.8%) received docetaxel, and eight patients (9.4%) received pazopanib. Recurrence occurred in 44 patients, and second-line chemotherapy was administered in 30 patients (14%).

Survival Analysis

The median follow-up duration was 65 months (95% CI, 54.3–75.64). The median OS of localized and metastatic disease was not reached vs 26 (95% CI: 16–35.5) months ($p< 0.01$) (Figure 2). The 3-year OS rates for localized and metastatic tumors were 84.9% and 40.0%, respectively. Statistically significant differences were observed in OS based on tumor sites ($p=0.03$), histological subtypes ($p=0.006$), T stage ($p=0.03$), Nodal metastasis ($p<0.001$), and metastasis at diagnosis ($p<0.001$). Cox regression analysis revealed that variables associated with better overall survival were primary site extremities, tumors less than 5 cm, negative regional lymph nodes, no metastasis, and treatment with surgery and radiotherapy. OS was significantly lower among elderly patients (≥65 years) than among adolescent and young adult (AYA) patients (15–39 years) ($p=0.002$). Although OS was worse in patients with tumor deep to fascia compared to those with superficial tumors, this difference was not statistically significant ($p=0.86$). Cox regression analysis of the variables associated with the overall survival of patients with STS is presented in Table 2. Local therapy for metastatic disease is associated with higher OS. The median OS for patients who underwent surgery, radiation, the combination of surgery and radiation, and no local treatment was 26, 23, 31, and 9 months, respectively ($p=0.004$) (Figure 3).

Discussion

This study provides an essential overview of the characteristics, treatment approaches, and outcomes of this rare malignancy within the region of a leading tertiary care hospital in SA that specializes in sarcoma care. These findings highlight several distinct features, including a relatively younger median age at diagnosis and a high prevalence of advanced disease at presentation. The clinical presentation was primarily characterized by painless swelling with a median symptom duration of 8 months. This emphasizes the need for increased awareness and early detection of STS among healthcare providers and the public. These results may reflect potential delays in diagnosis, lack of awareness, and disparities in access to healthcare within the region.

Table 1 Patient and Disease Characteristics, n=214

Characteristics	Number (%)
Age at diagnosis Median (IQR)	37 (25–49.5)
Gender	
Male	120 (56.1)
Female	94 (43.9)
Presentation	
Painless swelling	105 (49.1)
Painful swelling	77 (36.0)
Weight loss	4 (1.9)
Numbness/weakness	2 (0.9)
Fever	1 (0.5)
Jaundice	1 (0.5)
Incidental	1 (0.5)
NA	23 (10.7)
Primary sites	
Lower extremity	133 (62.1)
Thigh	76 (57.1)
Leg	39 (29.3)
Foot	18 (13.5)
Upper extremity	41 (19.2)
Forearm	10 (24.4)
Arm	29 (70.7)
Hand	2 (4.9)
Trunk	33 (15.4)
Retroperitoneum	2 (0.9)
Others/NA	5 (2.3)
T Stage	
T1 (≤5cm)	25 (11.7)
T2 (>5 to ≤10 cm)	68 (31.8)
T3 >10 to ≤15 cm)	71 (33.2)
T4 (>15 cm)	11 (5.1)
TX	39 (18.2)
Nodal metastases	
N0	165 (77.1)

(*Continued*)

Table 1 (Continued).

Characteristics	Number (%)
N1	41 (19.2)
Nx	8 (3.8)
Distant metastases	
M0	134 (62.6)
cM1	76 (35.5)
pM1	4 (1.9)
Metastatic Sites	
Lung (only)	42 (52.5)
Lymph node (only)	5 (6.2)
Lung and Lymph node	10 (12.5)
Lung and liver	8 (10.0)
Lung and bone	5 (6.2)
Lung and brain	3 (3.8)
Multiple sites	7 (8.8)

Abbreviation: NA, not available.

Our analysis of 214 patients revealed a median age of 37 years, similar to findings from Jordan (median age, 38 years) and younger than in other Middle Eastern and North African populations (47 years),[13,14] and markedly younger than in the Western population (67 years).[15,16] The younger age at diagnosis in our series could be related to the demographic profile of the SA population; however, these findings warrant further investigations to identify possible risk factors contributing to early-onset disease in the region. Male predominance in our cohort is consistent with regional reports and US databases.[14,17,18] Alternatively, some European studies have reported a higher incidence of STS in females, likely due to the inclusion of tumors arising from uterine and breast tissues.[19]

The lower limb was the most common site (62.1%), consistent with the existing literature,[14,20] and synovial sarcoma was the most common histological subtype, aligning with reports from other Middle Eastern countries.[13] In contrast, liposarcoma is more frequently reported in other regional series and Western populations.[14,17,21] This likely reflects potential differences in registry completeness, considering regional and ethnic differences in STS epidemiology.

Consistent with previous studies, the majority of patients in our cohort (>70%) presented with large tumors, with a median size of 10 cm.[22,23] The median diagnostic interval was 8 months, comparable with global reports, and likely contributed to the high metastatic rate by permitting progression even in extremity tumors, which are generally more amenable to early detection.[8,24,25] Previous studies have shown that patients with sarcomas in the trunk experience longer diagnostic intervals than those with extremity tumors (approximately 6.7 vs 3.2 months), highlighting the influence of tumor site on time to diagnosis.[25] Such delays, linked to poorer survival and greater metastatic risk, may result from patient factors, healthcare system limitations, and sociocultural barriers.[8,9] Overcoming them will require improved awareness, standardized referral pathways, equitable access to care, and management in high-volume multidisciplinary centers.[7,16,26]

Nearly 40% of our patients were diagnosed at the metastatic stage, which is higher than Western data, ranging from 10–20%.[3,22] This may be attributed to the prolonged diagnostic interval, which allowed disease progression, likely secondary to limited awareness, misdiagnosis, or the absence of streamlined referral pathways. A referral bias is also possible, as our tertiary center often receives more advanced cases. However, our cohort also showed a relatively high

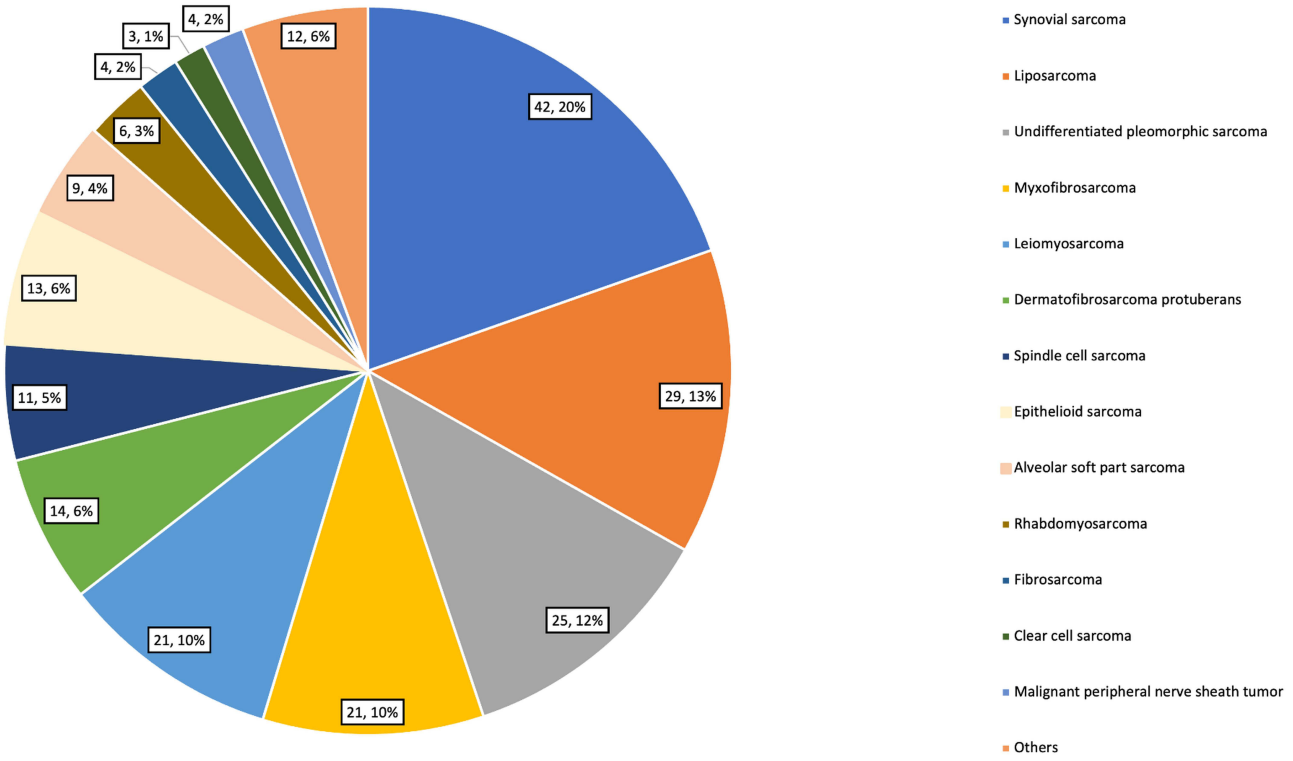

Figure 1 Distribution of histological subtypes of soft tissue sarcoma in the study cohort (n=214).

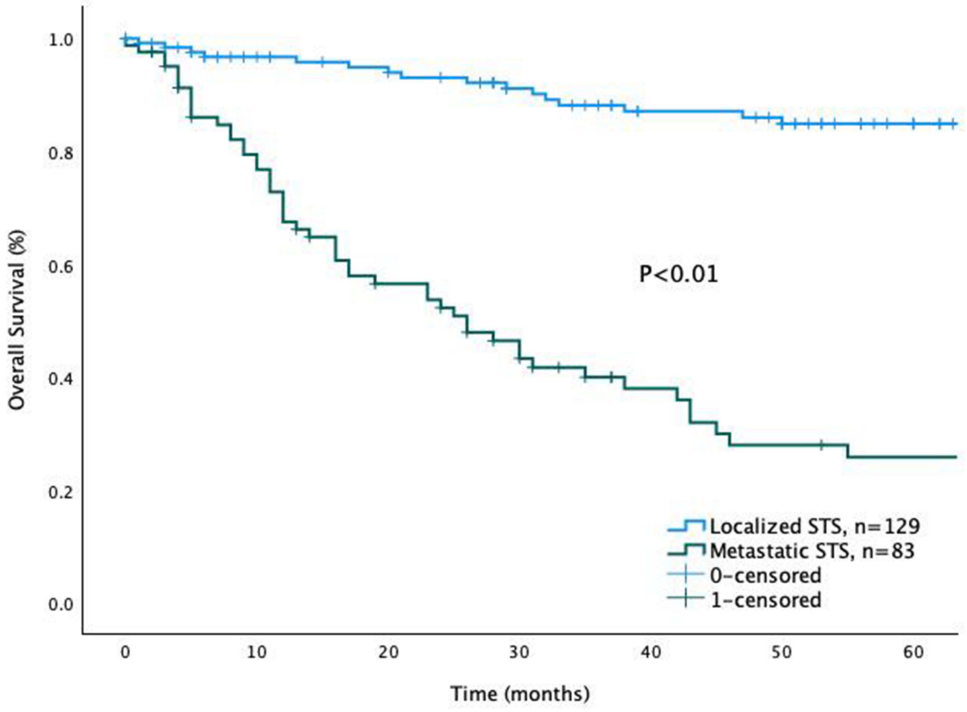

Figure 2 Kaplan–Meier curve for overall survival of patients with localized versus metastatic soft tissue sarcoma.

Table 2 Cox Regression of Variables Associated with Overall Survival of Patients with Soft Tissue Sarcoma

Variables	Univariant			Multivariant		
	Hazard Ratio	95% Confidence Interval	P-Value	Hazard Ratio	95% Confidence Interval	P-Value
Age						
15–39 years	Reference			Reference		
40–64 years	1.01	0.61–1.65	0.97	0.88	0.46–1.68	0.70
65 or above	2.09	0.93–4.69	0.07	6.05	1.96–18.72	0.002
Sex						
Male	1			1		
Female	1.22	0.77–1.94	0.38	1.42	0.77–2.94	0.25
Primary sites						
Trunk/others	Reference			Reference		
Extremities	0.46	0.28–0.78	0.004	0.38	0.15–0.98	0.04
T stage						
T1 (≤5cm)	Reference			Reference		
T2 (>5 to 10 cm)	3.05	1.05–8.84	0.04	2.67	0.60–11.95	0.19
T3 (≥10 to 15 cm)	3.68	1.26–10.68	0.01	3.62	0.80–16.37	0.09
T4 (>15 cm)	5.61	1.61–19.58	0.007	9.12	1.08–76.93	0.04
Nodal metastases						
N1	Reference			Reference		
N2	3.28	2.03–5.32	<0.001	1.08	0.46–2.51	0.84
Distant metastases						
M0	Reference			Reference		
M1	8.36	4.86–14.37	<0.001	8.77	4.14–18.58	<0.001
Tumor deep to fascia						
No	Reference			Reference		
Yes	2.08	0.88–4.86	0.09	1.10	0.35–3.40	0.86
Local Therapy						
None	Reference			Reference		
Surgery	0.24	0.11–0.53	<0.001	0.18	0.04–0.76	0.01
Radiation	0.69	0.27–1.74	0.44	0.18	0.03–0.87	0.03
Surgery and radiation	0.18	0.08–0.41	<0.001	0.13	0.03–0.60	0.009

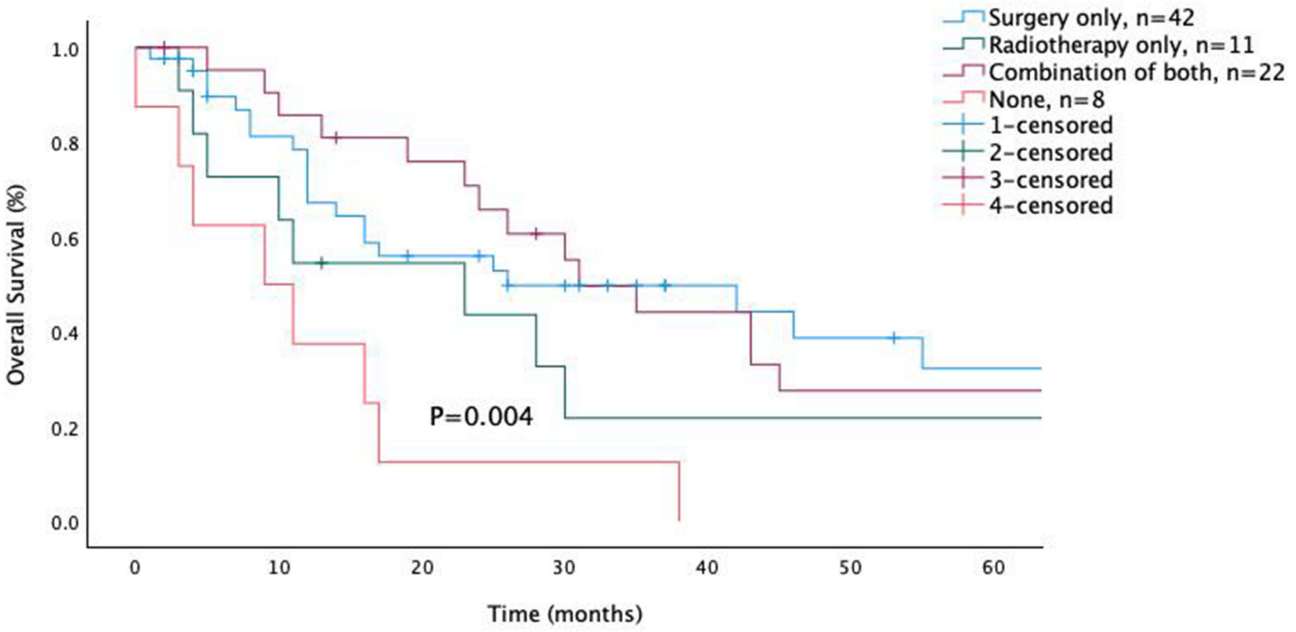

Figure 3 Kaplan–Meier curve for overall survival of metastatic soft tissue sarcoma based on local therapy modality (surgery, radiation, both, or none).

proportion of localized disease at diagnosis (61.2%), compared with the 62.0% metastatic rate reported from Middle Eastern and North African populations.[13] Perhaps this is due to a more significant proportion of patients being younger and having extremities as the primary site.

The treatment modalities employed in managing these patients, including surgery, radiation, and chemotherapy, reflect a multidisciplinary approach that is essential for effective STS management. The fact that 45.3% of the patients underwent surgical intervention and 41.6% received combined surgery and radiation resulted in an R0 resection rate of 57.5%, a figure likely lowered by the inclusion of patients with metastatic disease at presentation. The proportion of patients in our cohort receiving combined surgery and radiation (41.6%) includes all tumor sites. In contrast, 47% of patients reported in the U.S series had extremity soft-tissue sarcomas, limiting direct comparison.[27] In our cohort, radiation use was guided by tumor size, location, and margin status, consistent with evidence-based recommendations to reduce local recurrence. Synovial sarcoma tumors >5 cm were generally treated with chemotherapy, surgery, and radiation, consistent with international recommendations for high-risk STS aimed at improving local control and survival. Notably, the superior outcomes associated with R0 to local therapy in localized disease (96.9% three-year OS) reinforce the critical role of achieving complete tumor resection whenever feasible. The significant difference in the 3-year OS between localized disease in the extremities and trunk (90.9% vs 66.7%) highlights the importance of tumor location in prognosis. Moreover, the improved survival observed with local therapy in metastatic cases (median OS of 31 months for combined surgery and radiation vs 9 months for no local therapy) suggests the potential benefits of an aggressive multimodal approach for advanced-stage disease. However, this observation may in part reflect selection bias, as patients with better performance status or less aggressive disease were more likely to receive local therapy.

In our cohort, 39 patients underwent preoperative MRI, a critical tool for evaluating tumor size, local extent, and anatomical relationships. MRI findings may also provide insight into tumor grade, as features such as necrosis, signal heterogeneity, and peritumoral edema are more commonly observed in high-grade tumors.[28,29] Incorporating MRI into multidisciplinary decision-making enhances diagnostic precision, informs surgical planning, and facilitates personalized treatment approaches.

Saudi Arabia's healthcare system provides universal access through public and private sectors, but tertiary sarcoma care is centralized in a few major referral centers. Delays may occur due to limited awareness among primary care providers, non-standardized referral pathways, and distance-related access barriers. Expanding access to specialized multidisciplinary teams, improving education, and streamlining referrals could facilitate earlier diagnosis and better outcomes.

This study acknowledges the inherent limitations of its retrospective design, which may introduce selection bias and limit the generalizability of the findings to broader populations. Additionally, wide confidence intervals in some subgroups reflect small sample sizes and should be interpreted with caution. The lack of comprehensive data on key prognostic markers, including tumor grade and mitotic index (missing in 86% and 95.3% of cases), constrains a more detailed interpretation of the outcomes. Improving the quality and completeness of data will enable a better understanding of prognostic factors for survival outcomes. Therefore, standardizing reporting practices is essential to achieving these goals and establishing a more robust framework for future studies. Efforts should focus on establishing national registries and conducting prospective cohort studies. Collaborative networks among researchers, clinicians, and data scientists can further promote the sharing of best practices and insights, fostering a more comprehensive understanding of patient outcomes and treatment responses. This collaborative approach ultimately benefits patients by improving care strategies and outcomes.

Conclusion

This study contributes to the limited local data on STS in SA, highlighting its unique epidemiologic features, including a younger age at diagnosis and a high proportion of advanced-stage disease. These findings underscore the need for regional collaboration and prospective, multicenter research to characterize disease patterns further, improve outcomes, enhance diagnostic pathways, and strengthen data on key prognostic factors.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethical Considerations

This study was approved by the Research Advisory Council (RAC) of King Faisal Specialist Hospital & Research Centre (RAC number 2161205) with a waiver of informed consent. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2000). The participants remained anonymous, and no identifying or protected health information was recorded.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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