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Original Research Article

# A Hospital Based Clinical Assessment to Determine the Clinical Outcomes of Patients with Soft Tissue Sarcoma

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**Abstract**

**Aim:** The aim of the present study was to assess clinical outcomes of patients with soft tissue sarcoma.

**Methods:** The present study was conducted at IGIMS, Patna, Bihar, India for one year and 200 patients were included in the study. Demographic characteristics (age and sex), tumor-speci9c factors (site, histology, size, depth, surgical stage, and histologic grade), and treatment-speci9c factors (surgical margin and histological margin) data were collected from the patient medical records and reviewed.

**Results:** Male to female ratio was 40 to 60%. Median age was 53.5 years (range 18–84). Most patients had favorable RMH score (less than two 172/200, 86%); the remaining 14% of patients had an RMH score of two. Overall survival based on RMH score trended toward favoring lower scores, (Hazard Ratio = 2.0 (0.9, 4.6) for 1, 2 vs. 0, but was statistically inconclusive). Median OS was 24 months for RMH score 0 and was 12 months for patients with score 1–2 (P = 0.08). Performance status was also favorable with 192 patients (96%) with an ECOG 0–1. We found 14 different subtypes of sarcomas with 15 bone sarcomas and 50 soft tissue sarcomas.

**Conclusion:** STS present a treatment challenge due to their low incidence and atypical anatomic and histopathologic features. However, regardless of the treatment, long-term vigilance is required for these patients.

**Keywords:** clinical Outcomes, Soft Tissue Sarcomas.

## Introduction

Soft tissue sarcomas (STS) are rare heterogeneous tumors that account for <1% of all malignancies. [1] In general, 60% of STS in adults occur in the extremities [2], and only 15% occur in the upper limbs. [2-4] STS account for approximately 0.5% of all cancer-related deaths each year. [3] Approximately, 50% of STS of the upper extremities arise in the shoulder-upper arm region, 30%–40% in the elbow-forearm region, and only 10%–20% in the wrist-hand region.[5] The incidence of STS around the elbow is reported to be 3.8% of all soft tissue tumors.6 At present, surgery with wide margins is still the treatment of choice for localized STS in the extremities [7], and limb salvage surgery is preferred to maintain upper extremity function. [3]

Sarcomas are mesenchymal tumors of soft tissues and bone that are usually fatal when they progress beyond local control. Dating back to 1891, attempts have been made to treat sarcomas with immunotherapy [.8-11] These attempts were either with highly toxic "Coley's toxins" or less potent vaccine therapies as well as unsuccessful trials with interferons. Interestingly, osteosarcoma was one of the first cancers to get regulatory approval with an immunotherapeutic agent. Mifamurtide (L-MTPPE) is an agent that increased circulating TNFalpha and IL-6. It was approved in Europe for use in combination with adjuvant chemotherapy. [12,13] Alveolar soft part sarcoma has similarly shown response to immunotherapy with interferon, but only at the case report level. [14]

With the advent of modern immune checkpoint inhibitors several trials are ongoing to test the safety and efficacy of immunotherapy in sarcomas. Pre-clinical data suggests that tumor infiltrating lymphocytes (TILs) are an important positive prognostic indicator in multiple soft tissue sarcoma subtypes [15] including angiosarcoma [16] and gastrointestinal stromal tumor (GIST). [17] Especially with GIST, there is preclinical data to suggest that checkpoint blockade enhances activity of imatinib.[18] PD-L1 expression, which is an important biomarker of response to anti-PD-1 therapy for certain malignancies [19], has been investigated in sarcomas. One study found PD-L1 to be relatively uncommon except in GIST, spindle cell, and radiation associated sarcomas. [20] The SARC-028 study in particular showed signals of pembrolizumab activity in undifferentiated pleomorphic sarcoma and dedifferentiated liposarcoma. These two sarcoma cohorts are now undergoing expansion to further evaluate activity. [21] The results have been inconsistent across studies and while the overall trend is that immunotherapy doesn't have overwhelming activity in sarcomas as observed with melanoma or non-small cell lung cancer, it is clear that patients with certain sarcoma subtypes may respond and investigators continue to evaluate the use of immunotherapy in specific sarcomas such as alveolar soft part sarcoma. [22]

The aim of the present study was to assess clinical outcomes of patients with soft tissue sarcoma.

## Materials and Methods

The present study was conducted at IGIMS, Patna, Bihar, India for one year and 200 patients were included in the study. Demographic characteristics (age and sex), tumor-speci9c factors (site, histology, size, depth, surgical stage, and histologic grade), and treatment-speci9c factors (surgical margin and histological margin) data were collected from the patient medical records and reviewed.

Eligible patients had histologically confirmed invasive soft tissue sarcoma of the lung, bronchus, carina, or hilum with no known metastasis. Patients were

identified using site codes C340-C349 of the International Classification of Diseases for Oncology, third edition. Analysis was restricted to patients aged 20 years and older and underwent surgery, radiation therapy (RT), or both. Patients with Kaposi's sarcoma were excluded because the majority of these patients have acquired immunodeficiency syndrome, which would confound survival outcomes. Patients with rhabdomyosarcoma, Ewing's sarcoma, Askin tumor of soft tissue, peripheral neurectodermal tumor of soft tissue, and extrarenal rhabdoid tumor were also excluded from the analysis because the primary treatment of these tumors includes chemotherapy, which is not coded in the database.

### Statistical Analysis

All data were analyzed using R (version 2.13). Pearson's $\chi 2$ tests were used to analyze the frequency distribution of the categorical variables. Estimates of OS were calculated using the Kaplan–Meier method as a function on size, grade, and nodal status. Survival was also calculated for patients who underwent surgery alone, RT alone, or both. The log-rank test was used to determine whether differences in survival curves were statistically significant.

### Results

**Table 1: Patient characteristics**

| | |
|---|---|
| **Age** | |
| Median | 53.5 |
| Range | 18–84 |
| **Gender** | |
| Male | 80 |
| Female | 120 |
| **No. of metastatic sites** | |
| < 3 | 160 |
| >3 | 40 |
| **Albumin** | |
| > =3.5 g/dl | 90 |
| <3.5 g/dl | 110 |
| **RMH score** | |
| < 2 | 172 |
| >=2 | 28 |
| **ECOG PS** | |
| 0-1 | 192 |
| 2 | 8 |

Male to female ratio was 40 to 60%. Median age was 53.5 years (range 18–84). Most patients had favorable RMH score (less than two 172/200, 86%); the remaining 14% of patients had an RMH score of two. Overall survival based on RMH score trended toward favoring lower scores, (Hazard Ratio = 2.0 (0.9, 4.6) for 1, 2 vs. 0, but was statistically inconclusive). Median OS was 24 months for RMH score 0 and was 12 months for patients with score 1–2 (P = 0.08). Performance status was also favorable with 192 patients (96%) with an ECOG 0–1.

**Table 2: Histologic subtypes of sarcomas included in this study**

| | |
|---|---|
| Soft tissue sarcoma | 50 |
| Alveolar soft part sarcoma | 5 |
| Clear cell sarcoma | 2 |
| Desmoplastic small round cell tumor | 1 |
| Liposarcoma (Dedifferentiated) | 7 |
| Liposarcoma (Well-differentiated) | 2 |
| Gastrointestinal stromal tumor (GIST) | 10 |
| Leiomyosarcoma | 15 |
| Pleomorphic sarcoma | 1 |
| Sclerosing Epithelioid fibrosarcoma | 1 |
| Solitary fibrous tumor | 1 |
| Uterine carcinosarcoma | 1 |
| Bone sarcoma | 15 |
| Chondrosarcoma (High Grade, III) | 5 |
| Ewing sarcoma | 1 |
| Osteosarcoma | 5 |

We found 14 different subtypes of sarcomas with 15 bone sarcomas and 50 soft tissue sarcomas.

## Discussion

Metastatic, relapsed and refractory sarcomas continue to have a grave prognosis. There is considerable enthusiasm for developmental therapeutics in sarcomas with recent approvals of pazopanib, eribulin, trabectedin and olaratumab with doxorubicin. There are multiple trials ongoing with the combinations of these agents. [23-25]

Alektiar et al. [26] reported the clinical outcomes of STS arising in the knee and elbow. -eir study included 21 patients with elbow STS, wherein local recurrence developed in seven patients (33.3%). Although they analyzed prognostic factors, including knee STS, tumor size (>5 cm) was an independent prognostic factor of local recurrence. Emori et al. [27] reported a large series of STS in the elbow joint. Their study included 219 cases and local recurrence was observed in 21 cases. Gustafson and Arner [28] reported the clinical outcomes of STS arising in the upper extremity. Their study included 50 patients with STS in the upper arm, eight with STS in the elbow, and 40 with STS in the forearm. They reported that local recurrence developed in 15 of 28 patients who received inadequate treatment (surgery with an intralesional margin with or without adjuvant radiotherapy or surgery with a narrow margin without adjuvant radiotherapy). Additionally, local recurrence developed in 16 of 74 patients who received adequate treatment (surgery with a narrow margin with adjuvant radiotherapy or surgery with a wide or radical margin with or without adjuvant radiotherapy). -e authors considered that the tumor size in their series was relatively small compared with that in the lower extremity or trunk wall, which resulted in a favorable 5-yearmetastasis-free survival rate (72%).

Another interesting observation was seen in the patients with stable disease. It is entirely possible that some of the patients simply had indolent disease, such as the GIST and well-differentiated liposarcoma. However, osteosarcoma, dedifferentiated liposarcoma, and leiomyosarcoma are generally not considered indolent diseases and their stabilization in response to immunotherapy may serve as an indication of activity. While next generation sequencing (NGS) data was not available for the liposarcoma or leiomyosarcoma

patients, clinical grade NGS was performed on the osteosarcoma patient. This testing did not reveal a particularly high mutational load which is thought to increase response to immunotherapy. The response of the patients in our study along with recently reported abstracts of positive anti-PD-1 activity in diverse sarcomas suggests that earlier immunotherapy trials in sarcomas were not entirely correct in their negative experience. A recently completed phase II trial of pembrolizumab showed activity in undifferentiated pleomorphic sarcoma and dedifferentiated liposarcoma. [29] Another trial with advanced soft tissue sarcomas treated with pembrolizumab and metronomic cyclophosphamide yielded only one responder out of 50 treated patients. [30] While immunotherapy in sarcomas has shown small promise, we can say that it is unlikely to be the success that it has been in melanoma and non-small cell lung cancer. [31]

## Conclusion

In conclusion, STS present a treatment challenge due to their low incidence and atypical anatomic and histopathologic features. However, regardless of the treatment, long-term vigilance is required for these patients.

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