DOI: https://doi.org/10.54393/pjhs.v5i06.1689

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 6 (June 2024)

Original Article

Evaluation of Surgical Resection and Reconstruction Outcomes in Patients with Various Histological Subtypes of Soft Tissue Sarcomas: A Prospective Cohort Analysis

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ARTICLE INFO

Keywords:
Soft Tissue Sarcomas, Histological Subtypes, Surgical Resection

How to Cite:
Fatima, S., Akhlaque, R., Nasrullah, M., Amin, M., Imdad, S., & Imran, M. (2024). Evaluation of Surgical Resection and Reconstruction Outcomes in Patients with Various Histological Subtypes of Soft Tissue Sarcomas: A Prospective Cohort Analysis: Surgical Outcomes in Soft Tissue Sarcoma. Pakistan Journal of Health Sciences, 5(06). https://doi.org/10.54393/pjhs.v5i06.1689

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Received Date: 10th May, 2024
Acceptance Date: 24th June, 2024
Published Date: 30th June, 2024

ABSTRACT

Soft-tissue sarcomas (STS) are rare, especially as histological subtypes (more than 50). Despite being more prevalent in youngsters, their prevalence rises with age. **Objective:** To analyze the outcomes of surgical resection and subsequent reconstruction in patients with different histological subtypes of soft tissue sarcomas, focusing on the complications, recurrence rates, and overall survival. **Methods:** A prospective cohort study was conducted and data were collected from 14 patients treated between 2018 to 2022 at the Department of Plastic and Reconstructive Surgery, General Hospital, Lahore. The data included a detailed analysis of patient demographics, histological subtypes, surgical techniques, and postoperative outcomes, including complications, recurrence rates, and overall survival. **Results:** Soft tissue sarcoma was identified in 2 scalps, 2 arms, 3 forearms, 2 abdominal walls, 3 lower limbs, 1 nape of the neck, and 1 lumbar area. Two patients received neoadjuvant radiation and one chemotherapy. The tumors were 5–17.5 cm wide. Pleomorphic sarcoma was the most prevalent STS subtype, followed by liposarcoma and leiomyosarcoma in histology. This six-patient technique employed Latissimus dorsi, radial forearms, musculocutaneous gastrocnemius, free anterior lateral thigh (ALT) muscles, and year-end median. Complications occurred in 3 out of 14 patients who received flap reconstruction (complete flap failure in one patient, seroma in one patient, infection in one patient). The recurrence rate was 4 (28.6%) and survival rate was 13 (92.9%). **Conclusions:** This study concluded that R0 resection followed by immediate soft tissue reconstruction has helped in the management of such complex cases in terms of less complications and recurrence rate.

INTRODUCTION

Soft tissue sarcomas (STS) are an aggressive subtype of solid tumors that affect 1% of adults and 7% of children, with an annual incidence of 5 cases per 100,000 individuals [1]. A total of fifty distinct histological subtypes have been identified for STS. The most common STS in children is rhabdomyosarcoma, but undifferentiated pleomorphic sarcoma is more common in adults [2, 3]. Cervical sarcomas often present as soft, painless lumps. Both the patient and the clinician may fail to recognize the significance of swellings when the underlying reason is unclear. A much larger tumor is typically visible when a patient first visits the outpatient clinic after a delay in STS detection. Restoring these defects is a significant task for the plastic surgeon since complex abnormalities can result from the tumor's size and its connection with nearby tissues. Though the majority of STS are found on the limbs and trunk, a few may be seen in the retroperitoneal area [4]. When individuals with STS experience metastasis to the lungs, there's a good chance that the cancer will return locally. The main places for STS therapy should be tertiary care centers with specialized multidisciplinary teams of radiologists, pathologists, oncologists, and ablative and

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reconstructive surgeons [5, 6]. To get the best possible local therapy, it is essential to have sufficient resection margins as positive margins on surgical excision are the most important predictor of local recurrence [7]. The problem of attaining negative margins while keeping function is raised by the fact that STS typically occur near to or are principally associated with neurovascular systems. Results from studies using adjuvant and neoadjuvant radiation to treat cancer have demonstrated encouraging rates of limb salvage and sufficient resection margins. On the other hand, a lot of these removals are tricky and could need a lot of vascular repair or dissection [8]. There is a rare and difficult-to-treat subset of malignant tumors known as soft tissue sarcomas (STSs). These tumors are mesenchymal in origin and can develop anywhere in the body. Approximately half to two-thirds of STSs affect the extremities, which is why the name "extendity STSs" (ESTSs). As a therapy technique, surgery with negative margins which typically required amputation has provided the backbone [9, 10]. Disabilities and impairments that patients experience after undergoing amputation for ESTS therapy have caused significant distress due to the diminished level of functionality they experience. Results from a prior randomized prospective research comparing limb-sparing surgery with radiation to amputation for patients with ESTS found no change in OS or disease-free survival (DFS) [11]. Surgery for the treatment of ESTS is typically performed in conjunction with radiation, either before, during, or after the operation, to preserve the best possible structure and function of the limbs and joints. When treating non-metastatic sarcoma, it is crucial to remove the tumor completely while maintaining an adequate margin of healthy tissue. In STS, tumor resection with R0 margins is considered the gold standard [7]. By definition, "R0" resection involves removing the tumor's margins. As an alternative to the traditional practice of amputation, modern clinical practice includes limb-sparing resections for the majority of patients, all while maintaining sufficient survival rates [8]. Patients whose cancer has spread to other parts of the body may have adjuvant radiotherapy and chemotherapy as part of their treatments [9].

This study aimed to demonstrate how the tumor board's collective knowledge and the outcomes of interdisciplinary collaboration are critical to attaining both local disease management and disease-free survival.

METHODS

A prospective cohort analysis of all patients who underwent interdisciplinary surgical therapy for soft-tissue sarcomas at Lahore General Hospital, Lahore over a period of 5 years from 2018 to 2022 after getting approval with reference (111-2017). Fourteen individuals were considered for inclusion and patient's consent was obtained before study. Because the needed sample size was 14 patients, the estimation of the sample size was based on the prevalence of 18%, the margin of error was 10%, and the confidence interval was 95%. The non-probability purposive sampling approach was modified to fit the situation. Histologically verified STS diagnosis and therapy at our center were the inclusion criteria for this investigation. Patient demographics (median age and sex), cancer treatment modalities (neoadjuvant radiotherapy, neoadjuvant chemotherapy, adjuvant radiotherapy, and adjuvant chemotherapy), tumor characteristics (tumor location, tumor size, histological subtypes), reconstructive methods utilized post-tumor ablation, and post-operative follow-up were among the many pieces of information drawn from electronic health records. All the patients with a clinical history of pain and swelling in any region of the body with the size of the swelling equal to or greater than 5cm, progressive increase in the size of the swelling, or solid masses originating in deep subfascial planes were first investigated with X-ray to rule out bony tumors followed by MRI with contrast. The conventional method of diagnosis, after appropriate imaging evaluation, was doing several core needle biopsies (with needles >16G). For the superficial lesions, nevertheless, an incisional biopsy was performed. The senior surgeons were the ones who conducted the biopsies. The plan called for the last operation to remove the scar and the biopsy route without causing any harm. The research covered all individuals whose tumors were found to be soft tissue sarcoma. When the first diagnosis was made outside of our clinic, we always sought a second opinion from a pathologist. The American Joint Committee on Cancer (AJCC) approach was used for staging, which involved recording the tumor's location, size, and depth relative to the muscle fascia. Staging with the AJCC does not apply to certain types of cancer, such as angiosarcoma and Dermatofibrosarcoma Protuberans (DFSP). All such cases were then discussed in a tumor board meeting together with the pathologist, radiologist, ablative surgeon, plastic surgeon, and clinical oncologist. The management plan regarding neoadjuvant chemo/radiotherapy and excision of STS followed by reconstruction was delineated and documented. The recommendations of the tumor board were explained and thoroughly discussed with the patient including all surgical options, the pros and cons of each option, and the role of neo-adjuvant or adjuvant chemo/radiotherapy. Patients with Stage I-III tumors were planned for surgery however Stage IV tumors were not operated and were sent for radiation. The tumor resection was performed by the ablative surgeon (general surgeon/neurosurgeon and/or

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orthopedic surgeon). The R0 resection margins were obtained by achieving histopathologically negative margins on frozen section. Eight to ten tissue fragments were harvested from the tumor bed for the frozen section. After confirming margin clearance, the immediate reconstruction was carried out by the plastic surgery department. The radiation therapy was employed as a part of the standard treatment protocol in all tumors > 5cm in maximum dimension, high-grade tumor histology, and deeply located STS following primary wound healing in 3-4 weeks. Radiation therapy was not considered in cases where a true compartmental resection of the tumor-containing compartment was done. Although it is not typically recommended for adult-type soft tissue sarcomas, high-risk individuals may be offered adjuvant chemotherapy as an alternative therapeutic option. During the first two to three years, patients were monitored every three to four months. After that, biannually until the fifth year, and then annually after that. Outcomes of surgical resection and subsequent reconstruction in patients with different histological subtypes of soft tissue sarcomas, focusing on the complications, recurrence rates, and overall survival. SPSS version 23.0 was used for statistical analyses. Frequencies and percentages were used for categorical variables.

RESULTS

The median age of the patients was 42.1 years, where 8 patients were male while 6 patients were female. Among all, 11 patients were married and 3 were non married. Majority of the cases 9 had rural residency and 10 cases had poor socioeconomic status. Neoadjuvant radiation was administered to two patients, whereas one patient underwent neoadjuvant chemotherapy. Adjuvant radiation was given to nine individuals and adjuvant chemotherapy to two patients after surgery. The tumors ranged in size from 5 cm to 17.5 cm round (Table 1).

Table 1: Demographics of the Presented Cases

Variables	Frequency/Percentage
Median Age (Years)	42.1
Gender	
Male	8 (57.1%)
Female	6 (42.9%)
Marital Status	
Married	11 (78.6%)
Unmarried	3 (21.4%)
Residency	
Urban	5 (35.7%)
Rural	9 (64.3%)
Socio-economic status	
Poor	10 (71.4%)
Middle/High	4 (28.6%)
Techniques	
Neoadjuvant Radiation	2 (14.3%)
Neoadjuvant Chemotherapy	1 (7.1%)
Adjuvant Radiation	9 (64.3%)
Adjuvant Chemotherapy	2 (14.3%)
Mean Size of Tumor (cm)	11.4

It was found that 2 patients had soft tissue sarcoma of the scalp, and 02 of the arms, 03 patients had sarcoma of the forearm, 02 had abdominal wall sarcoma, 03 patients had lower limb sarcoma while 1 patient had STS at the nape of the neck, and 1 had STS of the lumbar area. Histopathological examination revealed that pleomorphic sarcoma, liposarcoma, and leiomyosarcoma were the most prevalent subtypes of STS. Spindle cell sarcoma, chondrosarcoma, synovial sarcoma, and dermatofibrosarcoma protuberans were among the other subtypes that were identified. Unclassified sarcoma was the diagnosis for one patient's sample. The most frequently used flap was Latissimus dorsi muscle in 6 patients, Radial forearm free flap in 3patients, vertical rectus abdominis myocutaneous (VRAM) flap (2 patients), while 1 patient's defect was reconstructed using a free anterior lateral thigh (ALT) flap. A musculocutaneous gastrocnemius flap was used for reconstruction in 2 patients (Table 2).

Table 2: Results Showing Tumor Location, Type, and Reconstruction Done

Area of Tumor	No. of cases	Nature of Tumor	Frequency/Percentage
Scalp	2	Dermatofibrosarcoma protuberans	Free Latissimus Dorsi Flap
		Pleomorphic sarcoma	Free Latissimus Dorsi Flap
Arm	2	Synovial sarcoma	Free Radial Forearm Flap
		Pleomorphic sarcoma	Free Radial Forearm Flap
Forearm	3	Spindle cell sarcoma	Free Latissimus Dorsi Flap
		Liposarcoma	Free Radial Forearm Flap
		Pleomorphic sarcoma	Free Anterolateral thigh Flap
Nape of Neck	1	Pleomorphic sarcoma	Pedicled Latissimus Dorsi Flap
Lumbar Area	1	Leiomyosarcoma	Pedicled Latissimus Dorsi Flap
Abdominal Wall	2	Leiomyosarcoma	Vertical Rectus Abdominis Flap
		Liposarcoma	Vertical Rectus Abdominis Flap
Lower Limb	3	Liposarcoma	Pedicled Gastrocnemius Flap

The median follow-up was 12 months. Complications occurred in 3 out of 14 patients who received flap reconstruction (complete flap failure in one patient, seroma in one patient, infection in one patient). Recurrence rate was 4 (28.6%) and survival rate was 13 (92.9%) (Table 3).

Table 3: Outcomes Among All Cases After Therapy

Variables	Frequency/Percentage
Complications	
Flap Failure	1 (7.1%)

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Seroma	1(7.1%)
Infection	1(7.1%)
Recurrence Rate	
Yes	4(28.6%)
No	10(71.4%)
Survival Rate	
Yes	13(92.9%)
No	1(7.1%)

After achieving R0 tumor resection under frozen section control, all patients required either a pedicled or a free flap for resurfacing the complex soft tissue defects. One complete free LAD flap loss was encountered for scalp reconstruction, for which a local scalp flap was performed. The other patient with seroma formation was dealt with ultrasound-guided aspiration while for one patient with infections, culture-specific intravenous antibiotics were administered for a period of 1 week.

Once the wounds healed in 3-4 weeks, patients were referred to medical oncologist for adjuvant radiotherapy/ chemotherapy. Secondary reconstructions for functional recovery of limbs included nerve grafting in 2 patients and tendon transfers in 2 patients(figure 1).

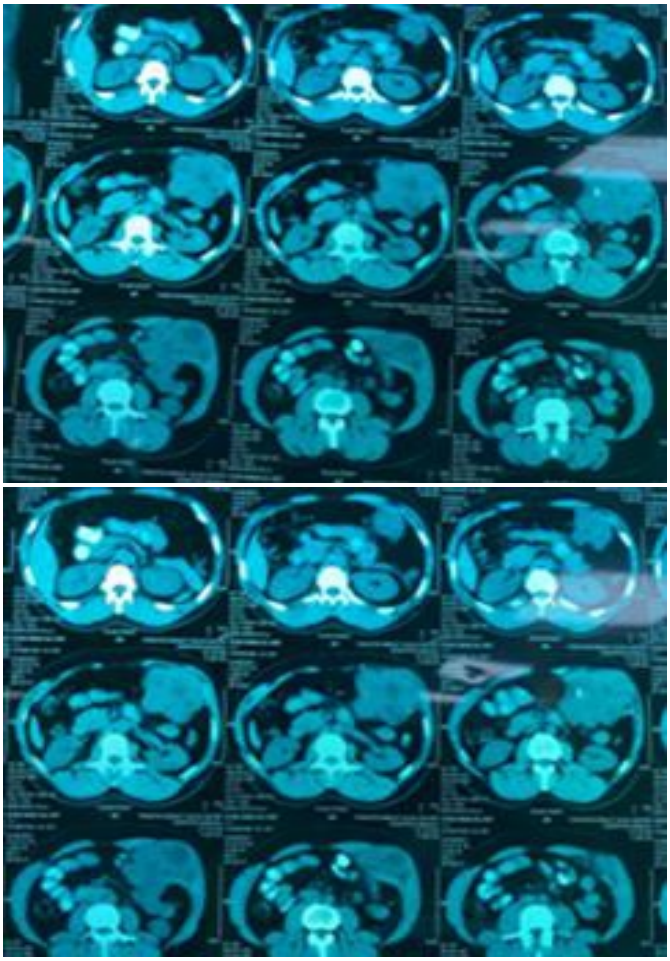

Figure 1: MRI Scans of Tumors

DISCUSSION

An early interdisciplinary strategy is necessary to prepare every patient receiving therapy for soft tissue sarcoma for excision and reconstruction. Urgent referral to a specialized sarcoma centre is required for all patients presenting with a soft-tissue tumor of unknown origin suspected of being sarcoma. When diagnosing STS, the gold standard diagnostic imaging method is magnetic resonance imaging (MRI) using diffusion-weighted imaging. Necrotic areas, fluctuating T2 signal intensities, and peritumoral postcontrast enhancement are hallmarks of high-grade (G3) tumors [10]. Also, MR can show you how big the tumor is, how far it has invaded if it has spread to other tissues, and how the lymph nodes are doing. There are three options for mass size and depth-based biopsy: core needle, incisional, and excisional. Excisional biopsies are a good choice for superficial masses with a diameter of 3 cm or less than 11 cm. With many passes and a gauge size of 16, core needle biopsy can detect STS subtypes with less problems compared to incisional biopsy, according to current research. Histological findings can differ and diagnostic errors are common since STS contains many distinct kinds of tumors. Because of the variety of possible STS diagnoses, only a highly trained sarcoma pathologist can be trusted with the task of analyzing biopsy results [11]. Medical oncologists, radiologists, pathologists, radiotherapists, ablative and plastic surgeons, and members of a multidisciplinary tumor board should convene to assess treatment regimens. Neoadjuvant therapies include but are not limited to, chemotherapy and radiation therapy. It is essential to have a multidisciplinary team look at patients before, during, and after surgery for a proper diagnosis. To reduce the chance of local recurrence, radiation is an important part of STS therapy regimens for Stages II, III, and IV [12, 13]. Even though no new evidence has emerged to support the claim that adjuvant or neoadjuvant radiation methods are better, the debate about how many despite the increased risk of acute wound complications and flap failure associated with neoadjuvant radiation, it does provide certain advantages, such as decreased edema and joint stiffness as well as lower fibrosis, in long-term follow-ups compared to adjuvant radiotherapy. Systemic chemotherapy is an effective treatment for advanced or metastatic tumors of the skin [14, 15]. Conventional cytotoxic chemotherapy has relied on anthracycline (doxorubicin) and ifosfamide derivatives [16, 17]. However, new experiments have cast doubt on their effectiveness owing to severe toxicity and poor treatment results. New targeted medicines, such as trabectedin for liposarcoma and leiomyosarcoma, have been developed as a result of discoveries in molecular etiology [18, 19]. Extensive excision is necessary after histological confirmation of STS to guarantee margins free of tumors as small as microscopic particles. Inadequate

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marginal resections cannot ensure R0 resection. Although amputation of the affected limb was once the norm for sarcoma treatment, recent data shows that R0 resection can provide the same or better long-term outcomes without the limb being amputated. By carefully removing the tumor while leaving intact surrounding tissue, a wide resection ideally makes the tumor undetectable. Radical tumor removal with neighboring muscle tissue and nerves preserved or functional deficiencies repaired by additional treatments are examples of how preservation of function is prioritized [20]. It is critical to immediately use vascularised soft tissue for defect restoration following R0 resection. Furthermore, it is not necessary to remove the whole compartment if the tumor does not extend into or through the muscle's origin or insertion. When combined with aggressive tumor removal, preserving function by removing nearby muscle tissue around the tumor was just as effective as removing the entire compartment in terms of long-term survival. To avoid damaging surrounding nerves due to inadequate tumor removal, epineural dissection is used. Although amputation of the leg is not always necessary, tumor infiltration of arteries and/or nerves necessitates resection and, if necessary, regeneration of these tissues [21]. When a tumor has progressed too far when a patient is too elderly or too sick to undergo complex repair, or in other severe cases, amputation of a limb may be required. Surgical treatment can be broadly classified as oncological excision, bone and soft tissue repair, and nerve and vascular or functional reconstruction [22]. The wide range of flaps used for reconstruction demonstrates the difficulty of surgically treating STS in the limbs [23]. Before choosing the best flap, it is important to study the location, diameter, depth, and nearby vessels. Surgeon discretion dictates whether reconstruction occurs simultaneously with tumor removal or after histological confirmation of an R0 resection. A two-step procedure can minimize complications caused by positive margins after the initial resection and allows for more exact planning of the required repair, but a one-step procedure has the benefits of less time spent in the hospital and faster recovery. In our study Complications occurred in 3 out of 14 patients who received flap reconstruction (complete flap failure in one patient, seroma in one patient, infection in one patient). The recurrence rate was 4 (28.6%) and the survival rate was 13 (92.9%). The results were in line with the previous research [17-20]. However, when problems are detected, a two-step method is necessary. Recent research has shown that NPWT, or a vacuum-assisted closure regimen, can lessen the occurrence of wound problems during the excision to the reconstruction process [24]. Before creating surgical procedures for each patient, it is crucial to evaluate the vascular status in the limbs, especially around the tumor [25]. Furthermore, to further enhance reconstruction safety and prevent flap loss, intraoperative imaging using indocyanine green angiography or blood flow analysis is an option [26]. It may be possible to avoid ligating the vessels during resection and avoid leaving no recipient vasculature to support the anastomosis of free flap vessels if a one-step approach is considered in cases where free flap reconstruction is necessary but the only large vessels in the tumor region are invading the tumor [27]. After the tumor is removed, there are no longer any recipient vessels. The recipient vasculature can be built as an arteriovenous loop for the rest of the therapy in a one- or two-step method. The ALT flap and the VRAM flap are two examples of pedicled flaps that may be used to conceal defects; they are commonly used on the anterior lateral thigh and in the groin [28]. These flaps can also be used in a free-flap fashion [29]. For greater anomalies, a combination of latissimus dorsi and para scapular or serratus anterior muscle flaps might be used to augment the flap area. Although nerve grafts can help restore large nerves that have been amputated after surgery, tendon transfers are often required for optimal motor recovery. Performing functional muscle transfers is also a common procedure. There is reason to question the study's validity due to the tiny sample size. The observed trends highlight the importance of early patient assessment for rapid reconstructive surgery following Ro resection; however, more study is required to confirm these results. The absence of an internal control group is only one of several limitations that must be acknowledged in this study. In addition, additional subgroup analysis is not feasible due to the series' short size and heterogeneity. Although our Institute is a national reference center, the amount of samples and diagnostic heterogeneity are correlated with the rarity of individual tumors.

CONCLUSIONS

It was concluded that R0 resection followed by immediate soft tissue reconstruction has helped in the management of such complex cases in terms of less complications and recurrence rate. Free flaps have revolutionized the entire management of soft tissue sarcomas as large defects can be reconstructed immediately. The multimodality approach remains the standard of care in such complex cases.

Authors Contribution

Conceptualization: SF, RA
Methodology: SI, MI
Formal analysis: MN, MAA
Writing-review and editing: SF, RA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

DOI: https://doi.org/10.54393/pjhs.v5i06.1689

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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