



Early Complications after Limb Salvage Procedures: Prospective Cross Sectional Study

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ABSTRACT

Introduction: Sarcomas are tumors that are mesenchymal in origin involving bone and soft tissues occurring in all age groups. Giant cell tumor, although benign, is locally aggressive and can also destroy the bone. Amputation was once considered primary treatment but now with advancements in diagnostic imaging modalities, surgical procedures and adjuvant therapies, limb salvage surgeries have become the preferred treatment modality.

The primary objective of our study was to determine the incidence of early complications occurring within the first thirty days in patients who underwent limb salvage surgery at our hospital. The secondary objective was to assess the association of these complications with patient-related factors, surgical modality, tumor characteristics and neoadjuvant therapy.

Methodology: All the patients with bone or soft tissue sarcoma and aggressive giant cell tumors of the extremities who underwent wide excision and limb salvage surgery from February 2020 to December 2021 were included in this study. Data were collected prospectively on follow-up visits in the clinic for one month. Data were compiled and analyzed using SPSS version 22. A p-value of <0.05 was considered significant throughout the study.

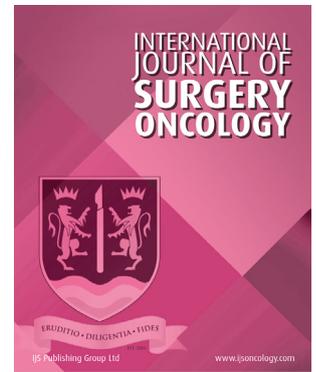
Results: A total of 60 patients were included in this study. The mean age of the patients was 39.90 years. Bone and soft tissue tumors were found in 35 and 25 patients respectively. A total of 13 patients experienced postoperative complications within 30 days of surgery. The association of these postoperative complications with gender distribution, prior comorbid conditions, type of tumor, anatomical location of the tumor and neoadjuvant therapy was found to be statistically insignificant.

Conclusion: The most frequently occurring postoperative complications are wound-related and the incidence of these complications is independent of the proposed risk factors.

Research registry number: Researchregistry4695.

HIGHLIGHTS

1. Limb salvage surgery though beneficial for patient, comes with pros and cons including early post-surgery complications.
2. Our study showed wound related complications are most commonly occurring in patients who underwent limb salvage surgery.
3. Surgical site infection followed by wound dehiscence was most frequently found early complication that occurred within 30 days of surgery.



CROSS SECTIONAL STUDY



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KEYWORDS:

Limb Salvage; Salvage Surgery;
Orthopaedic Oncology;
Musculoskeletal Cancer
Surgery

TO CITE THIS ARTICLE:

Ali Z, Saeed J, Umer M.
Early Complications after
Limb Salvage Procedures:
Prospective Cross Sectional
Study. *International Journal
of Surgery: Oncology*. 2022;
7(1), 75–80. DOI: [https://doi.
org/10.29337/ijsonco.143](https://doi.org/10.29337/ijsonco.143)

INTRODUCTION

Sarcomas are tumors of mesenchymal origin that make up a heterogeneous group of more than 80 tumors [1]. These can be broadly categorized into bone sarcomas including osteosarcoma, chondrosarcoma, multiple myeloma, Ewing sarcoma and soft tissue sarcomas comprising liposarcoma, fibrosarcoma, leiomyosarcoma, synovial sarcoma, rhabdomyosarcoma, pleomorphic sarcoma, malignant nerve sheath tumor & spindle cell sarcoma [2]. Epidemiological statistics show that bone sarcomas account for a total percentage of 0.2% of all malignancies with an incidence rate of 0.9 per 100000 people, annually [3]. Giant cell tumors are although non-cancerous but very aggressive locally, typically involving the metaphysis of long bones [4].

Historically, amputation was being adapted solely as the treatment of these musculoskeletal tumors to achieve sufficient margins. However, over the past years due to the advancement in diagnostic imaging modalities, surgical procedures and adjuvant therapies, limb salvage surgeries have now become the new treatment paradigm. The primary aim of the management is to control the local spread of the tumor with minimal complications, preserve the surrounding neurovascular and musculoskeletal structures, reconstruct the limb and restore its function [5]. Limb salvage surgeries thereby reduce morbidity and raise the quality of life. Considering the new treatment modalities, now amputation is only reserved for the cases in which tumors are extending beyond the compartment boundaries when there is extensive neurovascular damage or failure of the limb-sparing procedure [6]. Previously considered absolute contraindications to limb salvage surgery i.e., pathologic fractures and neurovascular bundle involvement are now considered relative contraindications [7, 8]. Limb sparing procedures include wide margin excision of the tumor in case of soft tissue tumor whereas in the case of bone sarcoma, the limb salvage procedure requires wide margin excision of the tumor, removal of the diseased bone and reconstruction of the limb via using grafts (allografts or autografts) or endoprosthesis [9].

Limb salvage surgeries have better cosmetic results and more functional outcomes. Tumor surgery, chemotherapy, radiation, and imaging technologies have all improved considerably over the past few years and due to this reason, the number of limb sarcoma survivorship studies (LSS) has increased [10]. There is research on complications of limb salvage surgeries in patients with malignancies from other world regions; however, data from our region is sparse [11, 12, 13].

STUDY RATIONALE

Complications of limb salvage surgery in a well-equipped hospital in Pakistan and what risk factors are likely to be associated with these complications. A higher complication rate would warrant a change in indications and surgical technique.

STUDY OBJECTIVE

The primary objective of our study was to determine the incidence of early complications occurring within the first thirty days in patients who underwent limb salvage surgery. The secondary objective was to assess the association of these complications with patient-related factors, surgical modality, tumor characteristics and neoadjuvant therapy.

METHODOLOGY

This prospective study was conducted at the Section of Orthopedics, Department of Surgery, Aga Khan hospital, Karachi. Appropriate approvals were obtained from the Hospital Ethical Review Committee.

All patients with primary bone or soft tissue sarcomas and aggressive giant cell tumors of the extremities who underwent limb salvage surgery from February 2020 to December 2021 were included in this study. Data was collected on follow-up visits of all these patients by a senior orthopaedic surgeon and a dedicated orthopedic research officer over thirty days. Patients who underwent only curettage for high-grade giant cell tumors and those who were lost to follow-up were excluded from this study.

Patient demographics, prior comorbid conditions, tumor characteristics, surgical modalities and the complications occurring in early post-operative were extracted as variables of interest. The data were assessed for local and systemic complications. A cut-off of 30 days was used to calculate the incidence of these post-procedural complications.

After the data was collected, it was compiled and analyzed by using SPSS (Statistical Package for the Social Sciences). A p-value of <0.05 was considered significant throughout the study. Quantitative variables such as age were reported as mean and standard deviation. Qualitative variables such as gender and complications were mentioned as frequency and percentage. The association of qualitative variables with the postoperative complications were assessed by using the chi-square/fisher exact test. This study has been registered in the research registry, the number is researchregistry4695 and it is being reported in line with STROCSS research reporting guidelines [14].

RESULTS

The mean age of our patients was 39.90 years (SD = 18.98) ranging from 4 years to 74 years. Of these patients, 41 were males and 19 were females. Twenty-one out of 60 patients had prior comorbid conditions accounting for 35%, with 25 per cent of patients having high blood pressure, 20% having diabetes, and 6.7% having a body mass index (BMI) greater than 25, compared to 65% of patients who did not

have any comorbid condition. Family history of tumors was found to be positive in 13.3% of cases.

Twenty-five patients had Bone tumors, while soft tissue tumors were present in 35 patients. The lower limb was the most common site of tumor involvement; there were 38 patients with lower limb tumors followed by upper limb tumors in 19 patients and pelvic tumors in 3 patients.

The final diagnosis in 11 patients was myxofibrosarcoma, 9 patients had osteosarcoma, 7 had Ewing's sarcoma and liposarcoma each and 5 had spindle cell sarcoma (Table 1).

Out of these 60 subjects, 23 underwent wide margin excision, 16 underwent WME+flap coverage, 14 underwent WME + endoprosthesis and 4, 2 and 1 underwent WME+ autograft reconstruction, hemipelvectomy and WME + fresh allograft reconstruction respectively. A total of 36 patients received neoadjuvant therapy in the form of chemotherapy/radiotherapy or a combination of both.

The total number of patients who experienced any complication following surgery was found to be 13. As shown in Table 2, most of these postoperative complications were wound related, 4 patients had deep infection followed by delayed wound healing in 3 patients and 1 patient experienced superficial site infection. Wound dehiscence occurred in one patient. One patient experienced a neurological complication of foot drop. On the twentieth postoperative day, 1 patient had disruption of pseudoarthrosis of the shoulder joint and similarly, 1 patient experienced postoperative hematoma collection on day 16. No systemic pulmonary or neurological complications were noted.

We studied the association between various parameters using chi-square tests and found no significant statistical association between early complications and gender, prior comorbid conditions, type of tumor, location of tumor and provision of neoadjuvant therapy (p -value > 0.05) Table 3.

DISCUSSION

Although limb salvage surgical techniques have advanced significantly in recent years, early postoperative complications continue to be a major cause of morbidity. According to our study, 21.7% of patients experienced complications in the first thirty days after surgery. In a retrospective study by Gallaway, Kathryn E et al. overall, 14.0% of patients reported at least one complication within the first 30 days after surgery for sarcoma of the limbs, out of which the most frequent complication was surgical site infection (superficial and deep both) making up 4% and 3% of the total patients followed by wound dehiscence which made up 1.8% [15]. These results are quite similar to our study in which out of 60 patients 4 had deep site infection and 1 had superficial site infection making up

TUMOR TYPES	FREQUENCY- n (%)
Myxofibrosarcoma	11
Osteosarcoma	9
Ewing sarcoma	7
Liposarcoma	7
Spindle cell sarcoma	5
Synovial sarcoma	4
Metastatic tumours	3
Giant cell tumour	3
Pleomorphic sarcoma	3
Chondrosarcoma	2
Malignant nerve sheath tumor	1
Leiomyosarcoma	1
Clear cell sarcoma	1
B cell lymphoma	1
Malignant melanoma	1
Squamous cell carcinoma	1
Total	60

Table 1 Types of Tumors.

COMPLICATIONS	n (%)
Deep infection	4 (6.7%)
Delayed wound healing	3 (5%)
Superficial site infection	1 (1.7%)
Wound dehiscence	1 (1.7%)
Neurovascular complications	1 (1.7%)
Disruption of pseudoarthrosis	1 (1.7%)
Hematoma collection	1 (1.7%)
Total complications	13 (21.7)

Table 2 Early Complication with 30 days of surgery.

	FREQUENCY – n (%)	p-value
<u>Gender</u>		0.552
Male	8 (19.5%)	
Female	5 (26.3%)	
<u>Comorbidities</u>		
Yes	6 (28.6%)	0.341
No	7 (17.9%)	
<u>Type of tumor</u>		
Bone tumor	6 (24.0%)	0.711
Soft tissue	7 (20.0%)	
<u>Anatomical location of the tumor</u>		0.392
Upper limb	6 (31.6%)	
Lower limb	7 (18.4%)	
Pelvis	0	
<u>Neoadjuvant therapy</u>		
Yes	10 (27.8%)	0.159
No	3 (12.5%)	

Table 3 Association of postoperative complications with patient-related factors and tumor characteristics.

6.7% and 1.7% respectively, and wound dehiscence was observed in one patient accounting for 1.7%.

Gharedhagi, Muhammad et al. in a retrospective cohort study including 40 patients reported a complication rate of 45.4% following limb salvage surgery which is quite higher than our study. This difference may be due to the longer duration of follow-up (24 months) as compared to our study which was 30 days only [16] and for such reason long-term complications such as allograft nonunion, prosthesis fracture and loosening, allograft fracture and implant failure were not reported in our study. Moore et al. in a retrospective study including 256 cases reported a 17.6% rate of major wound complications occurring in a median of 21.5 days after soft tissue sarcoma resection [17].

Additionally, a retrospective study by Yoichi Kaneuchi et al, reported that out of total of 65 patients aged <10 years with primary osteosarcoma who underwent limb salvage surgery, 46% faced postoperative complications out of which 24 patients developed early complications (<6 months) [18]. In our study, only 3 out of 60 patients were aged <10 years out of which 1 patient developed superficial site infection. However, the quoted study included only patients who were less than 10 years of age and in our study patients of all age groups were included which could account for the difference observed in this study.

Patient demographics including age, gender and prior comorbid conditions, type and location of the tumor, type of procedure and the provision of neoadjuvant or adjuvant therapies are all proposed risk factors for the occurrence of postoperative complications. A higher incidence of wound complications was linked to patients' comorbidities in the previous literature [17]. However, according to our findings, there is no significant association between the incidence of postoperative complications and patient demographics (p-value > 0.005).

Korah et al. concluded that the anatomical location of the tumor was one of the most important risk factors for postoperative wound complications. Anatomical differences, such as the proximity of critical neurovascular structures and joint spaces, complicate surgical resection. Concerning the location of sarcomas, previous literature has shown that wound complications were more common in instances involving the lower extremities [19]. In addition to being rare, pelvic sarcomas arise close to the neurovascular structures and viscera thereby posing a great challenge for their adequate resection [20]. On the contrary, according to our findings, most of the patients with upper limb sarcomas experienced early postoperative complications and the association between the anatomical location of the tumor and the occurrence of postoperative complications was statistically insignificant which may

be because our study is limited by small sample size (p-value = 0.392).

Neoadjuvant therapy is commonly used as an adjunct to surgery for high-grade tumors. Radiotherapy alone or radiotherapy along with chemotherapy can be utilized in combination with surgery to combat large, aggressive tumors that are difficult to remove. However, according to the previous literature preoperative radiation is linked to a higher risk of wound complications [17]. According to a study by Sullivan et al. the patients who receive preoperative radiotherapy are more likely to develop postoperative wound complications as compared to those who received radiation after surgery, so the size and location of the tumor, timing of surgery and duration of radiotherapy should be taken into account when making management decisions for a given patient [21]. Individuals with weakened immune systems, geriatric populations or patients with massive tumors are particularly susceptible in this regard [22]. Neoadjuvant chemotherapy is a notion that is still up for debate [23] and the majority of clinicians still don't accept it. A study by Gronhi et al. concluded that concomitant administration of chemotherapy and radiation therapy not only doubles the risk of high-grade thrombocytopenia but also one out of six patients experience postoperative wound complications [24]. However, there was an insignificant statistical association between the neoadjuvant therapy and the occurrence of complications according to our findings.

The study's limitations include the fact that it was conducted in a single location and the sample size was small which could be attributable to the low incidence of sarcomas in our population, implying that the findings cannot be generalized to the entire population. Designing multi-centred research studies to achieve a larger sample size will improve the accuracy and validity of these results.

CONCLUSION

The most frequently occurring early complications in the first month after limb salvage surgeries are wound-related and the incidence of these complications is independent of the proposed risk factors. However, due to cultural and financial constraints in our country, a lesser number of patients seek medical advice hence the incidence of these tumours reported is very low. Multicenter studies should be conducted to achieve a larger sample size so that occurrence of postoperative complications and their association with proposed risk factors can be studied in a better way.

ETHICS AND CONSENT

Ethical committee approval was sought before the commencement of this study.

COMPETING INTERESTS

The authors have no competing interests to declare.

AUTHOR CONTRIBUTIONS

Z. Ali was involved in manuscript writing, data collection and data analysis. J. Saeed was involved in critical review of the manuscript. M. Umer was involved in the study conception and supervision.

PROVENANCE AND PEER REVIEW

Not commissioned, externally peer-reviewed.

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TO CITE THIS ARTICLE:

Ali Z, Saeed J, Umer M. Early Complications after Limb Salvage Procedures: Prospective Cross Sectional Study. *International Journal of Surgery: Oncology*. 2022; 7(1), 75–80. DOI: <https://doi.org/10.29337/ijsonco.143>

Submitted: 10 August 2022 **Accepted:** 08 September 2022 **Published:** 23 September 2022

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