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LIMB SALVAGE SURGERY COMPARED TO AMPUTATION IN BONE AND SOFT TISSUE TUMORS: A CRITICAL ANALYSIS OF CURRENT EVIDENCE

Rana Muhammad Sohail Afzal khan[1], Shaheer Abdullah[2], Tooba Javaid[3], Muhammad Umer[4], Umair Ishfaq[5], Hasnat Gull[6]

[1]Final Year MBBS Student, Final Year MBBS, Hitec-IMS Taxila Cantt, Taxila

Email: ranasohail3610@gmail.com

[2]MBBS, House Officer, Hitec-IMS Taxila Cantt, Taxila, **Email**: shaheer.abdullah2@gmail.com

ORCID ID: https://orcid.org/0009-0000-5310-8603

[3]Final Year MBBS Student, Final Year MBBS, Hitec-IMS Taxila Cantt, Taxila

Email: toobajavaid01@gmail.com, mbbs.20.21.0468@hitec-ims.edu.pk

ORCID ID: https://orcid.org/000900027406340

[4]Final Year MBBS Student, Final Year MBBS, Hitec-IMS Taxila Cantt, Taxila,

Email: mu1247536@gmail.com, mbbs.20.21.0457@hitec-ims.edu.pk

ORCID ID: https://orcid.org/0009000899904857

[5]Final Year MBBS Student, Final Year MBBS, Hitec-IMS Taxila Cantt, Taxila

Email: muhammadumairishfaq@gmail.com, mbbs.20.21.0422@hitec-ims.edu.pk

ORCID ID: https://orcid.org/0009-0004-6344-5186

[6]4th Year MBBS Student, 4th Year MBBS, Rai Medical College Sargodha,

Email: gullhasnat1442@gmail.com

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Corresponding Author: Rana Muhammad Sohail Afzal khan, Final Year MBBS Student, Final Year MBBS, Hitec-IMS Taxila Cantt, Taxila

Contribution: Conceptualization, Study Design, Manuscript Drafting, Reviewing, Editing, Supervision, Final Approval, Accountability,

Email: ranasohail3610@gmail.com

ABSTRACT

Introduction: Bone and soft tissue sarcomas historically required amputation for local control. But the development of imaging, chemotherapy, radiotherapy, and surgical methods means that LSS (limb salvage surgery) becomes a treatment of choice in many cases, so that the tumor can be removed while limb function is retained.

Historical Perspective: Until the 1970s, amputation was the mainstay of musculoskeletal oncology treatment, before advancements in diagnostic imaging and systemic therapies made limb salvage procedures possible. Early reports showed equivalent survival after LSS versus amputation, and thus leading toward the change in attitude towards limb salvage.

Current Practices and Criteria for Surgical Choice: Selection for surgery is focused on achieving clear margins without impacting function. Limb salvage is recommended when the tumor is localized, without compromising the critical neurovascular bundle, and reconstruction can result in meaningful function. Amputation is still indicated in patients with tumor spread, no response to therapy or unachievable reconstruction. Surgical planning that includes multidisciplinary team assessment and patient's care is crucial.

Comparative Analysis of Outcomes: Survival is comparable overall between LSS and amputation with acceptable margins. Functional and psychological results generally favor LSS, and limb salvage is associated with increased rates of complications and possible need for reoperation. Quality of life evaluations tend to describe more favorable results after LSS, when rehabilitative treatment has been successful.

Challenges and Limitations: LSS may be associated with increased local recurrence, surgical complications, and economic burdens. Amputation although is more definitive, may result in speedier recovery and fewer reoperations in select cases.

Conclusion: Limb sparing surgery has similar oncologic results to amputation and has better functional and quality of life outcomes in selected cases. A personalized and multidisciplinary approach for overall survival and limb function plays a key role in the treatment of bone and soft tissue tumors.

Introduction

Neoplasms, constitutes a broad spectrum of bone and soft tissue tumors that can have a major impact on limb function as well as on survival of the patient (1,2). In the past, the treatment of malignant bone and soft-tissue tumors depended largely on amputation for local control and prevention of metastasis (2–4). Nevertheless, improvements in the techniques of diagnosis, imaging, chemotherapy, radiotherapy, and surgery have changed the treatment approach and limb salvage surgery (LSS) can now offer a therapeutic option to many patients (5–9). The need to remove the tumor with wide oncological margins and restore limb function, usually with reconstruction (prosthetic, involving a graft, with a biological method), characterizes limb salvage (7,10–12). Amputation in contrast removes the entire portion of the limb affected, and may be preferred in cases in which limb salvage would not be oncologically safe (5).

Many studies conducted in recent years throughout the world have examined the oncological and functional outcomes of limb salvage versus amputation (5). Some of the earlier meta-analyses and prospective studies had shown that LSS with adjuvant therapies offers the same overall survival (OS) as amputation in bone Sarcomas such as osteosarcoma and Ewing's sarcoma (6,10,13–15). Functional and psychosocial parameters were overall in favor of LSS with increasing interest in conservative surgical strategies even by the major oncological centers (16). Nevertheless, there are still concerns of an increased local recurrence rate, postoperative complications, brain damage, complex reoperations, when deciding on treatment (9,11,15).

Region specific studies however, especially from Asia and from resource-limited settings depict a more complex scenario (16–18). Reports on developing countries have pointed out that while technically limb salvage is a possibility and oncologically sound procedure in a selected group of patients, the results can be heavily influenced by time taken to make the diagnosis, availability of advanced reconstructive resources and post-operative rehabilitation services (9,17,19). And certain subtypes of tumors, large tumor loads or neurovascular involvement remain indications for primary amputation in order to maximize survival opportunities (17,20). The limb salvage versus amputation decision is, therefore, not just a surgical one but is multifactorial, driven by tumor biology, healthcare resources, patient desires and socio-economic considerations (5,17).

With the changing scenario in musculoskeletal oncology and controversies regarding best surgical options, it is important to critically analyse the existing evidence base (12,21). This narrative overview attempts to compare limb salvage surgery with amputation in survival, functional

outcomes, psychological effects, and quality of life through a systematic approach, and to describe issues, concerns, and research directions for the future. Collation of key evidence generated from recent research and available evidence to aid in clinical decision-making and take a step towards patient-specific care in the management of bone and soft tissue tumors is the objective of this review.

Historical Perspective

The history of treatment of bone and soft tissue tumors illustrates tremendous advancements in the disciplines of oncology, radiology, and surgical technology (4,11,14). During the first half of the 20th century, radical amputation was the treatment of choice for malignant musculoskeletal tumors (22,23). This was also related to diagnostic limitations without imaging, which made accurate tumor measurement difficult, and in the absence of chemotherapy and radiotherapy which provided realistic chance of cure (23,24). Consequently, amputation was accepted as the only way to obtain consistently acceptable local control and to prevent metastatic spread, not with-standing the substantial physical and psychological costs to the patien (2,25)t.

The 1970s were the transition of an era in musculoskeletal oncology (23). The development of imaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI) permitted improved preoperative identification of tumors, including evaluation of involvement of critical neurovascular structures (10,26,27). At the same time, multi-agent chemotherapy systems were introduced and led to improved systemic disease control in osteosarcoma and Ewing's sarcoma, thereby diminished the risk of distant metastasis (14,23,28,29). These advances made possible the attainment of wide surgical margins for without amputation, paving the way for limb-salvage surgery (LSS) (20).

Landmark research that was performed during this time period indicated that local control and overall survival rates similar to those of amputation are feasible with limb salvage when selected patients were treated appropriately (30). In addition, advances in reconstructive methods, including modular endoprostheses, vascularised bone grafts, and rotationplasty, also contributed to increased indication of LSS (9,31,32). With increased experience and improved results, limb-salvage surgery progressively replaced amputation as the surgery of choice performed in specialized centers particularly for tumors sparing the major neurovascular bundles (13). The transition from obligatory amputation to limb-sparing is one of the major success stories in interdisciplinary progress for the treatment of musculoskeletal tumors (33).

Current Practices and Criteria for Surgical Choice

Contemporary surgical treatment of bone and soft tissue tumors advocates a multidisciplinary strategy regarding the achievement of the oncological safety and the functional preservation (34). Option whisk between the limb salvage and amputation because it is a complex decision, which is based-on a detailed evaluation of such factors as the tumor type, patient-related variables, available facilities and patient preference (34,35). By having better systemic treatments and imaging techniques, limb preservation has become feasible for the majority of cases previously being considered amputation candidates (36).

Selection criteria for limb salvage include the ability to achieve wide surgical margins with preservation of critical neurovascular structures, a satisfactory response to neo adjuvant chemotherapy or radiotherapy, if applicable, and the presence of enough remaining tissue for meaningful functional reconstruction (36–38). Tumors that are well-localized with little invasion of surrounding muscles, nerves, or vessels are the best candidates for LSS (37). In contrast, when tumors encompass major arteries or nerves, when infection is uncontrolled, when there are multiple unsuccessful attempts at salvage, or when reconstruction would yield a non-functional or severely morbid extremity, primary amputation is still favored (18,27).

The types of reconstruction for limb salvage include a number of different methods depending on the location of anatomical site and extent of resection (18,34). These options may be in the form of endoprosthetic replacement (in particular those for large bone defects), allograft or autograft reconstruction, tissue based approaches which include vascularized fibular grafts, and on infrequent occasions rotationplasty for specific lower extremity tumours (24,39,40). In soft tissue tumors, for residual form and function, complicated flap reconstructions or skin grafts are required. Rehabilitation programs are fundamental in achieving the best post-surgery function, and frequently requiring a long period of time of physiotherapy and sometimes, mechanical aid (41). Patient factors, including age, comorbid conditions, occupation, psychological resilience, and expectations, are importantly considered when making decisions (41). An older and less active person might opt for a definitive amputation and prosthesis, while a younger, more active patient may be motivated by limb salvage despite multiple operations and an extended rehabilitation period (13,42). In addition, socioeconomic factors and availability of postoperative rehabilitation are important for outcomes, especially in resource poor environments where advanced reconstructive procedures may not be available (9,11,41). Accordingly, current principles favor

individualized (patient-centered) management through a multidisciplinary structure (tumor board) aiming at the maximal increase in both survival and quality of life (6,29).

Comparative Analysis of Outcomes

Survival Outcomes

Several series and meta-analyses support that, given appropriate margins, overall survival does not differ between amputation and limb salvage (9). According to Blacksin et al. observed no significant 5-year survival advantage dissimilarity among the two groups (43). Similarly, data from the Musculoskeletal Tumor Society and other high-volume cohorts confirm that limb salvage has no tumor outcome disadvantage over amputation (9,12,37,44).

Functional Outcomes

Limb salvage is generally possible if amputation does not offer any functional advantage, especially in the upper and distal lower extremities (25,41,45). Functional evaluations such as the Musculoskeletal Tumor Society (MSTS) score or Toronto Extremity Salvage Score (TESS) continue to demonstrate superior results for patients treated with LSS (9,12,14,33,44,46). Nevertheless, limb salvage may be accompanied by long-term problems including joint stiffness, muscle atrophy, and prosthesis-related problems, while the functional results of modern prosthetic devices are also far better for amputees (25,47).

Psychological and Emotional Consequences

Limb preservation is psychologically associated with superior body image, self-esteem, and emotional well-being (48). Amputation, despite the evolution of prosthetic technology, may present a significant psychological burden including depression, anxiety and change in self-image (16,25,48). However, other studies demonstrate that amputees are less affected by adverse psychological outcomes if there is good pre-operative counselling, rehabilitation services, and social support (5,48,49).

Quality of Life (QoL)

QOL results tend to favor limb salvage surgery in general. Patients record greater scores in domains such as mobility, social involvement, and independence (50). Reconstruction type, complications (i.e infection and mechanical failure), and the need of subsequent surgeries may, however, affect QoL in the long term (50,51). However, not only do prostetic wearers who adapt

well, amputated patients also undergo successful rehabilitation and can also have a good quality of life, the adaptation period is prolonged (50,52).

Problems and Limitations of Tumor Limb Salvage Therapy

Despite the fact that LSS has now become a fundamental practice of contemporary musculoskeletal oncology in high-income countries, there are still many problems with LSS (51,53). Local tumor recurrence and concern about the need for negative margins are an important consideration, especially for tumors in close proximity to critical neurovascular structures (29). This oncologic compromise may be less favorable than amputation in some cases, particularly if reoperation is not possible to achieve improved margins (54).

One of the limitations is that post-operative complications are more common in LSS than amputations (11). Complications can comprise prosthesis failure, infection, soft-tissue necrosis, wound disruption, or pathological fractures. Although the endoprosthetes are advantageous in many aspects, the mechanical wear as well as the loosening and breaking thereof can cause problems of various types, typically requiring a revision that is complex (55). In addition, patients with LSS tend to suffer from serial surgical interventions during the course of their therapy. These secondary procedures have a negative impact on overall morbidities and may prolong recovery (with longer physiotherapy and social support required). In some patients, the cumulative financial burden can exceed that of a properly planned amputation, which involves direct medical costs, work loss and permanent disability due to progressive gangrene (53,55). Primary amputation, however, despite a more radical approach, can represent a more definitive surgical treatment with a lower rate of recurrence in well selected patients. It is often related to shorter hospitalization, fewer complications, and lower rate of reoperation if the tumor is extensive or encase large vessels or nerves (34,50). The rehabilitation potential following amputation may be valuable in an area with a lack of advanced surgical skills, prosthetic maintenance and for the lack of a rehabilitation techniques. Thus, the choice of limb salvage must take into account not just the functional desires, but also the practical limitations of surgical possibility, healthcare setting, patient wishes, and long-term prognosis (51).

Emerging Trends and Future Directions.

Many advances are emerging in the field of limb salvage treatment as musculoskeletal oncology continues to develop. Volar Strategies One advance is the use of biologic reconstructions such as vascularized fibular grafts and an allograft-prosthesis composite for bony regeneration and

functional bypass, particularly in younger patients (22,54). In addition, the use of patient-specific 3D-printed endoprostheses is on the rise, that allow for a unique bone replacement designed to accommodate the patient's own anatomy, increase mechanical performance, and minimize mechanical failure of the prosthesis (54). Inpartial **intraoperative navigation and radio-guided surgery** also now exist as interventions that can improve margin control whilst leaving more of the healthy limb intact. These techniques minimize local recurrence and maximize the results of limb salvage procedures (3,37,39,41). Concomitant progress in **immunotherapy, targeted therapies, and neoadjuvant strategies** is also enhancing tumor response and reducing tumors in size before surgery, which in turn is broadening the potential applicability of limb-sparing interventions (30,36,48).

But these technological and therapeutic developments are not equally available everywhere. Knowledge-translation barriers exist and resource-strained environments have significant difficulties in adopting high-cost technologies and/or long-term rehabilitation programs (53,55). In these situations, the decision between LSS and amputation should be tailored to the specific patient and decided upon according to local facilities. The field would value large, prospective, multi-center studies, preferably including under-represented areas in order to gain more insights in long-term survival, functional outcome, and quality of life within different populations (55). And the inclusion of patient-reported outcomes in research paradigms will also be essential for informing future treatment choices and policies (48,54).

Conclusion

Available evidence indicates that when this is technically possible, limb salvage surgery is associated with a comparable oncological survival to amputation and greater functional, psychological and quality of life benefits. Still, patient selection is important, and the approach must be tailored to the patient, taking tumor characteristics, patient expectations and local resources into account. Multidisciplinary team participation and patient-centered counseling are important in achieving success irrespective of the type of surgery. As surgical and adjuvant rehabilitation procedures continue to improve, the outlook holds positive for improved success in preservation of life as well as limb in the treatment of bone and soft tissue tumors.

Authors' Contributions

1. **Rana Muhammad Sohail Afzal Khan**
   Contribution: Conceptualization, study design, manuscript drafting, reviewing, editing, supervision, final approval, accountability.
2. **Shaheer Abdullah**
   Contribution: Drafting, study design, manuscript writing, proofreading, critical revisions, final approval, accountability.
3. **Tooba Javaid**
   Contribution: Drafting writing significant sections of the manuscript, critical revisions, consistency check, final approval, accountability.
4. **Muhammad Umer**
   Contribution: Conclusion writing, proofreading, manuscript preparation, critical revisions, final approval, accountability.
5. **Umair Ishfaq**
   Contribution: Drafting writing significant sections of the manuscript, proofreading, reviewing, critical revisions, final approval, accountability.
6. **Hasnat Gull**
   Contribution: Drafting writing significant sections of the manuscript, critical revisions, consistency check, final approval, accountability.

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