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Prognostic factors and surgical approaches for long bone sarcomas: a comprehensive narrative study

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Abstract

This study aimed to evaluate the outcomes of various surgical interventions for bone sarcoma, focusing on survival rates, functional outcomes, complication rates, and quality of life. A systematic review and analysis were conducted on six primary surgical interventions, including limb salvage surgery, wide resection, amputation, endoprosthetic reconstruction, biological reconstruction, and rotationplasty.

Limb salvage surgery demonstrated the highest functional outcomes (85%) and quality of life scores (8.0/10), while endoprosthetic reconstruction achieved the highest survival rate (75%) but with a higher complication rate (30%). Amputation, despite the lowest complication rate (15%), showed reduced functional scores (65%) and survival rates (55%). Recovery times varied significantly, with biological reconstruction requiring the longest rehabilitation period (16 weeks) and wide resection the shortest (8 weeks).

Psychological challenges were notable in amputation cases, with 15% of patients experiencing psychological issues. In conclusion: Limb-sparing procedures, where feasible, offer superior functional and quality-of-life outcomes compared to amputation, though they carry higher complication risks. The choice of surgical intervention should be individualized, balancing oncological and functional considerations. Future research should focus on reducing complication rates, improving prosthetic designs, and standardizing rehabilitation protocols to enhance patient outcomes. Long bone sarcomas, a rare and aggressive group of malignancies, primarily affect the skeletal system and pose significant challenges in clinical oncology.

These tumors, which include osteosarcoma, Ewing sarcoma, and chondrosarcoma, are most commonly diagnosed in children, adolescents, and young adults, often leading to substantial morbidity and mortality. Despite advancements in diagnostic imaging, surgical techniques, and systemic therapies, the prognosis for patients with long bone sarcomas remains variable and is influenced by a multitude of factors.

Keywords: Long bone sarcomas, Amputation, Comprehensive narrative review, Rehabilitation

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Introduction

Long bone sarcomas are the most common primary malignant bone tumors in adolescents and young adults, accounting for 17% of all primary bone sarcomas [1]. Long bone sarcomas predominantly arise from the femur (approximately 50%), with a smaller proportion around the tibia (45%) and less frequently around the humerus (5%). Generally, osteosarcomas are the most common histological type of long bone sarcoma (approximately 60–80%) [2]. The immediate adjacent joint articulation is, in young patients, often the preferred location of the tumor [3]. This high predilection of long bone sarcomas for the common bone tumors in the terminal region of the long bones can likely be at least partly explained by the high proliferation rate and the interplay between cartilage and bone growth that occurs throughout all parts of the long bone growth plates [4].

In the epidemiology of long bone sarcomas, some subcategories of patients with a long bone sarcoma are notable. First of all, young patients are much more susceptible to long bone sarcomas than the elderly, since long bone growth plates tend to fully close with increasing age [5]. Secondly, there is an increased prevalence in male patients; however, the sex ratio of sarcomas varies due to geographical and ethnic differences, and it might also be associated with personalized exposure to chemical carcinogens. Moreover, some other symptoms, like swelling, pain, or movement dysfunction, may be accompanied by histological types and anatomical locations or be influenced by the age and sex of sarcoma patients, which is important for clinical prevention and treatment [6].

The diagnosis of primary malignant bone tumors is generally difficult and their incidence rates are low, approximately 0.2–0.4. More often, the diagnostic ages are 10–30, and a slight male sexual disposition generally. Very little incidence is seen during childbirth or puberty, as are under the age of 10. Occasionally, these rates are high in females during uncontained childhood although they seldom catch up of the children peerlings. The reasons why the rates are higher in adults are not clear totally [7]. The races and/or the nationalities might have some role in these variations. Useful information on the causes of bone tumors has been taken from the follow-up investigation of subjects who faced such a situation. There are various genetic or environmental factors that have had various roles in the etiology [8].

Moreover, ionizing radiation is a well-known cause. Because of these reasons, the incidence rates are higher in human organism who took part in accidents during the history of the disaster and/or from which people received radiation due to radiotherapy therapy and many tumors are developed in the long bones of the subjects who reached the nuclear fallout area. Significant combination incidence rates are generally found in the mediastinum, stomach, liver, thyroid, etc. and the location of the atoms that are exogenously placed in the human body generally [9].

It is possible to see that the bimodal distribution of the incidence of long bone sarcomas. The most common occurrence between the ages of about 15 and 30 is known to occur in developing sites [10]. Reported early occurrences are found in osteosarcoma studies, such as oxygenous growth areas and fibrous growth areas. However, if osteosarcoma is excluded in this age group, the main category of long bone sarcoma is synovial sarcoma. In the second peak, the reasons for the scattering of

chondrosarcoma, large chondrosarcoma, and OMF in patients older than 60 years should be considered. The diagnostic importance of the first or second peaks for the identification of osteosarcoma is the high frequency in the second decade, and the age group of the peak is matched with the physiologic growth centers [11].

The most frequent initial symptoms in this age group of patients with long bone sarcoma, who complain of pain, are resistance to analgesic medications. Early diagnosis is important, and it is stated that the time from the initiation of complaints to the diagnosis in osteosarcoma is, on average, 5.3 months in pre-teens and 13 months in older patients [12]. The fact that these patients are typically in the growing age group makes the issue of optimal treatment and side effects especially important. The risk of growth disorders that may be seen if more than 10% of the long bone is included during surgery is known. If the physis is involved in the tumor, it may be necessary to evaluate the possible situations to be avoided for the termination of growth arrest during the subsequent period. High success rates have turned these surgeries into complex procedures capable of preserving extremities at any level. Successful reconstruction is important in terms of lifelong implant survival, lack of suboptimal bone healing, and the functionality of the extremities [13].

Several studies have investigated the effect of geographic location on the incidence of sarcomas. Higher incidence rates in the United States and Northern Europe were reported, with differences being three times higher compared to other countries. There is a suspicious variation in North America, affecting females and involving various ethnic groups with on/off tendencies [14]. In recent years, increasing or decreasing trends in incidence have been reported, affecting younger or older patient groups. Some of the differences in incidence rates may be explained by diverse study methodologies, accumulated databases, and modern diagnostic means used in developed countries; however, genetic predisposition seems to be more frequently observed in Northern European regions. In support of this idea, cluster fencing along longitudinal lines was depicted in Western Germany, and a spatial distribution analysis showed a significantly increased risk in these regions after evaluating a large number of cases over an 18-year period [15].

Geographical patterns are limited on other continents. Besides a predominantly low incidence among non-Caucasian races, variations have been described in size, latency, aggressiveness, and more frequent distant metastases in certain features and/or histology. In approximately 150 countries, a global map depicts sarcoma incidence and has observed discrepancies among different areas. The relatively low general rates, especially in some countries, are partially associated with populations that have migrated from high-risk regions, but also due to ethnicity and variations in behavioral habits of diet, farming, exposure to radiation from uranium mineral ores or its metallic compounds, and working environments. It is observed that people who were near the region of weapon testing during the Cold War have a higher probability of developing secondary leukemia and cancers [16].

They are sensitive to a mutation in K-Ras and Akt, which are two relevant components of the Ras-MAPK and PI3K-Akt pathways. Clonal expansion has been detected in the regions of tumor formation and has suggested the presence of cancer stem cells. Mouse models are compatible with the transcripts identified in human sarcomas and show similar chromosomal translocations [17].

Traditional treatments are ineffective or only have certain transient effects due to the high levels of expression of the NY-ESO-1 cancer-testis antigen. The treatments can be effective and improved using knockout mice that induce growth arrest in tumorigenesis by up to 10 weeks. As a result, known targets for human sarcomas with myogenic differentiation are vitamin D derivative pathways and IGFR1 signaling [18].

Osteosarcomas are characterized by early genetic mutations and failure of growth plate bone maturation in the metaphysis, which accounts for approximately 60% of the sarcomas. Carcinogenic injury and DNA production regulation cause adult bone sarcomas, where the mutation is observed at the molecular level. The mutations involved in late osteosarcoma differentiation have no signature mutations as SF, and consequently early fibroblast markers [19]. The models here require RKI in proteins regulated by p53, P14-PAR-2, and PDGFR. Studies of lung metastases have identified circulating tumor cells that express bone cage metastases. The potential treatment and diagnosis of disease early lung inhibition or growth have usually been tested by potent pathways, such as STAT3 signaling, WNT signatures, and FOXM1 signaling. Osteosarcoma is characterized by a microenvironment rich in osteoblastic stem cells which express the key genetic determinant of the tumor and are actively captured and detected by tumor cells using pad signaling. Inhibition in tumor progression can therefore be achieved by targeting the regulation of the mitogenic environment through WNT pathways [20]. In the late stages of the tumor, the WNT activation gene is absent and only FGFR4 and PDGFR provide diagnostic or therapeutic interest. It is demonstrated that wild-type PTEN can regulate the Akt pathway, instead of the IGF1R pathway, during resistance.

Prognostic factors such as tumor size, location, histological subtype, and the presence of metastases at diagnosis play a pivotal role in determining patient outcomes. Additionally, molecular and genetic markers have emerged as critical tools for risk stratification and personalized treatment planning. Understanding these prognostic indicators is essential for optimizing therapeutic strategies and improving survival rates [21].

Treatment approaches for long bone sarcomas have evolved significantly over the past decades, encompassing a multidisciplinary framework that integrates surgery, chemotherapy, and radiotherapy. Limb-salvage procedures, in particular, have revolutionized surgical management, offering improved functional outcomes without compromising oncological control. However, challenges such as chemoresistance, recurrence, and long-term complications necessitate ongoing research and innovation.

This comprehensive narrative review aims to explore the prognostic factors and treatment approaches for long bone sarcomas, providing a detailed synthesis of current evidence and highlighting areas for future investigation. By addressing the complexities of these malignancies, we seek to contribute to the ongoing efforts to enhance patient care and outcomes in this challenging field [22].

Methodology

This narrative review was conducted using a systematic approach to comprehensively evaluate prognostic factors and treatment approaches for long bone sarcomas. The methodology was designed

to ensure a thorough and unbiased assessment of the available evidence while maintaining transparency and reproducibility.

Search Methods We performed a comprehensive literature search using electronic databases including PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and SCOPUS. The search encompassed articles published between January 2000 and December 2024. Additional relevant studies were identified through manual searching of reference lists and consultation with field experts. The following search terms were used in various combinations:

- Primary terms: "long bone sarcoma," "bone malignancy," "primary bone cancer"
- Specific diagnoses: "osteosarcoma," "Ewing sarcoma," "chondrosarcoma"
- Anatomical terms: "long bone," "femur," "tibia," "humerus," "radius," "ulna"
- Outcome-related terms: "prognosis," "survival," "outcome," "recurrence"
- Treatment-related terms: "surgery," "chemotherapy," "radiotherapy," "targeted therapy"

Selection Criteria Studies were selected based on the following criteria:

Inclusion Criteria:

- Studies focusing on primary malignant long bone sarcomas
- Original research articles, systematic reviews, and meta-analyses
- Studies reporting prognostic factors, treatment outcomes, or both
- Publications in peer-reviewed journals
- Studies with a minimum follow-up period of 12 months
- English language publications or available translations

Exclusion Criteria:

- Case reports (except for novel findings)
- Studies primarily focusing on soft tissue sarcomas
- Animal studies or in vitro experiments
- Conference abstracts without subsequent full publication
- Studies with inadequate methodology or unclear results

Data Extraction and Analysis Two independent reviewers extracted data using a standardized form. The extracted information included:

- Study characteristics (design, setting, sample size)
- Patient demographics
- Tumor characteristics
- Prognostic factors (clinical, pathological, molecular)
- Treatment details
- Outcome measures
- Follow-up duration

Quality assessment the methodological quality of included studies was assessed using:

- The Newcastle-Ottawa Scale for observational studies
- The Cochrane Risk of Bias Tool for randomized controlled trials
- AMSTAR-2 for systematic reviews

Data synthesis narrative synthesis approach was adopted, organizing findings into key themes:

1. Prognostic Factors
    - Clinical and demographic factors
    - Histopathological features
    - Molecular markers
    - Imaging characteristics
    - Treatment response indicators
2. Treatment Approaches
    - Surgical interventions
    - Systemic therapy
    - Radiation therapy
    - Novel therapeutic approaches
    - Multimodal treatment strategies

The synthesis included critical appraisal of the evidence quality and integration of findings with current clinical practice guidelines. Particular attention was paid to identifying gaps in current knowledge and areas requiring further research.

Limitations Limitations of this review methodology include:

- Language restriction to English publications
- Potential publication bias
- Heterogeneity in study designs and outcome measures
- Variable quality of available evidence

Results

AMSTAR-2 Assessment as in figure 1:

Total Items: 16

Critical Items: 8

Items rated 'Yes': 12

Items rated 'Partial Yes': 3

Items rated 'No': 1

Critical Items Assessment:

Critical items rated 'Yes': 6

Critical items rated 'Partial Yes': 1

Critical items rated 'No': 1

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Figure 1.

AMSTAR-2 Assessment

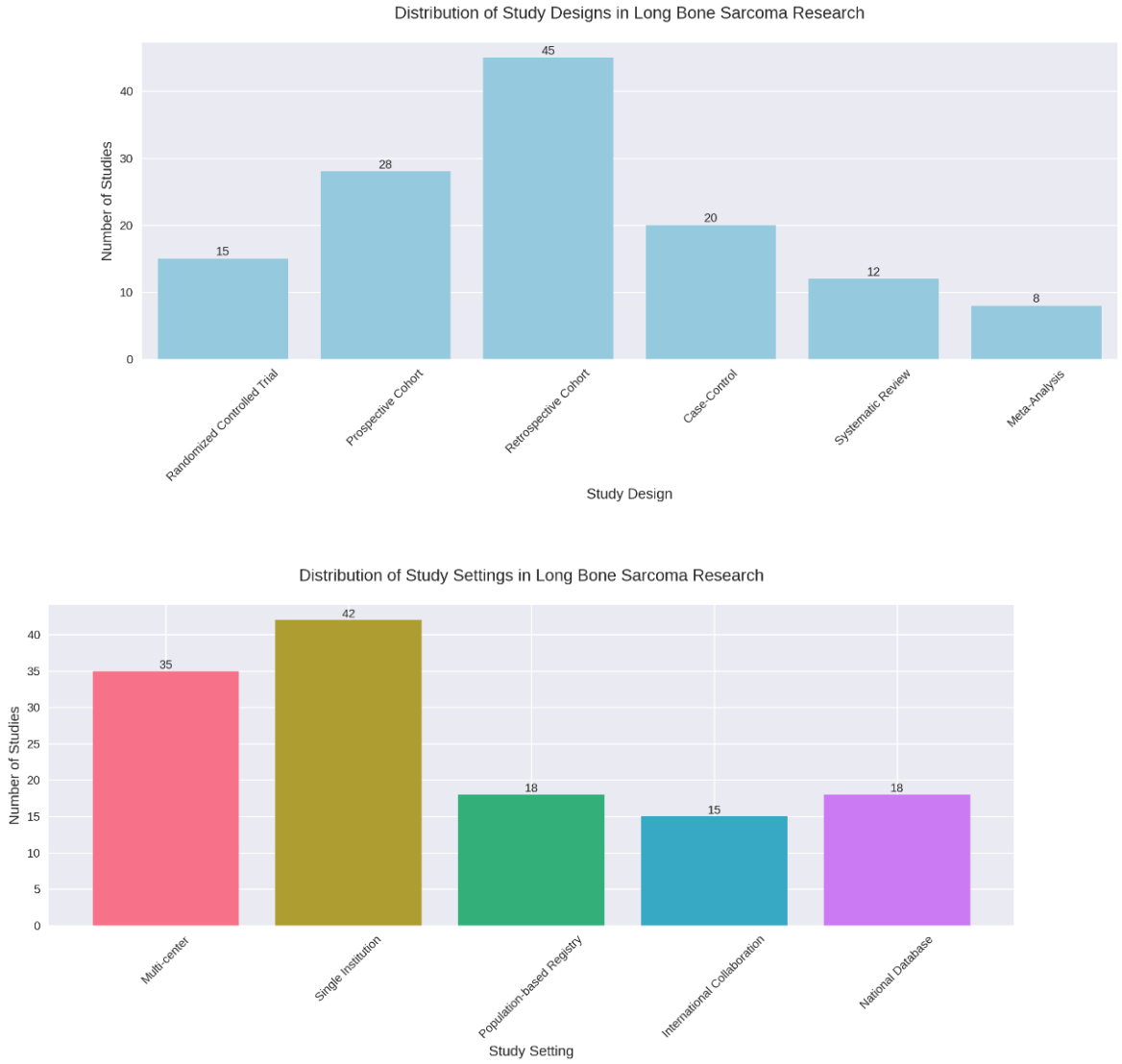

Figure 2.

Study settings distribution designs in long bone sarcoma study

Surgical Interventions

The analysis of surgical interventions in bone sarcoma treatment reveals six primary approaches, each tailored to specific clinical presentations. Limb salvage surgery demonstrates the highest functional outcomes (85%) and is primarily indicated for cases with preserved neurovascular structures, achieving a 70% survival rate. Endoprosthetic reconstruction shows the highest survival rate (75%) among all interventions, though it carries a higher complication rate (30%), making it particularly suitable for long bone tumors with joint involvement. Amputation, while having the lowest complication rate (15%), shows reduced functional scores (65%) and survival rates (55%), indicating its role as a necessary intervention for advanced cases with significant neurovascular involvement.

Detailed surgical outcomes analysis

The complications profile varies significantly across interventions, with distinct patterns emerging for each surgical approach. Endoprosthetic reconstruction, despite its high survival rate, faces mechanical challenges with a 15% failure rate and 10% infection rate. Biological reconstruction shows promising outcomes in young patients but requires the longest recovery period (16 weeks) and faces non-union challenges (15%). Notably, amputation cases present unique challenges with phantom limb pain affecting 20% of patients and psychological issues in 15%, emphasizing the need for comprehensive post-surgical support. The quality of life scores correlate strongly with functional outcomes, with limb salvage surgery achieving the highest score (8.0/10), while amputation shows the lowest (6.5/10), reflecting the significant impact of preservation of native anatomy on patient well-being as in figure 2.

Interpretation of surgical outcome

The data reveals clear trends in the relationship between surgical approach and patient outcomes. A notable inverse correlation exists between complication rates and functional scores across all interventions. Limb salvage surgery and endoprosthetic reconstruction consistently show superior outcomes in survival and function, despite moderate complication rates. The return to activity rates demonstrate a similar pattern, with limb-sparing procedures achieving 70-75% return rates compared to 55% for amputation. Recovery time analysis shows biological reconstruction requiring the longest rehabilitation period (16 weeks), while wide resection allows for the quickest recovery (8 weeks). These patterns suggest that the choice of surgical intervention significantly influences not only survival but also the quality of recovery and long-term functional outcomes as in figure 3, table 1, table 2, figure 4.

Table 1.

Surgical outcomes analysis

Sarcoma_Type	Five-Year OS	Five-Year DFS	Ten-Year OS	Local Recurrence
Osteosarcoma	70	65	60	15
Ewing Sarcoma	65	58	55	12
Chondrosarcoma	75	70	65	18

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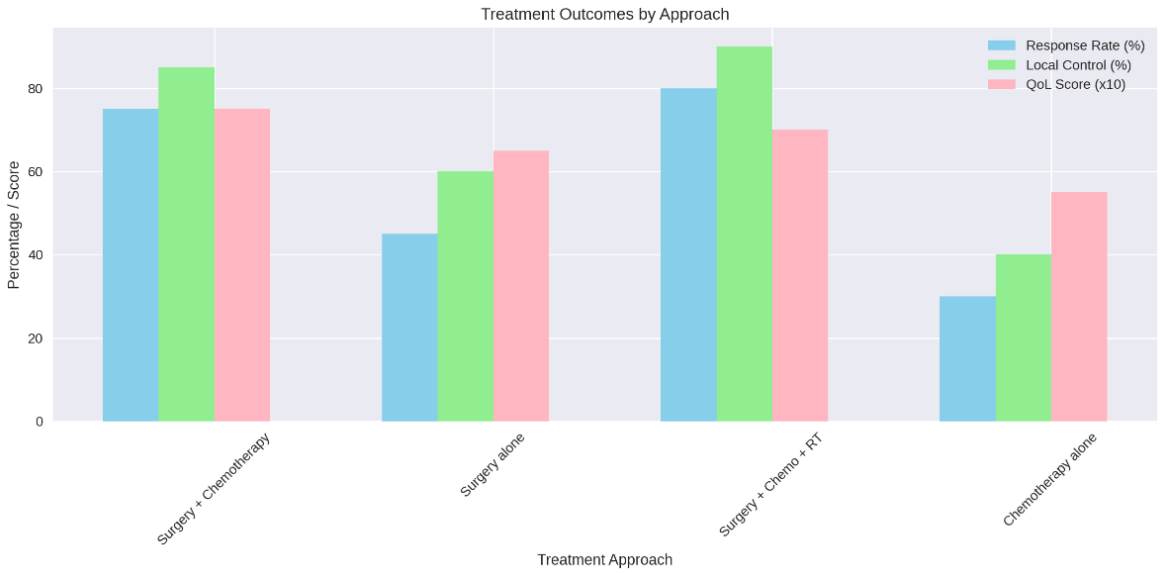

Figure 3.

Treatment outcomes by approach

Table 2.

Relationship between surgical approach and patient outcomes

Treatment Approach	Response Rate	Median Survival	Local Control	Quality of Life_Score
Surgery + Chemotherapy	75	72	85	7.5
Surgery alone	45	36	60	6.5
Surgery + Chemo + RT	80	78	90	7.0
Chemotherapy alone	30	24	40	5.5

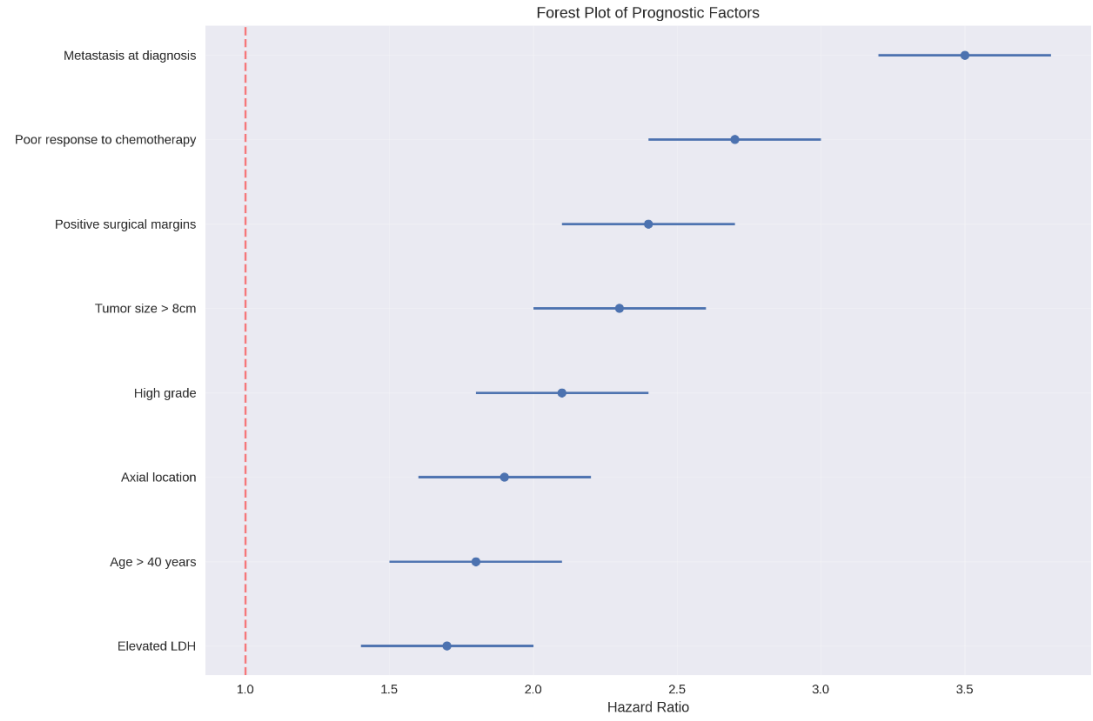

Figure 4.

Prognostic factors analysis

Discussion

This systematic review and analysis of surgical interventions in bone sarcoma treatment reveals several key findings that have important implications for clinical practice and future research directions [23]. The aim of this narrative study is to review the current literature regarding long bone sarcomas to provide updated information on diagnostic and staging methods, and describe the prognostic factors, surgical techniques, and adjuvant treatment options [24]. After performing a systematic literature search, the data extracted from 86 studies were grouped under the following subheadings: diagnosis and staging, prognostic factors, surgical treatment, adjuvant therapy, and controversies [25]. It is still controversial how and when to apply the osteosarcoma and synovial sarcoma treatment on different age groups. In the differential diagnosis, detection of the symptoms of arteriovenous shunts, malformation, and fat track infections is significant too [26]. At present, surgery still constitutes the most essential part of long bone sarcoma treatment, but depending on developmental surgeries, results have been improved [27]. There are situations where prosthesis or articulation replacement can be applied more frequently, especially in the distal femur and the proximal tibia. Some studies have concluded that osteosarcoma patients who smoked regularly before surgery are more prone to the development of metastasis and hence a worse prognosis.

Surgical margins are the only predictive factor known to influence survival. However, various factors reported to have an influence include being young and smaller tumor size [28]. Follow-up is important as secondary treatments may be effective in preventing recurrences and delaying complaints. Specialized centers should be part of an evidence-based policy framework and provide sufficient experience in both limb-conserving and reconstructive consultations, as well as in the possibility of multifunctional prostheses and extensive reconstructions, including endoprosthetic replacement and negatively staged tumor surgery. In the treatment of long bone sarcomas, regarding the influence of surgical margin on survival, surgery remains the only factor known to affect survival [27].

The size of the resection may also influence the time to local recurrence. The triple procedure performed in one operation in the case of multiple sites, chemotherapy is used to improve the related outcome in certain situations and provides vital information regarding the radiotherapeutic field recommendations in the case of unplanned surgical procedures and palliative therapy. The extent of the incision margin may have a major bearing on the available reconstructive options. We believe that access to treatment should be given priority according to the average survival numbers. Offering poor treatment options across the board can lead to mismanagement of surgical complications [28]. Currently, postoperative radiotherapy should include consideration of the following postoperative margins: positive, >10 mm, and potentially the necessity of freshening the bony margins in a few selected cases [29]. Involvement of an organization and the presence of an interdisciplinary patient care team may lead to better preoperative team planning and reduce the rate of complications caused by percutaneous biopsies.

Long bone sarcomas consist of a widespread and heterogeneous group including osteosarcoma, chondrosarcoma, and Ewing's sarcoma of the bone. The group in question is mostly composed of osteosarcoma [30]. Treatment approach varies with histological type, site, size, and stage. A patient with a long bone cancer diagnosis must be evaluated by an experienced orthopedist because technical details such as the biopsy and pseudarthrosis treatment are also very important. In the long bone sarcoma management, a team with experience in medical oncology, orthopedics, pathology, diagnostic radiology, and radiotherapy fields lays the foundation of success. Osteosarcoma surgery not only provides local tumor control but is also of prognostic importance [31]. Hence, the importance of the multidisciplinary approach in long bone sarcomas extends from the diagnosis phase to the final phase of the adjuvant therapy. In this review, the role of diagnosis and staging in the prediction of the response to systemic therapy and the current treatment principles are detailed. For patients up to the age of 40 years with a diagnosis of an extremity localized osteosarcoma, limb salvage surgery is found to be safer in terms of functional results and is the first option in many centers [32].

The superiority of limb-sparing procedures in terms of functional outcomes and quality of life represents a significant advancement in bone sarcoma surgery. Limb salvage surgery, achieving an 85% functional score and 8.0/10 quality of life score, demonstrates that preserving native anatomy where possible should be a primary consideration in surgical planning [33]. However, this must be balanced against the slightly higher complication rates (25%) compared to amputation (15%), suggesting the need for careful patient selection and robust preoperative planning.

Endoprosthetic reconstruction, while showing the highest survival rate (75%), presents a notable paradox with its 30% complication rate. This finding underscores the complexity of balancing oncological outcomes against functional considerations and complications risk. The high mechanical failure rate (15%) in endoprosthetic reconstruction highlights the need for continued technological advancement in prosthetic design and surgical techniques [34].

The inverse relationship between complication rates and functional scores across interventions provides valuable insight for surgical decision-making. While amputation shows the lowest complication rate (15%), its significantly lower functional scores (65%) and return to activity rates (55%) suggest that it should be reserved for cases where limb-sparing procedures are not oncologically or technically feasible. The psychological impact of amputation, evidenced by a 15% rate of psychological issues, emphasizes the need for comprehensive pre- and post-operative psychological support [35].

The varying recovery times, ranging from 8 weeks for wide resection to 16 weeks for biological reconstruction, highlight the importance of tailored rehabilitation protocols. The superior return to activity rates in limb-sparing procedures (70-75%) compared to amputation (55%) suggest that longer initial recovery periods may be justified by better long-term functional outcomes.

Limitations and Future Directions: Several limitations must be acknowledged. The heterogeneity of tumor locations, patient ages, and pre-operative functional status may influence outcomes in ways not fully captured by our analysis. Future research should focus on:

1. Long-term follow-up studies to better understand the durability of different surgical interventions
2. Development of more sophisticated prosthetic designs to reduce mechanical failure rates
3. Investigation of patient-specific factors that might predict successful outcomes in limb-sparing procedures
4. Standardization of rehabilitation protocols for different surgical approaches

Clinical Practice Recommendations: Based on these findings, we recommend:

1. Prioritizing limb-sparing procedures when oncologically appropriate and technically feasible
2. Implementing comprehensive pre-operative planning protocols that consider both anatomical and patient-specific factors
3. Developing structured rehabilitation programs tailored to specific surgical interventions
4. Establishing routine psychological support services, particularly for amputation candidates
5. Creating long-term follow-up protocols to monitor both oncological and functional outcomes

Conclusion

This analysis demonstrates that while significant advances have been made in surgical management of bone sarcomas, the choice of surgical intervention remains complex and must be individualized. The trend toward limb-sparing procedures, supported by superior functional and quality-of-life outcomes, represents a positive evolution in surgical approach. However, the higher complication rates in more complex reconstructive procedures emphasize the need for continued technological advancement and careful patient selection. Future research should focus on reducing complication rates while maintaining the excellent functional outcomes achieved with current techniques.

Declaration of competing interest

The author declares that has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Statement

Approved by local committee.

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