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Original Research Article

Evaluation of primary high-grade osteosarcoma by surgical resection in PT Birta city hospital

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ABSTRACT

Background: Classic OS had a 20% five-year survival rate during most of the 20th century. Adjuvant chemotherapy was first used to treat OS in the 1970s, raising survival rates to 50%. The standard course of treatment for OS includes surgery, neoadjuvant chemotherapy, and adjuvant chemotherapy. When treating a patient with soft tissue and bone sarcomas, the extent of surgical procedures is frequently described using surgical oncologic classifications. Radical resection refers to the removal of the whole bone or compartment harboring the tumor, whereas wide resection refers to the removal of the affected area of the bones with a cuff of healthy tissue.
Methods: The study conducted a retrospective analysis of 120 patients who visited to orthopedic outpatient department of PT Birta city hospital and research center, Nepal from October 2019 to November 2022. Radical resection was defined as the removal of the entire affected bone, while wide resection was described as partial bone excision. The baseline characteristics of the patients were analyzed and the data regarding radical and wide resection in osteosarcoma (OS) was evaluated.
Results: The analyzed report shows that 65/120 (54.1%) radical resections and 55/120 (45.8%) wide excisions were the extent of the resection. On the other hand, a central review of the extent of resection data revealed 100/120 (83.3%) wide excisions and 20/120 (16.6%) radical resections.
Conclusions: OS is currently treated with extensive resection, neoadjuvant chemotherapy, and adjuvant chemotherapy, with a strict emphasis on the overall intensity of treatment and prompt restart of post-resection chemotherapy.

Keywords: OS, Wide resection, Surgical resection, Chemotherapy

INTRODUCTION

The incidence of OS, a primary malignant bone tumor, is 3.4 per million persons per year worldwide.[1] Classic OS had a 20% five-year survival rate during most of the 20th century. Adjuvant chemotherapy was first used to treat OS in the 1970s, raising survival rates to 50%.[2,3] Amputation was the standard course of treatment for high-grade OS until the mid-1970s. By 1990, chemotherapy and limb salvage began to receive more attention in the treatment of high-grade OS. The survival rate is now greater than 65%.[4]

OS is categorized histologically by WHO as central, intramedullary, and surface tumors, with a variety of subtypes falling within each category.[5]

Over the years, advancements in technology and diagnostic methods have been made for OS. A

preoperative imaging protocol that includes at least two X-ray scans of the entire bone and the nearby joint should be followed for any suspected bone lesion.[6] On radiographs, the metaphysis of the bone will have an ill-defined lesion with osteoblastic and/or osteolytic regions, periosteal response, and a soft tissue mass. It is necessary to use magnetic resonance imaging (MRI) to assess the extent of bone marrow replacement, skip lesions, and expansion into the surrounding joint of the lesion, as well as its invasion into the soft tissue and neurovascular structures. The definition of cortical abnormalities, fracture sites, mineralization, and neurovascular involvement can be accomplished with the help of computed tomography (CT) scans. The extension of intraosseous tumors, metastases, and polyostotic involvement can all be seen using bone scintigraphy. A tool for displaying vascular anatomy may be angiography. Given that these regions frequently have vascular anatomic anomalies, it is useful for preoperative planning in patients with malignancies at the proximal tibia or shoulder girdle.[7,8]

The standard course of treatment for OS includes surgery, neoadjuvant chemotherapy, and adjuvant chemotherapy. Even after surgical amputation, the high-grade traditional OS survival rate was less than 20% prior to the use of chemotherapy, showing the presence of micro-metastases (usually pulmonary) before surgery. If the final pathology confirms the low grade, chemotherapy is often avoided and the low grade can typically be treated with excision alone.[9]

The aim of tumor surgery is to completely remove the tumor and all associated illnesses. Amputation versus limb salvage is the two surgical choices.[10] For 85-90% of individuals with OS, limb salvage surgery procedures offer a safe means of treatment. Resection and rebuilding are the two crucial processes in limb preservation. To completely eradicate a disease, resection is essential.[11] The next stage of limb salvage is reconstruction. Notably, non-weight-bearing bones like the proximal fibula and clavicle do not require repair because excision by itself does not result in functional losses.[12]

Amputation, which was originally the usual surgical course of action for OS, is now typically reserved for tumors that cannot be removed surgically and have soft tissue and neuromuscular contamination that cannot be repaired. According to numerous studies, limb preservation surgery offers greater daily function than amputation and is at least as effective as amputation in terms of survival. Osteointegration implants, which are used as a supplement to therapy in amputees to improve function, are a unique surgical procedure. These patients' survival rate at two years was 92%, and they generally reported improved prosthetic use and quality of life.[13,14]

OS was not treated with chemotherapy, and the prognosis was poor. Neoadjuvant chemotherapy, surgery, and adjuvant chemotherapy are now the recommended treatments for OS. The four chemotherapy drugs-methotrexate with leucovorin rescue, doxorubicin, cisplatin, and ifosfamide-are used in almost all treatment plans. Etoposide may potentially be used in the treatment of patients with metastatic illness.[15]

When treating a patient with soft tissue and bone sarcomas, the extent of surgical procedures is frequently described using surgical oncologic classifications. The intralesional, marginal, broad, and radical surgical classification systems used by the majority of sarcoma treatment facilities are those mentioned by Enneking et al. While the tumor is breached and removed piecemeal in intralesional excisions, it is eliminated through the so-called reactive zone in marginal excisions (the inflammatory area around the pseudocapsule). Because tumor cells are likely to be left behind, marginal and intralesional excisions are inappropriate surgical techniques for the eradication of sarcomas. Through a large or radical resection, a negative margin is what is intended by sarcoma excision. Radical resection refers to the removal of the whole bone or compartment harboring the tumor, whereas wide resection refers to the removal of the affected area of the bones with a cuff of healthy tissue (Figure 1). Most sarcomas can be safely removed by broad excision thanks to modern imaging technology and successful adjuvant therapy.[16,17]

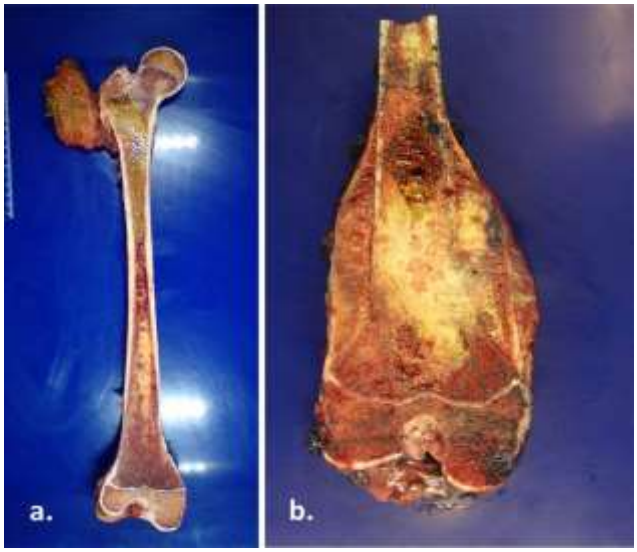

Figure 1 (a and b): Radical removal of an Ewing sarcoma from femur and wide distal femur excision for OS.

The excision of the whole bone compartment was necessary since the tumor covered almost the entire intramedullary section of the femur. To obtain a negative margin, only a part of the femur was removed.

There may be disparities in margin status between radical and wide resections of bone sarcoma because there are different oncologic surgical methods. In clinical trials, proper reporting of the resection status is crucial since faulty reporting could skew later data analysis. The general clinical opinion is that extensive or radical excision is equally beneficial for the local management of OS when combined with modern imaging and adequate adjuvant

therapy. However, there have yet to be any prospective studies to back this up. Additionally, historical data indicate that even in present-day therapy, marginal and intralesional resections raise possibility of recurrence.[18] Study aims to aims to evaluate the occurrence of surgical resection of high grade OS by its type in our hospital.

METHODS

Study design

The study conducted a retrospective analysis of patients for whom information on the degree of resection was available from PT Birta city hospital and research center. The study considered 120 patients in total who visited to orthopedic outpatient department of our hospital from October 2019 to November 2022. On the basis of our hospital's evaluation, at least one of the two orthopedic oncologists reviewed the surgical and pathology reports of patients who were thought to have received a wide or radical resection of the original tumor. Radical resection was defined as the removal of the entire affected bone, while wide resection was described as partial bone excision. The baseline characteristics of the patients were analyzed and the data regarding radical and wide resection in OS was evaluated.

Inclusion and exclusion criteria

Patients who were said to have received a broad or radical resection by the treating institution were included in this analysis. Patients who came to the outpatient department of our hospital who follow the study protocol and give informed consent for the study are included. Patients who provide informed consent for the study are included in the study. A total of 120 patients were included in the study.

For any reason (such as early death or departure from the research), patients who did not have their main tumor surgically removed were not included in this analysis. The clinical study did not accept patients who underwent resection prior to the initiation of chemotherapy, hence they were excluded from this analysis. Patients who did not follow the study protocol did not finish it, or did not provide consent were not included in the study.

Statistical analysis

We tested the claim that the likelihood of a discrepancy in the evaluation of radical according to central review and wide according to institutional review was equivalent to the likelihood of a discrepancy in the evaluation of wide according to central review and radical according to institutional review using McNemar's test.

Ethical approval

The patients were given a thorough explanation of the study by the authors. The patients' permissions have been gotten. The concerned hospital's ethical committee has accepted the study's methodology.

RESULTS

The analytical cohort for this analysis was made up of 120 patients who were said to have received a broad or radical resection. In Table 1, the clinical characteristics of these 120 patients are shown. The males (60%) are in high numbers than females (39.1%). The study found that the 28.33% of patients had stage IB cancer, 51.67% of patients had stage IIA cancer. There was no metastatic stage found.

Table 1: Baseline characteristics of patients who underwent tumor resection for high-grade OS, (n=120).

Characteristics	N	Percent (%)
Age at enrolment (in years)		
Median (range)	15 (6-41)	
Sex		
Male	72	60
Female	47	39.1
Stage		
IB	34	28.33
IIA	62	51.67
IIB	24	20
Primary sites		
Lower extremity		
Non-femur	39	32.5
Femur	58	48.3
Upper extremity	17	14.1
All other sites	6	5
Metastasis present at the time of enrolment		
Yes	20	16.7
No	101	84.1
Unknown	3	2.5

The analyzed report shows that 65/120 (54.1%) radical resections and 55/120 (45.8%) wide excisions were the extent of the resection. On the other hand, a central review of the extent of resection data revealed 100/120 (83.3%) wide excisions and 20/120 (16.6%) radical resections (Table 2).

Table 2: Concordance of institutional and central review of radical and wide resection in patients with newly diagnosed OS, (n=120).

Institutional reviews	Central review		Total
	Radical	Wide	
Radical	17	48	65
Wide	3	52	55
Total	20	100	120

DISCUSSION

Adjuvant chemotherapy given to patients with high-grade, localized OS following final surgical resection resulted in

a statistically significant improvement in disease-free and overall survival, which was sustained for 25 years. In patients who received adjuvant chemotherapy, tumor necrosis after just one cycle of neoadjuvant chemotherapy and radiotherapy was a predictor of overall survival and disease-free survival.[19,20]

Despite an increase in the use of adjuvant radiation over the last 30 years, surgery has remained the primary therapy for the majority of patients in Scandinavia with soft tissue sarcoma (STS). The Scandinavian sarcoma group (SSG) Register has kept track of patient and therapy characteristics since 1987. When the impact of updated radiation recommendations from 1998 was assessed, the accuracy of surgical margin evaluations across several Scandinavian institutions was looked into.[20,22]

Radical resections were frequently carried out for individuals with primary bone tumors prior to the development of efficient systemic medication for managing the microscopic disease. Orthopedic oncologists could remove less bone while still achieving oncologically acceptable margins and results thanks to the efficacy of chemotherapy in combination with cutting-edge imaging technology.[18,20] Although we are unsure if radical and wide resection results in different rates of local disease management, the degraded vernacular in reporting suggest a different course of action than was really taken, potentially corrupting any subsequent oncologic inferences.[17,20]

A famous study conducted at the Istituto Ortopedico Rizzoli characterized several critical margins in the management of OS.[12] There are four types of surgical margins: intralesional, marginal, broad, and radical. Whenever the tumor is accessed during surgery, an intralesional margin is formed. When the dissection penetrates or enters the reacting zone that envelops the tumor, a marginal margin is produced. When the reactive zone is avoided and the complete dissection is carried out through healthy tissues, a large margin is produced. When the whole myofascial or bony compartment, or compartments, containing the tumor, is removed, a radical margin is produced.[18,20]

Resection with wide margins is the guiding principle in the surgical resection of OS (removal of the tumor with a cuff of normal tissue covering it all around). This typically entails osteotomy of bone 2-3 cm away from the level of involvement and removing 2 cm of healthy tissue or a strong anatomical barrier (such as the fascial layer or articular cartilage).[21,22] After successful neoadjuvant therapy, it has also been suggested that thinner margins on bone are suitable for resection. Joint sparing resections that preserve the neighboring joint by using the open physis cartilage as a boundary is also oncologically sound. Some professionals have pushed for the use of computerized navigation for precise excision with safe margins based on imaging findings and maximum bone preservation.[22,24,25] Similar to this, the distraction of the growth plate is also performed prior to surgery to allow for the preservation of the physis while maintaining good excision margins. For verification of a negative margin at the location of the osteotomy, an intraoperative frozen piece of bone marrow should be supplied. In cases where saving the limb is not possible with tumor removal with wide margins, ablative surgery in the manner of amputation or disarticulation is required.[23,26]

It is difficult to reconstruct big segmental defects after resection. A good reconstruction should be long-lasting, compensate for the affected limb's loss of growth in the patients with the young skeletons, restore the limb's function and look as closely as feasible to normal, allow for the early rehabilitation, be affordable, and be easily accessible. There is no one perfect reconstruction technique, thus it is important to choose one that meets the patient's needs.[24,25]

Because it has a predictable functional outcome, enables early rehabilitation, enables intraoperative flexibility in size of reconstruction required, and is non-biological, it is unaffected by adjuvant chemotherapy, reconstruction with megaprosthesis is popular method of reconstruction. However, primary drawback of megaprostheses is their susceptibility to wear and strain, which might eventually cause loosening or breaking.[24-26]

Arthrodesis, intercalary repair, and osteoarticular grafts can all be treated using biological reconstruction. They rely on bone repair for recovery, which is impacted by adjuvant therapy and requires a lengthy recovery period. In particular, at locations like the proximal tibia, proximal femur, and proximal humerus, osteoarticular allografts have the benefit of good tendon reattachment for optimum function.[25-27]

The reported oncologic surgical classification discordance rate (wide vs. radical) was 43%. Patients who were classified as having undergone radical resection accounted for the majority of the discrepancies.[24] Although the precise cause of this high rate of discordance cannot be known with certainty, it is crucial to consider all of the possible causes. By extensive excision, OS s are typically eliminated. However, this procedure does not have a current procedural terminology (CPT) code.[23,24] Regardless of the amount of bone removed or the anatomic region, all CPT codes now use the description of "radical resection" for the surgical removal of bone cancer. The more patients who were reclassified as broad from radical may be an indication of the influence and limitations of the CPT coding system. Encourage surgical oncologists to refer to the actual extent of resection when naming the procedure rather than just the CPT code as another potential intervention.[17,19,20] This study is a single-centred study and so, it does not include variedtype of population and hence, the findings cannot be applied to the whole population. Also, this study did not include patients who received chemotherapy prior to the study.

CONCLUSION

The distal femoral and tibial of adolescents are the most prevalent sites for OS, a rare bone malignancy, to be detected. Early OS treatments frequently included surgical resection, such as amputation, or repair with auto- or allograft. Five-year survival rates have significantly enhanced as a result of the inclusion of neoadjuvant chemotherapy in treatment regimens. The study concluded that OS is currently treated with extensive resection, neoadjuvant chemotherapy, and adjuvant chemotherapy, with a strict emphasis on the overall intensity of treatment and prompt restart of post-resection chemotherapy. Immune therapy and targeted chemotherapy are making strides, and research into cutting-edge therapeutic modalities has so far produced encouraging preliminary findings.

It is difficult to surgically treat patients with OS. There is no discernible difference in survival between limb-salvaging procedures that are properly executed and amputations. The objectives of contemporary orthopedic oncology are optimal tumor excision and a functioning residual limb with improved patient and reconstructive survival. Regardless of whether the surgery involves limb-sparing or limb sacrifice, the removal of the tumor with proper margins should be the first priority. Individualized reconstruction should be done for each patient, taking their oncological, functional, and social demands into consideration.

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