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# Malignant bone tumors around the knee: A single-center experience

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## ABSTRACT

**Aim:** This study aimed to determine the frequency of malignant bone tumors (primary and metastatic) seen around the knee in our region, the patients' type and demographic characteristics, and the treatments' outcomes.

**Material and Method:** A retrospective analysis of the patients who were diagnosed and treated with histopathologically malignant tumors in the knee region in our hospital between 2004-2021 was performed from the hospital database. Patients' complaints, demographic information, and diagnostic and imaging findings were examined. In addition, tumor types, tumor localization, and treatments applied were analyzed.

**Results**: Malignant bone tumor was detected in 88 (35.7%) of 246 patients included in the study. The patients were 48 women and 40 men, with a mean age of 39.72±21.8 (6-76 years). A total of 88 patients were divided into the pediatric group (<18 years; n=39) and the adult group (≥18 years; n=49). The most common tumors were osteosarcoma in 54 (61.3%) and metastatic tumors in 22 (25%) patients. The most common localization of tumors was the distal femur with a rate of 75%. Metastasis was detected in 12 (18.2%) of 66 patients treated and followed up for primary malignant bone tumors. Limb sparing surgery was performed in 70 (79.5%), and various levels of amputation were performed in 14 (15.9%). Palliative radiotherapy was applied to two patients with metastatic lesions, while two patients who were in the neoadjuvant chemotherapy period died. The 5-year overall survival was 63.7%. Pediatric and adult age groups did not differ significantly in terms of survival (p=0.74), gender (p=0.585), and metastasis development (p=0.53).

**Conclusion:** The knee is a region that requires attention regarding bone tumors around it. As malignant bone tumors are rarely seen around the knee, a misdiagnosis may be made, and appropriate treatment may be delayed. Although the first diagnosis to come to mind for patients presenting with knee pain is trauma and growing pains, it must not be forgotten that a tumor could be the cause.

**Keywords:** bone tumors, malign, knee, surgery

## INTRODUCTION

The knee is the most common location for malignant bone tumors as well as many soft tissue sarcomas. The clinical presentation of these lesions usually includes pain and swelling associated with a palpable mass. In most primary bone tumors, the patient attributes their symptoms to traumatic events in the first place. This may lead to misdiagnoses and errors in the selection of the therapeutic approach. A treatment strategy in malignant bone tumors provided by a multidisciplinary team is the key factor for optimal management of such patients. In this study, cases of malignant bone tumors localized in the knee region, diagnosed and treated in our center, were reviewed in terms of various factors and treatment results.

Primary bone tumors are one of the most uncommon groups of oncological diseases. Of all tumors, approximately 1% are seen in the bones, and the majority of these are benign (1). According to the American Cancer Society data, 1,898,160 new cancer patients were diagnosed in 2021, and of these, a primary malignant bone tumor was determined in only 6310 (2).

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The reason for presentation to the hospital is generally painful or painless swelling. Patients with pain generally associate the pain with traumatic events. In particular, in the elderly patient group, symptoms associated with degenerative knee disorders can mask a bone tumor around the knee.

Diagnosis can be easily overlooked as the frequency is low in the general population, and therefore, the onset of treatment can be delayed. Starting treatment in the early stage is extremely important regarding tumor recurrence, metastasis, and survival (3-5).

This study aimed to determine the frequency of malignant bone tumors (primary and metastatic) seen around the knee in our region, the patients' type and demographic characteristics, and the treatments' outcomes.

## MATERIAL AND METHOD

A retrospective examination was made of patients with a bone tumor around the knee who presented at our hospital between 2004 and 2021. The study was carried out with the permission of Ondokuz Mayıs University/Training and Research Hospital, Noninvasive Clinical Ethics Committee (Decision No: 2022/178). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study included malignant bone lesions determined in the distal femur (the region 8 cm proximal from the joint line), the proximal tibia (8 cm distal from the joint line), the proximal fibula, and the patella. Soft tissue masses determined in the same region, lesions caused by reasons other than the tumor, synovial origin lesions, and benign bone tumors were excluded from the study. A record was made for each patient of the complaints on presentation, demographic information, diagnosis, radiographic imaging findings, and laboratory test results. The tumors of all the patients included in the study were diagnosed radiologically and/or pathologically. Then the tumor types, treatment applied, localization of the tumor, and demographic information was examined. The study flowchart is shown in **Figure 1**. Patients were divided into pediatric and adult age groups to investigate the effect of age groups on oncological outcomes. Analysis was performed in terms of factors of survival, gender, and metastasis development between these groups. The study flowchart is shown in **Figure 1.**

### Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS for Windows vn. 21.0 software (SPSS Inc., Chicago, IL, USA). Statistical values were stated as mean±standard deviation (SD), or median values for continuous variables, and as frequency (n) and percentage (%) for categorical variables. The effect of prognostic factors on survival was analyzed using Kaplan- Meier analysis and the Log Rank (Mantel-Cox) technique. A value of $p<0.05$ was considered statistically significant.

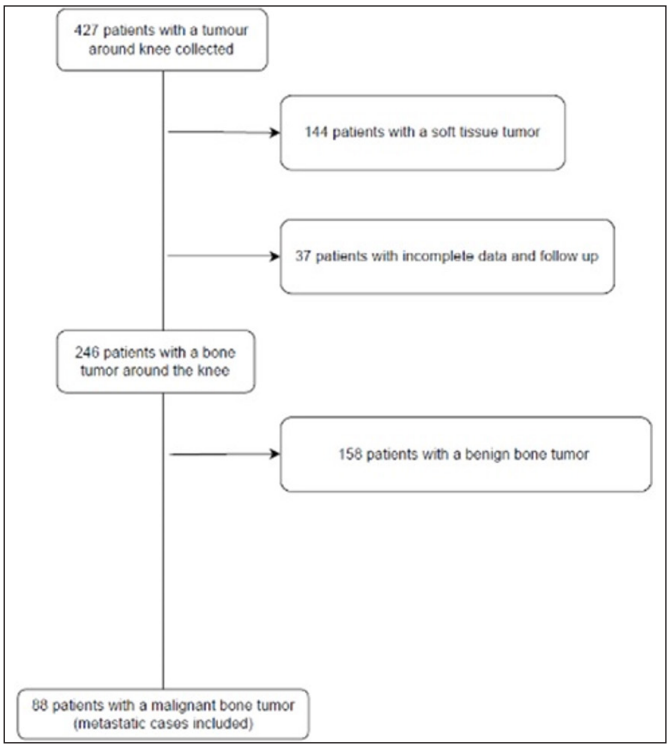


**Figure 1.** Study flowchart. The number of patients included in the study and demonstration of excluded patients.

## RESULTS

Of the 246 patients included in the study, 88 (35.7%) determined a malignant bone tumor The patients comprised 40 (45.4%) males and 48 (54.5%) females with a mean age of 39.72±21.8 years, and a mean follow-up period of 51.6 (3-156) months.

Osteosarcoma was determined in 54 (61.3%) patients, followed by metastatic tumors in 22 (25%). Ewing sarcoma was observed in 6 (7.2%) patients and chondrosarcoma in 6 (7.2%). The tumor was localized in the distal femur in 66 (75%) patients, in the proximal tibia in 18 (20.4%), in the proximal fibula in 3 (3.4%), and in the patella in 1 (1.2%) (**Table 1**).

Osteosarcoma was determined in 54 (61.3%) patients, localized in the distal femur in 42 (64.6%), and in the proximal tibia in 12 (18.75%). Of the six patients with Ewing sarcoma, localization was in the distal femur in 5 (83.3%) and the proximal fibula in 1 (16.6%). Surgical treatment was applied to 52 patients with osteosarcoma, as extremity-preserving surgery for 49 and amputation for 3. The 5-year survival rate was determined as 63.7%. Chondrosarcoma was determined in 6 patients, localized in the distal femur in 5 (83.3%) and the proximal tibia in 1 (16.6%).

In 12 (18.2%) of the 66 patients treated and followed up for primary malignant bone tumor, metastasis was determined. Of these, metastasis was to the lungs only in 8 patients and to the lungs together with multiple metastases in 4.

Of the 88 malignant bone tumors determined, 22 (25%) were metastatic lesions, localized in the distal femur in 14 (63.6%), the proximal tibia in 5 (22.7%), the proximal fibula in 2 (9%), and in the patella in 1 (4.5%) (**Table 1**).

**Table 1.** Demographic characteristics

| Parameters | n | % |
|---|---|---|
| Follow-up (months) | 51.6 (3-156) | |
| Age (mean) | 39.7±21.8 | |
| <18 | 39 | 44.3 |
| ≥18 | 49 | 67.1 |
| Sex | | |
| Male | 40 | 45.4 |
| Female | 48 | 54.5 |
| Tumor types | | |
| Osteosarcoma | 54 | 61.3 |
| Metastatic tumors | 22 | 25 |
| Ewing sarcoma | 6 | 7.2 |
| Chondrosarcoma | 6 | 7.2 |
| Localization | | |
| Distal femur | 66 | 75 |
| Proximal tibia | 18 | 20.4 |
| Proximal fibula | 3 | 3.4 |
| Patella | 1 | 1.2 |
| Complaints on presentation | | |
| Pain | 67 | 76.1 |
| Swelling | 9 | 10.2 |
| Pathologic fracture | 12 | 13.6 |
| Metastasis | | |
| Yes | 12 | 18.2 |
| No | 54 | 81.8 |

Of the 88 patients who presented with malignant bone tumors, extremity-preserving surgery was applied to 70 (79.5%), and amputation at various levels was performed on 14 (15.9%). Palliative radiotherapy was applied to two patients with metastatic lesions. Two (2.2%) patients were lost to mortality before surgical treatment could be applied.

The 5-year overall survival was 63.7%. The 5-year overall survival rates were 70.7% in the pediatric group and 57.9% in the adults (p=0.74). The 5-year survival rates of pediatric patients were 68.8% in males and 69.1% in females. In the adult group, it was found to be 46.6% and 61.2%, respectively(p=0.585). There was no statistical effect of metastasis development on overall survival in age groups(p=0.53) (**Table 2**).

**Table 2.** Evaluation of patient-related factors in terms of survival

| Parameters | 5-year overall survival | p value |
|---|---|---|
| Age group | 63.7% | |
| Pediatric/adult | 70.7% vs 57.9% | 0.740 |
| Sex | | |
| Male (pediatric/adult) | 68.8% vs 46.6% | |
| Female (pediatric/adult) | 69.1% vs 61.2%, | 0.585 |
| Patients with metastases | | |
| Pediatric/adult | 67.1% vs 62.7% | 0.531 |
| Total Patient | 63.7% | |

## DISCUSSION

Bone tumors are frequently seen in the knee region. In a study of 1925 patients in our clinic in 2014, of 687 bone tumors determined, 174 (25.3%) were in the knee region (6). In another study conducted in Turkey, Öztürk et al. (7) reported that of 1139 bone tumors determined, 246 (21.2%) were localized in the distal femur. The area of most involvement around the knee was the distal femur in the current study, consistent with the literature. In our study of 246 tumors, 162 (65.8%) were localized in the distal femur, 67 (27.2%) in the proximal tibia, 13 in the proximal fibula (5.2%), and 4 (1.6%) in the patella.

Pain is the most common reason for patients to present at the hospital. Swelling around the knee and restricted movement are frequently seen symptoms. Especially in patients of poor socioeconomic status, the reason for the first presentation at the hospital may be a pathological fracture. The incidence of pathological fracture development during diagnosis or while receiving chemotherapy has been reported to be 5-10% in the literature (6). Of the 88 patients in the current study, 67 (76.1%) presented with pain at the hospital. The complaint on presentation was swelling alone in 9 (10.2%) patients. The pathological fracture was seen in 12 (13.6%) patients. Of the 54 patients diagnosed with osteosarcoma, the pathological fracture was seen in 3 (5.5%), during diagnosis in 2, and while receiving neoadjuvant chemotherapy in 1. The incidence of pathological fracture was higher in patients with metastatic lesions. Of the 22 patients diagnosed with metastasis, nine presented at the hospital because of pathological fracture.

Osteosarcoma is the most frequently determined primary malignant bone tumor of all bone tumors(8). In a study by Bielack et al. (9) of 1702 patients with osteosarcoma, it was reported that 43% were localized in the distal femur and 23% in the proximal tibia. In the current study, osteosarcoma was the most common malignant tumor around the knee, determined in 54 (21.9%) of 246 patients. Consistent with findings in the literature, the most common site of localization in the current study was the distal femur (64.6%) (**Figure 2**).

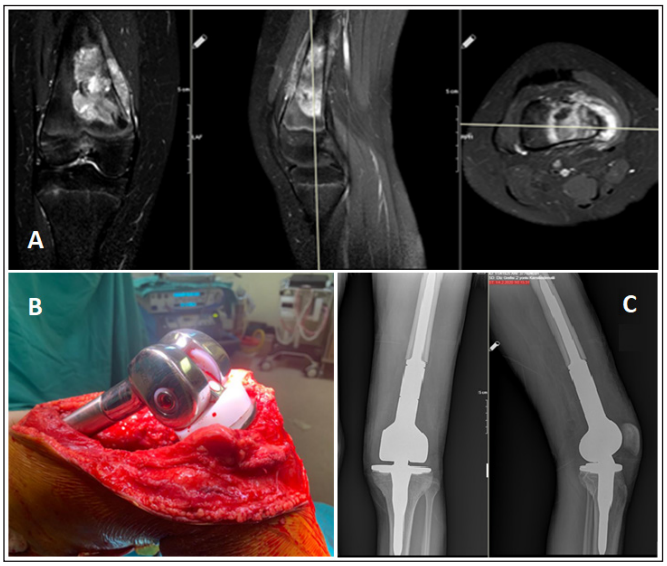


**Figure 2.** A) Images of osteosarcoma localized in the distal femur in different sections in MR T2 sequence B) Endoprosthetic prosthesis application after resection C) Postoperative AP and lateral radiographs

In a study by Marko et al. (10) of 9595 cases, metastasis was determined during the diagnosis of 18% of the patients with osteosarcoma. In the current study, there was seen to be metastasis in 4 (7.4%) patients during diagnosis, and of these, three were isolated lung metastasis. In the past, amputation was the gold standard in treating osteosarcoma. Still, in recent years, extremity-preserving surgery has come to the fore due to developments in chemotherapy, radiotherapy, and surgical techniques (11, 12). Simon et al. (13) evaluated 227 patients with sarcoma who were applied with extremity-preserving surgery or amputation and reported no difference in terms of survival of the patients. Two patients were lost to mortality in the current study while neoadjuvant chemotherapy was ongoing. The remaining 52 patients with osteosarcoma were treated surgically, with extremity-preserving surgery applied to 49 and amputation to 3 patients. In literature, the 5-year survival rate for patients aged <40 years with osteosarcoma has been reported in the range of 53%-71%(14, 15). In the current study, the 5-year survival rate was 71.4% in the pediatric age group and 62.5% in the adult group. Yao et al. (16) reported this rate as 57.66% in the pediatric age group, while Tina et al. (17) reported it as 86%.

Ewing sarcoma is rarely seen around the knee. It is determined more in the diaphysis of long bones and the metaphysic-diaphyseal junction (18, 19). It has been reported that 10% of Ewing sarcomas could be localized around the knee (20). Consistent with the literature, involvement around the knee was determined in 6 (10.9%) of the 55 patients determined with Ewing sarcoma in our clinic between 2004 and 2021. The localization was determined in the distal femur in 5 patients and the proximal fibula in 1.

In the current study, the 5-year survival rate was found to be 50%. In the literature, no study was found in terms of survival in Ewing sarcoma cases localized around the knee. This may be because this rare tumor often has diaphyseal involvement. However, since it is mostly seen in the pediatric age group, no comparison can be made with the adult group in terms of survival.

The worst prognosis criterion in Ewing sarcoma is metastasis at diagnosis. In a previous study, the 2-year disease-free survival rate was 32% in 39 patients with isolated lung metastasis and 20% in patients with widespread metastasis (21, 22). In the current study, there was metastasis during diagnosis in 2 patients with tumor localization in the distal femur. High femoral amputation was performed in 1 of these patients, followed by chemotherapy and radiotherapy.

The other primary malignant bone tumor localized around the knee that was determined in the current study was chondrosarcoma, localized in the distal femur in 5 patients and the proximal tibia in 1. There was seen to be lung metastasis in 1 patient during diagnosis. In 1 patient, there was involvement in the ipsilateral trochanter major together with lung metastasis. Hip disarticulation was applied to that patient and femoral amputation to the other five patients. In the current study, the 5-year survival rate was 33% in adult patients and 100% in the pediatric group. In the literature, we could not find any study in terms of the survival of chondrosarcoma localized around the knee.

After the liver and lungs, the bones are the 3rd most common region where metastasis is determined (23). Metastising tumors are usually lung, breast, prostate, kidney, and thyroid tumors (24). Of the bone lesions determined in the current study, 22 (25%) were seen to be metastatic lesions, of which 19 were metastasis from organs, and three were determined to be malignant mesenchymal tumor metastasis in adjacent tissue. There was metastasis in the distal femur in 14 patients, the proximal tibia in 5, the proximal fibula in 2, and the patella in 1 patient. A total of 9 patients presented at the hospital because of pathological fracture, and the most common reason for presentation in the other patients was pain.

Metastasis related to lung cancer was determined most often. Of the 9 cases of lung metastasis, involvement was in the distal femur in 7 and the proximal tibia in 2. Two patients presented at the hospital because of pathological fractures. Metastasis related to breast cancer was determined in 8 patients. Of these, involvement was in the distal femur in 7 and the patella in 1 and 3 patients presented with pathological fracture. Renal cell carcinoma metastasis was determined in 4 patients, all of which had a lesion in the distal femur, and all presented

at the hospital with a pathological fracture. Fracture fixation was applied to 3 patients, and in 1 patient, there was involvement in the ipsilateral femoral trochanteric region, so hip disarticulation was applied. Metastasis related to prostate cancer was determined in the distal femur of 1 patient. Surgical treatment was not applied to patients with multiple metastases.

It is known that the development of metastases has a negative effect on survival rates in malignant bone tumors. In our study, no statistical effect of metastasis development on overall survival was found in age groups ($p<0.05$). We think that this result may have been caused by the heterogeneity between the patient groups.

There were some limitations to this study, primarily the retrospective design. The data used were patients discussed in the tumor council, so the rates determined do not reflect the frequency of tumors seen in the general population. As this study was specific to a certain body area, some tumors such as chondrosarcoma and Ewing sarcoma were determined at low numbers. However, the fact that the groups are not homogeneous and the treatment methods are not standardized is an important limitation of the study.

## CONCLUSION

The knee is a region that requires attention regarding bone tumors around it. As malignant bone tumors are rarely seen around the knee, a misdiagnosis may be made, and appropriate treatment may be delayed. The tumor grade is critical in the treatment and survival of patients. Early diagnosis and treatment can be life-saving. Tumors may be localized around the knee in all age groups, but primary malignant tumors, in particular, are seen more often in the first two decades of life. Patients' active and healthy appearance in this age group may be misleading for clinicians. Although the first diagnosis to come to mind for patients presenting with knee pain is trauma and growing pains, it must not be forgotten that a tumor could be the cause.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Ondokuz Mayıs University/ Training and Research Hospital, Noninvasive Clinical Ethics Committee (Decision No: 2022/178).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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