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**Tülay Zenginkinet**
Department of Pathology, Istanbul Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

**Enes Kanay**
Department of Orthopaedics and Traumatology, Istanbul Medeniyet University Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

**Tarık Sarı**
Department of Orthopaedics and Traumatology, Istanbul Medeniyet University Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

**Salim Çağatay Akbulut**
Department of Orthopaedics and Traumatology, Istanbul Medeniyet University Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

**Muhlik Akyürek**
Maria-Josef Hospital, Greven, Germany

**Korhan Özkan**
Department of Orthopaedics and Traumatology, Istanbul Medeniyet University Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

**Corresponding Author:**
**Tülay Zenginkinet**
Department of Pathology, Istanbul Goztepe Professor Dr. Suleyman Yalcin City Hospital, Istanbul, Turkey

# Results of amputation after limb salvage surgery and primary amputation after diagnosis in malignant bone and soft tissue tumours

**Tülay Zenginkinet, Enes Kanay, Tarık Sarı, Salim Çağatay Akbulut, Muhlik Akyürek and Korhan Özkan**

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**Abstract**
**Introduction:** In the surgical treatment of malignant musculoskeletal tumours, limb sparing surgery and rarely amputation are preferred. In this study, we evaluated our patients who had undergone amputation after limb-salvage surgery or who had undergone primary amputation after diagnosis in our clinic.
**Methods:** In this study, a total of 18 patients who had undergone amputation due to complications after extremity-sparing surgeries performed due to primary bone, soft tissue sarcoma/carcinoma or benign aggressive bone and soft tissue tumour or who had direct amputation after the first diagnosis between the years 2015-2021 were evaluated retrospectively.
**Results:** A total of 18 patients (8 men, 10 women) underwent amputation in our clinic between 2015-2021; Twelve of them underwent secondary amputation after limb-sparing surgery (LSS). And primary amputation was performed in 6 patients after diagnosis. The mean age of the patients was 46.8 years. A total of 10 patients died in the post-amputation period. It was also observed that survival duration of the remaining 8 patients who had been still alive after amputation was 16,3 months (min/max: 6 months-36 months).
**Conclusion:** Today, limb salvage surgery has become the standard in malignant bone and soft tissue tumours of the extremities and the need for amputation is decreasing. Early referral of patients to reference centers and compliance with the necessary surgical rules in limb-sparing surgery can reduce the need for amputation and increase the success rate of limb salvage surgery.

**Keywords:** Malignant tumours, extremity-sparing surgery, amputation

## Introduction
Two main methods are preferred in the surgical treatment of malignant musculoskeletal tumors. These are limb-salvage surgery and rarely, amputation.
While extremity salvage surgery is applied as the basic principle in the treatment of both primary soft tissue and bone sarcomas and metastatic bone and soft tissue lesions, amputation has to be performed very rarely in recent years.
When these two methods are compared, considering that appropriate surgical margins are provided in both, it is seen that although there is no significant difference in terms of survival and life expectancy, limb-sparing surgery provides a better quality of life and functional capacity than amputation [1].
Although amputation was preferred more in the past years, especially in cases of delayed malignant bone and soft tissue tumours, limb salvage surgery has become the standard method thanks to the increase in experience gained in reconstructive surgery practices, developments in chemotherapy and radiotherapy regimens which are the current oncological treatment methods and innovations in imaging studies [1, 2].
There are 2 important rules to be considered in order to obtain better results than amputation in limb-sparing surgery. These are the provision of appropriate surgical margins and provision of satisfactory functionality of the reconstructed limb [2, 3].
Although amputations are rarely used in the field of orthopaedic oncology, they appear as an option in cases where limb-sparing surgery cannot be applied [4].

Amputation may become inevitable if a non-functional extremity occurs after resection, if there is a local recurrence that cannot be removed due to widespread contamination, or if success is not achieved in the treatment of persistent infection and/or ischemia after limb-sparing surgery [5, 6, 7].

## Material and Method

This study was conducted in accordance with patient consent and received approval from the Ethics Committee of the Istanbul Medeniyet University Prof Dr Süleyman Yalçın Göztepe City Hospital. Our patients who had been amputated due to complications after limb salvage surgery or who underwent direct amputation after the first diagnosis performed due to primary bone, soft tissue sarcoma/carcinoma or benign aggressive bone and soft tissue tumor between 2015-2021 in our hospital (Istanbul Medeniyet University Prof Dr Süleyman Yalçın Göztepe City Hospital), which is a tertiary musculoskeletal system oncology center, were included in this study.

In our study, we examined patients' demographic characteristics (Age and gender), tumor characteristics (Diagnosis, localization, depth, size and histopathological grade), surgical margins (Wide, marginal or intralesional), indications for amputation (Local recurrence, prosthetic infection, mechanical failure or skin necrosis) presence of metastases before amputation and during follow-up, survival after the first surgery, and survival times after amputation.

## Statistical Analysis

The data were analysed using IBM SPSS V23. Mean, standard deviation, median, frequency, ratio, minimum, and maximum values were used to present the study data in tables. Independent t test was used to compare two independent groups with normal distributions. Mann–Whitney U test was used for comparisons of two independent groups with non-normal distributions. Significance was evaluated at $p<0.05$.

## Results

The data of 18 patients (8 males, 10 females; mean age: 46.8 min/max (9-86 years)) who had undergone amputation in our clinic between 2015 and 2021 were retrospectively analysed (Table 1). Osteosarcoma in 5 patients (1 patient with chondroblastic, 2 patients with osteoblastic, 1 patient with de-differentiated parosteal and 1 patient with osteosarcoma secondary to radiotherapy), chondrosarcoma in 3 patients, Ewing sarcoma in 1 patient, rhabdomyosarcoma in 1 patient, giant cell bone tumor in 1 patient, giant cell tendon tumor in 1 patient, soft tissue sarcoma in 4 patients (Myxofibrosarcoma in 1 patient *[figure 1,2 and 3]*, undifferentiated pleomorphic sarcoma in 2 patients, epithelioid sarcoma in 1 patient), metastatic breast ca in 1 patient, and squamous cell carcinoma in 1 patient were detected.

After diagnosis, 6 patients underwent primary amputation. These were applied to 1 giant cell bone tumor, 1 diffuse type giant cell tendon tumor, 1 chondrosarcoma [figure4], 1 Ewing sarcoma, 1 undifferentiated pleomorphic soft tissue sarcoma and 1 osteosarcoma patient.

Two of these patients had benign aggressive bone and soft tissue tumors, giant cell bone tumor and giant cell tendon tumor, respectively. In our 4 patients with musculoskeletal tumors who underwent primary amputation, lung metastases were present before the amputation, and these patients died due to the disease during their follow-up.

Secondary amputation was performed in 12 patients who had been included in the study after limb-salvage surgery (LSS). Secondary amputation was applied with an oncological indication.to 10 of our patients who had developed relapse after LSS. Metastases were detected in 6 of these patients before amputation [figure 1, 2, 3]. In the remaining 4 patients, no metastasis was detected in the follow-ups after amputation.

LSS was applied to 2 of our patients and persistent infection developed in their follow-up. When these two patients were examined, it was seen that our first patient applied to us with squamous cell carcinoma recurrence in the proximal tibia after extremity salvage surgery at another center. This patient underwent reconstruction with extra-articular resection and arthrodesis-type intercalary prosthesis. In the follow-up, deep infection developed (first pseudomonas aeruginous, then staphylococcus haemolyticus were cultured) and a 2-stage revision was planned. However transfemoral amputation was performed following candida albicans infection that developed after a 2-stage revision.

In our other patient, revision surgery was performed in the 15th year after limb salvage surgery due to aseptic loosening findings in the mega prosthesis. Infection developed 3 months later, and staphylococcus epidermidis was grown in the deep tissue culture taken. Debridement, antibiotics and implant retention therapy (DAIR) procedure were performed.

In the follow-up, due to persistant infection, a 2-stage revision and free-flap was recommended due to accompanying soft tissue coverage problems, however, it was decided to proceed with transfemoral amputation due to the patient's accompanying comorbidities.

When the two groups who underwent primary amputation and secondary amputation after LSS were examined, no statistically significant difference was found between the survival times of patients with lung metastases before the amputation procedure. (The mean life expectancy of the group undergoing primary amputation was 7.75 months (2-14 months), and the mean life expectancy of the patient group who underwent amputation after LSS was 7.2 months (4-14 months) p value: 0.902). 5 of our patients who underwent LSS due to soft tissue and bone sarcoma in our clinic or in another center and then underwent secondary amputation due to recurrence in the follow-up, are still alive, and no metastatic focus was found in systemic scans with PET-CT. In the follow-up of 1 patient who underwent secondary amputation after LSS, lung metastases developed and metastasectomy was performed. The patient continues to live in the post-op 36th month.

In 7 of our patients who had to be amputated after limb salvage surgery, there was a history of operation in centers other than our clinic and a history of recurrence developed at various times. In six of these patients, the first surgical intervention was performed intralesionally in other centers. The first operations (Limb salvage surgery) of our other 5 patients who underwent secondary amputation due to recurrence during follow-up were performed in our clinic.

Except two patients, all other patients underwent amputation due to extensive neurovascular and compartmental involvement that did not permit limb-sparing surgery. According to pet-ct results during amputation, 3

patients had extensive multiple metastases and 7 patients had only lung metastases.

If the life expectancy of the patient group was examined, it was seen that 10 patients lost their lives in the post-amputation period and 8 patients survived. It was determined that two of these 8 patients were patients with benign aggressive soft tissue/bone lesions who underwent primary amputation, and the remaining 6 patients were from the group that had undergone secondary amputation. Considering our data on patient follow-ups after amputation, it was seen that 8 of our patients who were still alive at their last control had an average survival of 16.3 months (min/max: 6 months-36 months). This patient group can perform at least their basic daily living activities. It was observed that the average life expectancy of the patients who died during their follow-up was 7.3 months (min/max: 2 months/14 months) and the process resulted in loss secondary to the presence of recurrence/metastasis.

In addition, the average life expectancy of our 6 patients who underwent secondary amputation after LSS due to soft tissue-bone sarcoma died during their follow-up was calculated as 7 months (4-14 months), while those who underwent primary amputation due to soft tissue-bone sarcoma and died in their follow-ups, the average life expectancy of 4 patients was calculated as 7.75 months (2-14 months) with no statistically significant difference.

## Discussion

In this study, we aimed to reveal the histopathological and clinical features of musculoskeletal tumors of patients undergoing primary amputation or secondary amputation after limb-sparing surgery.

Previous studies have shown that patients with extremity sarcoma who require amputation have a worse prognosis because of multiple compartment involvement, diffuse neurovascular involvement, and larger tumors [8-11]. Therefore, we did not compare the survival of patients who needed amputation with those who underwent limb-sparing surgery in our study.

The most important factor causing primary amputation in our patient population was multi-compartmental involvement that would not allow limb-sparing surgery.

In the process of going to secondary amputation, the most important factor was the development of local recurrence. This was found to be consistent with the literature [11, 12]. In two of our patients, persistent infection caused amputation, while in one of these two patients, a soft tissue coverage problem was also accompanied.

Bone and joint defects after tumor resections are mostly reconstructed with mega prostheses. The size of the tumor and the soft tissue coverage problems that develop after the resection cause the infection rates to be higher than the traditional knee and hip arthroplasty.

A higher rate of amputation may be encountered, especially due to tissue covering problems that developed secondarily to tibial resection and the prosthesis applied afterward, and related infection [12].

In the early period (first 4 weeks) of prosthesis infections, the prosthesis can often be left in place with radical debridement and polyethylene replacement. In late infections, considering the biofilm layer formed, a two-stage revision procedure should generally be applied to overcome the infection.

In our study, a two-stage revision was performed in our patient with an infected megaprosthesis, but the process resulted in amputation due to persistent infection. In our other patient, the process went to amputation without a two-stage revision due to post-prosthetic deep infection, soft tissue covering problems and the patient's accompanying comorbidities.

When our patient population was examined, no local recurrence was encountered after amputation, and these results were found to be consistent with the results of Baysal Ö. *et al*.'s study [13]. This result was evaluated due to the negative surgical margins obtained after amputation in all patients.

In studies conducted by Stojadinovic A. *et al*. and Erstad D.J *et al*., the rates of distant organ metastases before amputation, in patients who had previously undergone limb-sparing surgery for extremity sarcomas were reported as 16.7% and 23.5%, respectively [5, 6]. In a study conducted in our country, Baysal Ö. *et al*. reported this rate as 52% [13]. In our study, this rate was found to be 50%. The most important reasons for this might be the delays of the patients in admission, the sociocultural characteristics triggered by the fear of losing limbs, and interventions made in institutions where there was not an orthopedic oncology center.

Six patients who underwent amputation after limb salvage surgery had their first surgery for existing musculoskeletal sarcoma in centers without an orthopedic oncology reference. Inadequate surgical margins led to recurrences that developed in the later period.

## Study Limitations

The retrospective design, limited patient group and numbers with various diagnoses (benign aggressive course, malignant course, patients with distant metastases) are one of the limitations of this study.

This is one of the rare studies presenting the clinical and histopathological features of amputated patients with musculoskeletal tumors in a developing country.

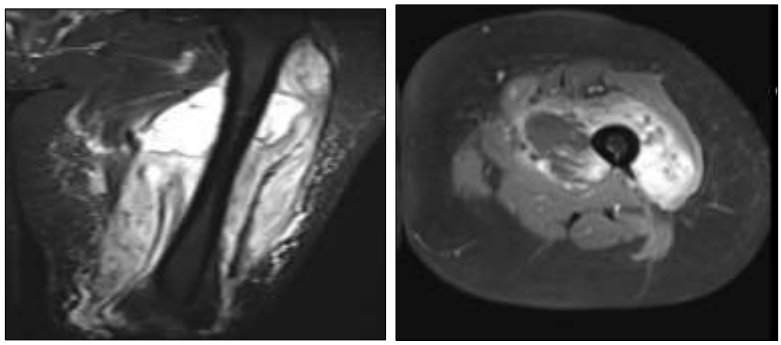

**Fıg 1: SS;** Age 55; myxofibroid sarcoma in left thigh

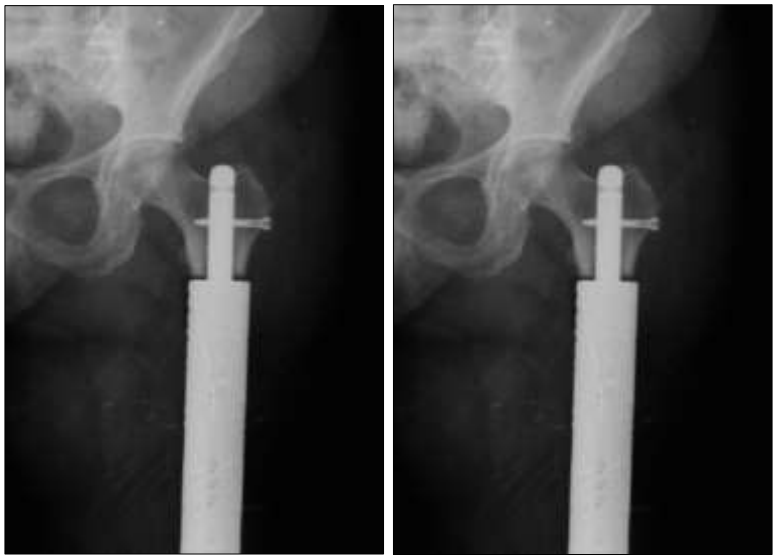

**Fig 2:** SS; Age 55; myxofibroid sarcoma in left thigh; after resection of the sarcoma with the involved bone

**Fig 3** SS; Age 55; myxofibroid sarcoma in left thigh local recurrence and hip desarticulation

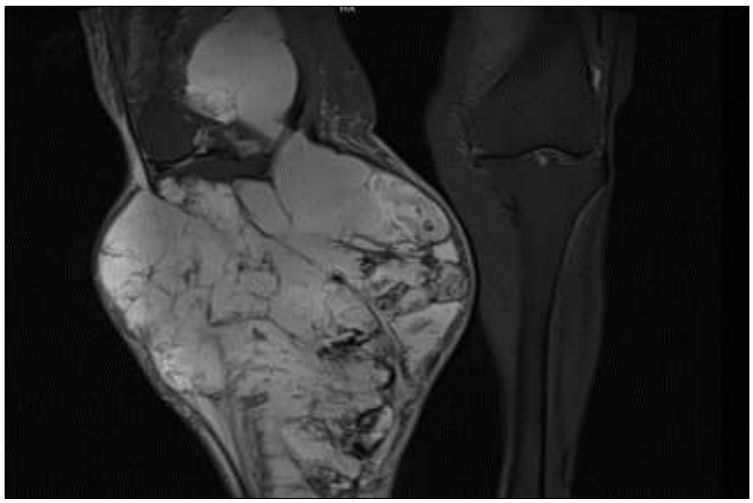

**Fig 4:** HM; Age 86; right cruris mixoid chondrosarcoma (Pre op image)

**Table 1:** Summary of the clinicopathological features of patients

| Name | Age | Survıval status | Sıze before amputatıon | Amputatıon type | Follow-up after surgery | Grade of tumour | Local recurrence | Indıcatıon of amputatıon | Metastasıs before amputatıon | Dıagnosıs & locatıon of tumor | Pathology | Follow-up (tıme) mean/ range |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| H.ö. (lss) | 66 | Alıve | Sıze before amputatıon 5-10 cm | Transfemoral amputatıon | After amputatıon;26 months alıve; no recurrence and met | Grade ıı | Local recurrence; 34 months after first resectıon | Local recurrence after lss (Neurovascular ınvolvement) | No | Chondrosarcoma ın rıght femur dıstal regıon | Grade ıı chondroasrcoma | 26 months/mean (11.3) range (2-36 months) |
| H.g. (lss) | 73 | Alıve | - no tumor before amputatıon | Transfemoral amputatıon | After amputatıon; 14 months alıve; no recurrence and met | Grade ııı | 2 tımes local recurrence (operated ın another clınıc) | Local recurrence after lss +persıstent ınfectıon | No | Squamous cell carcınoma ın the rıght knee | Squamous cell carcınoma | 14 months/mean (11.3) range (2-36 months) |
| S.d. (lss) | 44 | Alıve | Sıze before amputatıon 5-10 cm | Transfemoral amputatıon | After amputatıon;12 months alıve; no recurrence and met | Grade ııı | 1 local recurrence; 6 months after first resectıon (operated ın another clınıc) | Local recurrence after less (Neurovascular ınvolvement) | No | Chrondroblastıc osteosarcoma ın left cruris | Chrondroblastıc osteosarcoma | 12 months / mean (11.3) range (2-36 months) |
| H.a. | 19 | Alıve | Sıze before amputatıon 5-10 cm | Ray amputatıon | After amputatıon; 9 months alıve; no recurrence and met | - | No | Prımary amputatıon (neurovascular ınvolvement) | No | Gıant cell bone tumor ın the proxımal phalanx of the left hand 4th fınger | Gıant cell bone tumor | 9 months / mean (11.3) range (2-36 months) |
| S.d. (lss) | 42 | Exıtus | Sıze before amputatıon >10 cm | Transhumeral amputatıon | After amputatıon; 6. Month(decaesed) | - | 1 local recurrence 6 months after first resectıon (operated ın our clınıc) | Local recurrence after lss (neurovascular ınvolvement) | No | Breast carcınoma metastasıs on the rıght radıus head | Breast carcınoma metastasıs | 6 months / mean (11.3) range (2-36 months) |
| Ş.k. | 63 | Alıve | Sıze before amputatıon 5-10 cm | Fınger amputatıon | After amputatıon; 8 months alıve; no recurrence and met | - | No | Prımary amputatıon (neurovascular ınvolvement) | No | Tenosınovıal gıant cell tumor ın 3rd fınger of rıght hand | Tenosınovıal gıant cell tumor | 8 months / mean (11.3) range (2-36 months) |
| H.m. | 86 | Exıtus | Sıze before amputatıon >10 cm | Hıp desartıculatıon | After amputatıon; 2. Month(decaesed) | Grade ııı | No | Prımary amputatıon (neurovascular ınvolvement) | Met before amputatıon | Myxoıd chondrosarcoma ın rıght crurıst | Myxoıd chondrosarcoma | 2 months / mean (11.3) range (2-36 months) |
| Ö.y. (lss) | 18 | Alıve | Sıze before amputatıon >10 cm | Hıp desartıculatıon | After amputatıon; 36 months alıve; metastasectomy for lung | Grade ııı | Local recurrence 3 tımes (operated ın our clınıc) | Local recurrence after lss (neurovascular ınvolvement) | Met before amputatıon | Rhabdomyosarcoma ın left thıgh | Small round cell malıgn tumor wıth dıffused spındle cell areas (embrıonal rhabdomyosarcoma) | 36 months / mean (11.3) range (2-36 months) |
| A.a. (lss) | 74 | Exıtus | Sıze before amputatıon >10 cm | Hıp desartıculatıon | After amputatıon; 6. Month (Deceased) | Grade ııı | 1 local recurrence (operated ın another clınıc) | Local recurrence after lss (neurovascular ınvolvement) | Met before amputatıon | Soft tıssue sarcoma ın the left proxımal thıgh | Pleomorfıc sarcoma | 6 months / mean (11.3) range (2-36 months) |
| S.s. (lss) | 58 | Exıtus | Sıze before amputatıon >10 cm | Internal hemıpelvectomy | After amputatıon; 4. Month (Decaesed) | Grade ııı | Local recurrence 2 tımes (operated ın another clınıc) | Local recurrence after lss (neurovascular ınvolvement) | Met before amputatıon | Epıtheloıd sarcoma ın rıght thıgh | Epıteloıd sarcoma | 4 months / mean (11.3) range (2-36 months) |
| S.s. (lss) | 55 | Exıtus | Sıze before amputatıon >10 cm | Hıp desartıculatıon | After amputatıon; 6. Month (Decaesed) | Grade ııı | 1 local recurrence (operated ın our clınıc) | Local recurrence after lss (neurovascular ınvolvement) | Met before amputatıon | Myxofibroıd sarcoma ın left thıgh | Myxofibroıd sarcoma | 6 months / mean (11.3) range (2-36 months) |
| M.y. (lss) | 43 | Exıtus | Sıze before amputatıon >10 cm | External hemıpelvectomy | After amputatıon; 14. Month (Deceased) | Grade ııı | Local recurrence 2 tımes (first ın another, second ın our clınıc) | Local recurrence after lss (neurovascular ınvolvement) | Met before amputatıon | Rıght perıprosthetıc femur fracture (pathologıc) | Clear cell chondrosarcoma | 14 months / mean (11.3) range (2-36 months) |
| M.ö. | 72 | Exıtus | Sıze before amputatıon >10 cm | External hemıpelvectomy | After amputatıon; 4. Month(decaesed) | Grade ııı | No | Prımary amputatıon (neurovascular ınvolvement) | Met before amputatıon | Soft tıssue sarcoma ın left thıgh | Indıferentıfied pleomophıc sarcoma | 4 months / mean (11.3) range (2-36 months) |
| B.k. | 8 | Exıtus | Sıze before amputatıon >10 cm | Transhumeral amputatıon | After amputatıon; 11. Month(decaesed) | Grade ııı | No | Prımary amputatıon (neurovascular ınvolvement) | Met before amputatıon | Ewing sarcoma ın rıght elbow | Indıferentıfied malıgn round cell tumor (ewıng sarcoma) | 11 months / mean (11.3) range (2-36 months) |
| Y.t. | 21 | Exıtus | Sıze before amputatıon >10 cm | Transfemoral amputatıon | After amputatıon; 14. Month(decaesed) | Grade ııı | No | Prımary amputatıon (neurovascular ınvolvement) | Met before amputatıon | Osteosarcoma ın femur | Conventıonal osteosarcoma | 14 months / mean (11.3) range (2-36 months) |
| Mt (lss) | 53 | Exıtus | Sıze before amputatıon >10 cm | Internal hemipelvektomy | After amputatıon; 6. Month(decaesed) | Grade ııı | 1 local recurrence (operated ın another clınıc) | Local recurrence after lss + secondary ostetosarcoma | Met before amputatıon | Osteosarcoma ın pelvıc regıon | Secondary osteosarcoma due to radıotherapy | 6 months / mean (11.3) range (2-36 months) |
| St (lss) | 17 | Alıve | Sıze before amputatıon >10 cm | Transfemoral amputatıon | After amputatıon; 24 months alıve; no recurrence and met | Grade ııı | Local recurrence 2 tımes(operated ın another clınıc) | Local recurrence after lss (neurovascular ınvolvement) | No | Osteosarcoma ın femur dıstal regıon | De-dıferenced parosteal osteosarcoma | 24 months / mean (11.3) range (2-36 months) |
| R.b (lss) | 45 | Alıve | - no tumor before amputatıon | Transfemoral amputatıon | After amputatıon;2. Months alıve; no recurrence and met | Grade ııı | No | Local recurrence after lss+persıstent ınfectıons | No | Osteosarcoma ın proxımal tıbıa | Conventıonal osteosarcoma | 2 months / mean (11.3) range (2-36 months) |

## Conclusion

It may be extremely important to establish close contact with the psychologist and psychiatrist before the operations in order to convince both the patient and the family before it is too late for the operation and to reduce the psychological trauma that may occur.

The implementation of the amputation option for palliative purposes or for final treatment should be given at multidisciplinary orthopaedic oncology meetings.

Early referral of patients with musculoskeletal tumours to reference centres may reduce the need for amputation and increase the success rate of limb salvage surgery. A common consensus can be established in the future with studies to be conducted with larger patient groups.

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