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Clinical results of endoprosthetic reconstructions in metastatic and primary bone tumors

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Abstract

In this study, we aimed to compare the functional outcomes and survival of 38 patients with primary bone and metastatic bone tumors who were reconstructed with endoprosthesis. Thirty-eight patients who underwent endoprosthesis for malign bone tumors 2012- 2015 were included in the study. We retrospectively reviewed 38 patients, eight of whom underwent limb salvage with tumor resection prosthesis of tibia, 21 femur, and 9 humerus. When comparing functional outcomes, the revised Musculoskeletal Tumor Society (MSTS) scoring system was used for all surviving patients. The patients were evaluated in two groups as primary bone tumor and metastatic bone tumor. The mean follow-up period of 32 healthy and alive patients was 38 (12 to 98) months. While 12 patients were primary malign bone tumors, the other 26 patients had bone metastasis. All six patients who died during follow-up had a diagnosis of metastatic bone tumor. Periprosthetic infection was observed in two patients, recurrence tumor in one and prosthetic dislocation in one. It was found that the MSTS score in patients with primary bone tumors (22, 6) was statistically significantly higher than in patients with metastases (17, 6) ($p<0.05$). The score of the patients who had upper extremity (%22) reconstruction was found to be significantly higher than the lower extremity (%78) ($p<0.05$). It was determined that better functional results were obtained for patients with primary bone tumors than patients with bone metastasis. The low complication rates obtained because of this study, which had an average follow-up of 38 months, showed us that reconstruction with endoprosthesis is promising for tumors of the femur, tibia and humerus.

Keywords: Endoprosthesis, bone tumor, metastasis

Introduction

The main purpose in the treatment of malignant tumors in the musculoskeletal system; it is "life first, then quality life". Advances in chemotherapy and reconstructive methods play an important role in the development of limb salvage procedures. The age of the patient, localization and invasion of the tumor are effective in determining the most appropriate surgical method. Limb-salvaging reconstruction methods are; megaprosthesis (tumor resection prosthesis, endoprothesis and intercalaryprothesis), osteoarticular allografts, allograft-prosthesis systems, vascularized bone grafts, arthrodesis, extensible prostheses, rotationplasty and bone transport with Illizarov technique [1, 2]. When underletting these two conditions should be considered when undersetting these limb- salvaging methods in treatment: Survival rates should not be worse than amputation and adequate function should give to the limb. Limb salvage methods in treatment, two conditions should be considered: survival rates should not be worse than amputation and adequate function should be given to the limb. In limb salvage surgery, excision of the tumor with the appropriate margin and reconstruction with an endoprosthesis is used. In patients with survey less than 2 years undergoing reconstruction with an endoprosthesis, it provides great convenience for performing daily life activities [3]. This method has proven to be cost effective. Complications may occur in the long term. These; such as infection, aseptic loosening, mechanical failure [4]. Considering union problems in metastatic bone tumors, pathological fractures of weight-bearing joints such as the hip joint; megaprothesis can provide immediate stability and early function [5]. Biological fixation methods have become increasingly common in fixing megaprosthesis to bone tissue. In this way, sports activities can be done easily by providing sufficient muscle power [6]. Chemotherapy contributes negatively to bone healing. Therefore, it is associated with a high rate of fracture, nonunion, delayed union and infection [7]. The aim of this study was to

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determine the survival of reconstruction with a megaprosthesis that is one of the limb salvage methods, in malignant bone tumors. In addition, it was aimed to compare clinical results, functional results, complications and survival rates with the literature.

Materials and Methods

Ethics committee approval for the study was obtained from the scientific research and publication ethics committee of medicine faculty with the decision number 2020/1175. Informed consent was obtained from all patients included in the study. Thirty-eight patients with primary or metastatic bone tumors reconstructed with endoprosthesis between 2012 and 2019 were reviewed retrospectively. There were twenty-three men and fifteen women with a mean age of 60 years (21 to 86). The diagnosis included osteogenic sarcoma in three patients, chondrosarcoma in four, multiple myeloma in three, lymphoma in four, Ewing sarcoma in one and malignant mesenchymal tumor of bone in one. Patients diagnosed with bone metastasis: there were four renal cell carcinomas, nine lung carcinomas, five breast cancer, three prostate cancer and one rectal cancer (Table 1).

The resection site of the tumor was the tibia in eight patients, the femur in 21 and the humerus in nine. The mean bone length at which the resection was performed was 12.6 (4 to 30) cm. Comprehensive oncological evaluations and tumor council decision were made for all patients before surgery. In addition, radiographs, extremity MRI, thorax CT, and whole body scintigraphy were performed before the surgical intervention. When resection and endoprosthesis were indicated, patients were treated with a standard pre-postoperative chemotherapy. The incision area biopsied was excised ellipsoidal. A frozen section was sent to the pathology department at the level of the resected bone in each patient and the appropriate surgical margin was confirmed. All surgical incisions were made to include the biopsy wound. Patients older than 60 years and with metastatic tumors spent their first days postop in the intensive care unit for a short time. They were treated with antibiotics until the hemovac drain was removed and were discharged when they were medically stable. Early mobilization and weight bearing were underwent to all patients whose medical condition was stable. After the surgery, routine follow-ups were made once a month for the first three months and then every three months for up to a year. The records of all patients were reviewed for complications, including infection, recurrence, aseptic loosening, dislocation, and peri-prosthetic

Table 1. Histopathological diagnosis of 38 patients with endoprostheses (n:38)

Primary Bone Tumors (n:16)						
	Osteogenic Sarcom	Chondrosarcoma	Multiple Myeloma	Lymphoma	Ewing Sarcoma	Malignant Mesenchymal
N	3	4	3	4	1	1
Metastatic Bone Tumors (n:22)						
	Renal Cell Carcinoma	Lung Carcinoma	Breast Cancer	Prostate Cancer	Rectal Cancer	
N	4	9	5	3	1	

fracture. In addition, the patients were evaluated according to the failure classification after the tumor endoprosthesis made by Henderson et al [4]. The functional results were evaluated using the revised Musculoskeletal Tumor Society (MSTS) functional rating system for all surviving patients [8]. All surviving patients completed the MSTS questionnaire at their last visit or by telephone. The lower extremity group was given scores from 0 to 5 by asking about pain, function, mood, need for support, walking and stepping. The upper extremity group was given scores from 0 to 5 by asking about pain, function, mood and hand position, lifting and hand skills.

Data were given as median (minimum-maximum) and number (percentage). Conformity to normal distribution was made using the Shapiro-Wilk test. Mann-Whitney U test was used for statistical analysis and T test was used for independent samples. P <0.05 was considered statistically significant. IBM SPSS Statistics 26.0 program was used for analysis.

Examples of cases: The 56-year-old patient, who was followed-up for lung cancer, was admitted to our clinic with a pathological right humerus fracture. Relevant consultations and advanced imaging methods were made. Wide resection of the proximal humerus was performed, and reconstruction was achieved with a humeral proximal tumor prosthesis (Figure 1a, 1b, 1c).

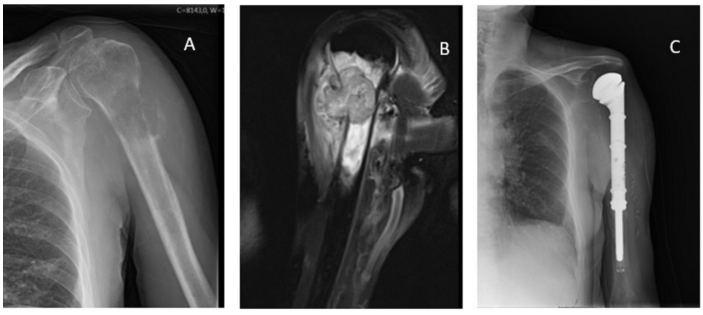

Figure 1. The 56-year-old man with lung carcinoma metastasis of bone showing (A) anterior-posterior and radiograph of the humerus showing a lytic lesion of the proximal third of the shaft. (B) MRI sagittal sequences show extensive destruction of the anterior and lateral cortex with associated soft-tissue mass. A 13 cm segment of bone was resected and reconstructed limb with the cemented endoprothesis implant, shown on (C) the anterior-posterior radiographs.

A 21-year-old male patient was admitted to our clinic with a right femoral shaft fracture. Pathological fracture was diagnosed because of CT and MRI. Biopsy was performed and diagnosed as Ewing sarcoma. (Figure 2a, 2b, 2c).

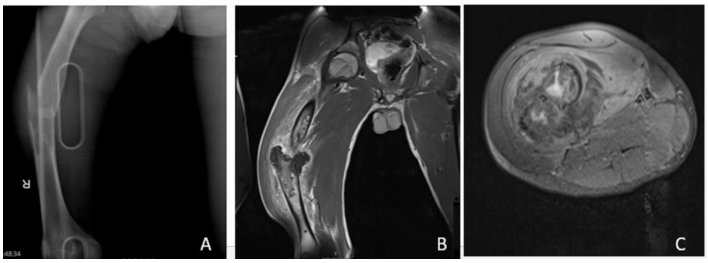

Figure 2. The 21-year-old man with Ewing sarcoma of bone showing (A) anterior-posterior and radiograph of the femur showing a lytic destructive lesion of the shaft. (B) MRI sagittal and (C) axial sequences show expansive destruction of the all cortex with a large associated soft-tissue mass.

After consultations and evaluations, 30 cm resection was performed to the right femur. It was reconstructed by resection tumor prosthesis. No recurrence was found in the 4-years follow-up (Figure 3a, 3b, 3c).

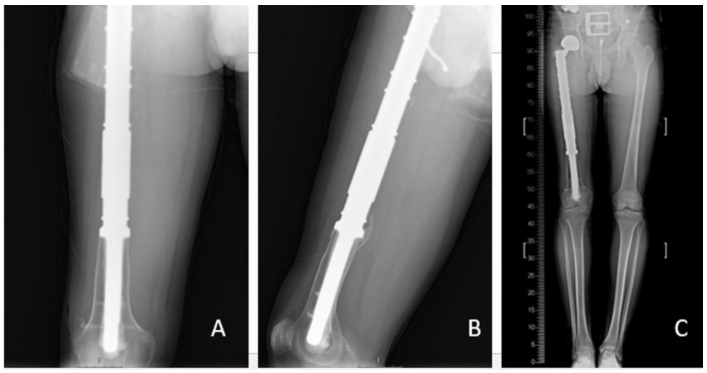

Figure 3. 30 cm segment of bone was resected and reconstructed limb with the cemented endoprothesis (intercalated) implant, shown on (A) the anterior-posterior, (B) lateral and (C) leg-length radiographs

Results

Six (15%) of 38 patients who underwent endoprostheses were excluded from the study in postoperative evaluations because they were dead. The mean age of 6 patients who died was 72 (57 to 86) years. Histopathological diagnoses of 6 patients who died were as follows: there were lung metastasis in three patients, renal cell tumor metastasis in one, rectal tumor metastasis in one and breast tumor metastasis in one. The mean age of 6 patients who died was 72 (57 to 86) years. The mean resection lengths of the patients who underwent tumor resection prosthesis were as follows: humerus was 12 (4 to 30) cm, femur was 12 (4 to 30) cm and tibia was 14 (4 to 23) centimeter. The mean follow-up period of 32 healthy and alive patients was 38 (12 to 98) months. During the follow-up of the patients, periprosthetic infection was observed in two patients and prosthetic dislocation in one patient. The patient with prosthetic dislocation was diagnosed with metastatic rectum. One of the patients who was developed periprosthetic infection undergone femur resection due to chondrosarcoma. The other patient had been distal femur resection due to breast ca metastasis. Two-stage prosthetic infection treatment method was underwent to these two patients. The patient, who underwent tibia proximal resection due to malignant mesenchymal tumor, revealed recurrence at the 6th month follow-up. Above-knee amputation was performed in this patient. None of the 16 patients with primary bone tumor died during the follow-up period. There were no major complications, except the infection that developed in patient with chondrosarcoma. The functional MSTS scores were obtained as 85% in 32 patients, while their mean total score was 17.2 (12 to 28). Results were excellent (76% to 100%) in six (19, 2%), good (51% to 75%) in 21 patients (67, 2%), fair (26% to 50%) in five patients (16%); results were good or excellent in 82% of cases. The average MSTS score of these seven patients was 23.8 (22 to 26). The average age of 25 patients who had endoprosthesis to the lower extremity (femur or tibia) and survived was 56 (21 to 86) years. The mean MSTS score of these 25 patients was 19.08 (12 to 28). The mean MSTS score of 16 patients with primary bone tumors was 22.6 (14 to 28). However the mean MSTS score of 16 patients with metastatic tumors was 17.6 (12 to 26). It was found that the MSTS score in patients with primary bone tumors was statistically significantly higher than in patients with metastases ($p<0.05$). The MSTS score of the patients who had upper extremity (%22) reconstruction was found to be significantly higher than the lower extremity (%78) ($p<0.05$). There was no statistically significant difference in the MSTS score between femur and tibia reconstructions (p:0.735). The mean age of patients with primary bone tumors was 51.3 (21 to 77) years. The mean age of patients with metastatic tumors was 66.1 (48 to 87) years. There was no statistically significant difference between bone resection length (4 to 28) and MSTS scores (Table 2).

Table 2. Details of 32 patients treated with endoprostheses

Primary Bone Tumors					
	N	**Mean age(year)**	**Resection length(cm)**	**MSTS**	**Complication**
Humerus	3	67.3	6	24	None
Femur	8	47.3	14	20.3	(n=1)+
Tibia	5	48.2	14.2	25.4	None
Metastatic Bone Tumors					
	N	**Mean age**	**Resection length(cm)**	**MSTS**	**Complication**
Humerus	4	64.2	11.1	23.75	None
Femur	11	66.8	11	15.3	(n=2)*+
Tibia	1	67	11	18	None

MSTS: Musculoskeletal Tumor Society Score. *: Dislocation. +: Infection

Discussion

The increase in the life expectancy of patients with malignant bone tumors has increased the expectation of limb salvage and maximum recovery. Reconstruction with endoprosthesis is one of the important options of limb salvage surgery in malignant bone tumors. Important points to be considered while performing the endoprosthesis reconstruction method, which is the most widely used limb salvage method, are as follows; morbidity of the technique, frequency of complications, patient expectation and durability of the implant. The large size of the tumor area limits the treatment methods that provide reconstruction. Reconstructive methods using Vascularized and non-vascularized autogenous bone grafts are insufficient for large defects and cause morbidity in the donor area [9]. Distraction osteogenesis is known to be useful in the treatment of large bone defects, but its use is limited in patients receiving treatment for malignant bone tumors. This method of treatment takes a long time and limits the neoadjuvant therapy of patients with malignant tumors [10]. The most widely used technique in the treatment of malignant bone tumors is allograft reconstruction. However, endoprostheses are often used for reconstruction. Allograft reconstruction method has disadvantages such as the possibility of infectious disease, immobilization for a long time for union, nonunion and infection [11, 12]. Endoprostheses have advantages such as early weight bearing and early mobilization. Mobilization is very important for the patient with malignant tumor. In a case series of 1261 patients who underwent endoprosthesis after tumor resection, 112 patients had limb amputation due to complications. In addition, in this study of Jeys et al. which was observed that complications decreased due to the increase in follow-up time [13]. During the 38 months mean follow-up period in our study, no amputation was observed in 31 patients except for the patient with malignant mesenchymal tumor. There were 534 failures in a review of 2174 patients in whom endoprosthesis was evaluated due to tumor resection [4]. In addition to this review, Henderson et al. failure classification was evaluated in five types [4]. Five modes of failure are described in this article: soft tissue failure (Type 1), aseptic loosening (Type 2), structural failures (Type 3), septic loosening or infection (Type 4), and tumor recurrence (Type 5). In addition, infection was the most common failure in this study [4]. Of the 32 patients, we followed up in our study, 2 infection and one had a hip dislocation. Of the two patients who developed infection, one was the proximal femur and the other was the distal femur resection. Aseptic loosening remains a major problem after replacing large bone defects with prostheses; In the literature, the incidence ranges from 4.9% to 9.6% 14,15. No aseptic loosening was found in our patients. In case of aseptic or septic loosening of the megaprosthesis, two-stage revision procedure is recommended [16, 17]. Two-stage procedure was performed in both patients who had failure due to infection. The patient who developed hip dislocation was diagnosed with rectal cancer and it was observed that dislocation developed due to mechanical structural failure. The patient with metastatic rectal cancer and hip dislocation underwent revision surgery in the second month. In 2015, in the study named "Survival of Modern Knee Tumor Megaprostheses", no significant difference was found in terms of MSTS scores in femur and tibia reconstructions [14]. Actually, in our study, no significant difference was found between the MSTS scores of the patients with 19 femur and six tibia. In addition, in that study of 223 patients, the MSTS score of the megaprosthesis and revisions had been found to be an average of 25, 2 [18]. In our study, the mean MSTS score was 17, 2. In our study, functional MSTS results were good or excellent in 82% of the cases. The mean MSTS function in patients undergoing endoprosthetic reconstruction varies between 78% and 86% in the literature, and this value is 72% (12-28) in our study [18-21]. We attributed the lower MSTS score in our study to the fact that we had more patients with metastatic tumors. Indeed, half of the patients in our study had metastatic tumors and had high comorbidity.

Conclusion

Endoprostheses for malign bone tumors result in reconstructions comparable with, if not better than, those of allografts. Considering its advantages such as function, appearance and emotional acceptance, the application of an endoprosthesis for limb salvage should be preferred over an ablative procedure. It was determined that better functional results were obtained for patients with primary bone tumors than patients with bone

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Ethics committee approval for the study was obtained from the scientific research and publication ethics committee of medicine faculty with the decision number 2020/1175.

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