Original Article

Reconstruction of Lower Extremity Primary Malignant and Metastatic Bone Tumours with Modular Endoprosthesis

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ABSTRACT

Introduction: This study is aimed to assess the functional results of cases with lower extremity malignant and metastatic bone tumours that were treated with modular tumour resection prostheses. **Materials and Methods:** 49 patients were retrospectively examined. 27 (55.1%) patients had a primary bone tumour, and 22 (44.9%) had a metastatic bone tumour. Although most tumours located in the proximal femur were metastatic, tumours located around the knee were mostly primary malignant bone tumours. The functional assessments of our patients were made according to the Musculoskeletal Tumour Society (MSTS) scoring system. The Student's *t*-test and the Chi-square test were used for statistical analyses. **Results:** 30 (61.2%) of the patients were men, and 19 (38.8%) were women. The average age was 46.2 ± 1.9 years. Tumours were located in the proximal femur in 27 (55.1%) patients, distal femur in 16 (32.7%) patients and proximal tibia in 6 (12.2%) patients. 14 (28.6%) patients had a pathological fracture on admission. The average follow-up period of our patients was 27.4 ± 3.4 months, and the average MSTS score was 74.3 ± 13%. Complications developed at any time in 34.7% of the patients, and the most common symptoms were aseptic loosening (8.2%) and prosthesis infection (8.2%). Local relapse was found in one (2%) patient. The 5-year survival rate was 68.3% in patients with a primary tumour and 30% in patients with a metastatic tumour. **Conclusion:** Although endoprosthesis reconstruction had advantages of giving very good functional results in the early phases, it was found to cause mechanical complications, especially in patients with primary bone tumours during the mid and late phases.

KEYWORDS: *Endoprosthesis reconstruction, extremity protective surgery, functional outcome, malignant bone tumours, metastatic bone tumours*

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INTRODUCTION

As a result of advancements in imaging techniques and oncological treatments, the use of new chemotherapeutic agents, improvements in radiotherapy and the experiences gained along with the technological improvements in primary malignant and metastatic bone tumours, many significant improvements have been observed in the prognosis and rates of survival over the last 25 years.[1,2] On reviewing previous studies, no significant difference was found between amputation and extremity protective surgery in terms of survival and the results following reconstruction using endoprostheses were perfect.[3] Thus, surgical treatment has tended towards extremity protective surgical interventions after 1990s.[4] This observation can be explained by the fact that extremity protective surgeries do not reduce survival; however, they do increase the rate of recurrence. The cooperation between reconstructive surgery and the field of oncology at present is more promising for the future.

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The main purpose of extremity protective surgical interventions is to totally eliminate the local disease without causing a major change in the patient's survival and function. Reconstruction with prostheses following resection during the surgical treatment of lower extremity primary malignant and metastatic bone tumours contributes greatly to this purpose. It is currently the preferred method as it enables rapid rehabilitation and mobilization with stability during the early post-surgical phase and has a low frequency of complications.[5]

The purpose of this study was to assess the functional response of patients who received reconstruction with an endoprosthesis following resection of lower extremity primary malignant and metastatic bone tumours and to assess the factors that can affect this response.

Materials and Methods

49 patients who received a modular-type tumour resection prosthesis (Megasystem-C prosthesis, Waldemar Link, Hamburg, Germany) in our clinic during 2000-2012 due to the presence of a lower extremity primary malignant and metastatic bone tumour and who had sufficient follow-ups were retrospectively assessed after permission was received from our local ethical board. The patients were analysed in terms of age, gender, direction, histological diagnosis, pathological fracture, treatment, functional outcome, complications, recurrence, patient survival, and the life of the prosthesis.

The Musculoskeletal Tumour Society (MSTS) scoring system was used to assess the functional results.[6] The MSTS scores of living and deceased patients were based on the scores calculated during their last examination. With this scoring system, a total of six parameters including pain, functional capacity, emotional acceptance, support use, walking distance, and way-of-walking were evaluated. Each parameter was scored between zero and five according to specific criteria, and the results were calculated in percentages by dividing by 30, which is the highest score. The MSTS scores obtained were classified as perfect 75%-100%, good 70%-74%, moderate 60%–69%, insufficient 50%–59% or bad <50%.

Statistical evaluation

After the data obtained from the study were coded, they were analysed with the SPSS 15.0 (SPSS Inc., Chicago, IL, USA) package program. The descriptive characteristics of the data were expressed as the average ± the standard deviation, numbers and percentages. The Shapiro-Wilk's test was used to determine whether the measurable variables were normally distributed. As the data was normally-distributed, the Student's *t*-test was used to make comparisons between groups. The Chi-square test was used for comparing the data obtained while scoring. The statistical significance level was accepted as $p < 0.05$ for all tests. A Kaplan–Meier analysis was used to calculate the survival rates.

Results

Of the 49 patients, 30 (61.2%) were men and 19 (38.8%) were women; the average age was 46.2 ± 1.9 years. The youngest patient was 13 years old, whereas the oldest one was 83 years old. The average age of patients with a primary bone tumour (N = 27) (36.2 ± 20 years) was significantly lower than that of patients with a metastatic bone tumour (N = 22) (58.4 ± 10 years) ($p < 0.01$). The age distributions (in years) were as follows in terms of localization: 57.7 ± 10.6 years in patients with proximal femur involvement (N = 27), 32.93 ± 21 years in patients with distal femur involvement (N = 16) and 29.8 ± 12 years in patients with proximal tibia involvement (N = 6). Patients with proximal femur involvement formed the oldest group, whereas patients with proximal tibia involvement formed the youngest group. When the patient's ages were analysed in terms of histological diagnoses, patients with osteosarcoma formed the youngest group, whereas patients with prostate carcinoma metastasis formed the oldest group [Table 1].

27 (55.1%) patients had a primary bone tumour, and 22 (44.9%) patients had a metastatic bone tumour. The tumour was in the proximal femur of 27 (55.1%) patients, in the distal femur of 16 (32.7%) patients and in the proximal tibia of 6 (12.2%) patients. 14 (28.6%) patients exhibited a pathological fracture at admission. The direction of the involvement was in the right lower

Table 1: Histologic diagnoses and age distribution as of ages

Histologic Diagnosis	Average (age)	N	Standart Deviation	Min	Max
Osteosarcoma	21,9	14	7,02	13	33
Giant Cell Tumor	27	1	.	27	27
Lymphoma	48	2	45,2	16	80
Multiple Myeloma	61	4	14,07	46	77
Malignant Fibrosis Hystiocytoma	50	2	12,7	41	59
Chondrosarcoma	51	4	4,43	46	56
Colon Cancer	67	2	0	67	67
Breast Cancer	50	4	14,6	33	68
Thyroid Cancer	53	2	9,8	46	60
Lung Cancer	57,1	11	4,5	50	65
Prostate Cancer	72,5	2	14,8	62	83
Renal Cancer	68	1	.	68	68
Total	46,2	49	19,6	13	83

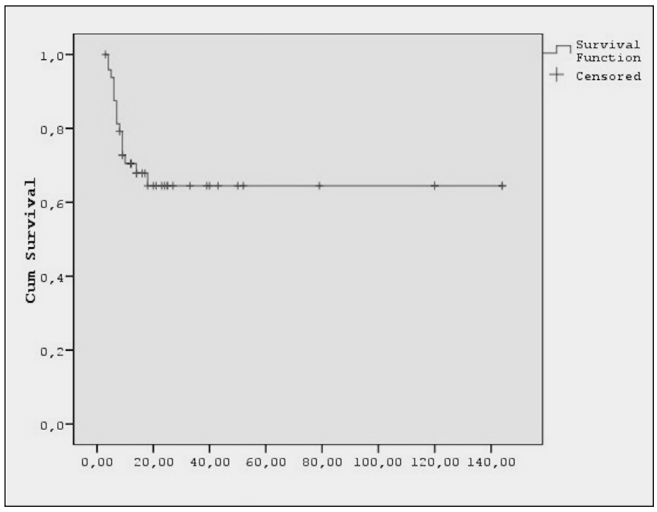

Figure 1: Survival rates of patients in months

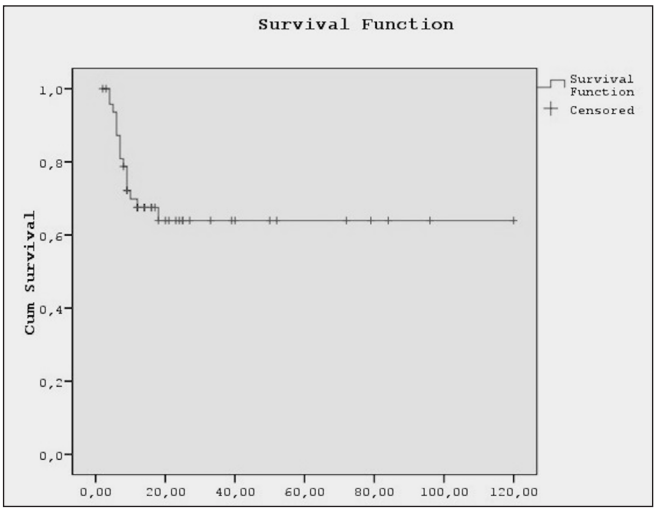

Figure 2: Prosthesis survival rates in months

Table 2: Follow-up times in terms of histologic diagnosis

Histologic Diagnosis	Average (month)	N	Standart Deviation	Min	Max
Osteosarcoma	51,5	14	50,2	3	144
Giant Cell Tumor	14	1	.	14	14
Lymphoma	19,5	2	4,9	16	23
Multiple Myeloma	17,7	4	8,8	6	25
Malignant Fibrosis Hystiocytoma	80	2	56,5	40	120
Chondrosarcoma	16	4	7	9	25
Colon Cancer	20,5	2	9,1	14	27
Breast Cancer	20	4	21,6	5	52
Thyroid Cancer	13,5	2	4,9	10	17
Lung Cancer	7,1	11	2,3	4	12
Prostate Cancer	13,5	2	6,3	9	18
Renal Cancer	20	1	.	20	20
Total	27,4	49	34,9	3	144

extremity in 17 (34.7%) patients and in the left lower extremity in 32 (65.3%) patients.

The average follow-up time for our patients was 27.4 ± 3.4 months. The average follow-up time for patients with a primary tumour was 39.6 ± 42.6 months, whereas for patients with a metastatic tumour was 12.4 ± 10.5 months. The average follow-up time was statistically significantly higher in the primary tumour group ($p < 0.05$). In terms of histological diagnoses, the longest follow-up time was in patients with malignant fibrous hystiocytoma (N = 2), whereas the shortest time was found in patients with long carcinoma metastasis (N = 11) [Table 2].

The average postoperative MSTS score of all patients was 74.3 ± 13.3. Although the average MSTS score was 81.2 ± 12.2 for the primary bone tumour group, the MSTS score was 65.8 ± 9.1 in the metastatic tumour group. The average MSTS score in primary tumour group was statistically significantly higher than that of the metastatic tumour group ($p < 0.05$). In all of the series, the following results were found: 24 perfect (49%), 9 good (18.4%), 11 moderate (22.4%), 3 insufficient (6.1%) and 2 bad (4.1%). Of the patients included in the study, 34.7% (17 patients) experienced a complication during their follow-up. The average time for the development of complications was 27.8 ± 2.9 months. Complications were as follows: prosthesis dislocation in two (4.1%) patients, prosthesis infection in four (8.2%) patients, periprostatic fracture in two (4.1%) patients, local recurrence in one (2%) patient, postoperative peroneal symptom in two (4.1%) patients, skin necrosis in two (4.1%) patients and aseptic loosening in four (8.2%) patients. The most common symptoms were aseptic loosening and prosthesis infection.

16 patients (33%), the average age of whom was 57.4 ± 13.4 years, died during the follow-up due to various reasons. 13 of the patients who died were men, and 3 were women. Their average follow-up time was 8 ± 3.6 months. 13 of these patients received proximal femur resection prosthesis, whereas 3 received distal femur resection prosthesis. In terms of histological diagnoses, one patient had multiple myeloma, two patients had breast carcinoma metastasis, one patient had thyroid medullar carcinoma metastasis, nine patients had lung carcinoma metastasis and two patients had prostate carcinoma metastasis. One patient, who had anosteocarcinoma located in the distal femur, received high femoral amputation after developing local recurrence during the 12th month. The patient died during the 14th month due to common lung metastasis. The patient with multiple myeloma died due to chronic

renal failure, and the other patients died due to advanced metastatic disease. None of our patients who received radiotherapy and chemotherapy died due to oncologic treatment.

Of the patients who had a primary bone tumour, 86.2% were alive during postoperative month 6, 71.3% were alive during postoperative month 12 and 68.3% were alive during postoperative month 60. Of the patients who had a metastatic bone tumour, 77% were alive during postoperative month 6, 45% were alive during postoperative month 12 and 30% were alive during postoperative month 60. According to the Kaplan–Meier analysis, survival times and rates in all cases were 87.5% during month 6, 79.2% during month 12 and 64% during month 60 [Figure 1].

The average prosthesis life was 32.2 ± 31 months in patients with a primary bone tumour (N = 27), 12.4 ± 10.5 months in patients with a metastatic bone tumour (N = 22) and was found to be statistically longer in patients with a primary bone tumour ($p < 0.05$). According to the Kaplan–Meier analysis, prosthesis survival in all cases was 93% during month 6, 67% during month 12, 64% during month 60 and 64% during month 120 [Figure 2].

Discussion

In primary malignant and metastatic bone tumours, resection, surgical excision of the tumour, including amputation, has been performed for many years. Extremity protective techniques were developed at the beginning of 1970s.[7,8] Developments in the prosthesis industry, as a result of recent technological advancements and experiences gained through the use of these implants, have increased the 5-year follow-up success of tumour endoprostheses from 20% to 85%. Consequently, extremity protective surgical interventions are now more commonly used than amputation in the treatment of bone tumours.[1] Reconstruction with an endoprosthesis has the advantages of stability, early load efficiency, being far from osteosynthesis concerns, and providing acute functional restoration.[9] However, in the long run, especially among younger cases, the need for revision caused by use, growth and other complications serve as a disadvantage.[1]

Yalnız *et al.*[1] performed modular tumour prosthesis on 23 patients with an average age of 49 years (between 14 and 81 years old), İlbeyli *et al.*[10] performed modular tumour prosthesis on 50 patients with an average age of 41.4 years (between 15 and 75 years old) and Qadir *et al.*[11] performed modular tumour prosthesis on 16 patients with an average age of 36.7 years (between 14 and 73 years old). The average age of the 49 patients in our series was 46.2 years (between 13 and 83 years old), and the age distribution was similar to that observed in previous studies. In previous studies, the average age of patients with a metastatic tumour was higher than that of patients with a primary malignant bone tumour.[1,10,11] Similarly, in our study, the average age of patients with a metastatic tumour was significantly higher than that of patients with a primary malignant bone tumour ($p < 0.05$). The patients with a proximal femur tumour represented the oldest group, whereas the patients with a tumour located within the proximal tibia formed the youngest group. We believe this is due to the fact that most of the patients with a tumour located in the proximal femur had a metastatic bone tumour, whereas almost all the patients with a tumour located in the proximal tibia had a primary malignant bone tumour.

The average follow-up time in our patients (primary and metastatic) was 27.4 months. Studies suggest that the follow-up time changes between month 1 and month 156; this average was similar to the values in our study.[1,10,11] Similar to preivous studies, the average follow-up time of the patients with a primary bone tumour was statistically significantly higher than that of patients with a metastatic bone tumour ($p < 0.05$). This situation can be explained by the fact that patients with a metastatic tumour were old and that they died during the early phase.

On comparing our functional results with those of previous studies, which assessed the overall (i.e., primary and metastatic) patients, among patients with an average MSTS score of 73.7% (43%-100%), we found that İlbeyli *et al.*[10] got perfect results in 10%, good results in 54%, moderate results in 32% and bad results in 4%. Similarly, Yalnız *et al.*[1] found the average MSTS score to be 58.9 % (40%-90%), Bruns *et al.*[12] found the score to be 83% (60%-100%) and Heisel *et al.*[13] found that the score to be 72%. In addition, good or perfect results were found in 94% of the patients. Qadir *et al.*[11] found the average MSTS score to be 72.3% in their series and found perfect results in 37% of their patients, good results in 31%, moderate results in 12%, insufficient results in 12% and bad results in 6% of their patients. In our series, the average MSTS score was 74.3% (46%-96%) and perfect results were found in 49% of our patients. In addition, we found good results in 18.4% of our patients, moderate results were found in 22.4%, insufficient results were found in 6.1% and bad results were found in 4.1% of our patients. The postoperative average MSTS scores of patients with a primary and metastatic tumour in our series were similar to those of previous studies and were found to be statistically higher among the primary tumour group when compared to those of the metastatic tumour group

($p < 0.05$). Similar to our study, Yalnız *et al.*[1] found that the average MSTS scores were significantly higher among the primary tumour group when compared to those of the metastatic tumour group ($p < 0.05$). These results can be associated with the fact that patients with a primary bone tumour are younger and have an increased rate of survival.

When the functional results of patients from previous studies who underwent a modular tumour resection prosthesis due to a pathological fracture were examined, the average MSTS score was calculated as 62.3% (44%-80%) by Hattori *et al.*[14] and as 64% by Natarajan *et al.*[15] In our series, the average MSTS score was calculated as 67.7% (58%-76%), and the average MSTS score of patients who did not have a pathological fracture was statistically significantly higher than that of patients with a pathological fracture ($p < 0.05$). This result was associated with the fact that most of the patients who underwent operations for a pathological fracture had advanced-stage metastatic disease, and thus, had comorbid systemic diseases and a general poor state of health.

When the general complication rates of previous studies that assessed primary and metastatic tumours together were examined, it was found that complication rates varied by study. In general, the most common complications were prosthesis infection, aseptic loosening and local recurrence.[1,10,11,13] Of the patients in our series, 34.7% developed complications during the course of follow-up. The most common complications in our study were prosthesis infection (8.2%) and aseptic loosening (8.2%). Complication rates were similar to those found in previous studies and the complication rates in the primary bone tumour group were statistically significantly higher than those of the metastatic tumour group ($p < 0.05$). We associate the higher complication rates observed among the primary bone tumour group with the longer follow-up time when compared with that of the metastatic group. Prosthesis dislocation in two patients was due to the body segment joint of the prosthesis. This was associated with the fact that the first series of the producing firm did not have screw fixation in the segment joint. This complication was not seen in the series that followed. It was thought that the aseptic softening observed in the four patients developed due to chemotherapy-induced bone necrosis in the early phases of prostheses that were applied without cement, and this situation was thought to result from the structure of the prosthesis.

When the general patient survival rates from previous studies that assessed primary and metastatic tumours together were examined, the survival rates in 5 years were 87% according to the Kaplan–Meier analysis in the series of Bruns *et al.*,[12] 74.5% in the Niimi *et al.*[16] series and 66.7% in the Natarajan *et al.*[15] series. In our series, the survival rates of patients, in general, according to Kaplan-Meier analysis was 87.5% during postoperative month 6, 79.2% during the first year and 64% during the fifth year. Survival rates in studies varied, and this is associated with the different rates of patients with primary and metastatic tumours in the different series. The survival rates of patients according to the Kaplan–Meier analysis in the series that had a modular tumour resection prosthesis due to a primary bone tumour was 93% for the 5-year survival rate as calculated by Schwartz *et al.*,[17] 93% for the 2-year survival rate and 87% for 10-year survival rate as calculated by Zimel *et al.*[18] and 88% for 5-year survival rate as calculated by Flint *et al.*[19] The survival rates of patients according to Kaplan–Meier analysis in series that had a modular tumour resection prosthesis due to the presence of a metastatic bone tumour was 86% for 6-month survival, 54% for 1-year survival, 37% for 2-year survival as calculated by Hattori *et al.*,[14] and 60% for 1-year survival, 38% for the 3-year survival and 30% for 5-year survival as calculated by Chan *et al.*[20]

Our series is similar that of previous studies, according to the Kaplan-Meier analysis, survival rates in patients with a primary bone tumour was 68.3% during year 5 and 30% in patients with a metastatic bone tumour during year 5.

Conclusion

Although endoprostheses provide very good functional results during the early phase, they may cause complications during the mid and late phases, especially in patients with primary bone tumours, as a result of their increased survival rates. With advances in technology, we believe that they will make great contributions and increase the quality of life for patients in this group.

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Conflicts of interest

There are no conflicts of interest.

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