Limb Salvage Surgery for Bone Tumors around the Knee: The Oncological and Functional Outcome—King Hussein Medical Center Experience

Raed Al-Zaben¹, Mohamed Alturk¹, Abdullah Alkhawaldah¹, Areej Al-Zaben² and Jamal Rahaymeh³

1. Orthopedic Surgery Department, Royal Medical Services, King Hussein Medical Center (Teaching Hospital of the Jordanian University), Amman 11855, Jordan

2. Biomedical Institute of technology, Royal Medical Services, Amman 11855, Jordan

3. Anesthesia Department, Royal Medical Services, King Hussein Medical Center (Teaching Hospital of the Jordanian University), Amman 11855, Jordan

Abstract: It is a challenge to save the lower limb with a malignant or invasive benign bone tumor around the knee. Retrospectively, we analyzed 30 patients with bone tumors around the knee region. The distal femur involved in 24 patients and proximal tibia in six patients. The tumors included 25 primary malignancies, two metastatic lesions and three giant cell tumors. The reconstruction procedures included 28 endoprosthesis replacements and two autogenous fibular grafts. The average follow-up was 35 months. Twelve patients died and 18 remained disease free. The five year survival rate of 25 patients with primary malignant bone tumors was 60%. The average MSTS (Musculoskeletal Tumor Society) functional score was 60% (range 20%-100%) in all patients. So we conclude that the limb-salvage procedures which accompanied with neo-adjuvant chemotherapy and post-operative chemotherapy are relatively safe. The functional outcome study has inherent limitations which are the inability to randomize treatment and the subjective of the measures, but we conclude that remaining 18 patients were active at home with efficient gait in home and outdoor at a mean of 30 months and those with more functional lower limbs had better quality of life. The infection was the leading cause of surgical complications which needed multi-staged surgery and associated with lower functional outcome. In our opinion, endoprosthesis should be considered as the treatment of choice for bone tumors around the knee joint. Advances in limb salvage surgery are, and will long continue to be, a great challenge for orthopedic oncologists of the 21st century.

Key words: Endoprosthesis, malignant bony tumor, knee, King Hussein.

1. Introduction

The knee region, consisting of the proximal tibia, distal femur and the surrounding soft tissue, is the commonest site of predilection for primary bone tumors. In the knee, the distal femur is the most common site, followed in descending order by proximal tibia [1-5]. The treatment of malignant or invasive benign bone tumors of the knee is a challenge to orthopedic oncologist surgeon. In the history, before the 1970s, the amputation and knee disarticulation were the main treatment for primary malignant bone

tumors around the knee [1, 2]. With better understanding of the biological behavior of musculoskeletal tumors, application of effective neo-adjuvant and adjuvant therapy and the development of bone defect reconstruction, 75% of malignant tumors around the knee can be safely resected through some limb salvage procedures [6-9]. In this paper, we investigate the clinical and functional outcomes of limb salvage operations for bone tumors of the knee. The knee joint was reconstructed with modular endoprosthesis (Hipokrat Modular Resection System, Hipokrat Custom Made Growing Endoprosthesis) designed by Dr. Kotz. The first endoprosthetic operation in King Hussein Medical

Corresponding author: Raed Al-Zaben, M.D., research field: orthopedic surgery. E-mail: zabenmw@yahoo.com.

Center was done in 2000 on a 38 year old patient with recurrent distal femur giant cell tumor (Fig. 1).

Endoprosthetic replacement offers several advantages, such as early mobilization and weight bearing, stability, a shorter operating time and hospital stay in comparison to biological reconstructions, and it allows the early introduction of postoperative adjuvant chemotherapy. Reconstruction with a modular endoprosthesis after resection of a bone tumor gives good functional results in most of the cases [1, 7, 10-16].

2. Patients and Methods

From January 2000 to December 2006, 30 patients with malignant or aggressive benign bone tumors of the knee, including 9 males and 21 females with a mean age of 34 years (range 12-74 years), were treated with limb salvage procedures. The tumors involved the distal femur in 24 patients and proximal tibia in 6 patients. Preoperatively, in addition to general routine

examinations and X-ray radiography, CT (computer tomography) and MRI (magnetic resonance imaging) scanning on the tumor sites and Isotope scan were performed in all the patients. Angiography was added if necessary. Through an evaluation of these examinations, the local and systemic tumor extent was determined, especially whether or not the neurovascular bundle and posterior compartment had been involved. Open biopsy was performed in all patients. According to clinical features, imaging and pathological examinations, the diagnoses and their Enneking's surgical classification were eleven osteosarcomas (IIB stage), one osteosarcomas (IA), three chondrosarcomas (1 IIB stage, 2 IIA stage), two malignant lymphoma (all IIA stage), eight Ewing's sarcomas (all IIB stage), three giant cell tumors (two recurrent and one combined pathological fractures) and two metastases (the primary malignancies were renal and lung carcinoma). Four patients had developed pathological fractures (Tables 1 and 2).

Fig. 1 The first endoprosthetic operation in King Hussein Medical Center was done in 2000 on a 38 year old patient with recurrent distal femur giant cell tumor.

Table 1 Histological type and anatomical location of bone tumors of the knee.

Tumor	Distal Femur	Proximal Tibia	Total	Percentage
Osteosarcoma	10	2	12	40%
Chondrosarcoma	3	-	3	10%
Ewing's sarcoma	4	4	8	26%
Lymphoma	2	-	2	7%
Bone giant cell tumor	3	-	3	10%
Metastasis	2	-	2	7%
Total	24	6	30	

Table 2 Number of Patients according to histological type and tumor grade.

Tumor type	Grade 1	Grade 2	Grade 3		Total no.
Benign bone tumors					
Giant cell tumor of bone	1	1	1		3
Primary bone tumors					
	Grade 1a	Grade 1b	Grade 2a	Grade 2b	
Osteosarcoma	0	0	1	11	12
Ewing's sarcoma	0	0	0	8	8
Chondrosarcoma	0	0	2	1	3
Lymphoma	0	0	2	0	2
Metastatic bone tumor					
	-	-	-	-	2
Total					30

As for other anatomical sites, limb salvage procedures for bone tumors around the knee comprise three steps: complete resection of tumors with safety margins, reconstruction of bone defects taking in consideration the length and joint line level, a good soft tissue covering [1, 2, 7]. All tumors were resected with wide margins, except for two resections which just reached marginal margins because the tumors were too large to be resected widely.

Following resection of the bone tumor, the reconstruction of bone defects depended upon factors such as the patients' desire, the tumor type and extension. Reconstruction procedures included 24 custom-made tumor prosthesis, four expandable growing endoprosthesis and two autogenous fibular grafts. Six patients needed vascular bypass done by vascular surgeons of our center. Soft tissue reconstruction, whose key points were reconstruction of the extensor system and preservation of joint line, was completed mainly through crossed suture and reattachment of the residual muscles and tendons around the knee to provide static and dynamic stability. The medial gastrocnemius muscle flaps were needed in six patients because too much soft tissue was resected to achieve complete resection and negatives margins.

Postoperatively, a dressing and back slap was applied to immobilize the involved knee for 3-4 weeks, and then a knee cage was used for a further 2-3 weeks. Simultaneous functional exercises of foot, ankle and hip were started as soon as possible. After the soft tissue had healed and the knee joint stabilized, the passive and active motion was started. All the patients

were instructed on their functional exercises and their limb function was evaluated according to the MSTS scoring system in regular follow-up. The patients with osteosarcoma and Ewing's sarcoma were started adjuvant chemotherapy 2 weeks after surgery. The patients with lymphoma and metastatic lesions were given other therapies by physicians of related departments.

3. Results

The postoperative follow-up was done at an out-patient clinic or via telephone interview. The average follow-up period was 30 (range 10-60) months. The patients were examined for complications and oncological and functional outcomes:

3.1 Complications

Deep infection had occurred in three patients and they were treated by the three stages procedure: (1) removal of primary endoprosthesis, (2) filling the gap with spacer for 12 weeks, (3) reinsertion of the endorprosthesis. The antibiotic was given during the three stages according to the culture results. uto-graft bone fracture occurred in one case two years later and it was treated by external fixation with autogenous bone graft to achieve arthrodesis (Fig. 2). Temporary common peroneal nerve palsy occurred in three cases which recovered in three months later spontaneously.

3.2 Oncological Outcome

Local recurrences occurred in two patients with osteosarcoma, of these one was treated by local excision

Fig. 2 A case of knee arthrodesis by Autograft which complicated with fracture and treated by external fixator.

Table 3 Complications of treatment. Number in parentheses represents the number of patients.

Complication	Diagnosis	Treatment	Final result
Local recurrence (2)	Osteosarcoma (2)	Re-resection (1)	NED (1)
		Amputation (1)	DOD (1)
Infections (3)	Osteosarcoma (3)	Extraction of EP + arthroplasty (3)	NED (2)
	Osteosarcoma (4)		DOD (4)
Local recurrence + Mets (8)	Ewing's sarcoma (2)	Resection of mets and recurrent(1)	DOD (2)
	Chondrosarcoma(1)		NED (1)
	Lymphoma (1)		DOD (1)
Mets alone (1)	Osteosarcoma (1)		DOD (1)
Death of primary disease (3)	Lymphoma (1)		DOD (1)
	Metastasis (2)		DOD (2)
Periprosthetic fractures (2)	Osteosarcoma (2)	Revision (2)	NED (2)

DOD: died of disease; NED: no evidence of disease; EP: endoprosthesis.

and had no evidence of disease and the other needed knee disarticulation and died after local relapse one year later. Local recurrences accompanied with distant metastases occurred in eight cases, of these one with chondrosarcoma was treated by resection of the recurrent and lung metastatic lesions and had no evidence of disease, and four cases with osteosarcoma opted out of therapy and died three months later, two cases with Ewing's sarcoma died four months later. One case with osteosarcomas abandoned therapy and died of their diseases. The two patients with metastases died of primary tumors within one year after surgery. One case with lymphoma died of hematopoiesis failure

and the other elderly patient died of myocardial infarction. Thus, there were 18 disease-free survivals at the latest follow-up. The five-year overall survival rate of 25 patients with primary malignant bone tumors was 60% (Table 3).

Peri-prosthetic fracture occurred in two patients and revisions by longer stems were done with good results. Metal breakage occurred once, also revision was done with a good results (Fig. 3).

3.3 Functional Outcome

The remaining lower limb function was evaluated according to the MSTS functional evaluation system

Fig. 3 25 year old female complicated by femoral steam breakage.

Fig. 4 An 18 year old female with proximal tibia Ewing's sarcoma.

Fig. 5 A 14 year old female with distal femur Ewing's sarcoma.

Fig. 6 A 22 year old male with distal femur osteosarcoma.

for the lower limb which consists of six items (pain, function, emotional, acceptance, support, walking and gate). The mean over all MSTS score was 60% (range 20%-100%) in 30 patients, respectively. The scores were 88% (range 77%-100%) in nine cases with uninvolved flexor and nor extensor system (3 giant cell tumor, 1 osteosarcoma, 1 lymphoma, 2 chondrosarcoma, 2 Ewing's sarcoma) (Fig. 4), 63% (range 77%-40%) in 17 cases with tumor resection and reconstruction of extensor system (Fig. 5), and 30% (range 20%-40%) in four patients with no extensor system function (Fig. 6).

4. Discussion

Chemotherapy has dramatically changed the cure rate of malignant bone tumors [6, 17-19]. Since the introduction of effective neo-adjuvant chemotherapy in the 1980s, more than 80% of patients with osteosarcoma of an extremity have been considered candidates for limb-salvage surgery, and that increased the trend of using the endoproshtesis for limb-salvage surgery.

More than two thirds of our patients (67.8%) were younger than 35, and almost half of them (47.8%) were under the age of 25. For medical, surgical and rehabilitative advances, limb-salvage surgery has surpassed amputation as the primary treatment for

primary malignant bone tumors in young children. Preservation of limb function in the pediatric oncology patient is the most challenging. In skeletally immature patients, the functional impairment due to the subsequent growth inhibition must be considered in conjunction with limb-salvage surgery [4, 8-10, 17, 18, 20].

Prosthetic reconstruction in the skeletally immature patient is demanding because of the necessity to cope with the expected disruption of limb growth after resection of one or more major growth plates and the high demands placed on implants by young patients. Expandable endoprosthesis have an important place in treating still growing children. Although endoprosthetic reconstruction in children is fraught with many problems, it is usually possible to obtain a good functional limb at skeletal maturity. Treatment must be strictly prioritized in terms of the patient's life, the limb, its function, length equalization and cosmetic appearance. Orthopedic intervention in the care of children and young adults with oncological conditions must be individualized [4, 9-11, 17, 20].

An individual approach to every patient is essential in order to choose the most suitable surgical treatment; for pathological fractures due to primary bone tumors, metastatic lesions or tumor-like lesions. The goal of surgical treatment is primarily to remove tumor, and

then to fill bone gap, restore function and minimize pain, thus improving the patient's quality of life [1, 2, 3, 8, 12, 14, 21, 22].

The relatively small number of patients with secondary bone tumor in our study does not represent the real incidence of these kinds of tumors, and only exceptionally do we treat such patients.

Three patients with tumor-like lesions (giant cell tumor) were treated by complete resection and endoprosthesis reconstruction: in one patient with grade 1 giant cell tumor, the reason was articular surface destruction, and in the other two patients the lesion size was more than 2/3 of the total width of the distal femur.

More than two-thirds of the patients began the orthopedic treatment of a malignant bone tumor at the point when histological activity of the tumor shifted to a more aggressive histological grade. Malignant bone tumors are of major concern in orthopedic surgery, and treatment should be started as soon as possible. Losing precious time, these patients come late to a specialist of orthopedic oncology, which is a sign of the inefficiency of our health system. Education of general physicians, physicians of other specialties and the general population should also be in the domain of the orthopedic oncologist (Fig. 5).

Deep infection was the most common complication, occurring in three patients in our study. In the literature, the rate of deep infection has ranges from 3%-10% [1,

11, 13, 23, 24]. Removal of the endoprosthesis, curettage, debridement, irrigation and filling the gaps with spacers for 3 months and reinsertion of the endoprosthesis again were performed in three patients; in two patients we had unsatisfactory final results: amputation following local recurrence in one patient and knee ankyloses in the other patient.

The second most common complication in treating our patients was local recurrence of the tumor. The data should be analyzed together with information about the tumor grade. The majority of the patients with malignant bone tumors had high grade tumors, which made the treatment more complicated. After local recurrence of the tumor without metastases in two patients, radical surgical treatment resulted in saving one patient, who is now disease free.

Periprosthetic fracture occurred in two patients: after a car accident in one, and during a sports activity in the other patient. Good functional status after surgery encourages the patient to go "beyond the limits" of the operated limb [25]. If there is no primary disease, treatment of such patients should not be a difficult problem.

5. Conclusions

Many studies have been performed to investigate endoprosthetic survival rates after tumor resection, but the results cannot be summarized and systematic review cannot be performed; mostly because of the small number of patients, as well as the different models and principles of endoprosthesis, but the survival rate is not worse than those were treated by amputation. The survival rate of the primary malignant bone tumors around the knee that were treated by endoprosthesis is 60% at 5 years, so we conclude that the limb-salvage procedures which accompanied with neo-adjuvant chemotherapy and post-operative chemotherapy are relatively safe. The functional outcome study has inherent limitations which are the inability to randomize treatment and the subjective of the measures, but we conclude that remaining 18

Fig. 5 A 18 year old male with distal femur osteosarcoma.

patients were active at home with efficient gait in home and outdoor at a mean of 30 months and those with more functional lower limbs had better quality of life. The infection was the leading cause of surgical complications which needed multi-staged surgery and associated with lower functional outcome. Specific long-term consequences of endoprosthetic reconstructions after tumor resection for the patient's affected limb are still unknown. In our opinion, endoprosthesis should be considered as the treatment of choice for bone tumors around the knee joint region. Advances in limb salvage surgery are, and will long continue to be, a great challenge for orthopedic oncologists of the 21st century.

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