Dorothy Fox. *Mideast Café.* Watercolor, 18″ × 24″.

Limb salvage management of selected patients with fractures of primary bone sarcoma does not appear to increase the risk of local recurrence or death.

Limb Salvage Management of Pathologic Fractures of Primary Malignant Bone Tumors

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Background: *Little is known about oncologic outcomes of patients with primary bone tumors complicated by a pathologic fracture and treated by limb salvage.*

Methods: *Our study included 17 men and 14 women aged 6 to 61 years (average age 17 years). All 31 patients had primary bone tumors complicated by a pathologic fracture. Diagnoses included osteosarcoma (17 patients), Ewing's sarcoma (10), malignant fibrous histiocytoma (3), and lymphoma (1). All received preoperative chemotherapy. The distal femur was affected in 13 patients, the proximal femur in 6, mid shaft femur in 4, the proximal humerus in 4, the proximal tibia in 3, and the fibula in 1. All patients underwent limb salvage and achieved a wide resection margin.*

Results: *The average follow-up period was 18 months (range 8 to 51 months). Two patients required amputation due to local recurrence. Six patients developed pulmonary metastases and eventually died.*

Conclusions: *A pathologic fracture of primary bone tumor is not always a contraindication for limb salvage since the oncologic outcome appears acceptable.*

Introduction

The principal goal in the management of patients who have a primary bone sarcoma is prolonging their survival. Primary bone sarcomas that require surgical resection can be treated by either amputation or limb salvage. Most studies comparing limb salvage and amputation reported that limb salvage had no adverse effect on the long-term survival of patients.[1]

Several contraindications to limb salvage have been developed to ensure that this treatment does not result in an inferior oncologic outcome.[2] Pathologic fracture of a primary bone sarcoma is considered a contraindication to limb salvage for two reasons: (1) the fracture results in a local hematoma with dissemination of tumor cells into adjacent tissues and adjacent joints, and (2) damage to the microcirculation may facilitate metastases.[3] On the other hand, several factors support limb salvage for primary bone sarcoma complicated by pathologic fractures.[4] These factors include the efficacy of neoadjuvant chemotherapy, healing of the fracture during the preoperative chemotherapy, thus facilitating manipulation during

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surgery, and the use of reconstructive modalities (eg, joint fusion and rotationplasty) that do not require functioning muscles after wide surgical resections.

This study evaluates the oncologic outcomes of limb salvage procedures that were used for 31 patients with primary bone sarcoma complicated by a pathologic fracture.

Materials and Methods

Our study included 31 patients (17 men and 14 women) with an average age of 17 years (range 6 to 61 years). All participants had primary bone tumors complicated by a pathologic fracture. The diagnoses were osteosarcoma (17 patients), Ewing's sarcoma (10), malignant fibrous histiocytoma (3), and lymphoma (1). The patients were staged by local radiography, magnetic resonance imaging (MRI), computed tomography of the chest, and technetium bone scan. All of the tumors were stage IIB according to the system proposed by Enneking et al.[5] Patients who were metastatic (stage III) at presentation were not included in this study. The distal femur was affected in 13 patients, the proximal femur in 7 patients, the mid shaft femur in 3 patients, the proximal humerus in 4 patients, the proximal tibia in 3 patients and the fibula in 1 patient (Table 1).

Fractures were present at the time of diagnosis and before the beginning of chemotherapy in 24 patients, whereas fractures occurred during preoperative chemotherapy in 7 patients. Until the time of surgery, all the fractures were managed at the time of occurrence by a plaster slab, a cast, or a Thomas splint, depending on the site of fracture. Pathologic fractures were divided into two groups — displaced (16 patients) and undisplaced (15 patients). Displaced fractures included major displacement, comminuted, segmental, washed out, and intercondylar fractures (Fig 1). Undisplaced fractures included cracks and minimally displaced fractures.

All patients received preoperative chemotherapy during which the pathologic fractures consolidated. Drugs included 4 cycles of doxorubicin and cisplatin. In

Table 1. — Diagnosis, Type of Reconstruction, Type of Fracture, Outcome of Fracture, and Oncologic Outcome in 31 Patients

Patient	Age	Sex	Diagnosis	Site	Fracture Type	Fracture Time	Fracture Outcome	Reconstruction	Local Recurrence	Metastases
1	16	F	OS	DF	UD	PC	U	VF		
2	17	M	OS	DF	UD	DC	U	MD		
3	16	M	OS	DF	UD	PC	U	VF	+	+
4	17	M	EW	PF	D	PC	U	RP		
5	10	F	EW	PH	D	PC	U	VF		+
6	20	F	EW	PF	D	PC	N	MD		
7	11	M	EW	PF	D	DC	U	RP		+
8	14	M	OS	PT	UD	PC	U	OA		
9	18	F	OS	DF	UD	PC	U	OA	+	+
10	40	M	L	PF	D	PC	U	MD		
11	11	F	OS	FM	D	PC	U	RP		
12	12	M	EW	FIB	UD	DC	U	WR		
13	17	F	EW	FM	D	PC	U	VF		
14	11	M	MF	DF	D	PC	N	RP		+
15	14	M	EW	PF	D	PC	U	RP		
16	12	F	OS	DF	D	PC	U	RP		
17	15	F	OS	PT	UD	PC	U	PDF		
18	16	F	OS	DF	UD	PC	U	VF		
19	17	F	EW	FM	D	PC	U	VF		
20	16	F	OS	DF	D	PC	N	VF		
21	12	M	OS	DF	D	DC	U	VF		
22	6	F	EW	PT	UD	DC	U	RP		+
23	19	F	OS	DF	UD	PC	U	PDF		
24	11	M	OS	PH	D	PC	U	PS		
25	10	F	OS	PH	UD	DC	U	PS		
26	28	M	MF	PH	UD	PC	N	PS		
27	14	M	OS	DF	UD	DC	U	MD		
28	61	M	MF	PF	D	PC	U	MD		
29	18	M	OS	DF	UD	PC	N	PDF		
30	17	M	EW	PF	D	PC	U	MD		
31	16	M	OS	DF	UD	PC	U	PDF		

Diagnosis: OS = osteosarcoma, EW = Ewing's sarcoma, MF = malignant fibrous histiocytoma, L = lymphoma
Site: DF = distal femur, PT = proximal tibia, FM = mid femur, PF = proximal femur, PH = proximal humerus, FIB = fibula
Fracture type: UD = undisplaced, D = displaced
Fracture time: PC = prechemotherapy, DC = during preoperative chemotherapy
Fracture outcome: U = united, N = not united
Reconstruction: RP = rotationplasty, VF = free vascularized fibular graft, PDF = pedicled fibular graft, PS = pedicled scapular crest graft, MD = modular prosthesis, OA = osteoarticular allograft, WR = wide resection only

26 patients, the fractures were solidly united both clinically and radiologically prior to surgery. In the remaining 5 patients, the fractures were not united radiologically, but clinically there was no gross abnormal mobility at the fracture site.

Limb salvage was then performed and a wide resection margin was achieved in all 31 patients. Reconstruction techniques were divided into three groups. In the first group, the adjacent joint was arthrodesed and included reconstruction by a free vascularized fibular graft (8 patients), pedicled fibular graft (4), and a pedicled scapular crest graft (3). In the second group, 7 patients underwent rotationplasty. In the third group, the function of the adjacent joint was preserved and included reconstruction by a modular prosthesis (6 patients) and an osteoarticular allograft (2 patients). No reconstruction was done for the patient who had fibular resection. All of the patients who had displaced fractures had their tumor resected by an "extended wide margin" and hence fell in the first or second group. An *extended wide margin* is a term we devised to define a margin that is larger than the regular wide margin but less than the radical margin. The dissection is done subfascially, and all the muscles in the compartment are resected with the tumor. The muscles are cut at the level on the bone osteotomy, and an extraarticular type of resection is done to include the adjacent joint with the specimen (Fig 2). None of the patients in this study received preoperative or postoperative radiotherapy.

Patients were examined clinically and radiologically every 6 weeks during the first 6 months, then every 3 months for the following 2 years, then every 6 months for 3 years, and then annually thereafter. Computed tomography scans of the chest were taken every 3 months in the first year, every 6 months in the second year, and then annually for 5 years. A bone scan was done every 6 months in the first year, then annually for 2 years.

Results

The mean follow-up period in this study was 18 months, ranging from 8 to 51 months. Two patients had local recurrence, one at 5 months and one at 12 months. They were managed by amputation but eventually died of metastatic

Fig 1. — Types of pathologic fractures: (A) undisplaced, (B) displaced, (C) segmental, (D) comminuted, (E) intercondylar, and (F) washed out.

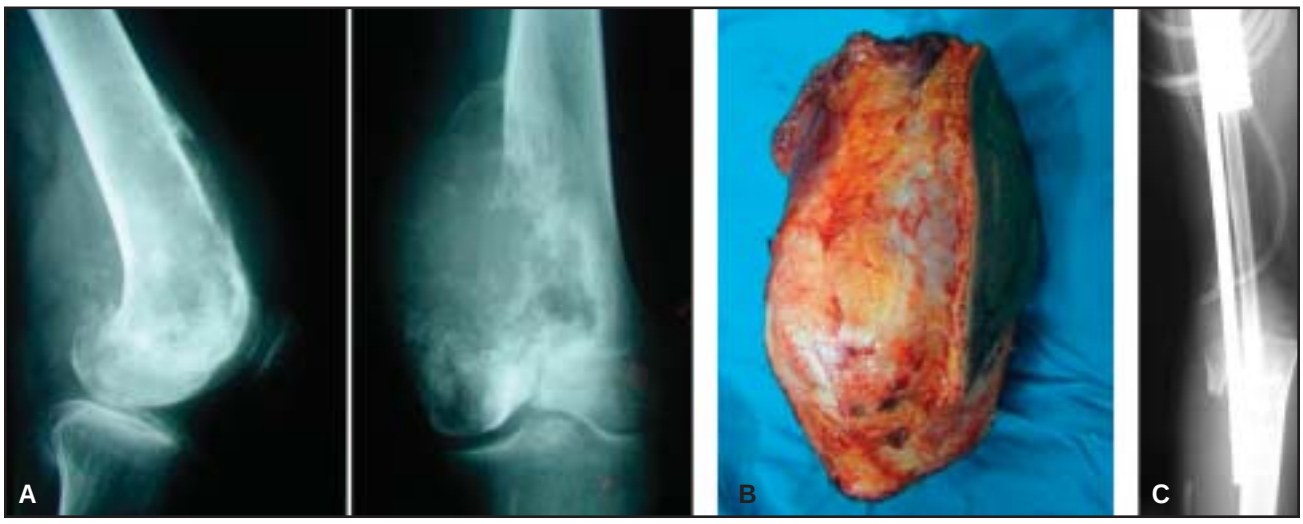

Fig 2. — Displaced intercondylar fracture in a distal femoral osteosarcoma. (A) is a preoperative radiograph, (B) shows the resected specimen including distal femur, proximal tibia, patella, and all the quadriceps muscles that were cut at the level of the osteotomy, and (C) is a postoperative radiograph showing reconstruction by a vascularized fibular graft.

disease, one at 8 months and one at 18 months following the original limb-sparing surgery. Pulmonary metastases occurred in 6 patients; 3 underwent lung metastasectomy, but all 6 ultimately died of metastatic disease.

We attempted to correlate the incidence of local recurrence and pulmonary metastases to the type of tumor, type of fracture, and type of surgery (Table 2).

Discussion

Several questions arise when developing a treatment strategy for patients who have a primary bone tumor that is complicated by a pathologic fracture: Is the presence of a pathologic fracture in a primary bone sarcoma a poor prognostic factor that mandates immediate amputation? Is the rate of local recurrence higher with limb salvage than with amputation? Is the oncologic outcome affected by the type, time, and outcome of the pathologic fracture or by the type of tumor or reconstruction? We attempted to answer these questions in this study. Although the results were not statistically significant due to small numbers, they suggest certain trends. This study may also serve as a source of data for future meta-analysis that can guide us in choosing the optimal management strategy for patients with pathologic fractures of primary bone tumors.

Table 2. — Local Recurrence and Pulmonary Metastases in Relation to Type of Tumor, Fracture, Timing, Fracture Union, and Reconstruction in 31 Patients

Factor	Local Recurrence	Pulmonary Metastases
Type of Tumor (No. of patients):		
Osteosarcoma (17)	2 (12%)	2 (12%)
Ewing's sarcoma (10)	—	3 (30%)
Malignant fibrous histiocytoma (3)	—	1 (33%)
Lymphoma (1)	—	—
Total (31)	2 (6%)	6 (19%)
Type of Fracture:		
Displaced (16)	2 (13%)	3 (19%)
Undisplaced (15)	—	3 (20%)
Total (31)	2 (6%)	6 (19%)
Time of Fracture:		
Prechemotherapy (24)	2 (8%)	4 (17%)
During chemotherapy (7)	—	2 (29%)
Total (31)	2 (6%)	6 (19%)
Fracture Union:		
United (26)	2 (8%)	5 (19%)
Not united (5)	—	1 (20%)
Total (31)	2 (6%)	6 (19%)
Type of Reconstruction:		
Free vascularized fibula (8)	1 (13%)	2 (25%)
Pedicled fibula (4)	—	—
Pedicled scapular crest (3)	—	—
Rotationplasty (7)	—	3 (43%)
Modular prosthesis (6)	—	—
Osteoarticular allograft (2)	1 (50%)	1 (50%)
Wide resection only (1)	—	—
Total (31)	2 (6%)	6 (19%)

Glasser et al[6] reported that the occurrence of a pathologic fracture in a primary bone tumor was associated with an impaired survival rate. The fracture probably denoted the aggressive nature of the tumor that ultimately caused the bone to fracture.[6] However, the survival of the patients with pathologic fractures of the primary bone tumors who underwent limb salvage was similar to those who had an amputation. The incidence of pulmonary metastases in our series was 19.3%. This is less than the 23% incidence rate reported by Scully et al,[7] but this may be due to our short follow-up period. When we compared the incidence of metastases in osteosarcoma patients in this series with a similar group of patients who did not sustain a pathologic fracture and were followed for the same period of time at our institution, we found that they had the same outcome (E. Safwan, MD, unpublished data, 2001). The local recurrence rate in our series was 6.5%, which is less than the 23% rate reported by Scully et al[7] and the 19% rate reported by Abudu et al.[3] However, most of the patients in the latter study had contaminated margins of tumor resection. Although the low incidence of local recurrence in our series may be attributed to the short follow-up period, we believe it resulted from our the use of extended wide margins of resection for all displaced fractures. Of the 22 patients in our study who had an extended wide margin of resection and reconstruction by rotationplasty or joint fusion, only 1 developed local recurrence. Joint fusion results in a functional outcome that is inferior to a mobile

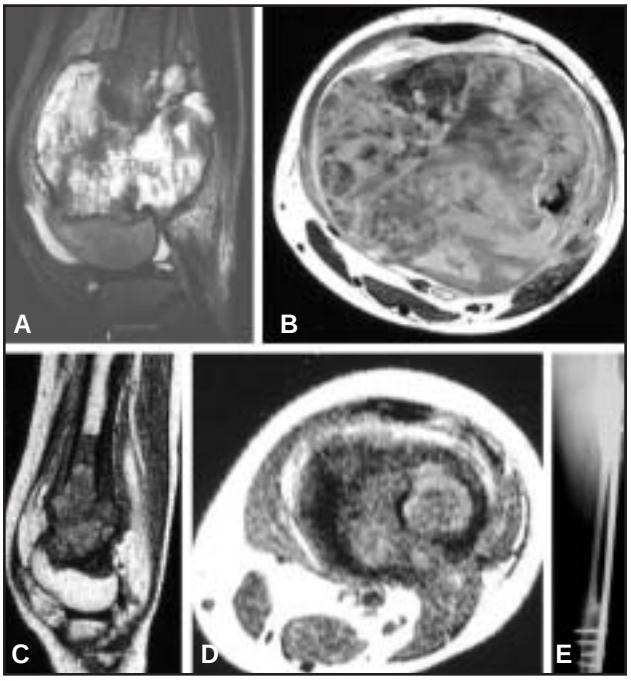

Fig 3. — Displaced fracture in a distal femoral osteosarcoma: (A) sagittal cut of an MRI before chemotherapy, (B) axial cut of an MRI before chemotherapy, (C, D) MRI performed following chemotherapy showing marked regression of tumor and healing of fracture, and (E) follow-up radiograph showing reconstruction by a vascularized fibular graft.

joint because patients have a visible limp, are limited in recreational activities, and experience variable emotional acceptance. However, most patients have no pain and can eventually walk with no support and for long distances. Moreover, it is a durable type of reconstruction that does not require future reoperations.

Healing of a pathologic fracture during chemotherapy can be problematic. However, in our series, fractures healed during the preoperative chemotherapy period in 26 (84%) of the 31 patients (Figs 3 and 4), which is similar to the 84% incidence rate reported by Jaffe et al.[8] Also, fracture union correlated with a high tumor necrosis percentage, thus indicating a good response to chemotherapy.[9] Tumors that are not sensitive to chemotherapy (eg, chondrosarcoma) may not be amenable to limb salvage if fractures have occurred. These types of tumors were not included in our study.

Two patients with local recurrence had displaced fractures that occurred before the beginning of chemotherapy. However, Scully et al[7] stated that neither the type nor the timing of the pathologic fractures affects the oncologic outcome.

Conclusions

Pathologic fractures of primary bone sarcoma should not be considered an absolute indication for amputation. Patients should be treated by neoadjuvant chemotherapy, and their tumors should then be resected with adequate margins that might entail performing an extended wide margin in some cases. In doing so, the oncologic outcome of these patients will probably not be jeopardized.

Studies reported in the literature describing the management of pathologic fractures of primary bone tumors are limited and include only small numbers of patients. Multi-institutional studies are needed to obtain statistically significant data that will assist in treating this patient population.

Fig 4. — Displaced fracture of a proximal femoral osteosarcoma. (A) is a preoperative radiograph following chemotherapy showing a united fracture, and (B) is a postoperative radiograph showing reconstruction by a modular prosthesis.

References

1. Simon MA, Aschliman MA, Thomas N, et al. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. *J Bone Joint Surg Am*. 1986;68A:1331-1337.

2. Simon MA. General considerations in malignant bone tumors. In: Simon MA, Springfield D, eds. *Surgery for Bone and Soft-Tissue Tumors*. Philadelphia, Pa: Lippincott-Raven; 1998.

3. Abudu A, Sferopoulos NK, Tillman RM, et al. The surgical treatment and outcome of pathological fractures in localized osteosarcoma. *J Bone Joint Surg Br*. 1996;78:694-698.

4. Scully SP, Temple HT, O'Keefe RJ, et al. The surgical treatment of patients with osteosarcoma who sustain a pathological fracture. *Clin Orthop*. 1996;324:227-232.

5. Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging musculoskeletal sarcoma. *Clin Orthop*. 1980;153:106-120.

6. Glasser DB, Lane JM, Huvos AG, et al. Survival, prognosis and therapeutic response in osteogenic sarcoma: the Memorial Hospital experience. *Cancer*. 1992;69:698-708.

7. Scully SP, Ghert MA, Zurakowski D, et al. Pathologic fracture in osteosarcoma: prognostic importance and treatment implications. *J Bone Joint Surg Am*. 2002;84-A:49-57. Erratum in: *J Bone Joint Surg Am*. 2002;84-A:622.

8. Jaffe N, Spears R, Eftekhari F, et al. Pathologic fracture in osteosarcoma: impact of chemotherapy on primary tumor and survival. *Cancer*. 1987;59:701-709.

9. Thompson RC Jr, Pritchard DJ, Nelson TE. Pathologic fractures in osteosarcoma. *J Bone Joint Surg Br*. 1992;74(suppl III):277.