Endoprosthetic Reconstruction After Resection of Musculoskeletal Tumors

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Abstract

In the literature, long-term survival of endoprosthetic reconstruction varies widely. Few long-term reports analyze both anatomical and disease-specific implant and patient survival.

We retrospectively reviewed the results of 489 patients who underwent resection of musculoskeletal tumor and reconstruction using an endoprosthetic device between December 1980 and August 2009. Implants were considered to have failed if the cemented components were revised for any reason, or the major body segment was removed for any reason. Implant survival, limb survival, and patient survival were determined using the Kaplan-Meier method.

Sixty-one (12.5%) of the 489 cases were revised at a mean follow-up of 6.6 years (range, 1 month to 27.3 years). Kaplan-Meier analysis revealed overall implant survival of 23.1% at 27 years (95% CI, 5.0% to 100.0%). At 15 years, modular implants outperformed older custom designs (90.8% and 59.6% survival, respectively; $P < .05$). Complications that led to failure of the limb-salvage effort included local recurrence (21 cases), infection (11), positive surgical margins (3), and intractable pain (1). Thirty-six amputations (7.4%) were performed. There were no cases of amputation performed as a direct outcome of mechanical failure.

Endoprosthetic implants provide a reliable, durable method of reconstruction after resection of musculoskeletal tumors.

As a result of improved adjuvant treatments, limb salvage is now the preferred method of managing the vast majority of localized skeletal malignancies.[1-3] There are various postresection reconstructive alternatives, including vascularized free-tissue transfer, osteoarticular allograft, allograft-prosthetic composite, and endoprosthetic replacement.[4,5] Although acceptable short-term function has been reported for virtually all these alternatives, their long-term durability is debatable.

The limb-salvage literature is difficult to interpret because of the wide variation in surgical techniques, implants, reconstructive methods, anatomical locations, and disease severity.[6-15] The present study included a large cohort of patients who underwent limb reconstruction performed with a relatively uniform surgical technique by a single surgeon at a single institution. We have previously published reports on subsets of the patients included in the present analysis,[16-18] but now we want to consolidate the data to determine whether differences in implant durability or complications would be noted across anatomical sites.

In the late 1970s, early failure of endoprosthetic reconstructive methods was widely predicted. Patients with a normal life expectancy are expected to require revision of an endoprosthetic reconstruction. Conversely, for patients with disseminated metastatic disease and a short life expectancy, endoprosthetic reconstruction likely provides durability. For patients with localized extremity malignancy, however, the most efficacious method of reconstruction after segmental bone resection is widely debated.

We conducted a study of the long-term durability and complications associated with limb salvage using an endoprosthetic implant. Specifically, we wanted to determine and compare (1) anatomy-specific implant durability, (2) anatomy-specific patient survival, and (3) incidence of complications that ultimately compromise the limb-salvage effort.

Materials and Methods

This study was approved by our institution's office for protection of research subjects. Between December 1980 and August 2009, surgeons at our institution performed 613 limb-salvage procedures using an endoprosthetic device for the reconstruction. For the present analysis, we excluded 45 cases in which various expandable devices were used, and another 79 cases treated for nononcologic indications. These criteria left 489 cases available for review.

The cohort included both custom (n = 202) and modu-

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Table I. Demographics of All Endoprosthetic Reconstructions Performed at Our Institution Between December 1980 and August 2009[a]

Location	Tumor	Nontumor	Expandable	Total
Distal femur	186	39	27	252
Proximal tibia	52	2	3	57
Proximal femur	86	16	4	106
Total femur	14	12	1	27
Distal humerus	13	1	0	14
Proximal humerus	100	8	4	112
Total humerus	7	1	5	13
Scapula	22	0	0	22
Intercalary	9	0	1	10
Total	**489**	**79**	**45**	**613**

[a]Present analysis includes 489 cases done for musculoskeletal tumor.

Table II. Disease Severity by Location

Location	Low Grade/ Benign	IIA/IIB	III	Total
Distal femur	43	122	21	186
Proximal tibia	9	43	0	52
Proximal femur	20	43	23	86
Total femur	0	12	2	14
Distal humerus	0	7	6	13
Proximal humerus	19	34	47	100
Total humerus	0	6	1	7
Scapula	6	14	2	22
Intercalary	1	7	1	9
Total	**98**	**288**	**103**	**489**

Table III. Outcomes by Location

Location	N	Revision	%	Recurrence	%	Amputation	%	Infection	%
Distal femur	186	35	18.8	13	7.0	18	9.7	6	3.2
Proximal tibia	52	10	19.2	3	5.8	5	9.6	3	5.8
Proximal femur	86	5	5.8	7	8.1	1	1.2	1	1.2
Total femur	14	2	14.3	1	7.1	2	14.3	4	28.6
Distal humerus	13	3	23.1	0	0.0	0	0.0	0	0.0
Proximal humerus	100	0	0.0	11	11.0	7	7.0	1	1.0
Total humerus	7	0	0.0	2	28.6	1	14.3	1	14.3
Scapula	22	1	4.5	2	9.1	1	4.5	1	4.5
Intercalary	9	5	55.6	0	0.0	1	11.1	0	0.0
Total	**489**	**61**	**12.5**	**39**	**8.0**	**36**	**7.4**	**17**	**3.5**

lar (n = 265) reconstructions of the distal femur (n = 186), proximal humerus (n = 100), proximal femur (n = 86), proximal tibia (n = 52), total femur (n = 14), distal humerus (n = 13), intercalary diaphysis (n = 9), and total humerus (n = 7) (**Table I**). All 22 scapular implants were custom. The vast majority of oncologic reconstructions were performed for high-grade localized disease (Enneking stage IIA/IIB lesions) (**Table II**). Resections followed generally accepted oncologic principles of obtaining a wide margin. Patients were followed with physical examination, localized imaging, and chest computed tomography quarterly for 2 years, semiannually for 2 years, and then annually. Sixteen patients were lost to follow-up.

Data collected included implant type (custom or modular), disease stage (according to the system described by Enneking and colleagues[19]), length of follow-up, implant survival, patient survival, and incidence of complications. Implants were considered to have failed if the cemented components were revised for any reason, or the major body segment was removed for any reason. Hinge mechanism and bushing failures were considered separately, as the endoprosthetic components were always retained. Amputation for any reason was considered a failure of the limb-salvage effort. Implant survival, limb survival, and patient survival were determined using the Kaplan-Meier method. Survival curves were compared using the log-rank method.

Results

Sixty-one (12.5%) of the 489 cemented components were revised at a mean follow-up of 6.6 years (range, 1 month to 27.3 years). Mean follow-up was 9.6 years (range, 3 months to 27.3 years) for patients who underwent reconstruction with a custom implant and 4.0 years (range, 1 month to 23.2 years) for patients who received a modular implant. Kaplan-Meier analysis revealed overall implant survival of 23.1% at 27 years (95% CI, 5.0% to 100.0%) (**Table III**). Twenty-seven years after surgery, the lowest rate of implant failure was seen in the upper extremity, followed by the proximal femur, the proximal tibia, and the

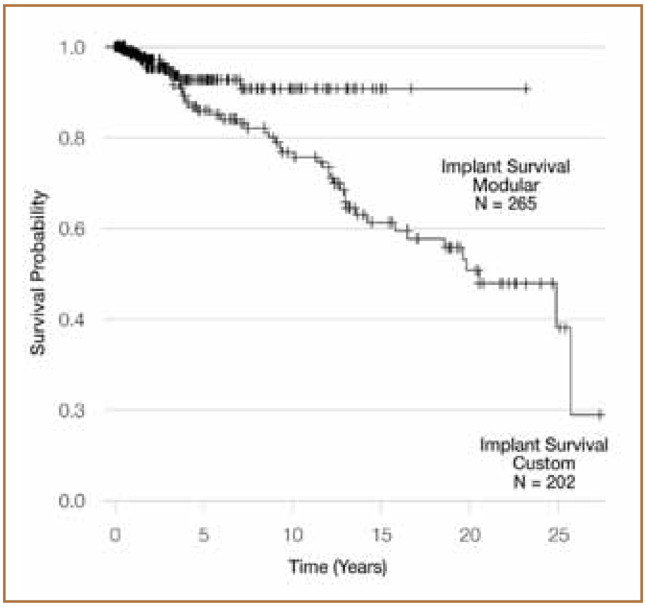

Figure 1. Kaplan-Meier survivorship analysis shows modular (n = 265) and custom (n = 202) implant survival using revision of stem or major body segment as endpoint. All 22 scapular implants were nonmodular and excluded from analysis.

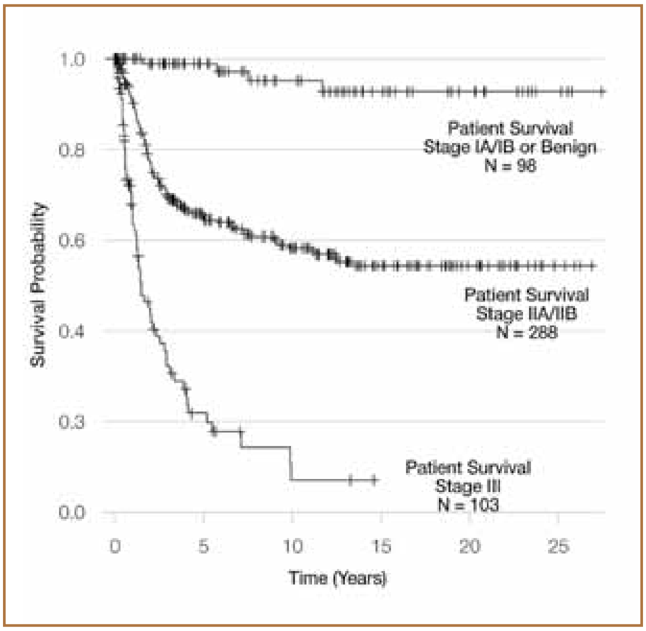

Figure 2. Kaplan-Meier survivorship analysis shows patient survival stratified by disease stage using death from disease as endpoint.

distal femur. At 15 years, modular implants outperformed older custom designs (90.8% and 59.6% survival, respectively; $P < .05$) (**Figure 1**). The change to modular implants had the largest impact on implant survival at the distal femur (51.7% vs 93.7%; $P < .05$). Modularity did not statistically improve implant durability in other anatomical locations. Placement of an intercalary implant carried the highest risk for revision (55.6%).

Disease-specific patient survival was best for patients with low-grade or benign disease (92.6%; 95% CI, 85.7% to 100%) and worst for those with stage III/metastatic disease (7.1%; 95% CI, 2.1% to 23.8%) (**Figure 2**). Patients with high-grade localized disease (Enneking stage IIA/IIB lesions) had overall 27-year disease-specific survival of 54.2% (95% CI, 47.7% to 61.5%). Patient survival among those with IIA/IIB lesions was highest for lesions in the proximal tibia (69.9%; 95% CI, 55.4% to 88.1%), followed by the distal femur (56.0%; 95% CI, 46.8% to 67.0%), the proximal femur (44%; 95% CI, 34.6% to 53.6%), and the upper extremity (43.5%; 95% CI, 29.5% to 64.0%) (**Figure 3A**). A statistically significant improvement in disease-specific survival was noted among patients with high-grade localized tumors treated after 1990, when ifosfamide was added to the typical chemotherapeutic regimen at our institution (67.5% vs 44.8%; $P < .05$).

Reasons for implant revision included aseptic loosening

Table IV. **Reasons for Implant Revision**

Reason	DFR	PTR	PFR	TF	DH	PH	TH	Scapula	Intercalary	Total
Aseptic loosening	22	7	3	—	3	—	—	—	2	37
Fatigue fracture	10	1	—	2	—	—	—	—	3	16
Severe osteolysis	—	—	1	—	—	—	—	—	—	1
Infection	2	1	1	—	—	—	—	—	—	4
Tumor recurrence	1	—	—	—	—	—	—	1	—	2
Periprosthetic fracture	—	1	—	—	—	—	—	—	—	1
Total	**35**	**10**	**5**	**2**	**3**	**0**	**0**	**1**	**5**	**61**

Abbreviations: DFR, distal femoral replacement; PTR, proximal tibia replacement; PFR, proximal femoral replacement; TF, total femur replacement; DH, distal humeral replacement; PH, proximal humeral replacement; TH, total humeral replacement.

Table V. **Causes of Limb-Salvage Failures**

Cause	n	%
Local recurrence	21	58.3
Infection	11	30.6
Positive margins	3	8.3
Intractable pain	1	2.8
Mechanical failure	0	0.0
Total	**36**	**100.0**

Table VI. **Fate of Local Recurrence**

Local Recurrence	n	%
Amputation	21	53.8
Palliation	18	46.2
Total	39	100.0
Died of disease	**32/39**	**82.1**

(n = 37), fatigue fracture of the implant (n = 16), infection (n = 4), tumor recurrence (n = 2), severe osteolysis (n = 1), and periprosthetic fracture (n = 1) (**Table IV**). Thirty-six amputations (7.4%) were performed among all patients for local recurrence (21 cases), infection (11), positive surgical margins (3), and intractable pain (1) (**Table V**). Total femur replacement carried the highest risk for both infection and amputation, followed by total humerus replacement. Incidence of local recurrence was highest among those who had undergone total humerus replacement. Eighteen of 39 total cases with local recurrence did not undergo repeat surgery, and were treated with palliation while the viable limb was maintained (**Table VI**). There were no cases of amputation performed for mechanical failure of the endoprosthesis.

Discussion

The rarity of musculoskeletal sarcomas makes it difficult to draw definitive conclusions about the optimal reconstructive method after tumor resection. The literature suggests endoprosthetic reconstruction certainly offers a durable and functional alternative to amputation.[20,21] However, the data across studies are difficult to interpret because of the varied surgical techniques, implant types, and patient demographics.[6-15] There are very few long-term reports that include data collected from a relatively uniform cohort of patients treated by the same surgeon using consistent surgical techniques and implants. We have previously reported the outcomes of the distal femoral, proximal tibial, and proximal femoral endoprostheses included in this study.[16-18] We wanted to combine that data with the data for the rest of our endoprosthetic reconstructions to compare outcomes across anatomical sites. Specifically, we aimed to determine the disease-specific and anatomy-specific implant survival, patient survival, and incidence of complications that compromised the limb-salvage effort.

The limitations of this study included the retrospective data collection and the loss of 16 patients to follow-up. Data were collected from available charts, and no patient was specifically recalled for the study. As a result, any complications or postoperative events not documented in the medical record may not have been included in the present analysis. The lost-to-follow-up quotient—the ratio of lost-to-follow-up patients to the number of failures reported—was much less than 1, and therefore the loss of the 16 patients to follow-up should not have significantly detracted from the validity of the data presented.[22]

In the literature, long-term survival of endoprosthetic reconstruction varies widely. Most long-term reports provide data regarding one anatomical location or one subset of patients. Very few long-term reports analyze both anatomical and disease-specific implant and patient survival to allow for conclusions to be reached about the efficacy of any one spe-

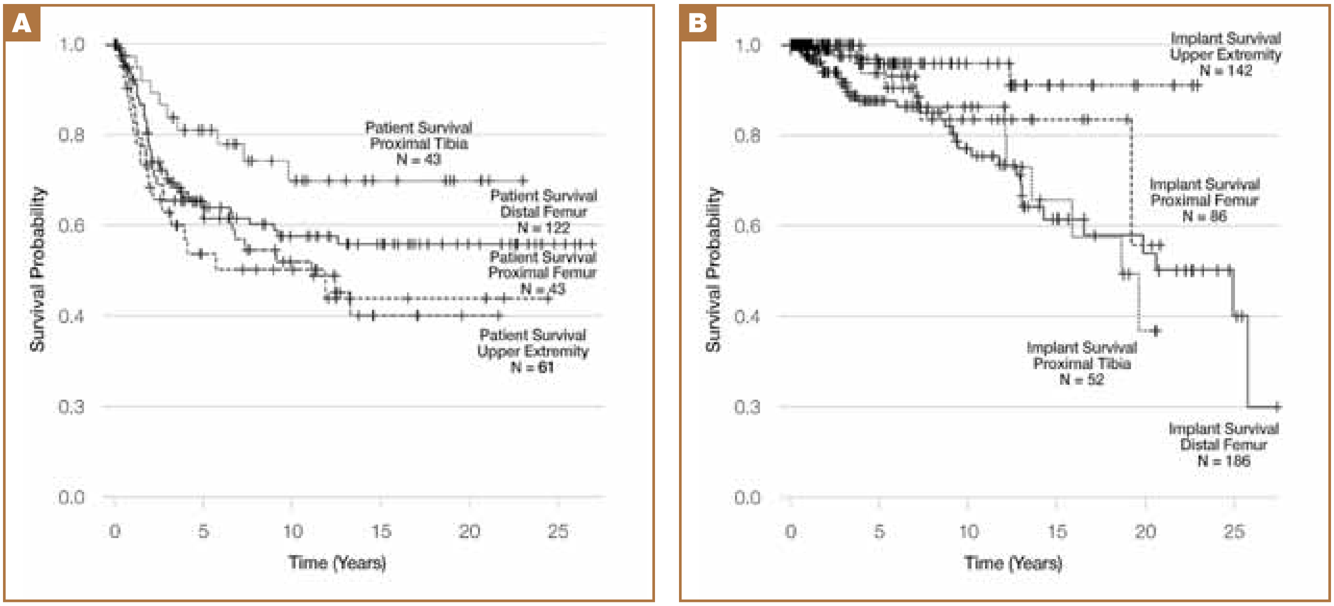

Figure 3. Outcomes by anatomical location. (A) Kaplan-Meier survivorship analysis shows patient survival among those with high-grade localized disease (Enneking stage IIA/IIB) stratified by disease location using death from disease as endpoint. (B) Kaplan-Meier survivorship analysis shows implant survival stratified by location using revision of stemmed implant as endpoint. Figure excludes intercalary implants (n = 9) and total femur implants (n = 14).

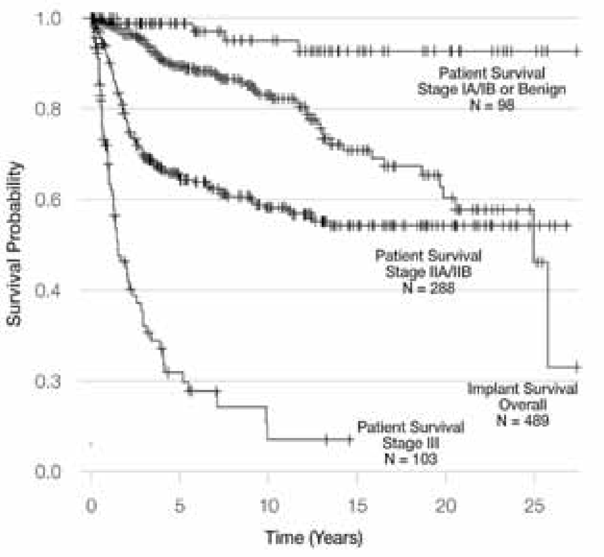

Figure 4. Kaplan-Meier survivorship analysis shows overall implant survival, along with patient survival stratified by disease stage.

cific treatment method. In one of the largest series reported, Jeys and colleagues[14] reported the results of more than 700 endoprosthetic replacements performed for musculoskeletal tumors. Much as in our study, the authors found a very low rate of amputation for mechanical failure, and most failures of the limb-salvage effort were caused by local recurrence (50%) and infection (48.6%). All implants in that series were custom-made, and the authors did not specify the method of implant fixation or analyze the cohort according to implant type. In contrast to our findings, the highest rate of amputation in that series was in the proximal tibia (18.4%). Gosheger and colleagues[12] reported the results of 250 patients treated in various anatomical locations with the Mutars prosthesis. The authors reported good results 5 years after surgery using cementless fixation in all implants and, similar to our study, found that implants in the upper extremity had the highest survival rate. Torbert and colleagues[23] reported on the 10-year survival of 139 patients who underwent endoprosthetic reconstruction for tumor. The authors found the highest rate of implant survival in the proximal femur and the lowest in the distal humerus. This finding echoes our results, with the exception that we also included intercalary implants, which are the only reconstructions that fared worse than distal humerus replacements.

Although patients with benign or localized disease were expected to have the highest survival rates, and patients with stage 3 or metastatic disease would have the lowest, our finding of variation in disease-specific survival among those with high-grade localized disease based on anatomical location is unique (**Figures 3A, 3B**). Indeed, we are unaware of any other long-term report that corroborates the finding of worse survival among patients with tumors localized to the upper extremity. In addition, our finding of improved disease-specific survival since 1990, when ifosfamide was added to our standard chemotherapeutic regimen, is interesting, and we believe this warrants further investigation. This finding is particularly important in light of some recent reports of improved long-term survival among patients with high-grade localized disease.[24,25]

Complications are virtually inevitable with any method of reconstruction after resection of a large musculoskeletal malignancy. Although other minor complications occurred during our study time frame, we specifically reported the complications that ultimately compromised the limb-salvage effort and resulted in amputation. Similar to the findings of other long-term series, infection and local recurrence were associated with the highest rate of amputation, while isolated mechanical failure did not directly result in any amputations. Patients with benign or localized disease who survive longer than 20 years should expect to undergo at least 1 revision procedure to treat failure of an endoprosthetic device (**Figure 4**).

Although intercalary implants carried the highest risk for revision, the most frequently encountered failures in this series were localized to the distal femur, particularly for implants of older designs. Modular implants most dramatically decreased the rate of mechanical failure when used in distal femoral applications. Prosthesis survival was longest for reconstructions involving the upper extremity, where unfortunately patient survival was worst. We noted a trend toward improved patient survival for those with high-grade localized disease during the later years of this study, possibly the result of an improved chemotherapeutic regimen. Endoprosthetic implants provide a reliable, durable method of reconstruction after resection of musculoskeletal tumors.

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