Endoprosthetic Reconstruction for the Treatment of Musculoskeletal Tumors of the Appendicular Skeleton and Pelvis

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Background: Excision of a bone tumor requires reconstruction if limb salvage is a priority. Reconstruction with an endoprosthetic implant is preferred in our unit, as the patient typically can return rapidly to full weight-bearing and functional activities. Long-term complications, such as deep infection, aseptic loosening, and mechanical failure of the implants, have led to concerns about the efficacy of reconstruction and the ability to revise failed implants while maintaining limb salvage in the longer term. The purpose of this study was to investigate the survival of endoprosthetic reconstructions in the medium to long term in order to determine the factors associated with their failure.

Methods: A consecutive series of 776 patients underwent endoprosthetic reconstruction following resection of a bone tumor at a minimum of ten years prior to this investigation. One hundred and nine children with a so-called growing endoprosthesis were excluded as they often require revision to an adult prosthesis near skeletal maturity. Six patients were excluded because of a lack of adequate follow-up data, leaving 661 patients for analysis. Kaplan-Meier survival analysis of the implant was performed, with implant revision for any cause (infection, local recurrence, and mechanical failure), mechanical failure alone, and amputation used as the end points.

Results: The mean duration of follow-up was fifteen years for patients who survived the original disease. Two hundred and twenty-seven patients (34%) had revision surgery because of mechanical failure (116 patients), infection (seventy-five patients), and locally recurrent disease (thirty-six patients). Implant survival at ten years was 75% with mechanical failure as the end point and 58% with failure from any cause as the end point. The limb salvage rate was 84% at twenty years.

Conclusions: We believe these medium to long-term results with first-generation endoprostheses are encouraging and justify the continued use of endoprostheses for reconstruction following the excision of a bone tumor.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

The surgical excision of bone tumors of the appendicular skeleton and pelvis requires a method of reconstruction of the bone defect if limb salvage is a priority. In the United Kingdom, reconstruction with endoprosthetic implants is the method of choice. It is believed that it affords the patient several advantages, including the ability to return rapidly to full weight-bearing functional activities, an important advantage when approximately 25% of the patients survive less than two years from the time of surgery[1]. Other advantages of endoprosthetic replacements include their initial reliability, wide availability, and proven cost-effectiveness[2]. However, the long-term complications of reconstructive surgery, such as deep infection[3], aseptic loosening[4], and mechanical failure of the implants, have led to concerns about the efficacy of this reconstruction method and the ability to revise a failed implant while maintaining limb salvage in the longer term[5]. These concerns are heightened in younger patients.

The purpose of this study was to investigate the fate of endoprosthetic replacements in patients who had been followed for more than ten years, in order to determine the long-

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TABLE I Diagnoses of Patients Treated by Endoprosthetic Replacement

Diagnosis	No. (%) of Patients	10-Year Implant Survival Rate with Additional Surgery for Any Cause as End Point
Osteosarcoma	283 (42.8)	50%
Chondrosarcoma	112 (16.9)	67%
Ewing sarcoma	64 (9.7)	54%
Metastatic disease	64 (9.7)	88%
Malignant fibrous histiocytoma	43 (6.5)	54%
Other	32 (4.8)	64%
Giant-cell tumor	29 (4.4)	61%
Fibrosarcoma	15 (2.3)	75%
Soft-tissue sarcoma	11 (1.7)	80%
Benign tumor	8 (1.2)	50%

term durability of endoprosthetic reconstruction for limb salvage.

Materials and Methods

Prior to 1996, a consecutive series of 776 patients with a musculoskeletal tumor underwent reconstruction with an endoprosthesis by one of three consultant surgeons (Rodney Sneath, R.J.G. and S.R.C.) at a tertiary referral unit. All reconstructions were performed with custom-made implants. We excluded 109 children who had a reconstruction with a so-called growing endoprosthesis. These implants invariably required revision to an adult prosthesis near skeletal maturity and thus would skew the revision rates. Our unit has a policy that all patients treated with an endoprosthetic replacement for a tumor are followed every three months for the first two years, every six months until the fifth year, and then annually thereafter. After ten years, the case of the patient is reviewed every two years or sooner if he or she has a problem. Patients who fail to return for follow-up are contacted. A total of six patients were excluded because of a lack of adequate follow-up data, leaving 661 patients suitable for analysis.

Electronic patient records have been kept on all patients seen in the unit since 1986, and data had been entered retrospectively for 236 patients (36%) seen before 1986. Patient records were retrieved for all patients in the study group. Demographic data, diagnosis, site of the neoplasm, operations performed, percentage of specimen necrosis, surgical complications, outcomes after surgery, date of last follow-up evaluation, the presence of metastases, local recurrence, and mortality were reviewed for all patients.

There were 370 men and 291 women in the study group. The mean age of the patients at presentation was thirty-four years (range, seven to eighty years). The most common indication for reconstruction was osteosarcoma in 283 patients (43%) (Table I). The most common Enneking stage[6] at presentation was IIB (a high-grade extracompartmental tumor), which was seen in 339 patients (51.3%).

The factors influencing implant survival were evaluated with univariate analysis with use of Kaplan-Meier curves and log-rank testing and with multivariate analysis performed with use of Cox proportional hazards. The factors tested included age at the time of the initial surgery, sex, diagnosis, stage, site, adjuvant therapy, and decade of implantation.

End points for survival analysis were revision surgery for any cause, revision for mechanical failure of the implant, and amputation. Revision surgery was defined as removal or exchange of the endoprosthetic metallic implant for any cause (including mechanical failure, infection, and locally recurrent disease). Mechanical failure included aseptic loosening, implant fracture, instability, periprosthetic fracture, pain, and stiffness. Revision surgery did not include routine maintenance surgery, such as rebushing of the hinges of the constrained knee implants or patellar resurfacing. Rebushing was required in thirty patients in whom the polyethylene bushings were exchanged without interfering with the metallic implant. One patient underwent patellar resurfacing without exchange of the metallic implant. The level of significance was set at $p = 0.05$.

Results

The overall patient survival was 52.7% at ten years and 45.7% at twenty years. The mean duration of follow-up was nine years for all patients and fifteen years (range, ten to thirty-five years) for the patients who survived the original disease. The most common site for the placement of the primary endoprosthesis was the distal end of the femur, which was involved in 228 patients (35%) (Table II).

A total of 227 patients (34%) underwent revision surgery. When the end point was revision surgery for mechanical failure, implant survival was 75% at ten years and 52% at twenty years (Fig. 1). Mechanical failure was inversely proportional to time ($y = 1–0.025x$; that is, a 2.5% rate of implant failure per year). However, with revision surgery for any cause as the end point, implant survival decreased to 58% at ten years

TABLE II Implant Survival Rate at Ten and Twenty Years (with Revision for Mechanical Failure and All Causes) and Amputation Rate According to Site of Prosthesis

Site	No. (%) of Implants	Survival Rate with Additional Major Surgery for Mechanical Failure as End Point (%)		Survival Rate with Additional Major Surgery for Any Cause as End Point (%)		No. (%) of Patients Requiring Amputation
		At 10 Years	At 20 Years	At 10 Years	At 20 Years	
Proximal end of femur	139 (21)	78.1	55.9	64.1	44.5	13 (9.4)
Femoral diaphysis	20 (3)	81.5	61.1	75.0	53.4	2 (10)
Distal end of femur	228 (34.5)	68.6	46.3	52.7	30.5	21 (9.2)
Total femur	7 (1)	100	–	100	–	0
Tibia	136 (20.6)	62.5	40.6	39.9	20.7	25 (18.4)
Humerus	103 (15.6)	90.7	73.1	84.7	66.7	6 (5.8)
Pelvis	28 (4.2)	87.1	76.2	59.9	44.9	5 (17.9)

and 38% at twenty years (Fig. 2). Failures due to all causes were treated with a one-stage revision in 141 patients, a two-stage revision in twenty-six patients, and primary amputation in sixty patients. The most common reasons for revision surgery were mechanical failure (116 patients; 51%), infection (seventy-five patients; 33%), and locally recurrent disease (thirty-six patients; 16%). The mean time to revision following primary surgery was 2.2 years (range, zero to thirty-four years) for any cause and 8.6 years (range, zero to thirty-four years) for mechanical failure. Aseptic loosening was the most common cause of mechanical failure (Table III), and it occurred in seventy-five patients at a mean of 9.4 years following implantation.

Two patients with deep infection were offered but declined revision surgery. One of them survived 10.3 years with modest intermittent wound drainage from a distal femoral replacement, and the other patient was living 10.5 years later with infection around a pelvic replacement; however, the implants in both patients were functioning well at the time of the last follow-up.

The only independent prognostic factors that were found to be significant on multivariate analysis, with revision for any cause as the end point, were the site of the prosthesis ($p = 0.001$) and the gender of the patient ($p = 0.04$). Factors such as the initial diagnosis, age at the time of implantation, adjuvant therapy, and tumor stage at presentation were associated with a trend to significance but failed to reach significance on multivariate analysis; however, they did reach significance on univariate analysis, which is a less robust method of analysis.

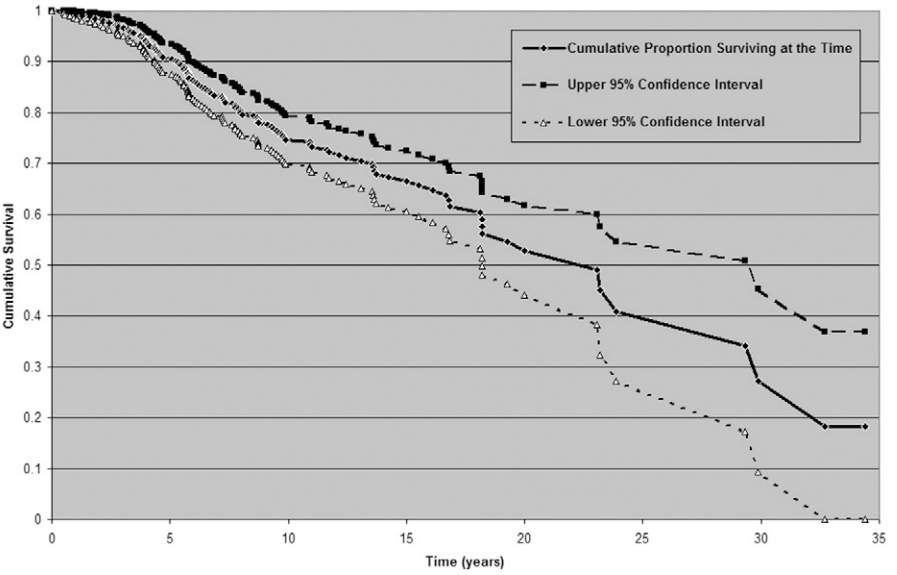

Fig. 1

Survival of the implants, with revision for mechanical failure as the end point.

TABLE III Recorded Complication Rates Related to Original Surgery

Complication	No. of Patients	Percentage of Patients
Aseptic loosening	75	28.6
Deep infection	75	28.6
Instability	54	20.6
Implant fracture	16	6.1
Periprosthetic fracture	7	2.7
Common peroneal nerve palsy	7	2.7
Pulmonary embolism	6	2.3
Rotational loosening	5	1.9
Excessive stiffness	5	1.9
Excessive pain	4	1.5
Proximal deep-vein thrombosis	3	1.1
Hematoma	3	1.1
Wrist drop	2	0.8
Total	262	40.0

Implant survival varied with respect to the site of implantation (Table II). The ten-year survival rate of the upper limb implants (85%) was significantly different from that of the lower limb implants (53.3%) and the pelvic prostheses (59.9%) ($p = 0.0001$). The cause of implant failure also varied among implantation sites (Table IV).

Patients with metastatic disease had the highest rate of implant survival because of the short life expectancy of the patients. The long-term survival rate for implants in patients with an aggressive benign condition was lower than that for implants in patients with a primary bone tumor because the former group had a high rate of infection (37.5%), which was commonly due to the multiple procedures that had been performed prior to the implantation of the prosthesis.

The decade when the prosthesis was implanted was found to be significant only with regard to the survival rate of tibial implants ($p = 0.01$), with revision for any reason as the end point. For other sites, the ten-year survival rate was 64.3% for prostheses implanted before 1980, 58.1% for those implanted from 1980 to 1984, 48.7% for those implanted from 1985 to 1990, and 63.7% for those implanted after 1990. For the tibial implants, the ten-year survival rate significantly improved from 33% for those implanted between 1980 and 1984 to 52% for those implanted since 1990. This is attributed to the routine use of gastrocnemius muscle flaps starting in 1988[3,7].

The ten-year implant survival rate, with revision for any cause as the end point, was 60.6% for patients who were less than twenty years old, 62.1% for patients from twenty to fifty years old, and 79% for patients over fifty years old ($p = 0.008$) (see Appendix). Young patients were more likely to have a failure

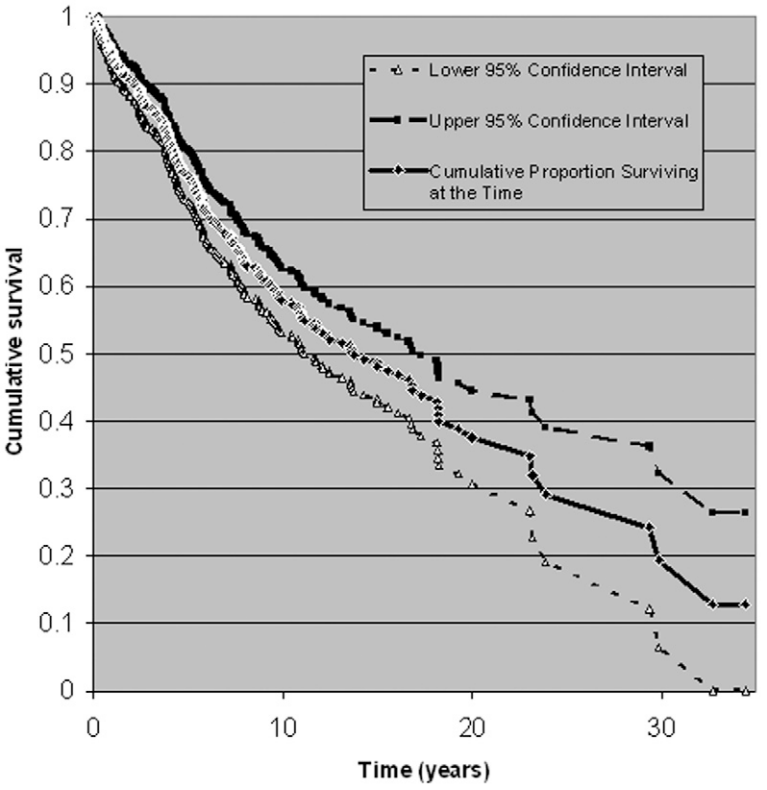

Fig. 2
Survival of the implants, with revision surgery for any cause as the end point.

TABLE IV Reason for Failure of Endoprostheses Stratified by Site of Implantation

	Site						
Reason for Failure	Distal End of Femur (N = 228)	Humerus (N = 103)	Femoral Diaphysis (N = 20)	Pelvis (N = 28)	Proximal End of Femur (N = 139)	Tibia (N = 136)	Total Femur (N = 7)
Aseptic loosening	31 (13.6%)	8 (8%)	3 (15%)	2 (7%)	15 (11%)	16 (12%)	
Implant fracture	5 (2.2%)	2 (2%)	0	0	0	8 (6%)	1 (14%)
Infection	29 (12.7%)	0	0	7 (25%)	11 (8%)	28 (21%)	
Instability	2 (0.9%)	1 (1%)	0	1 (4%)	3 (2%)	2 (2%)	
Local recurrent disease	12 (5.3%)	7 (7%)	2 (10%)	2 (7%)	7 (5%)	6 (4%)	
Pain	3 (1.3%)	0	0	0	1 (<1%)	0	
Periprosthetic fracture	2 (0.9%)	0	0	0	0	3 (2%)	1 (14%)
Rotational loosening	5 (2.2%)	0	0	0	0	0	
Stiffness	0	0	0	0	1 (<1%)	0	

because of mechanical causes ($p = 0.001$) (see Appendix). Men also had higher rates of failure than did women, with implant survival rates of 53% and 65%, respectively ($p = 0.007$).

The ten-year implant survival rate, with revision for any cause as the end point, was 82% for patients treated with surgery alone, 60% for those treated with surgery and chemotherapy, 78% for those treated with surgery and radiation therapy, and 51% for those treated with all modalities ($p < 0.0001$). The ten-year implant survival rate for patients with an Enneking stage-IA or IB (low-grade) tumor (74%) or those with a stage-III (metastatic) tumor (86%) was better than that for patients with an Enneking stage-IIA (high-grade intracompartmental) or stage-IIB (high-grade extracompartmental) tumor (48%) ($p = 0.0008$). This is a reflection of adjuvant therapy, which distorts the implant survival rate; low-grade tumors often did not require adjuvant therapy, and patients with stage-III disease often had a poor prognosis, with only 7% of such patients alive at ten years following surgery.

Amputation was performed in seventy (10.6%) of the 661 patients. It was done because of local recurrent disease in thirty-five patients (50%), infection in thirty-four patients (48.6%), and implant fracture in one patient. At the time of writing, there had been no amputations following failure because of aseptic loosening. On the basis of the numbers, no significant difference was detected in amputation rates between endoprostheses implanted for benign or malignant disease or on the basis of the age of the patient at presentation.

The rate of amputation decreased from 23% (fourteen) of the sixty patients treated prior to 1980 to 11% (fifteen) of the 136 patients treated from 1980 to 1984, to 11% (twenty-two) of the 209 patients treated from 1985 to 1990, and to 7.4% (nineteen) of the 256 patients treated in the years since 1990 ($p = 0.01$). The rates were also different with regard to the site of prosthesis implantation, with the highest rate for patients with a tibial implant (18.4%; twenty-five of 136 patients) and the lowest rate for those with a humeral implant (5.8%; six of 103 patients) ($p = 0.04$). The mean time to amputation was 3.9 years (range, 0.1 to 21 years), and 75% of the amputations occurred within 5.5 years (see Appendix).

A complication related to surgery occurred in 262 patients (40%) (Table III). Deep infection occurred in seventy-five patients (11.3%); twenty-six (35%) of them were treated by one-stage revision; twenty-six (35%), by two-stage revision; and twenty-three (31%), by primary amputation. The rate of primary amputation for infection among reconstructions performed prior to 1985 (twelve of nineteen patients) was higher than that of reconstructions done since 1985 (eleven of fifty-six patients) ($p = 0.015$), and an attempt at two-stage revision is now our routine procedure. One-stage revision was successful in controlling infection in nineteen (73%) of twenty-six patients, and two-stage revision was successful in twenty-two (85%) of twenty-six patients ($p = 0.026$). The median time to revision because of infection was 3.8 years after the time of the original reconstruction, with 13% (ten) of seventy-five deep infections seen more than ten years following the original reconstruction. The median time to revision for mechanical failure of an implant was 9.3 years after the time of the original reconstruction, with 10% (eleven) of 116 failures occurring eighteen years after the original reconstruction. The implants had survived without revision in 195 of 313 living patients at ten years, in thirty of seventy living patients at twenty years, and in only five of eight living patients at thirty years.

Discussion

The purpose of the study was to determine the durability of endoprosthetic replacements for the reconstruction of defects after tumor surgery. Patients with endoprostheses are exposed to major risks of infection, mechanical failure, and amputation; however, we demonstrated an ability to maintain limb salvage in 84% of the patients twenty years after reconstruction. The long-term survival of tumor endoprostheses may be regarded as poor compared with the 95% rate of sur-

vival at ten years for most modern hip implants[8]. However, patients with a tumor have a 10% rate of deep infection, a younger mean age at the time of surgery, and, frequently, reduced muscle function (from the radical dissection required for the wide tumor excision), causing altered joint biomechanics with consequent increased strain on both the prosthesis and the bone-prosthesis junction[3,4]. Patients with a tumor around the knee require removal of both the cruciate and the collateral ligaments, necessitating the use of a constrained fixed or a rotating-hinge prosthesis, which is accompanied by a weak extensor mechanism because of the soft-tissue excision, resulting in an increased rate of loosening and implant failure.

Our results are comparable with those in other reports on endoprosthetic replacements. Biau et al.[9] described ninety-one patients with a bone tumor about the knee who were treated with an endoprosthesis; thirty-six patients required removal of the implant. Gosheger et al., in a study of 250 patients treated with the Mutars prosthesis (Implantcast, Buxtehude, Germany), reported a five-year survival rate of 68.5% for implants in the lower limb, with an 8% rate of aseptic loosening[10]. Frink et al. reported that twenty-six of eighty-three patients had a revision after five years[11], and Torbert et al. reported an event-free prosthetic survival rate of 69% in a study of 139 patients at ten years[12]. Zeegen et al. showed a five-year prosthetic survival rate of 76%, with patients who underwent surgery for local recurrence excluded[13]. Mittermayer et al., in a study of 251 patients with a Kotz prosthesis (Howmedica, Rutherford, New Jersey), reported a 76% rate of prosthetic survival without aseptic loosening at ten years[14]. Shin et al. reported fifty revisions of 208 prostheses, with a survival rate of 65% of the custom-made prostheses at ten years[15], and Malawer and Chou noted a ten-year survival rate of 67% of the large-segment prostheses in eighty-two patients[16].

The debate continues about the long-term survival of metallic implants compared with the short-term complications of biological (autograft or allograft) reconstructions. Both techniques have their place in the surgeon's armamentarium, and studies have shown little difference in long-term survival. Futani et al.[17], in a study comparing the results of endoprosthetic reconstruction in twenty-eight children and those after biological reconstruction in twelve children, showed a ten-year survival rate of 51% for the endoprostheses and 46% for the biological reconstructions. In a report on allograft reconstruction around the knee in 116 patients, Brigman et al.[18] found that 37% of the patients regarded the procedure as a failure, 34% had a nonunion, 16% had a deep infection develop, and 12% required a later amputation. Muscolo et al.[19] reported good results after eighty allograft reconstructions. Of the sixty-two allografts available for review, fourteen failed (because of infection, local recurrence, bone resorption, or fracture) and the survival rate of the allograft was 78% at ten years. We are not aware of any published long-term results of a large series of biological reconstructions for all sites and diagnoses.

Our investigation is an observational retrospective cohort study, which has several weaknesses. The study period is long and the techniques and implants have evolved. The design of the distal femoral implant changed to include rotating platforms (to reduce torsional force) and hydroxyapatite-coated collars at the bone-prosthesis interface (to allow ongrowth of bone to decrease bending forces), leading to substantial improvements in implant survival[4,20,21]. The routine use of pedicled medial gastrocnemius flaps with tibial implants[7] and the increased use of plastic surgery have enhanced implant survival, dramatically reducing infection rates[3,7]. Early on, infections around implants were frequently treated with primary amputation; however, two-stage revision is now advocated as the primary treatment with good results[3], and no primary amputation for infection was performed after 1990.

This present study confirms the long-term durability of endoprosthetic reconstruction for limb salvage surgery, with the evolution of design and techniques improving the rate of implant survival but highlighting the problems of infection and aseptic loosening, which can have dire consequences for the patient and surgeon. Attempts to resolve both of these problems constitute the major challenge for the future of limb salvage surgery in patients with musculoskeletal tumors.

Appendix

eA A table showing the effect of patient age on implant survival and figures showing survival curves, with use of mechanical failure and amputation as the end points, are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM). ■

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