L. M. Jeys · R. J. Grimer · S. R. Carter · R. M. Tillman

Risk of amputation following limb salvage surgery with endoprosthetic replacement, in a consecutive series of 1261 patients

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Abstract Endoprosthetic replacements are commonly used for limb salvage following surgical excision of bone tumours. Advantages include initial reliability, rapid restoration of function and their ready availability. Potential long-term problems include loosening, infection and mechanical failure. Increasing problems may lead to the necessity for amputation; this paper assesses that risk. A total of 1,261 patients have undergone endoprosthetic replacements in our centre in the past 34 years, with a total of 6,507 patient years of follow up. A total of 112 patients have had subsequent amputation. The reasons for amputation were local recurrence in 71, infection in 38, mechanical failure in two and chronic pain in one. The proximal tibia had the greatest risk of amputation ($n=38/245$). The time to amputation varied from 2 days to 16 years, with a mean of 31 months. The risk of amputation decreased with time, although 10% took place after more than 5 years.

Résumé Les remplacements prothétiques sont couramment utilisés pour la réhabilitation d'un membre après excision chirurgicale d'une tumeur osseuse. Les avantages incluent fiabilité initiale et restauration rapide de la fonction. Les ennuis potentiels à long terme sont le descellement, l'infection et la faillite mécanique. Les problèmes croissants peuvent mener à la nécessité d'une amputation; ce travail étudie ce risque. Un total de 1261 malades a subi des remplacements prothétiques dans les 34 années passées, avec un total de 6507 années-patients de suivi. 112 malades ont eu une amputation dont les raisons étaient: récurrence locale pour 71, infection pour 38,

échec mécanique pour 2 et douleur chronique pour 1 cas. Le tibia proximal avait le plus grand risque d'amputation ($n=38/245$). Le délai d'amputation variait de 2 jours à 16 années, avec une moyenne de 31 mois. Le risque d'amputation diminue avec le temps, bien que 10% des amputations aient eu lieu après plus de 5 années.

Introduction

Endoprosthetic replacements are one of the most commonly used methods for limb salvage following surgical excision of bone tumours and are accepted as a suitable method of reconstruction [8, 10, 17, 21, 22]. They allow rapid restoration of function to the patient, and functional scores show better results than amputation [20]. They are readily available for replacement of many bones and joints, and some centres now have several decades of experience in their use [12, 19, 23] with long term results becoming available [1, 10, 11, 21, 22, 24]. It has been proven that they are also a very cost-effective way of treating bone tumours [9]. However, endoprosthetic replacements are associated with a greater risk of complications [8] and subsequent operations compared to amputation [20]. The patients endure long-term problems of wear, aseptic loosening, mechanical failure, infection and local recurrence [4, 12, 15, 16, 19, 23]. There is also a significant risk of amputation following endoprosthetic replacement [19, 2, 23]. This paper documents the scale and causes of this risk.

Methods

Prospective data is collected on all patients seen in our unit, and this is stored on a database. Information collected includes demographic details, diagnosis, stage, grade, treatment (including adjuvant), complications and outcomes. Using the database, it was possible to identify those patients who had an endoprosthetic replacement and those who had subsequent amputation, as well as the reasons for amputation. Patients who had died or were still alive with their prosthesis in situ were censored, whilst those who had an amputation for whatever reason were uncensored. Statistical analysis was performed using Kaplan-Meier Survival Analysis

L. M. Jeys · R. J. Grimer · S. R. Carter · R. M. Tillman
Royal Orthopaedic Hospital Oncology Service,
Bristol Road South, Northfield, Birmingham,
B31 2AP United Kingdom

L. M. Jeys (✉)
Waterstones House,
31A Green Abbey, Hade Edge, Holmfirth, West Yorkshire,
United Kingdom
e-mail: lee.jeys@btclick.com
Tel.: +44-1484-663551, Fax: +44-121-6854146

Fig. 1 Survivorship of all limbs following endoprosthetic replacement without amputation, using Kaplan-Meier analysis (95% confidence level)

Table 1 Amputation rates for each endoprosthetic replacement site

Site	Amputations		
	Total	Due to infection	Due to local recurrence
Proximal femur (<i>n</i> =264)	15 (5.7%)	5 (1.9%)	9 (3.4%)
Distal femur (<i>n</i> =492)	42 (8.5%)	12 (2.4%)	30 (6.1%)
Femur other (<i>n</i> =28)	1 (3.6%)	0 (0%)	1 (3.6%)
Tibia (<i>n</i> =245)	38 (15.5%)	19 (7.8%)	17 (6.9%)
Humerus (<i>n</i> =183)	11 (6%)	1 (0.6%)	10 (5.5%)
Pelvis (<i>n</i> =49)	5 (10.2%)	1 (2%)	4 (8.2%)

and Fisher PLSD tests using Statview package (SAS Institute, Cary, USA). We identified the cause for amputations, estimated the risk of amputation stratified by diagnosis, endoprosthetic replacement site and complication and produced survival analyses of the endoprosthetic replacements.

Results

Data was retrieved on 1,261 patients who had undergone endoprosthetic replacements in our centre over 34 years, with a follow-up of 6,507 patient years. The overall patient survival was 60% at 5 years, 54% at 10 years and 40% at 20 years. The majority of endoprosthetic replacements were femoral (*n*=784, 62%), of which 492 were distal femoral replacements, 264 proximal femoral replacements and 28 total or mid-shaft replacements. Other sites were tibial (*n*=245, 19%), humeral (*n*=183, 15%) and pelvic (*n*=49, 4%). Overall limb survival without amputation was excellent, with a 20-year survival of 91% by Kaplan-Meier survival analysis (Fig. 1).

Overall risk of amputation was 8.9% (*n*=112). Reasons for amputation were for control of local recurrence (*n*=71, 63%), infection (*n*=38, 34%), mechanical failure of the prosthesis (*n*=2, 2%) and persistent pain (*n*=1, 1%) (Table 1). It was found that local recurrence was the sin-

Fig. 2 Survivorship of limbs following endoprosthetic replacements without amputations comparing patients with and without local recurrence, using Kaplan-Meier analysis (95% confidence level)

Fig. 3 Distribution of time to amputation

gle biggest risk factor to limb survival. The 10-year limb survival fell to only 43% following local recurrence of the disease (Fig. 2), and this was statistically significant ($p \leq 0.0001$) compared to the risk of amputation in patients without local recurrence. The risk of amputation following proven infection of an endoprosthetic replacement was 19% compared to the risk for amputation with a local recurrence, which was 36%.

For each endoprosthetic replacement site, local tumour recurrence was the most common cause of amputation, except for tibial endoprosthetic replacements where infection played an equally causative role. Risk of amputation was lowest in the proximal femoral replacements (5.5%) and highest in the tibial replacements (15.5%). It was found that patients with tibial replacements had a statistically higher risk of amputation compared to patients with replacements at other sites ($p=0.001$).

Time to amputation ranged from 2 days to 16 1/2 years, with a mean of 31 months. Median time to amputation was 32 months for infection and 13 months for local recurrence. Amputation risk decreased with time, although 10% took place more than 5 years after insertion. Late amputations occurred due to both infection and local recurrence (Fig. 3). It was also found that replacements inserted prior to 1980 had a survival statistically less than those inserted since 1980. The patient's presenting diagnosis, age, subsequent chemotherapy and type of replacement (standard or extendable) were not statistically significant risk factors for amputation.

Discussion

The overall risk of amputation following endoprosthetic replacement in our experience is comparable or lower than reported in other series [19, 20, 23]. However, at 8.9%, this represents a significant risk to limb salvage, which increases with tibial replacements to 15.5%. Survival analysis shows that the vast majority of patients are able to keep their affected limb following replacement for their lifespan. This may, obviously, require several operations and possibly revision of the prosthesis.

Local recurrence was a precursor to amputation in two thirds of cases, and further improvements in adjuvant therapy may help to reduce this risk. The control and possibly early detection of local recurrences may prove to be the key in avoiding amputation. Infection, also a major cause of late amputation, is a problem in all forms of limb salvage surgery, and satisfactory methods of both prevention and treatment have yet to be identified [2, 6, 7, 13, 14, 18]. Patients with tibial replacements have high rates of amputation. Improvement in coverage (e.g. gastrocnemius flaps) and prosthesis design may help increase function as well as reduce infection rates. This may be a plausible explanation for the reduction in amputation rates for patients with tibial replacements since 1980, together with better adjuvant therapies [3, 5]. Grimer et al. [10], in 1999, showed a reduction in the risk of infection from 36% to 12% with tibial replacements following the routine use of gastrocnemius flaps. Our results show that the amputation rate prior to their routine use was 37.2% ($n=16/43$), which has been reduced to 13.6% ($n=22/161$). This further compounds evidence for the routine use of gastrocnemius flaps in tibial replacements.

Effective early detection and treatment of deep infection in endoprosthetic replacements may allow increased limb survival. Interestingly, there was no statistical difference between limb survival with extendable and adult replacements despite the increased risk of infection with repeated lengthening procedures [1, 23].

The presenting diagnosis did not statistically alter limb survival. In particular, there was no increased risk for patients receiving chemotherapy despite possible increased risks of infection associated with adjuvant therapy. It is interesting to note that survivorship of limbs

without amputation was not statistically different when benign and primary tumours were compared; the cumulative survivorship of limbs at 10 years for benign conditions was 84% (95% CI; 94%–74%) compared to 87% (95% CI; 90%–84%) for malignant conditions. This may be due to the fact that most replacements for benign conditions were for giant cell tumours, which have a high rate of local recurrence, and there is no reason to believe that they should have a higher infection rate than other tumours. The number of patients receiving radiotherapy following replacement was too small to draw any significant conclusions about the risk to limb survival. Not surprisingly, over half of the amputations occurred within the first 18 months of replacement insertion; however, a significant proportion required late amputations. Late amputations occurred for both infection and local recurrence, indicating that these complications are equally as serious whenever they arise.

Importantly, however, the risk of amputation did not increase with time, suggesting that, despite the increasing cumulative risk of complications with the passage of time, this does not result in an increased incidence of amputation. In particular, mechanical problems such as aseptic loosening are not proving to be a cause of late amputations.

Endoprosthetic replacements provide a reliable method of long-term limb salvage with a low but ever-present risk of subsequent amputation. Tibial replacements have a higher rate of amputations, with infection playing a significant role. Local recurrence and infection are both harbingers of amputation. An improved method of preventing both local recurrence and infection will lead to a reduction in amputation risk. In our experience, mechanical failure does not seem to constitute a significant risk to late amputation, even in young patients.

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