Endoprosthetic replacement of the distal femur for bone tumours
LONG-TERM RESULTS

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We investigated whether improvements in design have altered the outcome for patients undergoing endoprosthetic replacement of the distal femur after resection of a tumour. Survival of the implant and ‘servicing’ procedures have been documented using a prospective database, review of the design of the implant and case records. In total, 335 patients underwent a distal femoral replacement, 162 having a fixed-hinge design and 173 a rotating-hinge. The median age of the patients was 24 years (interquartile range 17 to 48).

A total of 192 patients remained alive with a mean follow-up of 12 years (5 to 30). The risk of revision for any reason was 17% at five years, 33% at ten years and 58% at 20 years. Aseptic loosening was the main reason for revision of the fixed-hinge knees while infection and fracture of the stem were the most common for the rotating-hinge implant. The risk of revision for aseptic loosening was 35% at ten years with the fixed-hinge knee, which has, however, been replaced by the rotating-hinge knee with a hydroxyapatite collar. The overall risk of revision for any reason fell by 52% when the rotating-hinge implant was used.

Improvements in the design of distal femoral endoprostheses have significantly decreased the need for revision operations, but infection remains a serious problem. We believe that a cemented, rotating-hinge prosthesis with a hydroxyapatite collar offers the best chance of long-term survival of the prosthesis.

The distal femur is the most common site for primary malignant bone tumours. Over the past 30 years, limb salvage has replaced amputation as the mainstay of surgical treatment, principally because of improvements in imaging, chemotherapy, surgical technique and in the design of the prostheses.1-3 Simon et al4 have compared the results of limb-sparing surgery with those of amputation in patients with osteosarcoma and have concluded that limb salvage does not compromise long-term survival although it may lead to an increased risk of local recurrence. Limb salvage has also been shown to be more cost-effective than amputation.5

Endoprosthetic replacement is one method of reconstruction after resection of a tumour. It has the advantage that patients recover rapidly and can bear weight early.6-8 The main complications of its use are local recurrence, infection, aseptic loosening, mechanical failure and fracture, either of the prosthesis or of bone.9-13 Therefore, other methods have been advocated, but despite the potential complications endoprosthetic replacement has continued to be used not only in the treatment of primary bone tumours, but for metastatic and other non-tumourous conditions.14-17

To date there have been no large studies on the long-term complications of endoprosthetic replacement of the distal femur. We therefore report our experience of over 30 years employing this procedure, and compare the results of the use of a fixed-hinge prosthesis with those of a rotating-hinge design.

Patients and Methods
Between March 1973 and December 2000, 428 consecutive patients underwent resection of the distal femur and endoprosthetic replacement. A total of 12 overseas patients with no documented follow-up and 81 children with an extendable endoprosthesis were excluded, leaving 335 patients in the study group.22 There were 198 male and 137 female patients with a median age of 24 (interquartile range (IQR) 17 to 48). Most (307) were treated for primary bone tumours, osteosarcoma being the most common diagnosis (Table I). Details of each patient’s diagnosis, treatment and outcome were entered prospectively into a database. The operations were all carried out at a
All the prostheses were custom-made and 328 were designed and manufactured at the Department of Biomedical Engineering of the Institute of Orthopaedics of University College, London (latterly Stanmore Implants Worldwide, Stanmore, United Kingdom), six were made by Biomet (Howmedica Stryker, Newbury, United Kingdom) and one by Howmedica (Howmedica Stryker). Before 1992, 162 fixed-hinge distal femoral endoprostheses were employed. Between 1992 and 2000, 173 rotating-hinge endoprostheses were employed of which 143 had a hydroxyapatite (HA) collar and were cemented, 15 had no HA collar and were cemented, and 15 had an HA collar but were uncemented (Fig. 1). The patients with a rotating-hinge device were slightly older than those with a fixed-hinge prosthesis (median ages 29 (IQR 18 to 52) and 23 (IQR 17 to 41), respectively, p = 0.01). This was because a higher proportion of patients had an endoprosthesis for metastatic disease. The bushes in the femoral component were made of ultra-high-molecular-weight polyethylene (UHMWPE). The HA collar had been incorporated on the femoral component at the prosthesis-bone junction in the expectation that there would be osseointegration which would decrease late aseptic loosening (Fig. 2).

All the operations were performed in a clean-air theatre. Antibiotic prophylaxis was given at the time of surgery and for up to 24 hours post-operatively. The operation was performed with the patient supine, through a longitudinal incision which excised the biopsy track and was deepened into a medial parapatellar approach to the knee. The proportion of the excised femoral shaft varied between 25% and 75%. Resection of the tumour was carried out according to the oncological principles defined by Enneking, Spanier and Goodman23 endeavouring to achieve a wide margin of resection. A total of 320 stems were implanted with low-viscosity cement, introduced with a gun, and 15 were uncemented. The patella was not resurfaced unless an extra-articular resection was required.

All patients were allowed partial weight-bearing, progressing to full weight-bearing by the time that they left hospital two weeks after their operation. After six weeks, they returned for a period of intensive inpatient physiotherapy. They were then followed up every three months for two years, then at six months for five years, and annually thereafter.

Outcome analysis. Failure was defined as the time in years from the date of the original surgery to the measured event (e.g. revision). In 1993 Unwin et al7 suggested that failure should be classified as biological (infection), biomechanical (loosening and bone fracture) or mechanical. The last can be further divided into failure of the prosthesis such as breakage, and servicing procedures such as rebushing. To this we must add oncological failure. We therefore considered failure under the following headings:

1. The need for any further operation, whatever the cause (rebushing, revision, excision for local recurrence, amputation etc).
2. The need for any revision of the prosthesis or part of the prosthesis because of failure of the implant (e.g. aseptic loosening, fracture of the implant, infection, breakage etc).
3. The incidence of failure of limb salvage because of amputation.
4. The incidence of the two main complications of aseptic loosening and infection.

We used Kaplan-Meier survival curves to assess the rate of failure of the prostheses. Patients were censored for statistical analysis (observation stopped before the event occurred) if their endoprosthesis had not failed by the time of their last assessment or if an alternative event, such as amputation, had made them no longer susceptible to that risk.

Table I. Diagnosis of patients managed by endoprosthetic replacement

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteosarcoma</td>
<td>188</td>
</tr>
<tr>
<td>MFH*/spindle-cell sarcoma</td>
<td>65</td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td>29</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>19</td>
</tr>
<tr>
<td>Giant-cell tumour</td>
<td>17</td>
</tr>
<tr>
<td>Ewing’s sarcoma</td>
<td>8</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
</tr>
</tbody>
</table>

*MFH, malignant fibrous histiocytoma
Results

The mean follow-up was for 12 years (5 to 30). At this stage, 192 patients (57%) remained alive.

Of the series, 36 patients (10.7%) had an amputation and the risk was 9% at five years rising to 17% at 20 years. The most common reasons were local recurrence (20 cases (6%)) and infection (15 cases (4.5%)). The remaining patient required an early amputation for ischaemia. A total of 32 patients (9.6%) developed deep infection, after a median of 13 months (IQR 4 to 37). Seven needed early amputation and 25 had a two-stage revision in an attempt to control the infection. This was successful in 17 but failed in eight, with these patients eventually requiring amputation. We found no difference in the risk for amputation or infection between the fixed-hinge and rotating-hinge endoprostheses.

Kaplan-Meier analysis, using any further surgery as the end-point, demonstrated a 61% estimated risk of failure at 10 years. The reasons for this included local recurrence, infection, revision, rebushings and fracture. A total of 81 patients (24%) needed a revision procedure.

Seven implants fractured (one fixed-hinge, six rotating-hinge). Two revisions were carried out for persistent pain of uncertain cause. Rebushing of the primary endoprosthesis was needed in 55 prostheses (45 fixed-hinge, 10 rotating-hinge) and seven required multiple rebushings (5 twice, 1 three times and 1 four times). The mean time from implantation to rebushing was 11 years (1 to 15). Patellar resurfacing was required in eight cases for patellofemoral pain, but was also carried out at the time of revision for other causes if the patella looked particularly worn. It was more commonly needed with fixed-hinge than with rotating-hinge endoprostheses, probably because of improvements in the design of the patellofemoral bearing surface in the latter (Fig. 1).

Survivorship of the fixed- and rotating-hinge designs were compared using Kaplan-Meier analysis (Figs 3 and 4). The outcome, taking revision of the implant as an end-point, is shown in Figure 3. The early rates of failure were similar, but there was later divergence. Early failure was usually due to infection or breakage of the prosthesis whereas late failure was more likely to be due to aseptic loosening. If aseptic loosening was taken as the end-point, the rotating-hinge design with an HA collar was least likely to fail (p < 0.0001). The risk of revision for aseptic loosening of a fixed-hinge was 35% at ten years compared with 24% for a rotating-hinge without an HA collar and 0% for a rotating-hinge with an HA collar (Fig. 4). Two patients with rotating-hinge prostheses and HA collars had revision for thigh pain. In one this was due to a fungal infection, but in the other there was no evidence of infection or loosening, although the pain was relieved by revision. Aseptic loosening was the most common reason for revision of a fixed-hinge knee and appeared to be a problem which continued with time, whereas infection and fracture of the stem were the most common reasons for failure of rotating-hinge implants.

Gender, diagnosis and the decade of treatment did not affect the rate of complications or survival of the prosthesis, but patients over the age of 60 years at the time of implantation had a significantly lower rate of mechanical loosening and revision than those under the age of 60 years.
Discussion

Limb-salvage surgery has replaced amputation as the treatment for primary bone tumours of the distal femur. This has been achieved without adversely affecting survival, mainly due to improvements in chemotherapy.\textsuperscript{3,4,12,24} Limb salvage offers considerable advantages in terms of function, appearance and psychological acceptance,\textsuperscript{25,26} and is generally considered to be cost-effective when compared with amputation.\textsuperscript{5}

Resection of the distal femur necessarily sacrifices all the knee ligaments thereby requiring a constrained or semi-constrained articulation for its reconstruction. The use of constrained knees has not been entirely successful in patients with osteoarthritis, and since most patients with resections of tumours around the knee are young, a high rate of failure can be expected.\textsuperscript{27} Previous reports have highlighted the high incidence of complications after this type of surgery.\textsuperscript{28} The definition of ‘failure’ varies from series to series and the available short-term results may underestimate the rate of failure. One of the largest and most frequently quoted papers on endoprostheses is that of Unwin et al\textsuperscript{9} who produced a detailed analysis of 1001 implants, but only used the end-point of aseptic loosening. We have shown that failure can take many forms, some of which may result in complete loss of the limb (local recurrence and infection), revision of the prosthesis (infection, loosening, fracture of the implant) and relatively simple ‘servicing’ of the prosthesis (rebushing, patellofemoral problems).

We suggest that in future comparisons the following definitions should be used:

1. The risk of amputation.
2. The risk of infection.
3. The risk of mechanical failure resulting in revision.
4. The risk of further surgery from any cause.

We have demonstrated these risks in Table II.

Amputation after distal femoral replacement was required in 36 patients (10.7%). In 20 cases it was carried out for local recurrence of disease. The rates of amputation in other series range from 4% at a minimum follow-up of two years\textsuperscript{19} to between 10% after ten years\textsuperscript{29} and 15%.\textsuperscript{30} The risk of a patient requiring an amputation is related to the rate of local recurrence as well as to the risk of infection.

In the period of our study we carried out limb salvage on 85% of patients with tumours of the distal femur. The rate of local recurrence can clearly be reduced by having a higher amputation rate initially, particularly for patients with large tumours in whom only a marginal excision can be achieved, but this has not been shown to lead to any improved overall survival, particularly for osteosarcoma.\textsuperscript{31}

In such situations the surgeon should discuss with the patient the risks and benefits of limb-salvage surgery compared with amputation.

Several authors have highlighted the problem of infection after limb salvage,\textsuperscript{7,13,19,21,32} in which it is as frequent as after allografting.\textsuperscript{28,33} The median time to infection in our series was 13 months and although many of these early infections were related to chemotherapy and central line infections, there were an equal number of late infections, many of which developed quite spontaneously without apparent cause many years after the original operation. Extra-articular resection was rarely performed and it is therefore not possible to draw meaningful conclusions as to whether this subgroup was at any altered risk in terms of infection, loosening or functional outcome. This high, continuing risk of infection is an ongoing problem in orthopaedic oncology and methods of preventing it are actively sought.\textsuperscript{34}

Revision for a fractured implant was needed in seven cases (2%), one in the fixed-hinge and six in the rotating-hinge group. This is probably due to the more complex construction of the rotating-hinge implant. All of the fractures were in the tibial yoke where the rotating component is

<table>
<thead>
<tr>
<th>Risk</th>
<th>5 yrs</th>
<th>10 yrs</th>
<th>15 yrs</th>
<th>20 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>9</td>
<td>15</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Infection</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Revision</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>17</td>
<td>33</td>
<td>49</td>
<td>58</td>
</tr>
<tr>
<td>Fixed-hinge</td>
<td>17</td>
<td>42</td>
<td>56</td>
<td>64</td>
</tr>
<tr>
<td>Rotating-hinge</td>
<td>17</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any surgery</td>
<td>38</td>
<td>61</td>
<td>75</td>
<td>89</td>
</tr>
<tr>
<td>Aseptic loosening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed-hinge</td>
<td>13</td>
<td>35</td>
<td>44</td>
<td>55</td>
</tr>
<tr>
<td>Rotating-hinge either no HA\textsuperscript{*} or no cement</td>
<td>24</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotating-hinge with HA Nil Nil</td>
<td></td>
<td></td>
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</tbody>
</table>

\textsuperscript{*} HA, hydroxyapatite
inserted into a tibial tray. These were invariably painless and the patient simply noticed increased instability of the knee. Such fractures should be revised immediately to avoid damage to the UHMWPE surface from the broken ends. Rates of fracture of up to 6% have been reported elsewhere.7,21,30

The survival analysis does not take into account every procedure which the patient undergoes during the lifetime of that implant. The UHMWPE bushings allow for a staged mechanism of failure and wear out before the implant itself fails or loosens. In our series 16% of all patients required one or more rebushings of the primary implant (55 rebushings) and a smaller number needed rebushing of revised implants. In previous studies, up to 42% of patients have required rebushing procedures.21 The patella was not resurfaced routinely at the primary operation and only 2% of patients needed this at a later stage.

Patients should be informed that servicing procedures, such as the replacement of bushings, may be required and in young patients are almost inevitable.

Our results show that overall 24% of the patients required a revision of their prosthesis. However, since the rate of revision rose with time it is essential that these figures are reported as Kaplan-Meier survival. Reported rates of revision range from 9% with a maximum follow-up of eight years35 to 35%.11,30,36 A number of studies have been published with short- to medium-term survival rates of up to 87% at three years and 67% to 88% at five years; the results at ten years show a decrease to a survival of 48% to 65%, and only very limited data are available at 20 years, with survival of up to 53%.7,11,29,37 Small series on the use of modular endoprosthetic systems have been published.38,39 Larger series have been published with the Howmedica modular replacement (Howmedica Stryker) and the Kotz modular femoral and tibial resection systems (Stryker Howmedica Osteonics, Rutherford, New Jersey). The series of Zeegen et al35 reported the outcome of 55 distal femoral replacements with eight proximal tibial replacements, generating a three-year Kaplan-Meier survival with failure due to loosening, mechanical failure or infection of 87% for the modular knee subgroup. The series of Mittermayer et al40 and Capanna et al21 with the Kotz modular femur and tibia resection system showed a survival at ten years of 76% without aseptic loosening and with good or excellent results in 75% at a mean of 51 months, respectively.

It is disappointing to report that failure due to both infection and local recurrence has not improved with time. Mechanical problems, and in particular aseptic loosening, appear to have been prevented by the introduction of the rotating-hinge knee in combination with an HA collar. Loosening rates of 5% to 16% with short follow-up11,19 and of 5% to 28% with longer follow-up have previously been reported2,7,29,30 Shih et al41 compared the outcome of patients with constrained and rotating-hinge endo-

prostheses, and found good or excellent results in 33% of the former and 69% of the latter group with a revision rate of 42% in the fixed-hinged group. Roberts et al10 showed a five-year survival of 72% (64% at seven years for a fixed-hinge design). Survival of 88% at five years for a rotating-hinge design15 has been reported with good functional and radiological results demonstrated for the rotating-hinge.19,42

The use of an HA collar at the prosthesis-bone junction allows osseointegration of the prosthesis with the host bone (Fig. 2) and has successfully prevented the problems of aseptic loosening seen in the previous generation of prostheses. There were a small number of rotating-hinge prostheses in our series without an HA collar and these were at significant risk of aseptic loosening. The use of a rotating-hinge has slightly increased the risk of mechanical failure due to breakage of the implant, but has significantly reduced the need for rebushing procedures. The decreased rate of UHMWPE wear may also have helped to decrease the incidence of loosening.

No benefits in any form have been received or will be received from a commer-
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References


