ORIGINAL ARTICLE

Intercalary defects reconstruction of the femur and tibia after primary malignant bone tumour resection. A series of 13 cases

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Malignant Bone tumour;
Autograft;
Allograft;
Bone tumour resection;
Bone reconstruction

Summary
Introduction: Performing intercalary segment reconstruction after malignant bone tumour resection results in both mechanical and biological challenges. Fixation must be solid enough to avoid short-term or mid-term mechanical failure. The use of an allograft or autograft must ensure long-term survival of the reconstruction. The goal of this study was to analyse the clinical and radiological outcomes of these reconstructions.

Patients and methods: Thirteen patients were operated on eight femurs and five tibias. The median age was 20 years old (range 14–50). The most common diagnosis was osteosarcoma. The median resection length was 15 cm (Q1–Q3: 6–26). A plate was used for fixation in nine cases and an intramedullary locked nail in four cases. An isolated bone autograft was used in two cases, an isolated bone allograft in one case, a dual autograft-allograft composite in six cases, and vascularised fibula and allograft combination in four cases.

Results: The cumulative probability of union was 46% (95% CI: 0–99%) at 1 year; at the final follow-up, union was achieved in 12 patients (92%). Because of non-unions, 13 iterative procedures were needed to obtain these results. A non-displaced fracture of a cuboid-shaped tibial graft occurred in one patient, which was treated conservatively. Three infections occurred.

Discussion: The results of intercalary segmental defects reconstruction after bone tumour resection were good, both from an oncologic and radiological point-of-view. One or more iterative procedures are sometimes needed to finally obtain bone union. We prefer to use a free rectangular cuboidal tibial graft since reconstruction with a vascularised autograft is technically more difficult. The choice of fixation methods is still controversial and no approach was found to be superior.

Level of evidence: Level IV. Retrospective study.
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Introduction

Primary, malignant bone tumours are rare. They represent less than 1% of all cancers and have an estimated incidence of six per million per year [1]. The life expectancy of patients operated for a malignant bone tumour has increased, particularly due to advances in chemotherapy. This has resulted in changes to the initial surgical management, with fewer amputations and more conservative treatments [2–4]. A prosthesis is often used to reconstruct the metaphysis or metaphysis-epiphysis junction, the most common regions for a tumour [5–7]. Conversely, tumours distal to the epiphysis are rarer. The possibility of joint preservation exists but post-resection reconstruction methods are not standardised.

Malignant bone tumours located at the metaphysis-diaphysis junction of long bones in the lower limb are amenable to a resection and intercalary reconstruction procedure that preserves the proximal joint, however the long-term outcome of this reconstruction is not well defined. One aspect of this procedure requires that the fixation be solid enough to avoid mechanical failure of the reconstruction in the short and medium term. The location and extent of resection determine the choice of fixation methods [8,9]. The other aspect is the need for the bone allograft (cryopreserved or irradiated) or autograft to integrate into the host bone where the resection was performed and ensure the long-term survival of the reconstruction.

Resection and intercalary reconstruction often results in mechanical problems: non-union rates range from 17 to 57% in various series [10–18]. These can be attributed to either mechanical (fixation stability) or biological (graft integration) failures. Secondary fractures are a common complication (between 9 and 19% in various series [10–15,19,20]) because the grafted and intercalated bone segments are not repopulated. These mechanical and biological failures arise from insufficient stability of the initial fixation [14,16,21]. Infection is also a common complication [15] of this lengthy and damaging surgery, which is often performed in immunosuppressed patients.

We performed a retrospective study to evaluate the clinical and radiological outcomes of patients who underwent a resection and intercalary reconstruction of a primary bone tumour in the lower limb. The goal was to assess the time needed for bone union to occur and to critically analyse the mechanical, infectious and biological challenges of the different surgical methods used.

Patients and methods

This was a single centre, retrospective study on a series of 13 patients operated on between 1996 and 2005 in the orthopaedic surgery department of the Cochin Hospital in Paris, a group specialised in musculoskeletal tumour surgery. All of the procedures were performed by surgeons who were experienced in tumour surgery. The inclusion criteria were: patients with a primary malignant bone tumour of the lower limb; tumour located at the diaphysis, metaphysis or metaphysis-diaphysis junction; resection and intercalary reconstruction surgery. Patients with a secondary or benign bone tumour, tumour located at the epiphysis, patients where the bone resection left some bone continuity, patients with a prosthesis reconstruction or amputation were excluded.

During this defined period, 13 of the 159 patients operated for a primary bone tumour in the lower limb corresponded to the inclusion criteria. The median age was 20 years old [range: 14–50]; there were six men and seven women. Osteosarcoma was the most common diagnosis (Table 1). Eight tumours were in the femur and five in the tibia. In eight cases, the tumour was located at the diaphysis (four in the femur and four in the tibia), in three cases the location was the metaphysis-diaphysis junction (two in the femur and one in the tibia) and in two cases the location was the metaphysis (both in the femur). One patient (patient 6) had a metastatic disease with bone and lung involvement. Ten patients had adjuvant chemotherapy. Two patients had postoperative radiotherapy (patients 4, 6).

Resection was performed according to the surgical principles for primary malignant bone tumours [22]. The tumour...
was removed as a block, leaving a layer of healthy tissue in contact with the tumour. The height of the bone cuts were based on preoperative MRI, performed before the chemotherapy if applicable, so that 2 cm of healthy bone remained. The scar and biopsy track were removed in block with the resected piece. The median length of resection (Fig. 1) was 15 cm (first and third quartile [Q1–Q3]: 6–26). The resected edges showed no signs of contamination in 12 patients and microscopic contamination in one patient (patient 5).

Different surgical techniques were used to reconstruct the 13 resected bone segments. Three cortical-cancellous autografts were harvested from the tibia in the shape of a rectangular cuboid (patients 7, 8, 9). In two cases, two cortical rectangular cuboid pieces of about 10 cm in length were embedded into the proximal and distal shafts on both sides of the resection; in one case, only one piece was used.

Two massive allografts were performed, an isolated one in the femur (patient 6) and one in the tibia in combination with an iliac crest cancellous bone autograft (patient 10).

In four cases, a vascularised fibula bone graft was encased into a massive allograft (patients 1, 2, 11, 13). The fibula was included in the diaphysis of massive femur or tibia allografts and jutted out about 1 cm above the allograft, such that it was embedded into the two host bone segments on both sides of the resection (Fig. 2 and 3). Each time, the graft was performed as a second surgical procedure a few months after the resection. A cement spacer was used to stabilise the fixation between the two surgical procedures.

Finally, in four cases (patients 3, 4, 5, 12), a massive allograft was used in combination with a cortical-cancellous rectangular cuboidal tibia graft harvested from the contralateral side. The 10 massive allografts (five femurs and
five tibias) were taken from the bone bank at Cochin hospital and had been previously frozen and irradiated.

Cancellous bone was added to improve the strength of the fixation in eight cases. In six patients, the bone came from the contralateral tibia (patients 3, 4, 5, 7, 9, 12), the ipsilateral iliac crest in one patient (patient 10) and a banked femoral head in one patient (patient 8). This bone was packed in at the junction between the host bone and cortical graft. In cases of tibial resection, a graft between the tibia and fibula was systematically performed with this cancellous bone.

A plate was used for fixation in nine patients (five femoral and four tibial reconstructions) and an intramedullary locked nail in four patients (three femoral and one tibial reconstruction) (Table 2). When an allograft was used, the plates were set up as a bridge with typically one or two screws at the end of each allograft and at least three screws on both sides of the resection (Fig. 4). The nails acted as a

<table>
<thead>
<tr>
<th>Patient</th>
<th>Resection</th>
<th>Fixation</th>
<th>Graft</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + VF</td>
<td>Non-union</td>
</tr>
<tr>
<td></td>
<td>Metaphysis</td>
<td></td>
<td></td>
<td>ALLI Compartment syndrome</td>
</tr>
<tr>
<td>2</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + VF</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Diaphysis</td>
<td>Intramedullary locked nail</td>
<td>Allo + auto cortical-cancellous</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Diaphysis</td>
<td>Intramedullary locked nail</td>
<td>Allo + auto cortical-cancellous</td>
<td>Non-union Fracture</td>
</tr>
<tr>
<td>5</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + auto cortical-cancellous</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>Diaphysis</td>
<td>Intramedullary locked nail</td>
<td>Allo</td>
<td>Non-union</td>
</tr>
<tr>
<td>7</td>
<td>Metaphysis</td>
<td>Plate</td>
<td>Auto cortical-cancellous</td>
<td>Sepsis Hematoma</td>
</tr>
<tr>
<td>8</td>
<td>Metaphysis</td>
<td>Plate</td>
<td>Allo + auto cortical-cancellous</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Auto cortical-cancellous</td>
<td>Fracture</td>
</tr>
<tr>
<td>10</td>
<td>Diaphysis</td>
<td>Intramedullary locked nail</td>
<td>Allo + cancellous auto (iliac crest)</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + VF</td>
<td>Non-union Sepsis LPN paralysis</td>
</tr>
<tr>
<td>12</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + auto cortical-cancellous</td>
<td>Sepsis</td>
</tr>
<tr>
<td>13</td>
<td>Diaphysis</td>
<td>Plate</td>
<td>Allo + VF</td>
<td>No</td>
</tr>
</tbody>
</table>

VF: vascularised fibula; ALLI: acute lower limb ischemia; LPN: lateral popliteal nerve.

**Figure 4** Intercalary resection of an osteoblastic osteosarcoma at the metaphysis-diaphysis junction of the tibia and reconstruction with a plate, massive allograft and cortical-cancellous autograft (case 12). A: preoperative; B: immediately postoperative; C: 39-month follow-up.

bridge over the bone graft and were systematically locked at the distal and proximal ends (Fig. 5).

The primary outcome was the time needed for union in the reconstruction. A union was defined as the presence of fusion between the host bone and graft at both ends and full weight-bearing without pain. The time was calculated from the resection date, including for procedures done in multiple steps such as the vascularised fibula graft. Secondary outcome measures were the cumulative probability of surgical revision, independent of the reason, and the cumulative probability of surgical revision for mechanical reasons only. The cumulative probability of events under consideration were estimated by taking into account competitive risks, notably death, and depending on the event of interest, revisions due to infection, tumour or other reasons [23].

The cumulative probability estimates are given with their 95% confidence intervals (95% CI). Quantitative data are reported with the median and first and third quartile (Q1–Q3), except if specified otherwise. The analyses were performed with the R software [24].

Results

The median duration of hospitalisation was 12 days (Q1–Q3: 9–21). The median follow-up was 48 months (Q1–Q3: 24–131). At the last follow-up, 12 patients were still alive with no evidence of disease and one patient (patient 6) was alive with on-going disease. There was no morbidity at the autograft donor sites. There was no local tumour recurrence.

The cumulative probability of union was 46% (95% CI: 0%–99%) at 1 year and 90% (95% CI: 0%–100%) at 5 years (Fig. 6). At the last follow-up, 12 patients (92%) had graft union. The union occurred without further procedures in nine patients and after one additional procedure in four other patients. One patient (patient 6) did not have union at the last follow-up. However, no procedure was planned because of this patient’s poor general status (Ewing sarcoma with lung and bone metastases). The cumulative probability of surgical revision, independent of the reason, was 38% at 1 year (95% CI: 0%–97%) and 88% at 5 years (1%–100%). The cumulative probability of surgical revision for mechanical reasons was 23% (95% CI: 0%–99%) at 1 year and 73% at 5 year (95% CI: 0%–100%). Ten patients were re-operated for a total of 22 procedures. Thirteen procedures in eight patients were performed for mechanical reasons, six procedures were performed for infection reasons in three patients and three procedures were performed in one patient for other reasons.

Seven procedures for mechanical reasons and two for infection reasons were performed in four patients where union was not initially achieved. Three patients (patients 1, 4, 8) required decortication with a cortical-cancellous bone autograft from the ipsilateral iliac crest; two of these patients needed the fixation material changed and one did not. The fourth patient (patient 11) required six procedures, four for mechanical reasons and two for infection reasons, before union was achieved. The first procedure consisted of the second surgical intervention for the initial reconstruction, with placement of a vascularised fibula inside an allograft sleeve. Three years and four months after tumour

Figure 5  Intercalary resection of a chondroblastic osteosarcoma at the femur diaphysis and reconstruction with an intramedullary locked nail, massive allograft and cortical-cancellous autograft (case 3). A: preoperative; B: immediately postoperative; C: 39-month follow-up.

Figure 6  Cumulative incidence of the recorded events.
Table 3 Published results.

<table>
<thead>
<tr>
<th>Series</th>
<th>Case</th>
<th>Average follow-up (months)</th>
<th>Type of graft</th>
<th>Non-union (%)</th>
<th>Sepsis (%)</th>
<th>Fracture (%)</th>
<th>Local recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kreig [9]</td>
<td>16</td>
<td>49</td>
<td>Irradiated massive auto + VF</td>
<td>16</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Muscolo [18]</td>
<td>59</td>
<td>60</td>
<td>Frozen massive allo</td>
<td>15</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Donati [20]</td>
<td>113</td>
<td>12</td>
<td>Frozen massive allo</td>
<td>57</td>
<td>14</td>
<td>15.5</td>
<td>0</td>
</tr>
<tr>
<td>Enneking [25]</td>
<td>40</td>
<td>42</td>
<td>Cortical autograft + VF</td>
<td>33</td>
<td>5</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Sugiura [26]</td>
<td>19</td>
<td>57</td>
<td>Sterilised massive auto</td>
<td>32</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Ahmed [27]</td>
<td>31</td>
<td>69</td>
<td>Sterilised massive auto</td>
<td>6</td>
<td>16</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Manabe [28]</td>
<td>23</td>
<td>52</td>
<td>Sterilised massive auto</td>
<td>8</td>
<td>20</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Khattak [29]</td>
<td>12</td>
<td>49</td>
<td>Sterilised massive auto</td>
<td>8</td>
<td>41</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Sugiura [30]</td>
<td>15</td>
<td>48</td>
<td>Sterilised massive auto</td>
<td>14</td>
<td>13</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Uyttendaele [31]</td>
<td>15</td>
<td>60</td>
<td>Irradiated massive auto</td>
<td>6</td>
<td>13</td>
<td>?</td>
<td>13</td>
</tr>
<tr>
<td>Araki [32]</td>
<td>20</td>
<td>45</td>
<td>Irradiated massive auto</td>
<td>20</td>
<td>15</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

Auto: autograft; Allo: allograft; VF: vascularised fibula graft.

Discussion

In this study, clinical and radiological results in 13 patients were evaluated after resection of a primary bone tumour in the lower limb followed by intercalary reconstruction with a bone graft.

This work has limitations that can affect the internal and external validity of the results. First, the small number of patient did not allow us to analyse the effect of the different co-variables, such as the type of graft or fixation hardware, on the time needed for bone union. Second, the reconstructions were heterogeneous and the estimated results have a certain amount of uncertainty because of the small number of subjects analysed. However, these limitations are directly related to the low incidence of malignant bone tumours and they are prevalent in other published series.

Primary malignant bone tumours are truly rare and their initial surgical management has become more conservative [2–4]. These tumours are amenable to a resection and intercalary reconstruction procedure that spares the neighbouring joint, but reconstruction lead to particular problems and the long-term outcome is not well defined. Non-unions, infections and fractures are the most common complications of the initial reconstruction with placement of a vascularised fibula graft with allograft sleeve; two hardware removal procedures; one total knee arthroplasty with prosthesis for osteoarthritis. Three procedures were performed for other reasons in a single patient (patient 1): a femoro-popliteal bypass using a saphenous vein was needed as a second intervention on the day of the reconstruction procedure because of acute ischemia of the operated lower limb due to superficial femoral artery thrombosis during the anastomosis of the vascularised fibular graft; an aneponeurosis release had to be performed the next day because of compartment syndrome secondary to revascularisation of this bypass; another procedure for a keloid scar was performed later on. A non-displaced fracture in the cuboid tibial autograft occurred in one patient (patient 9); unloading of the limb for one and half months was sufficient to obtain union.

that require one or more additional procedures (Table 3). In retrospective series of 53 to 112 patients, where results of the resection and intercalary reconstruction of malignant bone tumours are reported with an average follow-up of 25 to 63 months, the non-union rate of massive allografts at the final follow-up was from 1 to 17% [14-16,20]. When isolated autografts are used in the reconstruction, retrospective series with eight to 40 patients with an average follow-up of between 20 and 69 months reported a non-union rate between 0 and 10% at the last follow-up [9,25—33]. The following factors were listed as being related to delayed union: type of graft, fixation, length of resection, associated chemotherapy [17]. Union occurs more quickly when a vascularised fibula graft is used [26,34,35], but instead of this long and difficult technique, we prefer to add a rectangular cuboid-shaped piece of tibia to the allograft, as this can be carried out easily, induces little pain, and provides a sufficient amount of cancellous and cortical bone. Different reconstruction techniques have been used with similar results [8,9,13,15,18] (Table 3).

There were three infection cases that resolved after one or more surgical revisions and appropriate antibiotic treatment. In a retrospective series with 53 patients after resection and intercalary reconstruction of malignant bone tumours by allograft, Gebhardt [14] found a 30% infection rate, despite a shorter follow-up than ours (25 versus 55 months). In cases of reconstruction with an isolated autograft, retrospective series with 12 to 40 patients found an infection rate between 0 and 42% [9,25—32]. The infection rate seems related to the length of the resection and recourse to adjuvant chemotherapy [14]. It is less when a vascularised fibula graft is used [35]. Our results are comparable to studies reporting on results of reconstruction using isolated autografts (Table 3).

One case of fracture was reported, which was treated conservatively. The fracture rate ranged from 9 to 19% in retrospective series with 26 to 120 patients where reconstruction was carried out with massive allografts after intercalary resection of malignant bone tumours [10—14,19,20,36] (Table 3). When isolated autografts are used, retrospective series with 12 to 40 patients have found a fracture rate ranging from 0 to 45% [9,25—30,32]. The length of the resection, type of graft and type of fixation were reported as being related to the risk of secondary fracture [21,25,37—42]. It seems that fixation with plates or intramedullary nails are less likely to result in fractures than fixation with screws alone [9,32]. We prefer to use intramedullary locked nails when resection is performed at the diaphysis, and plates or reconstruction with a vascularised fibula in metaphysis-diaphysis junction cases. We no longer recommend a two-step procedure because of the difficulty encountered during secondary dissection and as a consequence, increased risk of acute ischemia in the lower limb following the surgery.

Conclusion

Mechanical results of intercalary segment reconstruction after resection of a bone tumour were satisfactory, with bone union occurring in more than 90% of patients. However, union takes a long time and secondary procedures are often needed because of non-union or infection. Patients must be informed of these risks. We recommend adding a rectangular cuboid tibial autograft to the intercalary allograft during a single surgical procedure, as this is simpler to perform than a vascularised fibula graft. The intercalary allograft and fixation ensure immediate mechanical stability until the autograft can integrate sufficiently to ensure the long-term survival of the reconstruction. The use of an intramedullary locked nail is favoured after resection at the diaphysis, while the use of plates should be limited to reconstruction after resection at the metaphysis-diaphysis.

Disclosure of interest

The authors declare they have no conflicts of interest concerning this article.

References


