Limb salvage surgery in bone tumors: A prospective study in a single centre

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ABSTRACT
Limb salvage surgery includes all of the surgical procedures designed to accomplish removal of a malignant tumor and reconstruction of the limb with an acceptable oncologic, functional, and cosmetic result. Patient of Bone tumors of extremities presented to our centre from August 2011 to February 2012 were taken in to study. It has been a prospective, observational study. The study analyses a single centre experience of limb conservation in cases of primary bone tumors. The patients’ record were used for pre operative staging; neoadjuvant therapy used, if any; surgical procedure done; follow-up for prosthesis related complications and overall survival achieved. Total of 30 cases studied, included 20 males and 10 females. Median age at diagnosis of 22.8 (3–53) years. Upper limb involvement was present in 14 patients and lower limb in 16 patients. The malignant bone tumors were present in 21 patients (70 %), benign tumors in 8 (26 %), and one patient of solitary upper humeral metastatic lesion in an operated case of renal cell carcinoma. The most common diagnosis was osteosarcoma in 10 patients (33 %). Highest number of patients were treated with various methods of Arthrodesis (15/30, 50%) followed by Endoprostheses (13/30, 43%).High grade tumors (grade 2b and grade 3) were found in the majority of malignant bone tumors, 18 of 21 (86 %). Overall complications rate was 20%. All the patients of limb salvage have very good function; with an average Muscukoskeletal tumor society score of 25.5 out of a maximum possible 30 with range 21-29. The follow-up was 2 years. Four of our patients developed pulmonary metastasis and one patient developed brain & bony metastasis during follow up after surgery. In total, during the follow-up period, 4 patients 3 with osteosarcoma and 1 with Ewing sarcoma died due to tumor. 26 patients of 30 (86.7%) were still living with the salvaged limb at the last follow-up. Prosthetic survivorship rate was 100% at 2 year. Limb sparing surgery for bone tumors results in satisfactory results in terms of tumor control and limb function.

Key words: Bone tumor, Limb salvage, Modular prosthesis, arthrodesis

INTRODUCTION
Limb salvage surgery includes all of the surgical procedures designed to accomplish removal of a malignant tumor and reconstruction of the limb with an acceptable oncologic, functional, and cosmetic result. In the recent past, most sarcomas were treated by amputation. Limb salvage surgery has all but replaced amputation as the treatment of choice for sarcomas of the extremities. This dramatic change came about as the result of two important developments: effective chemotherapy and precision imaging techniques. Today, up to 90% of sarcomas in the extremities are treated with limb salvage surgery. 2Limb sparing surgical procedures have improved the quality of life of survivors.

Various methods are being used to restore the skeletal continuity after en-bloc excision of the tumor. These include custom made endoprostheses, autogenous bone grafts, allogenous bone grafts, osteochondral grafts, composite grafts, and in some cases only complete excision without any reconstruction. It has been shown that the functional level of the patients is better after limb salvage and they have better psychological adjustment when compared to amputation. Long term studies showed that limb salvage operations, performed with wide margins and chemotherapy did not compromise the survival or local control compared to an amputation. 3Cheaper and yet effective chemotherapy protocols and low cost indigenously manufactured megaprosthesis have allowed limb salvage surgery to develop even in the poorer countries. We describe a single centre experience of various methods of reconstruction in Limb Salvage.

MATERIALS AND METHODS
Study design: Patient of Bone tumors of extremities presented to our centre from August 2011 to February 2012 were taken in to study. A total number of 30 patients randomly selected. It has been a prospective, observational study

Sample selection inclusion criteria:
- Patients admitted to GCRI requiring surgery
- Both genders
- Cases of any age

Exclusion Criteria: Patients with bone tumors in whom limb salvage was not possible. The criteria used to determine if the limb was worthy of salvage were as follows:
1. The major neurovascular bundle is free of tumor.
2. Wide resection of the affected bone with a normal muscle cuff in all directions is possible.
3. All previous biopsy sites and all potentially contaminated tissues can be removed en bloc.
4. Bone can be resected 3 to 4 cm beyond abnormal uptake as determined by bone scan.
5. The adjacent joint and joint capsule can be resected.
6. Adequate motor reconstruction can be accomplished by regional muscle transfers.
7. Adequate soft tissue coverage is possible to decrease the risk of skin flap necrosis and secondary infection.

Investigations: Standard Investigations done at our Centre for all the patients include X ray of the part involved and of the chest, Computed Tomography of the part and of the chest, and magnetic resonance imaging of the part. Following non invasive investigations, biopsy of the lesion is performed. At our institute we prefer core needle biopsies/J-Needle biopsies. Metastatic workup also includes Positron Emission Tomography/Computed Tomography (PET/CT) and Tc 99 M Bone Scan.

Neoadjuvant Therapy: All patients of Osteosarcoma and Ewing’s sarcoma were given neoadjuvant chemotherapy (15/30, 50%). In Osteosarcoma, we used P+A Regime in six patient and P+A>HDMTX+I+A in four patient and VACM/IE for Ewing’s sarcoma. Cycle repeated every three weeks. Patients were reassessed both clinically and radiological after third cycle of chemotherapy. Definitive surgery was done three weeks after third cycle of neoadjuvant chemotherapy.

Surgical Approach: The surgery was performed according to the general principles of limb salvage surgery as outlined previously. We have used various methods of reconstruction that include arthrodesis and the modular segmental replacement system prosthesis.

Postoperative Follow-up: Isometric exercises and mobilization with crutches were started on 2nd postoperative day. The patients thereafter received adjuvant chemotherapy tailored to the degree of response seen to the neoadjuvant chemotherapy as evident on histopathology report.

Post Discharge Follow-Up: Sequential X-rays of operated extremities at 6 weekly till the bone union has occurred, then 3 monthly for 2 years was done. Oncological follow-up with every 3 monthly Chest X-ray, 6 monthly CT-Chest, CT scan of Local part when needed for Malignant bone tumors and 3 monthly local X-ray, yearly chest X-ray for Benign tumor was done.

Functional outcome assessed by Musculoskeletal Tumor Society Rating scale done when the reconstruction was functioning. Intraoperative, immediate postoperative and follow-up complications were noted.

Patients were followed up for a period of two years.

RESULTS

Demography: Total 30 cases of bony tumors were taken into study from August 2011 to February 2012, which included 20 males and 10 females with a mean age at diagnosis of 22.8 (3–53) years. The youngest patient in our study was 3 years old and oldest was 53 years old. The youngest male was 3 years while female was of 9 years.

Clinical presentation: Upper limb involvement was present in 14 patients and lower limb in 16 patients. Tumor was localized most in proximal humerus (10 patients, 33%), followed by distal femur in 9 patients (30%), proximal femur in 3 patients (10%), middle femur 1 patient (3%), proximal tibia in 2 patients (7%), distal tibia in 1 patient (3%), middle radius 1 patient (3%), and distal radius 3 patients (10%) (Figure 2).

The malignant bone tumors were present in 21 patients (70%), benign tumors in 8 (26%), and one patient of solitary upper humeral
metastatic lesion in an operated case of renal cell carcinoma. The most common diagnosis was osteosarcoma in 10 patients (33%), giant cell tumor of bone in 8 patients (26%), Ewing sarcoma in 5 patients (16%), Chondrosarcoma in 5 (16%), Fibrosarcoma in 1 patient (3%) and solitary upper humeral metastatic lesion in 1 patient (3%). Osteosarcoma and Giant cell tumor occurred most in Distal Femur (5/10, 50% and 3/8, 37% respectively) (Figure 2).

**Figure 1: Age & Sex Distribution of Cases**

**Figure 2: Composite Distribution of Tumor Types**

**Figure 3: MSTSS% Score**

**Methods of reconstructions:** In our study, highest number of patients were treated with various methods of Arthrodesis (15/30, 50%) followed by Endoprostheses (7/30, 23%) (Table 1)

**Histopathology:** High grade tumors (grade 2b and grade 3) were found in the majority of
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malignant bone tumors, 18 of 21 (86%). Detailed histological findings and tumor grades are shown in Table 2.

NED: no evidence of disease, AWD: alive with disease, DOD: died of disease

**Functional outcome:** All the patients of limb salvage have very good function; with an average Musculoskeletal tumor society score of 25.5 out of a maximum possible 30 with range 21-29 and 95% Confidence Interval 24.77-26.23. The mean functional score was 85% (Figure 3).

**Table 1: Methods of Reconstruction**

<table>
<thead>
<tr>
<th>Type of Reconstruction</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthrodesis</td>
<td></td>
</tr>
<tr>
<td>Plating &amp; fixation</td>
<td>3</td>
</tr>
<tr>
<td>Plating &amp; bone graft</td>
<td>3</td>
</tr>
<tr>
<td>Nailing</td>
<td>1</td>
</tr>
<tr>
<td>Bone graft + Metallic implant</td>
<td>1</td>
</tr>
<tr>
<td>Nail + fibular graft</td>
<td>2</td>
</tr>
<tr>
<td>Pseudoarthrosis</td>
<td>1</td>
</tr>
<tr>
<td>Turn-o-plasty+Plating</td>
<td>4</td>
</tr>
<tr>
<td>No reconstruction</td>
<td>1</td>
</tr>
<tr>
<td>Endoprosthes (Mega) shoulder prosthesis.</td>
<td>7</td>
</tr>
<tr>
<td>THR</td>
<td>3</td>
</tr>
<tr>
<td>TKR</td>
<td>3</td>
</tr>
<tr>
<td>Rotationalplasty</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 2: Histopathological Grade Distribution of the Operated Tumors**

Benign Bone Tumors

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giant Cell Tumor</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

Malignant Bone Tumors

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grade</th>
<th>Grade</th>
<th>Grade</th>
<th>Grade</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1a</td>
<td>1b</td>
<td>2a</td>
<td>2b</td>
<td>3</td>
</tr>
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<td>3</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>22</td>
</tr>
</tbody>
</table>

Complications: 6 patients (20%) had complications details of which, treatment methods, and final results are shown in Table 3.

**Table 3: Complication, Their Treatment and Final Outcome**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Final result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonunion- Implant failure</td>
<td>GCT(1)</td>
<td>Nail removal+ Plating+Grafting</td>
<td>NED</td>
</tr>
<tr>
<td>Fracture of clavicle</td>
<td>Chondrosarcoma(1)</td>
<td>Planting &amp; fixation</td>
<td>NED</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>Fibrosarcoma(1)</td>
<td>B-K amputation</td>
<td>AWD (Lungmets)</td>
</tr>
<tr>
<td></td>
<td>Osteosarcoma(1)</td>
<td>Hip disarticulation</td>
<td>DOD (Lungmets)</td>
</tr>
<tr>
<td></td>
<td>Solitary humeral mets(1)</td>
<td>Chemotherapy</td>
<td>AWD</td>
</tr>
<tr>
<td></td>
<td>Chondrosarcoma(1)</td>
<td>Open reduction</td>
<td>NED</td>
</tr>
</tbody>
</table>

Follow up outcome: The follow-up was of 2 years. Four of our patients developed pulmonary metastasis and one patient developed brain & bony metastasis during follow up after surgery. One patient underwent pulmonary metastectomy but died of disease at the last follow up. Patients who died due to tumor are as follows: 3 of 10 patients with osteosarcoma (30.0%), 1 of 5 patients with Ewing sarcoma (20%). Osteosarcoma patients died due to pulmonary metastasis, while Ewing sarcoma patient died due to brain and bony metastasis. One patient of Fibrosarcoma was still alive with pulmonary metastasis at last follow-up. In total, during the follow-up period, 4 patients died due to tumor. 26 patients of 30 (86.7%) were still living with the salvaged limb at the last follow-up. Survival rate of prosthesis is 100%. At the last control examination, patients showed no evidence of the primary disease.

**DISCUSSION**

Our study included 20 males and 10 females with a mean age at diagnosis of 22.8 (3–53) years. Osteosarcoma is the commonest malignant bone tumor. It accounted for 33% (10/30) of all bone tumors and 45% (10/21) of the malignant type in our series. Most common site of osteosarcoma was distal femur. In European osteosarcoma intergroup study 202 by Grimmer RJ et al, the most common site of tumor was distal femur followed by proximal tibia, fibula and proximal femur. In our study the most common site of tumor was proximal humerus (10/30) followed by distal femur (9/30). Before the use of chemotherapy (which began in the 1970s), osteosarcoma was treated primarily with surgical resection (usually
amputation). Despite such good local control, more than 80% of patients subsequently developed recurrent disease that typically presented as pulmonary metastases. The high recurrence rate indicates that most patients have micro metastatic disease at the time of diagnosis. The “neoadjuvant (pre-operative) chemotherapy” has the theoretical advantage of addressing these occult micro metastases. It has been found to facilitate subsequent surgical removal by causing tumor shrinkage and also by “sterilizing” the reactive zone around the tumor by destroying microscopic disease at the periphery of the primary lesion. Patients in whom there has been a good histopathologic response to neoadjuvant chemotherapy (>95% tumor cell kill or necrosis) have a better prognosis than those whose tumors do not respond as favorably. One patient in our study had > 90% response to neoadjuvant chemotherapy and 7 patients had between 60-90%. All 4 patients who died had a poor response to neoadjuvant chemotherapy (< 60%). In our series, during the follow-up, 4 out of 22 cases of malignant tumors died. The cumulative 2-year survivorship was 81.8%. Other similar series report 5 year survivorship ranging from 28% to 76%. It must be borne in mind there were relatively larger percentage of high grade tumors in our series and also that it includes chondrosarcoma which do not have a viable and effective chemotherapy regimen.

**Figure 4: Intraoperative and Postoperative photograph of limb with Prosthesis**

Currently endoprosthetic reconstruction is performed with the use of modular prosthesis. A rigorous rehabilitation program can be initiated immediately after implantation, allowing early joint range of motion and weight bearing. Prosthetic reconstruction carries a lower risk of deep infection than do allografts, and nonunion is not a concern because there are no osteosynthesis sites.

In our study, highest number of patients were treated with various methods of Arthrodesis (15/30, 50%) followed by Endoprosthesis (13/30, 43%). Endoprosthetic use also avoids the risk of disease transmission and immune responses that exist with allograft reconstruction. We had an overall complication rate of 20% and a prosthetic survivorship of 100% at 2 year.

**CONCLUSION**

The surgical management of patients with malignant tumors of bone is challenging. Limb salvage surgery includes all of the surgical procedures designed to accomplish removal of a malignant tumor and reconstruction of the limb with an acceptable oncologic, functional, and cosmetic result. Our study showed that limb salvage operations, performed with wide margins and chemotherapy did not compromise the survival or local control compared to an amputation. For our sample, limb sparing surgery for bone tumors resulted in satisfactory
results in terms of tumor control and limb function. Cheaper and yet effective chemotherapy protocols and low cost indigenously manufactured megaprosthesis have allowed limb salvage surgery to develop even in the poorer countries. Amputation remains as a valid procedure in cases where limb preservation is not possible.

REFERENCES
21. Enneking WF, Shirley PD (1997) Resection-


