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Limb Salvage Surgery in Bone Tumors: A Single Institutional Study- K.M.I.O Experience

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Abstract
Introduction: *Limb salvage surgery is the procedure which helps to remove tumours of Extremities and reconstruction is done with acceptable oncologic, functional and cosmetic results. The first priority is given for oncologic clearance followed by functional result. There is a change in trend all over the world from Amputations to Limb Salvage Surgery for appropriate candidates because of effective chemotherapy regimens, newer imaging techniques, advanced radiotherapy precision delivery, better reconstructive options and advances in Bio-Engineering.*
Materials and Methodology: *A retrospective analysis of 50 patients treated by Limb Salvage procedures in Bone tumours during a 5 year period from (2007–2011) in our Regional cancer centre which is also a tertiary care referral center was done. Before consideration of limb preservation procedures, all the patients were appropriately staged and assessed at a multidisciplinary tumour board meet. All patients with a proven histopathology of Osteosarcoma and Ewing's sarcoma were given neoadjuvant chemotherapy. At our centre, we use 3 cycles of IAP (Ifosfamide 1.5 gm/m^2 Day 1–3, Adriamycin 25 mg/m^2 Day 1–3, Cisplatin 90 mg/m^2) as neoadjuvant for Osteosarcomas and 4 cycles of IE/VAC (alternating, Ifosfamide 2 gm/m^2 Day 1–3, Etoposide 100 mg/m^2 Day 1–3, Vincristine 1.4 mg/m^2, Adriamycin 60 mg/m^{2,} Cyclophosphamide 600 mg/m^2) for Ewing's sarcoma. Response to chemotherapy was assessed by Imaging modalities and compared with previous imaging findings. The surgery was performed according to the general principles of limb salvage surgery.*
Results: *Most of the patients underwent surgery under general anaesthesia and few under spinal/epidural anaesthesia. General principles of limb salvage surgery was followed strictly.*
The medium resection length as 15 cm (range 6-25). The largest resections were performed in distal femur 16 cm (range 12-25), followed by proximal femur 15 cm (range 6-25), proximal Tibia 12 cm (range 7-15). Extra reconstructive interventions were needed for soft tissue coverage around knee joint in Osteosarcoma patients who have received neoadjuvant chemotherapy. Complications specific to endoprosthetic reconstruction may be related to mechanical or biological factors. Fatigue failure, aseptic loosening, Local Recurrence , peri-prosthetic fracture
Conclusion: *The surgical management of patients with bone tumors of bone is challenging, particularly malignant tumors. Limb sparing surgery is a safe procedure, oncologically sound, provides good functional and cosmetic results. Appropriate patient selection for limb sparing procedure is essential to ensure good and consistent result.*
Keywords: *L.S.S, Endoprosthesis, Neoadjuvant Therapy, Bio-Engineering.*

Introduction

Limb salvage surgery is the procedure which helps to remove tumours of Extremities and reconstruction is done with acceptable oncologic, functional and cosmetic results. The first priority is given for oncologic clearance followed by functional result. There is a change in trend all over the world from Amputations to Limb Salvage Surgery for appropriate candidates because of effective chemotherapy regimens, newer imaging techniques, advanced radiotherapy precision delivery, better reconstructive options and advances in Bio-Engineering.

Aims and Objectives

This study is aimed at identifying clinic-pathological characteristics, surgical strategies, prognostic factors and complications following treatment.

Methods and Materials

A retrospective analysis of 50 patients treated by Limb Salvage procedures in Bone tumours during a 5 year period from (2007–2011) in our Regional cancer centre which is also a tertiary care referral center was done.

Standard Investigations done at our Centre for all the patients include: Plain X ray of the part involved with adjacent joint, X ray- chest. All the patients underwent Bone scintiscan (Tc99m) to rule out polyosteotic lesions. Computed Axial Tomography of the chest (to rule out pulmonary metastasis). Computed Tomography of the part followed by complimentary Magnetic Resonance Imaging of the part is done, in some patients angiography is also considered. All these findings were recorded. Following non invasive investigations, biopsy of the lesion is performed.

At our institute we prefer core needle biopsies/J-Needle biopsies (image guided biopsies are preferred in deep seated tumours which are difficult to palpate). An open biopsy was performed in a few selected cases when core biopsies failed to achieve diagnosis. All biopsies were performed by a trained Oncosurgeon and planned in such a way that the biopsy scar can be safely included in the incision while performing definitive surgery. All Biopsy specimens were evaluated and reported by trained Oncopatho-logist. At our institution, the use of Fine Needle Aspiration Cytology is generally restricted to the confirmation of suspected metastasis.

Neo adjuvant Therapy

Before consideration of limb preservation procedures, all the patients were appropriately staged and assessed at a multidisciplinary tumour board meet. All patients with a proven histopathology of Osteosarcoma and Ewing's sarcoma were given neoadjuvant chemotherapy. At our centre, we use 3 cycles of IAP (Ifosfamide 1.5 gm/m^2 Day 1–3, Adriamycin 25 mg/m^2 Day 1–3, Cisplatin 90 mg/m^2) as neoadjuvant for Osteosarcomas and 4 cycles of IE/VAC (alternating, Ifosfamide 2 gm/m^2 Day 1–3, Etoposide 100 mg/m^2 Day 1–3, Vincristine 1.4 mg/m^2, Adriamycin 60 mg/$m^{2,}$ Cyclophosp-hamide 600 mg/m^2) for Ewing's sarcoma. Response to chemotherapy was assessed by Imaging modalities and compared with previous imaging findings.

The Principles of LSS were followed

The surgery was performed according to the general principles of limb salvage surgery as outlined below.

Wide excision of the affected bone with a normal muscle cuff in all directions is possible. All previous biopsy scar sites and all potentially contaminated tissues to be removed enbloc. The adjacent joint and joint capsule can be resected. The major neurovascular bundle is free of tumor. Adequate motor reconstruction can be accomplished by regional muscle transfers. Adequate soft tissue coverage is possible to decrease the risk of skin flap necrosis and secondary infection.

The various prosthesis used is mentioned below:

1. Modular Segmental Replacement System (MSRS) prosthesis (with a bipolar component) for the proximal part of the

humerus and the proximal part of the femur.
2. Custom Made Prosthesis (CMP) for distal part of femur and proximal part of the tibia.
3. Austin Moore Prosthesis (AMP) for the proximal part of the humerus and proximal part of the femur.
4. Extra Cortical plate and screw fixation for arthrodesis done in two cases.

All stems are cemented in places. All the endoprosthetic equipment were procured from:
Eagle Osteon Technology, Chennai. India
Mishra Dhatu Nigam Limited, Hyderabad, India

Post Operative Follow-up: For all patients Isometric exercises and mobilization with crutches was started on second postoperative day. These patients there after received adjuvant chemotherapy tailored to the degree of response seen to the neo adjuvant chemotherapy as evident on histopathology report.

Post Discharge Follow-up: The patients were followed up on monthly basis for six months, three monthly basis for one year, Six monthly bases for two years. On follow-up visits, a thorough clinical examination was carried out along with digital X-ray of the involved part. Chest X- Ray was done routinely followed by CT Scan of the chest done, if a suspect lesion was seen in digital X- Ray chest. Bone scan was done as a routine on yearly basis, while PET-CT scan was reserved for suspected metastatic lesions.

Results

In the study period, a total of 50 cases were studied which included 28 males and 22 females with a median age at diagnosis of 29 (15–60) years Fig1. Clinical Presentation of 50 patients given in the table1. Upper limb involvement was present in 08 patients and Lower limb involvement was present in 42 patients. In Histopathogical Distribution, Benign tumors ie Giant cell tumor 22 (44%) and Malignant tumors ie (Ewing's, Osteo, Chondro Sarcomas) 28(56%) was seen. Among 28 malignant tumours Ewing's sarcoma reported 04 pts (08%), Osteosarcoma 21 pts (42%) and Chondrosarcoma 03 pts (06%).

Most of the patients underwent surgery under general anaesthesia and few under spinal/epidural anaesthesia. General principles of limb salvage surgery was followed strictly.

The medium resection length as 15 cm (range 6-25). The largest resections were performed in distal femur 16 cm (range 12-25), followed by proximal femur 15 cm (range 6-25), proximal Tibia 12 cm (range 7-15). Extra reconstructive interventions were needed for soft tissue coverage around knee joint in Osteosarcoma patients who have received neo adjuvant chemotherapy.

Histopathology-Grade: High grade tumors (grade 2a and 2b) were found in the majority of malignant bone tumors, 26 of 28 patients (92.3%). Detailed histopathological tumor types and tumor grades distribution are shown in following Table2.

Complications following L.S.S:

Fig 3. Complications are not uncommon with any type of limb sparing procedures. Majority of these patients have altered immune system from chronic disease, Chemotherapy, Anaemia, thrombocyto-penia. Many patients have a tendency for wound infection. Complications specific to endoprosthetic reconstruction may be related to mechanical or biological factors. Fatigue failure, aseptic loosening, Local Recurrence, peri-prosthetic fracture Table3.

Follow-up: The median follow-up is 5 years (range: 3–7). 19 of 50 patients had follow-up for more than 5 years. 06 of our patients developed pulmonary metastasis during follow up after surgery. Patients who died due to tumor are as follows: 07 of 21 patients with osteosarcoma (33.3%), 1 of 4 patients with Ewing's sarcoma (25%) 1 of 3 patients with chondrosarcoma (33.3%). In total, during the follow-up period, 9 patients died due to tumor. 41 patients of 50 are still alive with the endoprosthesis at the last follow-up.

Fig1: Age Distribution of 50 patients Based on Gender

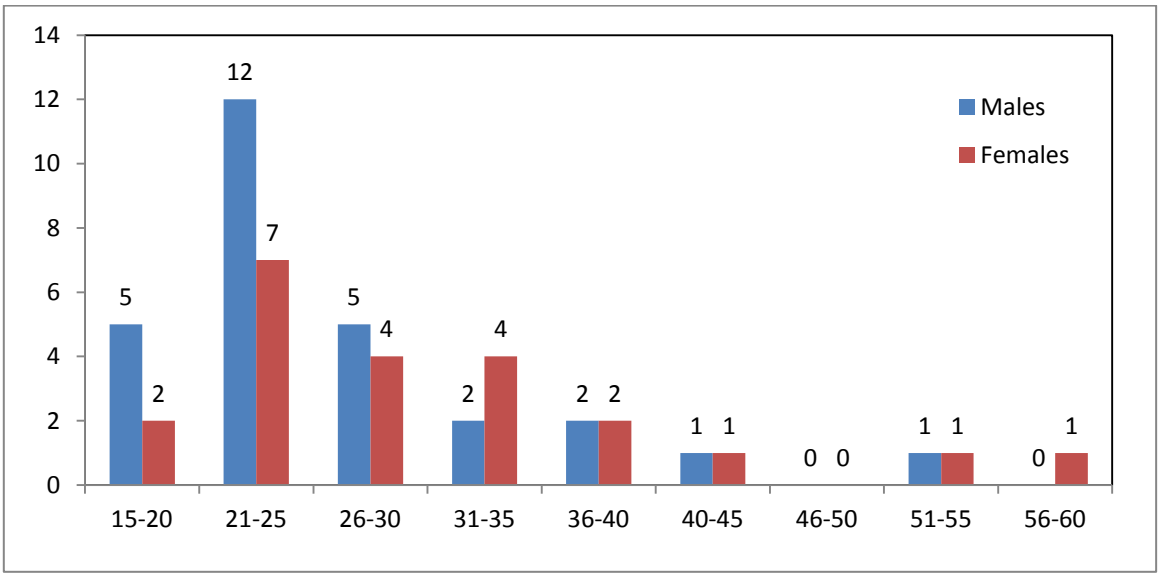

Fig 2: Limb Sparing Surgical Procedure

Fig 3: Complications following L.S.S

Table 1: Anatomical Localization of Tumors

Site	#	%
Proximal Humerus	8	16
Proximal Femur	19	38
Distal Femur	22	44
Proximal Tibia	1	2
Total	**50**	**100**

Table 2: Histopathological Distribution of Tumours

Histopathology	Grade 1		Grade 2		Grade 3	Total
Benign tumour						
Giant cell tumor	1		7		14	22
Malignant tumour						
	Grade 1a	Grade 1b	Grade 2a	Grade 2b	Grade 3	Total
Ewing's sarcoma	0	0	1	3	0	4
Osteo sarcoma	1	1	4	15	0	21
Chandro sarcoma	0	0	0	3	0	3
Total	1	1	5	21	0	28

Table 3: Complications of L.S.S

Complication	Diagnosis	Treatment	Final outcome
Wound infection	Ewing's sarcoma (02)	Debridement	NED
	Osteo sarcoma (03)	Debridement	NED
Aseptic Loosening	Giant cell tumor (03)	Implant Reapplied	NED
	Osteo sarcoma (02)	Implant Reapplied	NED
Peri-prosthetic fracture	Osteo sarcoma (01)	Elongation of Endoprosthesis	NED
Fracture of prosthesis	Giant cell tumor (01)	Revision Surgery	NED
Local Recurrance	Osteo sarcoma (04)	Re-Resection (1)	Death
		Amputation(03)	

Discussion

Primary malignant bone tumors are relatively uncommon lesions. Before the 1970s, management routinely consisted of trans bone amputations or disarticulations, with dismal survival rates (10% to 20%). With the development of more effective chemotherapeutic agents and treatment protocols in the 1970s and 1980s, survival rates improved. This along with better imaging modalities, allowed the focus of management to shift to limb preservation [1–3]. Osteosarcoma is the commonest malignant bone tumor[4]. It accounted for 42% of all bone tumors and 75% of the malignant type in our series. 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[4]. 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 [5, 6]. Additionally, in some patients with a relative contraindication to limb salvage, such as a pathologic fracture in the upper extremity, the use of chemotherapy with a favourable response may allow limb salvage to be considered[7]. It also provides oncologists with an important risk parameter. Patients in whom there has been a good histopathology response to neoadjuvant chemotherapy (>95 % tumor cell kill or necrosis) have a better prognosis than those whose tumors do not respond as favourably[8]. Hence, we use neo adjuvant chemotherapy as a routine for Osteosarcoma and Ewing's sarcoma. In our series, during the follow-up, 09 out of 28 cases of malignant tumors died. The cumulative 5-years survivorship was 38 %. Other similar series report 5 year survivor ship ranging from 28% to 76 % [9]. 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 have a viable and effective chemotherapy regimen.

Currently, 80% to 85% of patients with primary malignant bone tumors involving the extremities

(osteosarcoma, Ewing's sarcoma, and chondrosarcoma) can be treated safely with wide resection and limb preservation with or without reconstruction[9]. Limb-salvage surgery was as safe as an amputation in the management of patients with high-grade osteosarcoma. Thereafter, there have been multiple recent studies which indicate that limb preservation is the norm in bone tumors.[10–13].

Limb-salvage procedures can be divided into two groups: arthrodesis or arthroplasty. An arthrodesis is usually obtained using bone allografts [13], vascularised autografts[14] or both. An arthrodesis provides a stable, durable reconstruction which requires limited postoperative follow-up. But the inherent disadvantages include the loss of joint function, increased energy expenditure, and the additional abnormal mechanical stress to other joints.[15]

An arthroplasty preserves the joint. This can be accomplished with an allograft [16 and17] or a metallic prosthesis. Early metal designs were custom made, resulting in obvious manufacturing delays between diagnosis and reconstruction; consequently, intraoperative flexibility was limited .However, malignant bone tumors are dynamic tumors that change with time and treatment. Hence, currently endoprosthetic reconstruction is performed with the use of modular prosthesis. Modularity of prosthetic design allows intraoperative flexibility based on the final amount of tissue resected. A rigorous rehabilitation program can be initiated immedi-ately after implantation, allowing early joint range of motion and weight bearing. Prosthetic reconstruction carries a lower risk of deep infection than the allografts and non union is not a concern because there are no osteosynthesis sites.

Endoprosthetic use also avoids the risk of disease transmission and immune responses that exists with allograft reconstruction. Longevity, complications, and functional outcome vary by anatomic site, type of prosthesis, and fixation technique.[16- 19] In our series, we have used the modular segmental-replacement system prosthesis as the preferred modality for limb preservation. The advantages of the modular segmental-replacement system prosthesis include simplicity, adaptability and reduced operating time. We had an overall complication rate of 32% and a prosthetic survivorship of 82% at 5 years. Many studies have been performed to investigate endoprosthetic survival rates after tumor resection, but the results cannot be summarized and systematic review cannot be performed, mostly because of a small number of patients, as well as different models and principles of endoprosthesis. Tumor endoprosthetic survival rates are mostly about 60% to 80% at 5 years, and 40–70 % at 10 years.[20–22] For the current rotating-hinge knee design, reported follow-up is limited to approximately 10 years. Malawer et al.[23] in 1995 showed an 83%survival of prostheses at 5 years and 67% at 10 years. They had a revision rate of 15%, infection rate of 13%, amputation rate of 11%, and local recurrence rate of 6%. Overall, 44% of patients had at least one complication.

In an attempt to determine prosthesis and extremity survivorship, Horowitz et al.[24] reviewed their experience with 93 prosthetic reconstructions over 8 years: 16 proximal femur, 61 distal femur, and 16 proximal tibia. Minimum follow-up was 24 months (mean, 80 months). Prosthesis survival at 5 years was 88%, 59%, and 54% for proximal femur, distal femur, and proximal tibia reconstructions, respectively. The overall event-free prosthesis survival was 63% at 5 years and 36% at 10 years. Limb survival for the entire group was 87% at 5 years and 81% at 10 years.

Loosening, dislocation is the most common complication after primary or secondary femur endoprosthetic reconstruction, regardless the indication. In our series we noted 5 patients (10 %) with loosening of endoprosthesis, who were then managed successfully with re application of endoprosthesis. Periprosthetic fracture occurred in 1(2 %) patient during sport activity and was managed with endoprosthetic elongation.

Malawer et al. noted aseptic loosening as cause for failure in approximately 20 % at 5 years and 30 % at 10 years. Similarly, a review of other series too noted an incidence of this complication ranging from 5–30 %. Another common complication is infection. The incidence of infection was 10 % in our study. In the previous literature, the rate of deep infection has ranged from 4 to more than 30 %.[25] Curettage, debridement and irrigation were performed in these patients, we had satisfactory final results.

The location of bone tumors in the growing areas of bone commonly mandates the removal of the affected growth plate. Subsequent continued growth in the contra lateral extremity results in limb-length inequality which result in orthopaedic dysfunction. Expandable prosthesis were developed to address this issue. Custom expandable prostheses system consists of a fixed stem with a screw or a multiple plate extension mechanism. The obvious disadvantage in all these systems is that a surgical procedure is required for the subsequent expansions.

Conclusion

The surgical management of patients with bone tumors of bone is challenging, particularly malignant tumors. Limb sparing surgery is a safe procedure, oncologically sound, provides good functional and cosmetic results. Appropriate patient selection for limb sparing procedure is essential to ensure good and consistent result.

The reconstructive options for skeleton defects plays major role in L.S.S like resection arthridesis, osteaarticular allografts, endo prosthesis and allograft-prothesis composite.

The modular segmental replacement system prosthesis favoured by us in limb sparing surgery for bone tumors gives satisfactory result in terms of tumor control and limb function.

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