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Functional Outcome of Limb Salvage Surgery by Megaprosthesis for Malignant Bone Tumors-Mid and Long Term Follow Up

Manish R Shah[1], Manisha M Shah[2], Aditya K. Agrawal[1], Malkesh D Shah[3], Sarvang M Desai[4]

[1]MBBS, MS (Orthopaedics), Associate Professor, Department of Orthopaedics, Dhiraj Hospital, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth Deemed to be University, Waghodia, Vadodara-391760, Gujarat, India; [2]MBBS, MD (Pathology), Assistant Professor, Department of Pathology, Medical College and SSG Hospital, Vadodara, Gujarat, India; [3]MBBS, MS (Orthopaedics), Assistant Professor, Department of Orthopaedics, Dhiraj Hospital, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth Deemed to be University, Waghodia, Vadodara, Gujarat, India; [4]MBBS, MS (Orthopaedics), Professor, Department of Orthopaedics, Dhiraj Hospital, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth Deemed to be University, Waghodia, Vadodara, Gujarat, India.

ABSTRACT

Purpose: The gold standard treatment for primary bone sarcoma is limb saving (salvage) procedure in the indicated case. Today, limb saving surgery is considered safe and routine for approximately 90 % of patients with malignant bone tumours involving extremity. In our retrospective study of 40 patients having malignant bone tumour treated by limb salvage and mega prosthesis replacement of different regions like proximal humerus, proximal femur, distal femur, proximal tibia, we have studied mid and long term follow-ups in terms of life expectancy (survival), recurrence, implant-related complications, and functional outcome.

Methods: Retrospective study of 40 patients treated by limb salvage surgery using mega prosthesis during the study period (2014 to 2020). All patients were confirmed by biopsy. Neo-adjuvant chemotherapy was given as per the case. Results were analyzed at follow-up ranging from 2 years to 6 years with a mean of 3.2 years.

Results: 15 out of 40 (37.5%) were more than 5 years and 28 out of 40 (70%) were more than 3 years of follow-ups. Osteosarcoma was the commonest tumour (55%). There were no implant-related complications. 37 out of 40 (92.5%) patients with mega prosthesis were found to be tumour-free and without any complications on the last follow up.

Conclusion: Limb salvage surgery for malignant bone tumours by mega prosthesis is a good treatment in selected cases. It gives good tumour control and good functional life.

Key Words: Limb salvage surgery, Mega prosthesis, Malignant bone tumour, Sarcoma, Osteosarcoma, Ewing`s sarcoma

INTRODUCTION

Today, limb saving-surgery is considered the gold standard treatment for approximately 90 % of patients with primary bone sarcomas involving extremity.[1] There is always some confusion amongst general Orthopaedic surgeons regarding the diagnosis of malignant bone tumours. Out of different methods, the surgeon needs to choose the method and implant of his choice and can be customized as per the condition of the patient.[2] Some studies have reported a comparison of the patients treated by limb salvage versus amputation.[3;6;9]

Local recurrence rate in amputation is reported similar to limb salvage by some studies.[4] However, some studies reported fewer metastases rate in limb salvage surgery[5] and some reported a higher local recurrence rate in limb salvage surgery in comparison to amputation.[6] Cosmetic satisfaction is reported better after limb salvage.[7] Up to 1980s amputation was the only treatment offered to such patients.[8] Advancements in procedures for diagnosis, improvements in radiotherapy and chemotherapeutic agents helped in improving the results of limb salvage surgeries.[1,2] Due to increasing awareness amongst general orthopaedic surgeons and patients, we need to study mid and long-term results of such surgeries.

In our retrospective study of 40 patients having malignant bone tumour treated by limb salvage and mega prosthesis

Corresponding Author:

Dr. Manish R Shah, MBBS MS (Orthopaedics), Associate Professor, Department of Orthopaedics, Dhiraj Hospital, Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth Deemed to be University, Waghodia, Vadodara-391760, Gujarat, India; Email: manishshah2001in@yahoo.co.in

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replacement of different regions like proximal humerus, proximal femur, distal femur, and proximal tibia, we have studied mid and long term follow-ups in terms of life expectancy (survival), recurrence, implant-related complications, and functional outcome. We aimed to study different types of malignant bone tumours, mid and long term clinical and functional results, tumour-related complication, mainly recurrence and implant-related complications.

MATERIAL AND METHODS

A Retrospective study of 40 patients treated by limb salvage surgery using mega prosthesis during the study period (2014 to 2020) was carried out. Informed and written participation consent obtained from all patients and IRB clearance obtained.

Inclusion criteria were patient having Primary malignant bone tumour proved by biopsy. All patients were thoroughly investigated for the suitability of mega prosthetic replacement after wide marginal resection. All patients were thoroughly investigated for the absence of any metastasis. Patients with secondaries with pathological fracture and having reasonably life expectancy (primary fully treated) (Tumour board decision) were included too.

Patients having benign bone tumours and patients who refused to participate or refused for follow up were excluded.

Criteria for limb salvage were followed in all patients like wide marginal excision possible as per MRI and Bone scan, Extra-articular dissection of joint possible, Absence of vascular involvement and presence of collaterals in the lower limb, Presence of sufficient soft tissue for reconstruction, Absence of metastasis in primary bone tumours and secondary in bone with a pathological fracture with full treatment of primary and reasonable life expectancy of the patient.

Thorough History and examination were done in all patients. X-ray of the Local part and the full length of extremity, X-ray chest, USG abdomen to rule out metastases, PET scan, MRI and CT scan (in selected cases), Bone scan, Blood investigations were done as per routine protocol.

Trucut needle biopsy was done in all cases and SOS open biopsy if a needle biopsy is not conclusive. CT Guided biopsy was advised in deep-seated lesions. A Biopsy was done by the surgeon who is going to do the final treatment.

A preoperative protocol of Neoadjuvant chemotherapy for Osteosarcoma and Ewing`s sarcoma as per the decision of the one physician was followed. Blood investigations, preanaesthetic check-ups and repeat MRI after chemotherapy were done before surgery.

Standard aseptic precautions were followed. A scar of the biopsy was included in the final specimen. Wide marginal resection was done (3cm as per MRI measurement). An intraoperative frozen section was done in all cases to confirm the absence of malignancy in the proximal canal. Trial implantation was done to confirm the size of the implant, limb length discrepancy and vascular compromise during surgery. Final implantation was cemented in all cases. Whenever possible mesh (hernia mesh) was used to wrap implant and attach soft tissues for better functional outcome.

Postoperatively static exercise was started from 2nd postoperative day. Partial or Non-weight bearing was advised as per the case. Joint splintage was given for 4 to 6 weeks in the distal femur and proximal tibia malignancies. Pouch arm sling was given for proximal humerus cases for 4 to 6 weeks.

The final decision of chemotherapy and/or radiotherapy was taken after histopathology report (considering margin positive/negative, type of malignancy, and tumour necrosis).

Routine follow-ups were monthly intervals for 3 months, Bi-monthly for the next 6 months, and Quarterly thereafter. In all visits, clinical examination, chest X-ray, and routine blood investigations were done. PET scan was advised in suspected cases of recurrence.

RESULTS

Out of 40 patients, 28 were males and 12 were females. Age was ranging from 9 years to 68 years with a mean of 29 years. Out of 40 patients, 28 were from the age group 11 to 30 years (70%) (Table 1).

Table 1: Age and Sex Distribution

Age Group (Years)	Male	Female
0-10	0	2
11-20	10	2
21-30	10	6
31-40	2	0
41-50	0	0
51-60	2	2
61-70	4	0
Total	**28**	**12**

Types of malignancies are shown in (Table 2). Commonest was osteosarcoma (22 cases-55%) followed by chondrosarcoma (15%).

Table 2: Type of Malignancy

Type of Malignancy	Number	Percentage
Osteosarcoma	22	55
Chondrosarcoma	06	15
Ewing`s sarcoma	04	10
Secondaries with pathological fracture	04	10

Table 2: *(Continued)*

Type of Malignancy	Number	Percentage
Aggressive GCT	02	5
Spindle cell sarcoma	01	2.5
Synovial sarcoma	01	2.5
Total	**40**	100

Upper limb involvement was 10% (4/40) and lower limb involvement was in 90% (36/40). Distal femur involvement was commonest (45%) followed by proximal tibia involvement (30%) (Table 3).

Table 3: Anatomical Sites Involved

UPPER LIMB	LOWER LIMB
Proximal Humerus (4/40)-10%	The proximal femur (6/40)-15%
	A distal femur (18/40)-45%
	Proximal tibia (12/40)-30%

Longest resection (31 cm) was in case of distal femur malignancy for osteosarcoma (Figure 1, 2 and 3). Mean resection was 16cm (range 10 cm to 31 cm).

Soft tissue construction was done by available muscles in most of the cases. In all cases of proximal tibia resection, medial gastrocnemius flap and extensor mechanism reconstruction was done. Prolene mesh was used in some cases (Figure 4). Skin grafting was required in 4 cases. Out of those four cases, 1 was due to poor open biopsy done elsewhere (Figure 5) and in the rest 3 cases, the defect was big as the tumour was quite big (Figure 6).

Complications like superficial infection (1 case), delayed infection (1 case), flap necrosis (1case) (Figure 7), and recurrence (2 cases) were encountered. Details and final treatment are mentioned in (Table 4). No implant-related complications were found in any of the cases. In our study infection occurred in 3 patients (7.5%) (including one flap necrosis). However, all did well after debridement and one required a plastic surgeon`s intervention.

Table 4: Complications and Treatment Done

Complication	Diagnosis	Treatment Done	Final Outcome	Last Followup
Superficial infection (with in a month of surgery)	Aggressive GCT distal femur	Debridement	Wound healed satisfactorily	Patient OK
Delayed infection (after 3 months of surgery)	Distal femur Osteosarcoma	Debridement	Wound healed satisfactorily	Patient OK
Flap necrosis (7 days post operative)	Ewing`s sarcoma proximal tibia	Re-surgery and closure done by plastic surgeon by mobilization of gastrocnemius by posterior midline incision	Healed in 4 weeks time	Patient OK
Tumour recurrence (2 years after surgery)	Osteosarcoma	Above knee amputation	Patient walking with prosthesis	Patient OK
Tumour recurrence (1.5 years after surgery)	Synovial sarcoma proximal tibia	Above knee amputation	Patient walking with prosthesis	Patient OK

All patients were followed up as per routine protocol. Follow up ranges from 2 years to 6 years with a mean of 3.2 years. 15 out of 40 (37.5%) were more than 5 years and 28 out of 40 (70%) were more than 3 years of follow-ups. One patient of secondaries from carcinoma of the breast with pathological fracture sub-trochanter died within a week of surgery probably due to pulmonary embolism. One patient with synovial sarcoma had pulmonary metastasis probably because he had not taken postoperative radiotherapy and was lost to follow up after surgery. He was treated by above-knee amputation and chemotherapy. He was having no problems on last follow up. So, 37 out of 40 (92.5%) patients with mega prosthesis were found to be tumour-free and without any complications on the last follow-up.

In conditions, which were relative contraindications for limb salvage surgery (pathological fractures); it is now possible to give good functional life to the patients due to advancement in chemotherapy [10, 32]. We have treated 4 patients with pathological fractures in our series. Out of which one female patient expired in a week of surgery probably due to pulmonary embolism. Other patients with proximal humerus involvement were doing well at the final follow up. The patient with aggressive GCT was having distal femur pathological fracture too and she was doing well at the final follow-up. In terms of evaluation by the MSTS scoring system, the following results were found (Table 5).

Table 5: MSTS score and region involved

Region involved	MSTS score (Out of 35)
Knee (Distal femur + Proximal tibia)	20
Proximal femur	22
Proximal humerus	15

The following scores were higher in respective regions as per the MSTS scoring system. (Table 6). All patients got functional movements and 37 out of 40 (92.5) returned to original work (Figure 8).

Table 6: Region involved and functional MSTS score

Region involved	MSTS score
Knee (Distal femur + Proximal tibia)	- Functional activity - Emotional acceptance
Proximal femur	- Hip abduction
Proximal humerus	- Combined movements - Deformity (ROM)/Stability - Shoulder abduction strength

Neo-adjuvant chemotherapy was given to all our patients having osteosarcoma and Ewing's sarcoma. All except one patient are surviving at an average follow-up of 3.2 years (ranging from 2 years to 6 years). Other studies have reported 5 years survival rate ranging from 28% to 76% .In our series, there were no implant-related complications found. There were no revisions due to implant failure. Apart from 2 amputations and 1 death; out of 40 patients, 37 patients were doing well with follow-up ranging from 2 to 6 years (mean 3.2 years).

DISCUSSION

Over the last few decades, limb salvage surgery for malignant bone tumours has become the treatment of choice.[9-11] As per recent literature, the function of extremity can be preserved by achieving good local tumour control. Harris et al.[1,2,3] showed a comparison of amputees and limb salvage patients. The study found better emotional acceptance in limb preserving surgery patients; though it showed equal functional results in both groups[4,8,12] though reported differently by others . Survival rates are also comparable.[4,13,14]

Osteosarcoma is the commonest malignant bone tumour.[10] It was found in 22 out of 40 patients (55%) in our series. Even after amputation in the olden days, there was pulmonary metastasis in the majority of cases which was probably due to local micrometastasis even after proper surgical resection.[7,15] Neo-adjuvant (chemotherapy given before surgery) reduces the size of the tumours and reduces chances of micrometastasis.[11,12] Adjuvant chemotherapy (chemotherapy given after surgery) further helps to clear micrometastasis. We have used Prolene mesh in some of our cases and proved that it helps gain better functional come in knee and shoulder joints. Studies recommend the use of the mesh to improve shoulder joint stability.[16]

We have also observed that after the report of the final specimen, the patients in whom post-chemotherapy tumour necrosis was more than 90% behaved well.[14,17] At present limb salvage is the method of choice for primary malignant bone tumours which improves the psychosocial acceptance of the person in the society.[15,18] Simon et al. published a multicentre study of 227 patients and shown that there is no difference in survival rate at the end of 5 years in the patients treated by amputation and limb saving surgeries of different types.[19] Amputation is not an easily accepted option for any family as the patients are usually young and are the main bread earners. Other methods of limb salvage like arthrodesis or allograft reconstruction carry the risk of a non-union, disease transmission, and immune response-related problems. Arthrodesis gives stress to other joints and the patient walks with a limp. So, giving a good life to the patient with the functional joint by modular prosthesis is always good for the patient and family.[17,19] The prosthetic replacement has a lower risk of the above complications however final results depend upon the size, nature of the tumour, an implant used, and surgical technique.[18,19] The modularity of newer designs allows us to assemble the implant on the table as per the length of the resected tumour.

Other studies have shown good results with a mega prosthesis but they cannot be compared due to different prosthesis used and different numbers of patients. Reported 5-year survival after implant surgery ranges from 60% to 80% 29. And 10-year survival ranges from 40% to 70%.[20] Malawer and colleagues [20] in 1995 reported an 83% survival of metallic implant at 5 years and 67 % at 10 years. They had a revision surgery rate of 15 %, an infection rate of 13 %, and an amputation rate of 11 % and, a local recurrence rate of 6%. Total, 44% of patients had at least one complication. In another study by Horowitz and others, [21] overall event-free metallic implant longevity was 63% at 5 years and 36 % at 10years. Extremity survival for the whole group was 87% at 5years and 81 % at 10 years.[21]

The commonest complication apart from the above is infection. It ranges from 4% to more than 30% in other studies.[18] Regarding implant options for the paediatric age group with an open epiphyseal plate, epiphysiodesis of opposite normal side or Ilizarov lengthening are options to maintain limb length equality. We have one patient of 9 years of age, and in future, we are planning to do either.[7] Regarding the option of expandable implant, the cost is the major issue, and later date lengthening either by surgical intervention or by the

magnetic field can be done. However, we do not have such experience. However, it is a study involving follow-up ranging from 2 to 6 years with a mean of 3.2 years. So, we have labelled it as mid to long-term follow-up. Long term study with more number of patients is needed for better judgment.

CONCLUSION

Limb salvage surgery by mega prosthesis requires good infrastructure. A Team of Oncophysician, oncosurgeon and radiation oncologist is a must. Cost is a major concern too. So, if this option cannot be worked out; we can think of amputation, rotationplasty or arthrodesis. In a study by some surgeons, functional results of rotationplasty are superior to amputation or limb salvage. We do not have that many numbers of other methods for comparison. Limb salvage surgery for malignant bone tumours by mega prosthesis is a good treatment in selected cases. It gives good tumour control and good functional life. However, it needs proper infrastructure and team-based approach. If it cannot be worked out for any reason, amputation can be a good option.

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Conflict of Interest

None for any of the author.

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Figure 1: Osteosarcoma (Longest Resection-31 cm).

Figure 2: Longest Resection (31 cm).

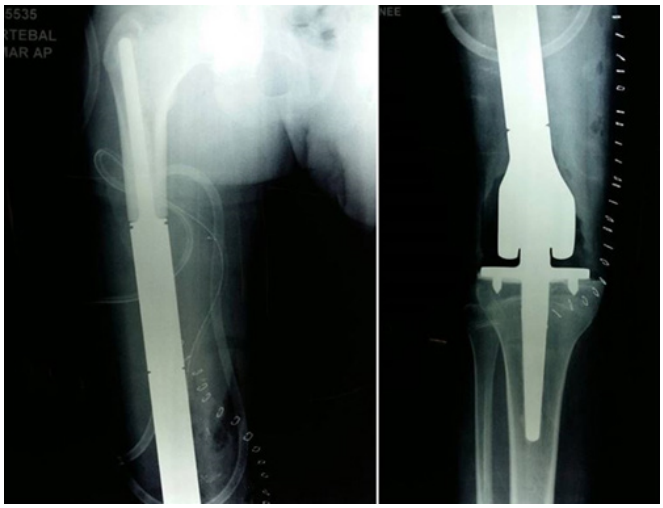

Figure 3: Post Operative X-ray of Longest Femur Resection.

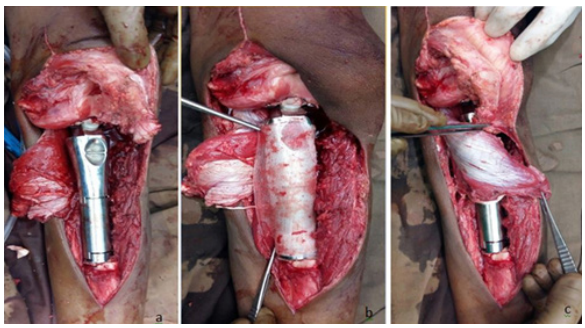

Figure 4: Use of Mesh for Reconstruction (Proximal Tibia). (a) Prosthesis in situ, (b) Mesh wrapped around prosthesis, (c) Gastrocnemius flap around mesh.

Figure 5: STSG for Closure of Wound (Problem Due to Open Biopsy Done Elsewhere).

Figure 6: STSG required due to Big Tumor Size.

Figure 7: Complication (Flap Necrosis Treated by Resurgery).

Figure 8: Functional Movements at Follow Up.