Comparison of Limb Salvage with Mega Prosthesis Versus Auto Graft Reconstruction after Cryotherapy in Adolescent Patients with Limb Sarcomas.

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ABSTRACT

Objective: To compare the functional outcome of limb salvage in adolescent limb sarcomas treated with Mega Prosthesis Versus Auto Graft Reconstruction as assessed with Musculoskeletal Tumor Society(MSTS) rating Scale.

Methods: This retrospective Cohort study was conducted in department of Surgical Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Center Lahore. The medical record of all adolescent (11 to 16 years) patients with limb sarcoma who underwent wide local excision and reconstruction with liquid nitrogen treated auto graft or mega prosthesis operated during the time period extending from 15th January 2018 to 15th December 2021 was reviewed. Both modalities of treatments were compared for functional outcome as assessed with MSTS scoring scale at one year with 0 to 100% score and the higher MSTS score indicating better functional outcome.

Results: The records of 35 patients were reviewed. Male patients were 26(74.28%) and females were 09(25.71%). The mean age was 15.8±3.6 years. The predominant type of tumor was Osteosarcoma(77.1%,n=27) and the commonest location was distal femur (40 %,n=14) and proximal tibia(40 %,n=14). Mega prosthesis replacement was done in 20(57.14%) patients while auto graft reconstruction was done in 15(42.85%) patients. At one year the mean MSTS score was 25± 5.6 (83.33) in patients with mega prosthesis and 20±7.5(66.66%) in auto graft(P<0.05).

Conclusion: Adolescent patients with limb sarcomas treated with Mega prosthesis yielded better functional outcomes when compared with auto graft reconstruction after cryosterilization.

Keywords: Limb salvage, Mega prosthesis, Musculoskeletal Tumor Society, Sarcoma.

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INTRODUCTION

Musculoskeletal sarcomas constitute 12% of pediatrics neoplasms and around 80% of these sarcomas arise from soft tissues and 20% are of bony origin.[1,2] Extensive tumor resection with simultaneous biological reconstruction or use of mega prosthesis or combination have made limb salvage possible. Limb salvage surgery has gained popularity owing to advances in neoadjuvant and adjuvant therapy, surgical techniques and prosthesis designs.[3] The prime objective of limb salvage surgery is to achieve wide resection with tumor free margins followed by stable reconstruction to ensure good functional outcomes but with minimal morbidity.[4] Modern Mega prosthesis designs can provide early functional return with reasonable long-term survival.[5] Mega prosthesis in skeletally mature Sarcoma patients remains the gold standard and a viable option in in adolescent patients with predicted Leg-Length Discrepancy (LLD) less than 3 cm at skeletal maturity but with some limitations. Several

complications of Mega prosthesis like infection, instability and limb length discrepancy have been reported in the literature.[6] Biological reconstruction can be achieved with distraction osteogenesis, vascularized auto graft, non-vascularized auto graft, allograft irradiated bone, and frozen bone. [7] One of the biological methods of treating bone Sarcomas with liquid nitrogen treated auto graft was first described by Tsuchiya and showed good and excellent limb salvage results. [8] Subsequent studies had also shown better results with liquid nitrogen-treated bone reconstruction.[9] Some studies however, have documented complications like non union and impaired wound healing and technical difficulties with the use of liquid nitrogen treated auto graft used for reconstruction.[10]

The objective of our study was to compare the functional outcome of limb salvage in adolescent limb sarcomas treated with Mega Prosthesis Versus Auto Graft Reconstruction.

METHODS

We conducted this retrospective Cohort study in department of Surgical Oncology Shaukat Khanum Memorial Cancer Hospital and Research Center Lahore. The medical record of all adolescent (11 to 16 years) patients with limb sarcoma who underwent wide local excision and reconstruction with liquid nitrogen treated auto graft or mega prosthesis operated during the time period extending from 15th January 2018 to 15th December 2021 was reviewed. Patients with recurrent tumor, metastasis, pathological fracture at presentation or operated elsewhere initially were excluded from the study. This study was conducted after taking approval from the Institutional Review Board and data concerning all the variables were collected from the hospital information system (HIS) and entered in the pre-designed forms. A standard uniform management protocol was adopted for each case. All patients were skeletally immature with the predicted remaining overall growth of less than 3 cm calculated with the Multiplier method. After completion of workup, all cases were discussed in a Multidisciplinary meeting with X-rays and MRI of the affected extremity, histological diagnosis, Bone scan CT chest. All patients of Osteosarcoma had Neoadjuvant Chemotherapy consisted of two cycles of MAP(Methotrexate, Doxorubicin, Cisplatin) chemotherapy according to EUROMOS(European and American Osteosarcoma Study Group) protocol[11] while Ewing sarcoma received 6 cycles of VDC/IE(Vincristine, Doxorubicin, and Cyclophosphamide alternating with Ifosfamide and Etoposide).[12] After neoadjuvant chemotherapy patients were reassessed clinically and radiologically with a repeat MRI of the affected limb and CT scan chest, re-discussed in a Multidisciplinary meeting and a further plan was devised.

Before operation pre-operative templating was done by using patients' cross-sectional images. Patients with adequate diaphyseal canal, femoral Inter-epicondylar distance, posterior tibial slope, and tibial size and predicted limb length discrepancy of less than 3cm at skeletal maturity were reconstructed with mega prosthesis after tumor excision. Patients in which adult mega prosthesis was not possible based upon templating and had predicted limb length discrepancy of less than 3 cm at skeletal maturity were reconstructed with liquid nitrogen treated auto graft after tumor excision. After wide local excision the frozen section from proximal and distal bone ends were tested to confirm tumor-free margins.

For reconstruction using mega prosthesis the resected bone was sent for histopathology and reconstruction was done with modular mega prosthesis Limb Preserving System (LPS).

For auto graft reconstruction we used the free freezing method for bone treatment in which resected bone was dissected out from soft tissue envelope. The bone was reamed so the medullary canal was free from any gross tumor. Then drill holes were done in it before liquid nitrogen treatment. Resected bone was placed in the specialized sterile container and dipped in liquid nitrogen for 20 minutes followed by placing it at room temperature for another 15 minutes after which it was dipped in normal saline for 10 minutes to complete the cycle. The liquid nitrogen-treated auto graft was used to reconstruct defects and fixed with locking plates or intramedullary nails. Gastrocnemius flap and split-thickness graft was used for coverage in some cases in tumors around the knee joint.

All the patients were followed every 6th week to check for wound status and limb length discrepancy. X-ray of the operated limb was done on every visit. CT scan chest and bone scan were advised 04 monthly for surveillance. Both modalities of treatments were compared for functional outcome as assessed with MSTS[13] scoring scale at one year with a score ranging from 0 to 30(converted to 0 to 100%)with higher MSTS score indicating better functional outcome. We also compared the reoperation rate, chemotherapy breaks (> 3-week) in adjuvant chemotherapy after surgery, hospital stay,

conversion to amputation and limb length discrepancy in both groups.

We analyzed our data with SPSS version 24. Frequencies and percentages were calculated for quantitative variables while mean and standard deviation was calculated for qualitative variables. The MSTS score in both groups was compared and P value was calculated using independent sample-t test Qualitative variables were compared using Chi-square test. Student's t test was used for comparison of continuous variables. P value <0.05 was considered significant. Data was presented in table where necessary.

RESULTS

In this study 35 patients were included. Majority (74.28%,n=26) of our patients were male while female patients were 09(25.71%). The mean age of our sample was 15.8±3.6 years. The predominant type of tumor was Osteosarcoma (77.14%,n=27) followed by Ewing Sarcoma ((14.28%,n=5) and Chondrosarcoma (8.57%,n=3).Tumor location was distal Femur in 14(40%) patients, proximal Tibia in 14(40%), proximal Femur in 03 (8.57 %),proximal Humerus in 02 (5.71 %),distal Tibia in 01 (2.85 %) and distal Radius in 01 (2.85 %) patient. Mega prosthesis replacement was done in 20(57.14%) patients while auto graft reconstruction was done in 15(42.85%) patients. The mean follow up period was 15.6±3.7 months(range 12.2 to 17.4 months). At one year the mean MSTS score was 25± 5.6 (83.33) in patients with mega prosthesis and 20±7.5(66.66%) in auto graft (P=0.002).No statistically significant difference was noted in MSTS score for distal femur and proximal tibia. The comparison of surgical outcome of other variables of mega prosthesis versus auto graft reconstruction is shown in table I. A statistically significant(P<0.05) better surgical outcome was noted in Mega prosthesis group in terms of lesser chemotherapy break, less infection and wound dehiscence, less hospital stay, limb length discrepancy, amputation and re surgery rates.

Table I: Comparison of surgical outcome of Mega prosthesis versus auto graft reconstruction in adolescent limb sarcomas.

S. No	Outcome Variables	Mega Prosthesis group (n=20,57.14%)	Auto graft reconstruction group (n=15,42.85%)	*P* value
1	**Chemotherapy breaks(delay >3 weeks)**	02(10%)	09(60%)	0.02
2	**Infection**	--	04(26.66%)	0.01
3	**Wound dehiscence**	02(10%)	05(33.33%)	0.01
4	**Hospital Stay**			0.001
	< 05 days	16 (80%)	04 (26.66%)	
	5-10 days	02 (10%)	05 (33.33%)	
	>10 days	02 (10%)	06 (40%)	
5	**Limb length discrepancy**			0.03
	< 02 cm	14 (70%)	12 (80%)	
	2-3cm	05 (25%)	03 (20%)	
	3-4cm	01 (05%)	--	
6	**Conversion to amputation**			0.01
	Yes	01 (5%)	03 (20%)	
	No	19 (95%)	12 (80%)	
7	**Re-surgery**			0.01
	Yes	02 (10%)	09 (60%)	
	No	18 (90%)	06 (40%)	

DISCUSSION

Allograft reconstruction of limb sarcomas has many limitations particularly in developing countries where bone banks are not yet established. Therefore alternative methods have been developed to re-use the resected bone for reconstruction after irradiation,[14] autoclaving[15], and pasteurization.[16] But these methods require special equipment and firm thermal control. Moreover thermal treatment adversely affects the biomechanical properties of auto graft including loss of osteo-induction.[17]

Freezing the Sarcoma affected resected bone with liquid nitrogen is a viable option as it has shown to retain its osteo-conduction and osteo-induction properties as demonstrated in many studies.[18]

In our study we had documented an increased overall complication rate in auto graft treated with liquid nitrogen compared to the Mega prosthesis. The most common issue in liquid nitrogen treated group was wound dehiscence in 5 (33.33%) patients that had resulted in chemotherapeutic delays, hinders post-operative recovery and prolonged hospital stay. Skin necrosis after liquid nitrogen treated auto graft is comparable with Li Y and colleagues[19] who noted that 05(31.25%) patients in their series developed skin necrosis or superficial infection. Contrary to the above Higuchi et al[20] did not show any complication of skin necrosis after liquid nitrogen treatment in their series.

Imran et al [21] was of the opinion that delayed adjuvant chemotherapy of more than 21 days resulted in an increased risk of recurrence and mortality. The adjuvant chemotherapy is effective in preventing micro metastasis spread and local recurrence with increased survival.[22] In our study delay in chemotherapy was more frequent in the liquid nitrogen group(60%,n=9) than in mega prosthesis reconstruction(10%,n=02).This can result in increased local recurrence and decreased survival rate. Liquid nitrogen treated auto graft patient had increased hospital stay due to higher skin-related complication, infection, and reoperation rate in this group. Increased hospital stay is associated with increase in treatment cost, hospital-induced psychosis, infection in an immunocompromised patient and decrease patient satisfaction. [23]

We assessed the post operative functional status of our patients with Musculoskeletal Tumor Society(MSTS) rating Scale and noted mean MSTS score of 25± 5.6 (83.33%) in patients with mega prosthesis and 20±7.5(66.66%) in the auto graft($P<0.05$) at one year follow up. Kamal treated[5] 35 patients with mega prosthesis including 26(57.6%) adolescent patients with age 11 to 20 years. At one year follow up mean MSTS score was 78.7%. Sharil and Nawaz[24] treated 34 distal femur and 20 proximal tibia with endoprosthesis.They documented mean MSTS of 21.13(70.43%) altogether while MSTS for distal femur group was 21.94(73.13%) and proximal tibia was 19.75(65.83%). Ji and colleagues[25] treated 15 skeletally immature osteosarcoma of distal femur with mean age 10 years and noted MSTS of 82.7. Araki *et al* [26] treated 37 patients of osteosarcoma with frozen autograft reconstruction. The mean age was 15 to 39 years. The MSTS was excellent in 8(89%) and good in 1(11%) in patients under 14 years. The MSTS score in patients of 15 to 39 years of age was excellent in 4(78%) and good in 3(17%). Tsuchiya[8] treated 28 patients with age range 10 to 68 years and noted excellent limb function in 20(71.4%),good in 3(10.7%),fair in 3(10.7%) and poor in 2(7.1%).

The design of our study was retrospective Cohort. Our sample size was small. Our follow up period was short. We recommend further studies on this topic to address all these limitations and verify our results.

CONCLUSION

Adolescent patients with limb sarcomas treated with Mega prosthesis yielded better functional outcomes when compared with auto graft reconstruction after cryosterilization.

Conflict of Interest: None

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