

Outcome of Osteosarcoma, Recurrence, Complications, Metastasis and Survival

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ABSTRACT

We retrospectively evaluated data of 25 patients with Osteosarcoma. These patients were treated by either limb salvage surgery with endoprosthesis reconstruction or limb amputation. We explore whether the complications, recurrences, metastasis and survival are the same or not between limb-salvage and amputation groups. We conclude that Limb-salvage surgery reduces the risk of relapse compared with amputation in the treatment of patients with osteosarcoma. The disease free survival and overall survival at 2 years follow up are significantly better after limb salvage surgery as compared to limb amputation. Furthermore, there was no difference in the metastasis and complication rate in both the groups.

Keywords: Osteosarcoma, recurrence, complications, metastasis, survival

INTRODUCTION

Osteosarcoma is the most common primary malignant bone tumor in children and adolescents, accounting for 4% of all childhood cancers worldwide. In India, the incidence varies from 4.7% to 11.6%, where this malignancy is associated with significant morbidity and mortality.¹ Historically amputation was done, resulting in complete loss of extremity but with advances in chemotherapy, imaging and reconstruction techniques have made limb salvage surgeries more feasible.² Limb preservation surgery can be complex. Perhaps the most complicated and

potentially life altering decision involves choosing the type of surgical procedure that will balance maximum potential for cure with an acceptable aesthetic outcome, long term mobility and quality of life. There are number of treatment options for reconstruction, these include manufactured endoprosthesis devices, bulk allografts, biological constructs or combination of the these elements. Theoretically, limb preservation increases the rate of local recurrence, but in experienced hands it can be performed with little or no increase in local recurrence compared to amputation.³ Beyond survival there is little information on physical impairment and disability, but evaluation of functional outcome is becoming more important in the increasing proportion of long term survivors. Over the past three decades the focus has now shifted from controversy over the various forms of limb salvage to methods enhancing functional and oncological outcome after endoprosthesis replacement.⁴ One of the main difficulties of OSA is to achieve wide resection margins and at the same time to restore function and stability. The objective of this study was to investigate the complications, recurrence, metastasis and survival after limb salvage surgeries and limb amputation.

LITERATURE REVIEW

Renard et al in the year 2000 evaluated the functional results and the complications after several limb-saving and ablative

treatments because of lower extremity bone sarcoma. Complications were 3 times more common after limb-salvage procedures and 4 times more common after endoprosthetic reconstructions compared to after ablative procedures.⁴

Rose et al in 2006 sought to examine the disease-specific survival and risk of late recurrence or dedifferentiation in a cohort of 29 patients with average of 15.8 years follow up. Disease-free survival was 83%, with five patients dying of disease at an average of 26 months after presentation. Limb-salvage therapy seems to offer survival equivalent to amputation, and there does not seem to be a substantial risk of late recurrence, dedifferentiation, or disease progression.³³

Jiang et al conducted a meta-analysis in 2014 to explore whether the relapse, 5-year survival and metastasis are the same or not between limb-salvage and amputation groups. A total of 89 studies were identified and seven articles with 200 cases in the limb-salvage surgery group and 84 subjects in the amputation group were included in the meta-analysis. The pooled data indicated that no statistical difference of risk for developing relapse between limb-salvage and amputation was found. The 5-year survival rate of patients underwent limb-salvage surgery was smaller than patients received amputation, the metastasis rate of patients underwent limb-salvage surgery was significant decreased compared with patients received amputation They concluded that Limb-salvage surgery does not increased the risk of relapse compared with amputation in the treatment of patients with osteosarcoma.⁶

Puri et al in 2014 did a retrospective analysis of 18 cases of periosteal osteosarcoma. There were 2 local recurrences at 9 months and 18 months post surgery. Pulmonary metastasis occurred in 4 cases (22%).14 patients were alive and their disease free survival at 5 years was 77.8% and overall survival rate was 83.3 %.⁷

Laitinen et al conducted a retrospective of 80 patients in 2015 to evaluate the

prognostic and therapeutic factors which influence the oncological outcome of parosteal osteosarcoma. Overall survival was 91.8% at five years and 87.8% at ten years. Local recurrence occurred in 14 (17.5%) patients and was associated with big tumor size and on histology recurrences were dedifferentiated high-grade tumors.⁸ Bohler et al in 2018 retrospectively evaluated data of 49 patients with humeral osteosarcoma. All patients underwent resection and Endoprosthetic reconstruction. Eleven patients (22%) had at least one complication. The estimated cumulative incidence for the first complication was 18% at one year, 23% at five years, and 28% at ten years, respectively. Soft tissue failure was the most common complication. In conclusion, Endoprosthetic reconstruction is a good treatment method with an acceptable complication rate.⁹

MATERIALS & METHODS

We obtained data retrospectively from our prospective tumor registry as well as from medical and radiological records of patients who were diagnosed with osteosarcoma. 25 patients with osteosarcoma were treated, 17 underwent Limb salvage surgery and 8 underwent amputation. We compared the complications, recurrence, metastasis and survival in these two groups of patients.

RESULT

Anatomic site relation with the treatment method

Site	Limb Salvage Surgery	Amputation	Total
1.Proximal tibia	5	4	9
2.Distal femur	8	1	9
3.Proximal humerus	1	3	4
4.Proximal femur	1	0	1
5.Others	2	0	2
Total	17	8	25

Recurrence

In our series we found 4 cases of local recurrence ,1 case in Limb Salvage Surgery Group and 3 cases in Amputation group, and it was found to be statistically different(p value =0.044) (Table 1).

Table 1: Recurrence among Limb Salvage surgery and Limb Amputation

Local Recurrence	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 YES	1	5.9%	3	37.5%	4	16%	P=0.044
2 No	16	94.1%	5	62.5%	21	84%	
3 Total	17		8		25		

Metastasis

We reported 8 cases of patients with metastasis. 4 cases were in limb salvage surgery group and 4 cases in amputation group. The occurrence of metastasis was not significant difference between both the groups (p value=0.359) (Table 2). Table 3 shows the sites of metastasis.

Table 2: Metastasis in different treatment groups

Metastasis	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 YES	4	23.5%	4	50%	8	32%	P=0.359
2 No	13	76.5%	4	50%	17	68%	
3 Total	17		8		25		

Table 3: Showing site of metastasis in different treatment groups

Metastasis	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 Pulmonary	2	50%	4	100%	6	75%	P=0.263
2 Bony metastasis	1	25%	0	0%	1	12.5%	
3 Others	1	25%	0	0%	1	12.5%	
3 Total	4		4		8		

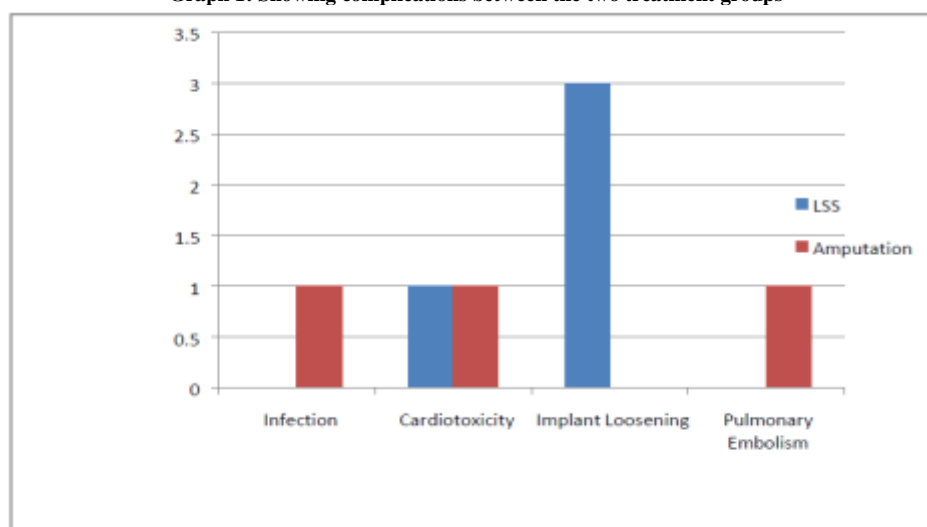
Complications

We had 7 cases of complications, 4 in limb salvage surgery group and 3 in amputation group. The occurrence of complications was not found to be significant in both the groups (p value=0.639). (Table 4 and Graph 1)

Table 4: Showing complications between the two treatment groups

Complications	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 Infection	0	0%	1	33.3%	1	14.28%	P=0.639
2 Cardiotoxicity	1	25%	1	0	2	28.56%	
3 Implant Loosening	3	75%	0	33.3%	3	42.85%	
4 Pulmonary embolism	0	0%	1	33.3%	1	14.28%	
6 Total	4		3		7		

Graph 1: Showing complications between the two treatment groups



Disease free survival at 2 years follow up

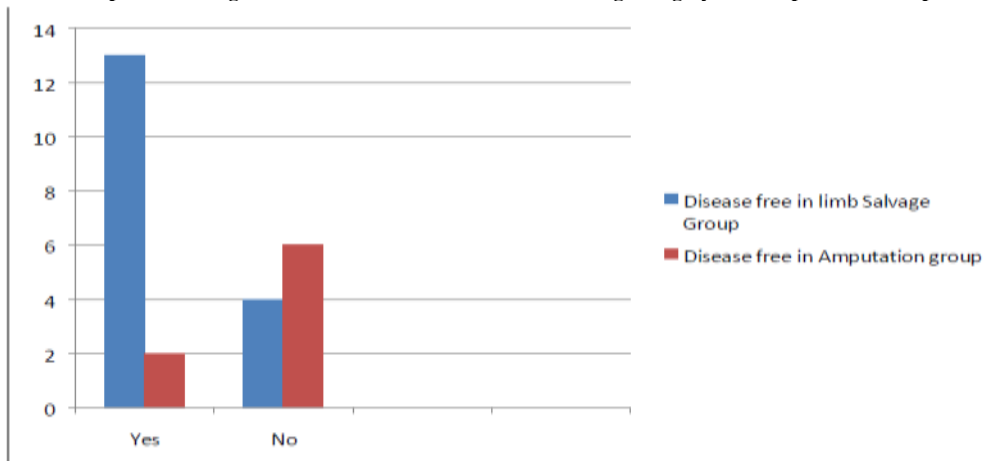
Disease free survival was calculated between the Limb Salvage surgery group and the Amputation group and there was

found to be statistically significant difference between the 2 treatment methods (p value=0.044)(Table 5 and Graph 2).

Table 5: Showing Disease free survival between limb Salvage Surgery and Amputation Group

Disease free	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 YES	13	76.47%	2	25%	15	60%	P=0.044
2 No	4	23.52%	6	75%	10	40%	
3 Total	17		8		25		

Graph 2: Showing Disease free survival between limb Salvage Surgery and Amputation Group



Overall survival at 2 years follow up

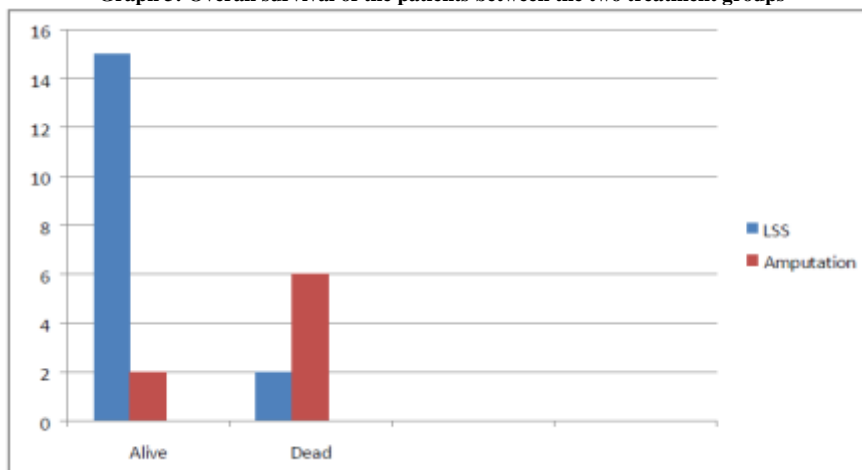
In our series we had 17 alive patients while 8 patients died. 2 patients died in the limb salvage surgery group and 6 patients died in

the Amputation group. There was found to be significant difference (p value=0.004) (Table 6 and Graph 3).

Table 6: Overall survival of the patients between the two treatment groups

Disease free	Limb salvage group		Amputation group		Total patients		P value
	Number in group	Percentage in group	Number in group	Percentage in group	Total Number	Percentage	
1 Alive	15	88.2%	2	25%	17	68%	P=0.004
2 Dead	2	11.6%	6	75%	8	32%	
3 Total	17		8		25		

Graph 3: Overall survival of the patients between the two treatment groups



DISCUSSION

In our series we had 2 cases of cardiotoxicity, 1 patient with infection, 3 patient had implant loosening and 1 had pulmonary embolism. No significant difference in the complication between the two groups (p value=0.639). Contrary to our results Rand et al found complications were 3 times more common after limb salvage procedure and 4 times more common after endoprosthetic reconstruction compared to after ablative procedures. Arpaci et al reported surgery complications in 3 out of 22 patients.¹⁰ Bohler et al concluded that endoprosthetic reconstruction is a good treatment method with acceptable complication rate.

Out of 17 patients treated we had 4 cases of recurrence. The recurrence rate was significantly higher in limb amputation group (p value=0.044) (3 patients, 37.5%) than patients treated with Limb Salvage Surgery, 1 patient (5.9%). On the other hand Picci et al reported the local recurrence rate in limb salvage and amputation group was 7 and 2.4% respectively, in patients with high grade had osteosarcoma.¹¹ Wright et al found local recurrence in 15% and survival of 75% in limb salvage surgeries.¹² Bacci et al. reported that local relapse occurred in 5% of surgically-treated patients with osteosarcoma who had an inadequate surgical margin.¹³

At 2 years follow up we found metastasis in 8 patients. 4 (23.5%) out of the 17 patients who were treated by limb salvage surgery and 4 (50%) out of the 8 patients treated by limb amputation developed metastasis. We found no significant difference between the 2 groups (p value=0.359). Laitinen et al found pulmonary metastasis in 12 (14%) patients.⁸ While in our study we found higher percentage of pulmonary metastasis was (6 patients, 75%), bony metastasis was found in 1 patient (12.5%) which lead to paraplegia, while 1 patient (12.5%) had pulmonary embolism.

At 2 years follow up, 13 (76.47%) out of 17 patients treated with Limb Salvage Surgery and 2 (25%) out of 8 patients treated

with Limb Amputation were disease free. There is a significant difference in the disease free survival between both the treatment groups at the end of 2 years (p value =0.044). Rose et al found disease free survival was 83% in Limb Salvage resection.⁵ Arpaci et al found 3 years overall survival and disease free survival were 83% and 70% respectively in Limb Sparing Surgery.¹⁰ Contrary to our results Jiang et al found 5 year survival rate in limb salvage surgery was smaller than patients with amputation.⁶ Li et al found the overall Kaplan- Meyer survival was 82% in limb salvage surgery.¹⁴ Maruland et al stated that there is no difference in survival rate between patients undergoing limb-salvage procedures and amputations, whereas there is a high trend of local recurrence with limb-salvage.¹⁵ At 2 years follow up, 15 (88.2%) out of 17 patients, and 2 (25%) out of 8 patients were alive in the limb salvage and the amputation group respectively. We found significant difference (p value=0.004) between the overall survival of two treatment groups. Kumar et al observed the overall survival was 42% at 10 years, overall survival in limb salvage was 93%.¹⁶

CONCLUSION

We conclude that the disease free survival and overall survival at 2 years follow up are significantly better after limb salvage surgery as compared to limb amputation. Besides there were fewer recurrences in the limb salvage group. There was no difference in the metastasis and complication rate in both the groups.

Declaration by Authors

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