

# Factors Affecting Survival in Osteosarcoma

Varun Sachdeva<sup>1</sup>, Richa Mehra<sup>2</sup>

<sup>1</sup>MS Orthopaedics, Zonal Hospital Mandi (H.P.)

<sup>2</sup>MS ENT Zonal Hospital Mandi (H.P.)

Corresponding Author: Richa Mehra

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## ABSTRACT

Endoprosthetic reconstruction, the most common option in limb-salvage surgeries, is an attractive alternative to other surgical options and plays a key role in keeping the patients quality of life since it provide early mobilization, stability, and weight-bearing for patients. The aim of limb-salvage surgery is to maximally preserve a limb with a satisfactory function and to avoid the psychological and cosmetic problems caused by amputations. With the addition of neoadjuvant chemotherapy to treatment protocols, five-year survival rates have dramatically increased. Today, amputation is not a first choice anymore. There is a significant difference in the disease free survival between the limb salvage and amputation group at the end of 2 years ( p value =0.044). Significant difference was found between the tumour volume and the survival of the patient (p value=0.012). 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. There is no significant difference between the Huvos Grade and the overall survival of the patient (p value=0.121).

**Keywords:** LSS-Limb salvage surgery

## INTRODUCTION

Osteosarcoma is a rare bone tumour found in areas of rapid bone turnover, most commonly the distal femur and proximal tibia of adolescent patients. Osteosarcoma is the most common type of malignant bone tumour in the region of the knee.<sup>1</sup> Prior to

the advent of chemotherapy, osteosarcoma was a fatal disease. Today most osteosarcoma patients receive neoadjuvant chemotherapy followed by surgical resection and a regime of chemotherapy post-operatively.<sup>2</sup> 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.<sup>3</sup> 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 endoprosthetic devices, bulk allografts, biological constructs or combination of these elements. In this study we aim to study the affect of Limb preservation surgery and amputation on the survival in twenty five patients of Osteosarcoma.

## LITERATURE REVIEW

In the 1970s, Jaffe published the first significant success of chemotherapy, showing that methotrexate was a useful agent to manage metastases in advanced disease.<sup>4</sup> As new cytotoxic agents were discovered, the use of chemotherapy blossomed, but the practice remained controversial until a landmark study in 1985 which showed an increase in 6-year survival

from 11 to 61% with the addition of multi-agent chemotherapy.<sup>5</sup> The 5-year survival in osteosarcoma in the first half of the 20th century was less than 20%.<sup>6</sup> These patients were mainly treated by limb amputation and most of them died of lung metastases.<sup>7</sup> Since then, long-term survival for patients with localized osteosarcoma has improved to approximately 60% due to the newly-introduced multi-agent chemotherapy together with gradually-improved surgical techniques in the 1970s, but has remained largely unchanged since then. By contrast, the long-term survival of patients with metastatic osteosarcoma still remains at 25–30%.<sup>8</sup> A study performed at Memorial Sloan Kettering found similar increase in survival with chemotherapy that was given

before surgery (neoadjuvant) showing that it was safe to delay surgery for treatment.<sup>9</sup> The patient’s age has been found to correlate with survival; the poorest survival is among older individuals. Death rates for osteosarcoma have steadily declined by approximately 1.3% per year. The 5-year overall survival rate is about 68%, regardless of sex.<sup>10</sup>

**MATERIALS & METHODS**

Twenty five patients with biopsy proven Osteosarcoma presenting to Government Medical College and Hospital, Chandigarh, who were treated by either amputation or limb salvage surgery were assessed for the various survival factors using the Chi Square Test.

**RESULT**

**Table 1: Relation between tumour volume and the Disease free survival of the patients**

Tumour volume	Disease free survival in Limb salvage group		Disease free survival in Amputation group		Total patients		P value
	Yes	NO	Yes	no	Total Number	Percentage	
<200cm <sup>3</sup>	6	2	0	1	9	50%	P=0.268
>200cm <sup>3</sup>	4	1	2	2	9	50%	
Total	13		5		18		

Significant difference was found between the tumour volume and the survival of the patient (p value=0.012)(Table 1)

**Table 2: Relation between tumour volume and the overall survival of the patients**

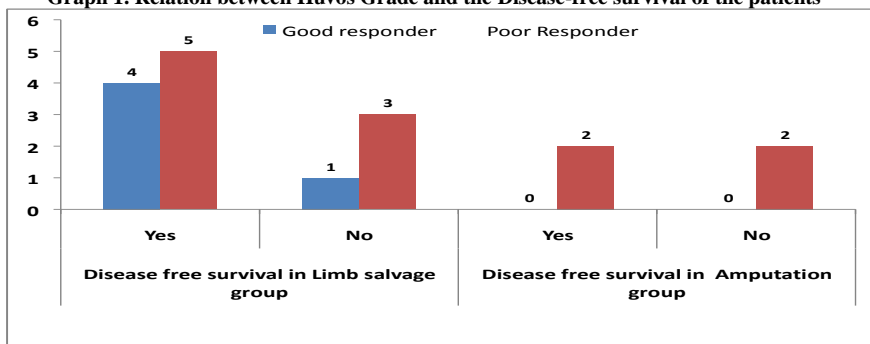
Tumour volume	Limb salvage group		Amputation group		Total patients		P value
	Alive	Dead	Alive	Dead	Total Number	Percentage	
<200cm <sup>3</sup>	8	0	0	1	9	50%	P=0.012
>200cm <sup>3</sup>	5	0	2	2	9	50%	
Total	13		5		18		

Table 2 shows a Significant difference between the tumour volume and the survival of the patient. (p value=0.012)

**Table 3: Relation between Huvos Grade and the Disease free survival of the patients**

Huvos grade	Disease free Survival in Limb salvage group		Disease free survival in Amputation group		Total patients		P value
	Yes	NO	Yes	No	Total Number	Percentage	
Good Responder	4	1	0	0	5	29.41%	P=0.584
Poor responder	5	3	2	2	12	70.58%	
Total	13		4		17		

**Graph 1. Relation between Huvos Grade and the Disease-free survival of the patients**

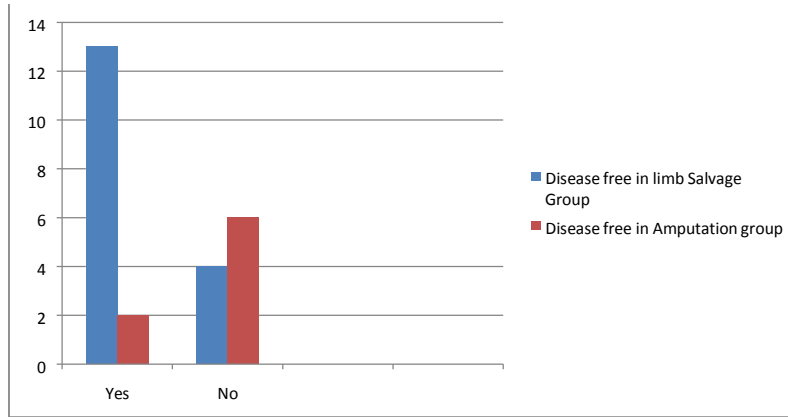


No significant difference was found between the Huvos Grade and the disease free survival of the patient (p value=0.584). (Table 3 and Graph 1)

**Table 4: 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**

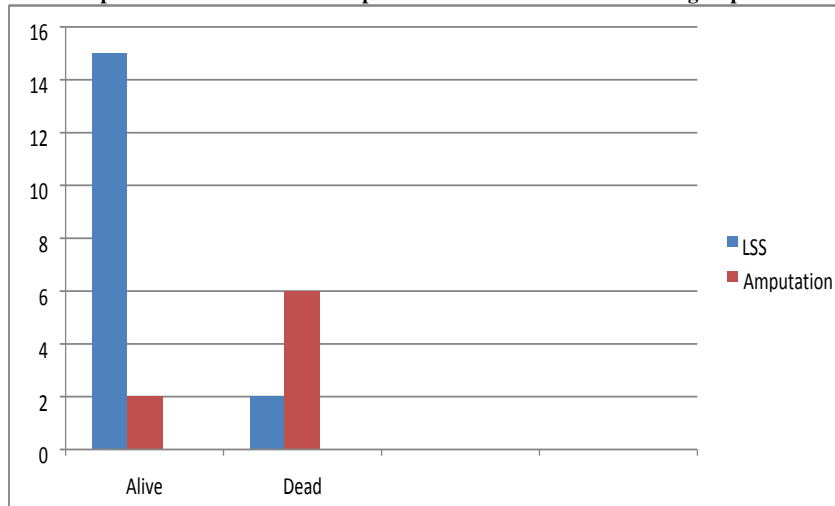


Disease free survival was calculated between the Limb Salvage surgery group and the Amputation group and there was found to be statistically significant difference between the 2 treatment methods (p value=0.044).(Table 4 and Graph 2)

**Table 5: 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**



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 in the over all survival between both the groups (p value=0.004).(Table 5 and Graph 3)

**DISCUSSION**

The choice of treatment options in osteosarcoma depends on tumor grade, location, and response to neoadjuvant

chemotherapy. Limb-salvage surgery is currently the gold standard in osteosarcoma treatment. The aim of limb-salvage surgery is to maximally preserve a limb

with a satisfactory function and to avoid the psychological and cosmetic problems caused by amputations. With the addition of neoadjuvant chemotherapy to treatment protocols, five-year survival rates have dramatically increased. Today, amputation is not a first choice anymore owing to advances made in chemotherapy, surgical techniques, surgical devices, and diagnostic methods. Endoprosthetic reconstruction, the most common option in limb-salvage surgeries, is an attractive alternative to other surgical options and plays a key role in keeping the patients quality of life since it provide early mobilization, stability, and weight-bearing for patients. On the other hand, the disadvantages of endoprosthesis surgery have to be considered, such as infection, loosening of prosthesis, joint stiffness, limb-shortening or lengthening and implant fracture.

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).

Tumour volume was calculated using the MRI reports and two groups were made with tumour volume  $<200\text{cm}^3$  and  $>200\text{cm}^3$ . Reports were not available for 7 patients, for the rest 17 patients, where tumour volume was known, no significant difference was found between tumour volume and the treatment (p value=0.294) or the disease free survival ( p value =0.269).Significant difference was found between the tumour volume and the survival of the patient (p value=0.012) . 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.

## CONCLUSION

We conclude that the tumour volume significantly affects the overall survival in patients with osteosarcoma. However there was no difference in survival with the Huvos grading. The disease free survival and overall survival were significantly better in the limb salvage group as compared to the amputation group, which favours the recent advancement towards limb salvage with endo prosthetic devices.

### *Declaration by Authors*

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**Conflict of Interest:** The authors declare no conflict of interest.

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