Advances in Tumor Management Modalities, Surgery Prevails As Best Predictor of Survival for Osteosarcoma: An Analysis of Primary Osseous Tumor Characteristics, Management, and Outcomes from the National Cancer Database (NCDB)

Taylor D. Ottesen, BS, Blake N. Shultz, BS, Alana M. Munger, MD, Cosmas Sibindi, BS, Alp Yurter, BS, Arya R. Varthi, MD, Jonathan N. Grauer, MD

Yale School of Medicine, Department of Orthopaedics and Rehabilitation, New Haven, Connecticut

Background

Primary osseous tumors, such as osteosarcoma, are relatively uncommon. Most studies about their characteristics, management, and outcomes have limited patient numbers and combine varied tumor histology. Further, the management of such neoplasms has evolved significantly within the past decade, as surgical techniques, adjuvant therapies, and molecular-targeted treatment modalities. and as such, most studies are from a single-institution with varying tumor histology making them difficult to study.

Questions/Purposes

Given osteosarcoma treatment advances, the current study sought to investigate the effect of various treatment modalities and demographic risk factors on the outcomes of primary osteosarcoma using the large National Cancer Database (NCDB).

Materials and Methods

Osteosarcoma patients from the 2004-2015 NCDB datasets were separated into three cohorts based on primary tumor location: axial, appendicular, and other. Demographic and treatment data as well as one-, five-, and 10-year survival were determined for each group. Multivariate Cox analysis was performed showing the correlation of demographic and treatment variables with the likelihood of death at any given time within each group. Kaplan Meier survival curves were generated showing the correlation of survival with distant metastases and year of diagnosis.

Results

Of 4,430 osteosarcoma patients identified, 810 cases were axial and 3,435 were appendicular. Multivariate Cox analysis showed that the likelihood of death for all patients significantly increased with age category, distant metastases (Incidence Rate Ratio (IRR=3.83, p≤0.001), and treatment with radiation alone (IRR=7.35, p<0.001) and significantly decreased for appendicular primary site (IRR=0.71, p<0.001), and treatment with surgery alone (IRR=0.38, p<0.001) or surgery plus chemotherapy (IRR=0.60, p<0.001).

Analysis of axial and appendicular tumors separately, the likelihood of death for the axial group significantly increased with age, distant metastases (IRR=3.39, p<0.001), and treatment with chemotherapy (IRR=1.68, p=0.001), but decreased with surgical treatment (IRR=0.44, p<0.001). Additionally, the likelihood of death for the appendicular group increased significantly with age, metastases (IRR=3.96 p<0.001), and radiation treatment (IRR=16.575, p=0.006), and decreased significantly for females (IRR=0.80, p<0.001), surgical treatment (IRR=0.30, p<0.001), and treatment with surgery plus chemotherapy (IRR=0.48, p<0.001).

Figure 1: *Long-term survival of all patients with and without distant metastases at the time of presentation (p < 0.001).*

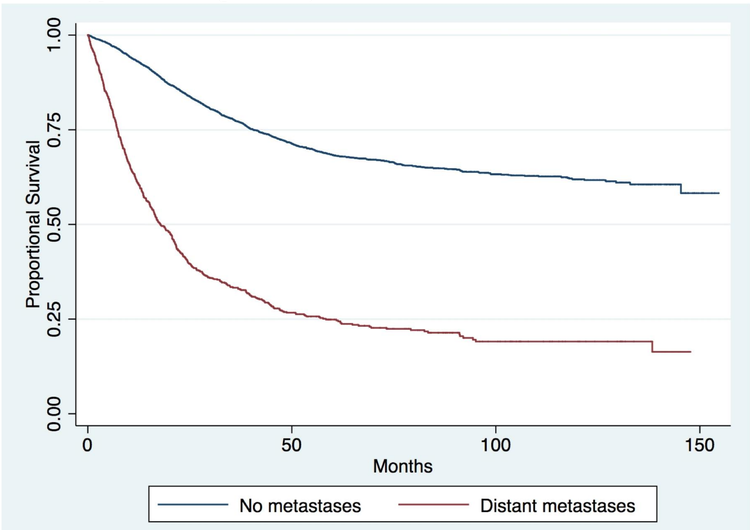


Table 1*: Multivariate Cox analysis of the likelihood of death at any given time for demographic and operative variables for the axial cohort*

Likelihood of death at any given time	IRR*	95% Confidence Interval			p-value
Age Category					
< 23	Ref	Ref		Ref	Ref
23-45	1.325	1.137	-	1.545	**<0.001**
46-62	2.107	1.734	-	2.561	**<0.001**
62+	3.528	2.695	-	4.619	**<0.001**
Sex					
Male	Ref	Ref		Ref	Ref
Female	0.798	0.707	-	0.9	**<0.001**
Metastasis at time of diagnosis					
Yes	3.958	3.478	-	4.505	**<0.001**
Year of diagnosis					
2004-2007	Ref	Ref		Ref	Ref
2008-2011	1.102	0.966	-	1.258	0.149
2012-2015	0.965	0.815	-	1.142	0.677
Treatment choice			-		
None	Ref	Ref		Ref	Ref
Surgery	0.305	0.227	-	0.411	**<0.001**
Radiation	16.575	2.263	-	121.416	**0.006**
Chemotherapy	0.919	0.707	-	1.193	0.525
Surgery and radiation	0.599	0.309	-	1.165	0.131
Surgery and chemotherapy	0.476	0.375	-	0.605	**<0.001**
Radiation and chemotherapy	5.62	0.767	-	41.161	0.089
Unknown	0.363	0.217	-	0.606	**<0.001**

***IRR = Incidence Rate Ratio; defined as the incidence rate of the exposed population divided by the total number of people at risk of death at any one point in time.**

Table 2: Multivariate Cox analysis of the likelihood of death at any given time for demographic and operative variables for `the appendicular cohort.

Likelihood of death at any given time	IRR*	95% Confidence Interval			p-value
Age Category					
< 23	Ref	Ref		Ref	Ref
23-45	1.496	1.094	-	2.045	**0.012**
46-62	2.243	1.614	-	3.117	**<0.001**
62+	4.088	2.776	-	6.020	**<0.001**
Sex					
Male	Ref	Ref		Ref	Ref
Female	0.782	0.641	-	0.955	0.016
Metastasis at time of diagnosis					
Yes	3.393	2.659	-	4.330	**< 0.001**
Year of diagnosis					
2004-2007	Ref	Ref		Ref	Ref
2008-2011	1.008	0.804	-	1.263	0.947
2012-2015	0.844	0.644	-	1.106	0.218
Treatment choice					
None	Ref	Ref		Ref	Ref
Surgery	0.443	0.309	-	0.637	**< 0.001**
Radiation	4.533	1.044	-	19.683	0.044
Chemotherapy	1.682	1.241	-	2.279	**0.001**
Surgery and radiation	0.840	0.514	-	1.372	0.486
Surgery and chemotherapy	0.788	0.592	-	1.049	0.103
Radiation and chemotherapy	8.244	1.046	-	64.997	0.045
Unknown	0.883	0.533	-	1.465	0.631

***IRR = Incidence Rate Ratio; defined as the incidence rate of the exposed population divided by the total number of people at risk of death at any one point in time.**

Figure 2**:** *Long-term survival of patients in the axial, appendicular, and other cohorts (p < 0.001).*

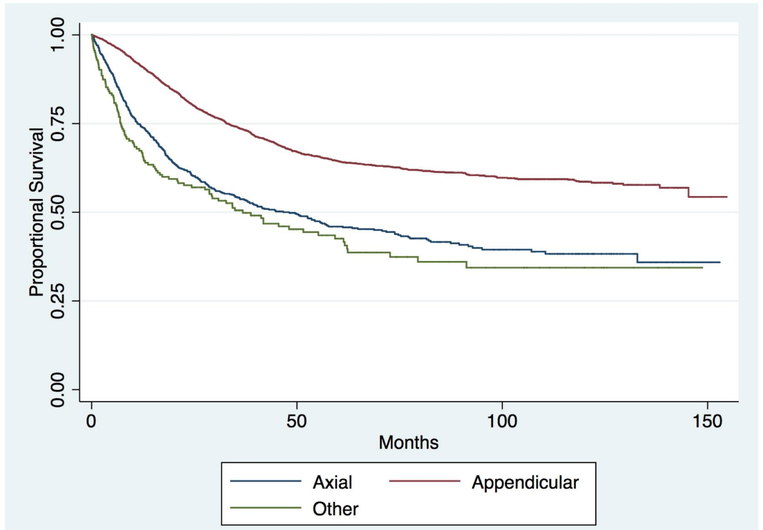
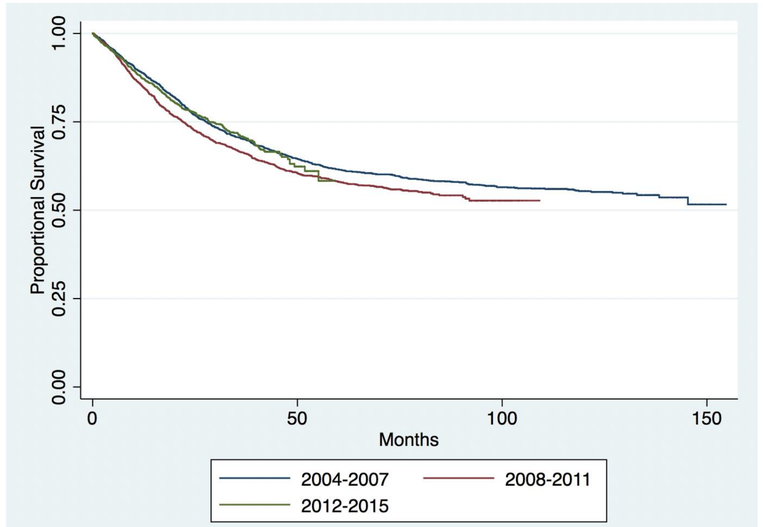


Figure 3*: Long-term survival of patients in the three era groups (p = 0.022).*



Conclusions

Despite advances in tumor management, the current study found surgical excision to be the best predictor of survival for both axial and appendicular osteosarcomas. There is no difference in patient survival from 2004 to 2015 suggesting that newer therapies may be equally effective compared to traditional management of osteosarcoma. Presence of distant metastases is a significant, poor prognostic sign as is increasing age and male gender. Presence of primary osteosarcoma of the appendicular skeleton was found to be a good prognostic sign when compared to axial involvement potentially due to ease of operability.

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