Inferior Outcomes for Osteosarcoma After Non-Adherence with NCCN Guidelines in the United States: Nationwide Results

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INTRODUCTION:

Adherence to evidence-based treatment guidelines and its survival impact remains unclear for bone sarcomas. This study aimed to determine rates of, survival outcomes and factors associated with adherence to the National Comprehensive Cancer Network (NCCN) treatment guideline for osteosarcoma.

METHODS:

Patients within the National Cancer Data Base treated for osteosarcoma from 2004 to 2015 were identified. Adherence to histology/stage-specific NCCN guidelines was determined and overall survival was estimated according to the adherence. Multivariate logistic regression analyses (MVA) were performed to determine factors associated with adherence/nonadherence.

RESULTS:

Among 5,086 patients included in the final cohort, 3,482 (75.5%) received recommended treatment described in the NCCN guideline. Adherence rates for low-grade/parosteal, periosteal (intermittent-grade), high-grade (localized), and metastatic osteosarcoma were 86.8%, 82.4%, 70.1%, and 93.5%, respectively. Overall survival was significantly higher in patients with adherent treatment versus nonadherent treatment across all histology/stages: low-grade/parosteal/periosteal, 89.3% versus 79.6% (5-year; P = 0.029); high-grade (localized), 66.6% versus 45.6% (P < 0.001); metastatic, 22.3% versus 5.0% (P < 0.001). For low-grade/parosteal and periosteal osteosarcoma, major factor of nonadherence to the guideline was positive surgical margin, which was seen in 11.3% and 8.1%, respectively. For high-grade OS (localized), factors regarded as nonadherence to the guideline included no receipt of chemotherapy (11.3%) or surgical treatment (10.8%), and positive surgical margin (9.5%). On MVA, receipt of sarcoma care at academic/research institute was an only factor that was commonly and independently associated with the receipt of adherent treatments for all of the histological subtypes in patients with localized osteosarcoma.

DISCUSSION AND CONCLUSION:

The treatment adherence to the NCCN guideline for osteosarcoma was associated with improved survival outcomes. Receipt of sarcoma care at academic/research institutes was associated with higher adherence rates, highlighting the importance of referral to the specialized institutes for osteosarcoma regardless of the histological subtype and tumor stage.

Figure 1

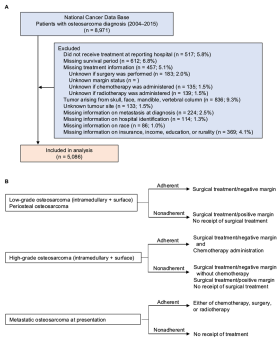

Figure 2

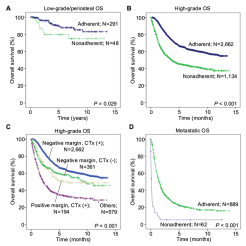

Table 1. Patient demographic, clinical, and hospital-related characteristics

Characteristics	Total (N = 5086)	Low-grade OS (N = 205; 5.2%)		Intermediate OS (N = 76 ; 1.9%)		High-grade OS (N = 3796; 74.6%)		Metastatic OS (N = 911; 18.7%)		p value
	N	N	(%)	N	(%)	N	(%)	N	(%)	
Age (median)	21	29		27		20		19		<0.001
<65 year	3613	71.2%	159	75.9%	60	85.1%	2761	69.4%	633	69.6%
≥65 year	1473	28.9%	47	24.1%	16	14.9%	1035	26.6%	317	30.4%
Sex										0.031
Male	2954	56.1%	76	36.2%	40	54.9%	2142	53.9%	547	59.6%
Female	2132	43.9%	129	63.8%	26	45.1%	1654	46.1%	364	40.4%
Race										0.062
White	3295	64.6%	174	85.4%	47	63.1%	2417	63.8%	615	67.5%
Black	827	16.2%	30	14.1%	13	20.5%	648	16.9%	141	15.4%
Hispanic	661	13.4%	29	13.9%	9	13.8%	520	12.4%	143	15.1%
Asian	172	3.4%	7	3.0%	3	4.5%	135	3.4%	27	2.9%
Other	131	2.7%	5	1.3%	1	1.4%	95	2.3%	27	1.8%
Comorbidity										0.152
0	4573	89.9%	157	69.4%	70	94.6%	3427	89.2%	838	89.1%
1	430	8.3%	32	14.4%	2	4.2%	303	7.8%	87	9.1%
2	86	1.9%	7	1.3%	1	1.0%	66	1.7%	26	2.7%
Tumor size										<0.001
5.1-8.0cm	1730	34.0%	118	56.6%	25	47.2%	1158	34.1%	203	17.2%
10.0-15.0cm	2570	50.6%	102	38.5%	38	44.8%	1932	48.6%	509	54.5%
>15.0cm	781	15.4%	17	4.7%	8	7.7%	706	12.8%	219	28.3%
Tumor site										<0.001
Extremity	4261	83.8%	218	97.4%	79	94.6%	3224	85.1%	739	74.6%
Trunk	825	16.2%	7	2.6%	4	5.4%	572	14.9%	242	25.4%
Facility type										<0.001
Academic/research	3706	72.9%	213	85.4%	50	67.6%	2773	68.7%	670	70.5%
Comprehensive community	728	14.3%	12	4.8%	9	12.2%	556	14.5%	141	15.2%
Community	68	1.4%	2	0.8%	1	1.4%	44	1.1%	19	2.1%
Integrated network	583	11.7%	24	12.9%	14	18.9%	472	18.5%	112	11.8%
Region										<0.001
Private	1040	19.6%	178	86.4%	48	64.9%	2135	56.2%	503	52.7%
Medicare	1777	33.5%	18	9.3%	3	4.3%	408	18.3%	312	34.9%
Medicaid	1115	21.0%	46	17.4%	14	21.6%	812	20.7%	221	24.8%
Other government	1123	21.2%	19	10.2%	6	10.8%	827	22.0%	271	30.4%
Uninsured	247	4.5%	12	7.2%	4	5.4%	172	4.3%	52	5.3%
Zip-median income ($) (year)										0.642
< 35,999	876	16.2%	45	17.8%	13	17.6%	736	18.4%	169	18.8%
36,000-47,999	1293	24.1%	55	20.8%	23	30.1%	929	23.4%	243	26.0%
48,000-62,999	1347	25.1%	60	22.6%	18	23.7%	1000	25.1%	269	28.8%
> 63,000	1134	20.6%	60	22.2%	13	23.7%	1134	28.5%	242	26.2%
Zip-median educ (%)										0.089
< 13%	1204	23.7%	75	28.3%	13	17.6%	914	23.6%	302	33.2%
13%-20.9	1454	28.4%	80	25.2%	23	31.2%	1127	28.3%	224	27.8%
21.0%-25.9	1446	28.4%	60	24.5%	23	30.2%	995	28.6%	261	27.6%
> 26.0	1044	20.5%	45	17.6%	15	20.5%	760	19.1%	224	25.6%
Rurality										0.254
Metropolitan	4277	84.1%	218	86.8%	58	76.4%	3188	83.5%	763	82.2%
Suburban	765	15.0%	30	12.0%	12	24.0%	505	13.2%	218	14.6%
Rural	164	3.2%	7	2.8%	4	5.4%	71	1.8%	32	2.3%
Distance										0.063
<25 miles	2455	48.4%	95	38.0%	20	31.2%	1508	39.4%	310	35.8%
25-50 miles	2441	48.1%	96	38.2%	25	39.2%	1539	38.7%	381	40.5%
51-100 miles	770	15.1%	42	12.8%	15	23.2%	575	14.1%	138	14.1%
>100 miles	400	8.1%	32	20.6%	7	9.4%	544	13.9%	111	14.2%
Median income										0.048
North	665	13.1%	33	13.0%	10	13.0%	513	13.5%	131	13.6%
Mountain	267	5.3%	13	7.3%	2	2.7%	227	5.7%	40	5.2%
West North Central	397	8.0%	16	7.0%	6	8.1%	284	7.5%	91	9.4%
East North Central	840	16.6%	34	15.6%	9	12.2%	642	16.9%	155	16.0%
South Atlantic	770	15.2%	42	18.8%	12	16.8%	571	15.0%	145	15.2%
New England	135	2.7%	7	2.6%	1	1.4%	98	2.5%	33	3.4%
West South Central	400	7.9%	13	7.2%	5	6.8%	301	7.9%	75	7.9%
East South Central	224	4.4%	12	5.7%	3	4.0%	170	4.5%	39	4.2%
South Atlantic	1212	23.8%	60	22.8%	22	29.7%	856	22.5%	282	32.0%

Table 2. Multivariate analysis with logistic regression model adjusted for covariates to estimate the adherence to the CPG in patients for high-grade osteosarcoma

Covariate	Adjusted Odds Ratio (OR)	95% CI	p value
Age (years)			
<60 year	1	Reference	
>60 year	2.28	1.68-2.77	<0.001
Sex			
Male	1	Reference	
Female	1.19	1.01-1.39	0.036
Race			
White	1	Reference	
Black	1.32	1.03-1.68	0.027
Hispanic	1.25	0.96-1.64	0.102
Asian	1.07	0.68-1.68	0.783
Other	1.16	0.66-1.98	0.582
Comorbidity index			
0	1	Reference	
1	0.86	0.64-1.16	0.321
≥ 2	1.21	0.67-2.18	0.523
Tumor size (cm)			
≤8.0 cm	1	Reference	
>8.0 cm	0.79	0.66-0.93	0.086
Unknown	2.32	1.98-2.68	<0.001
Tumor site			
Extremity	1	Reference	
Trunk	3.68	2.98-4.58	<0.001
Facility			
Conventional OS	1	Reference	
Telangiectatic OS	0.87	0.43-1.04	0.072
Small cell OS	0.96	0.39-2.38	0.932
Low-grade OS	1.45	0.53-3.98	0.469
High-grade surface OS	1.45	0.53-3.38	0.395
Facility type			
Community/research	1	Reference	
Academic/research	1.32	1.18-1.71	<0.001
Insurance status			
Private	1	Reference	
Medicare	3.76	2.65-4.56	<0.001
Medicaid	1.29	0.90-1.84	0.161
Other government	1.27	0.75-2.14	0.341
Uninsured	1.78	1.25-2.55	0.002
Zip-median level income ($)			
< 35,999	1	Reference	
36,000-47,999	0.98	0.68-1.14	0.349
48,000-62,999	0.94	0.63-1.11	0.214
> 63,999	0.89	0.64-1.24	0.550
Zip-median education (%)			
<7%	1	Reference	
7-12.9%	1.30	0.78-1.27	0.970
13-20.9%	1.12	0.79-1.59	0.407
≥21%	0.77	0.56-1.08	0.137
Rurality			
Rural	1	Reference	
Suburban	1.17	0.95-1.51	0.238
Metropolitan	1.31	0.94-2.32	0.150
Facility location			
Pacific	0.96	0.72-1.28	0.785
Mountain	0.80	0.53-1.21	0.291
West North Central	0.89	0.53-1.28	0.601
East North Central	0.89	0.68-1.15	0.382
Middle Atlantic	1.16	0.86-1.51	0.287
New England	0.69	0.41-1.18	0.179
West South Central	1.12	0.79-1.59	0.527
East South Central	1.16	0.78-1.66	0.379
South Atlantic	1	Reference	
Distance			
<25 miles	1	Reference	
11-50 miles	0.88	0.72-1.07	0.205
51-100 miles	0.76	0.60-1.03	0.084
>100 miles	0.54	0.40-.84	0.001