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Association between Treatment at High-Volume Facilities and Improved Overall Survival in Soft Tissue Sarcomas

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Abstract

Background—Soft tissue sarcomas (STS) are rare malignancies requiring complex multidisciplinary management. Therefore, facilities with high sarcoma case volume may demonstrate superior outcomes. We hypothesized that STS treatment at high-volume facilities is associated with improved overall survival (OS).

Methods—Patients 18 years with non-metastatic STS treated with surgery and radiotherapy at a single facility from 2004–2013 were identified from the National Cancer Database (NCDB). Facilities were dichotomized into high-volume (HV) and low-volume (LV) cohorts based on total case volume over the study period. OS was assessed using multivariable Cox regression with propensity-score matching. Patterns of care were assessed using multivariable logistic regression analysis.

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Results—Of 9,025 total patients, 1,578 (17%) and 7,447 (83%) were treated at HV and LV facilities, respectively. On multivariable analysis, high educational attainment, larger tumor size, higher grade, and negative surgical margins were statistically significantly associated with treatment at HV facilities; conversely, black race and non-metropolitan residence were negative predictors of treatment at HV facilities. On propensity-score matched multivariable analysis, treatment at HV facilities versus LV facilities was associated with improved OS (hazard ratio (HR) = 0.87, 95% CI: 0.80–0.95, $p = 0.001$). Older age, lack of insurance, greater comorbidity, larger tumor size, higher tumor grade, and positive surgical margins were associated with statistically significantly worse OS.

Conclusions—In this observational cohort study using the NCDB, receipt of surgery and radiotherapy at HV facilities was associated with improved OS for patients with STS. Potential socio-demographic disparities limit access to care at HV facilities for certain populations. Our findings highlight the importance of receipt of care at HV facilities for patients with STS, and warrant further study into improving access to care at HV facilities.

Keywords

Sarcoma; Radiotherapy; Surgery; Hospital Volume; Healthcare Disparities

Introduction

Soft tissue sarcomas (STS) are a rare and heterogeneous group of malignant mesenchymal tumors consisting of more than 50 different histologic subtypes that comprise less than 1 percent of all adult malignancies.¹ Optimal care of patients with STS requires a multidisciplinary approach involving surgery, radiation oncology, medical oncology, radiology, and pathology. Given the rare nature of these cancers, and the complexity of diagnosis and treatment, National Comprehensive Cancer Network (NCCN) guidelines recommend that all patients with STS “be evaluated and managed by a multidisciplinary team with extensive expertise and experience in the treatment of sarcoma.”²

Facility case volume, defined as the number of cases of a particular disease managed by a treatment facility, is commonly used as a proxy for management expertise and experience.³ A growing body of literature has elucidated an association between facility case volume and improved patient outcomes for both oncologic^{4,5} and non-oncologic conditions.^{6–8} Such volume-outcomes studies in patients with STS are limited.⁹ Therefore, we assessed a large modern cohort of patients using a nationwide cancer registry to explore the relationship between facility case volume and overall survival (OS) in STS. Given the uncommon nature of STS and its multifaceted treatment paradigm, we hypothesized that treatment at high-volume (HV) facilities is associated with improved OS compared to treatment at low-volume (LV) facilities.

Materials and Methods

Data Source

The study cohort was identified from the National Cancer Database (NCDB),^{10,11} a national cancer registry that is sponsored by the American College of Surgeons and the American

Cancer Society, which draws on hospital registry data from more than 1,500 Commission on Cancer (CoC) accredited facilities in the United States and Puerto Rico. The database captures approximately 70% of incident cancers in these regions and contains more than 34 million unique cancer cases. Data are collected prospectively from CoC-accredited program cancer registries with nationally standardized data coding definitions.¹²

Study Population

Inclusion criteria consisted of patients 18 years of age with non-metastatic STS treated with definitive surgery and either pre-operative or post-operative external beam radiotherapy from 2004–2013. The entire course of surgical and radiation treatment must have been performed at the reporting facility; patients treated at multiple facilities were excluded. Common adult STS histologies such as undifferentiated/unclassified histology, undifferentiated pleomorphic sarcoma, liposarcoma, leiomyosarcoma, fibrosarcoma, synovial sarcoma, and angiosarcoma were included; histologies primarily encountered in the pediatric population and those primarily treated with chemotherapy such as rhabdomyosarcoma and Ewing sarcoma were excluded. Patients with STS arising in the head and neck, extremities, thorax, trunk, abdomen and pelvis (*International Classification of Diseases for Oncology, Third Edition*, codes 490 – 499) were included. The cohort was limited to those who received between 4,000 to 7,500 cGy of total radiation dose, which we felt to be a conventional dose range for treatment of STS. Lastly, patients with missing follow-up information were excluded, culminating in a final cohort of 9,205 patients (Figure 1).

Patient Cohorts and Variables

For the primary analysis, the study cohort was dichotomized into HV facilities and LV facilities arms. HV facilities (n=11) were defined as facilities in the top 1 percentile (99th percentile or higher) by case volume (79–252 cases) over the study period; the remainder of the facilities were defined as LV facilities. The 99th percentile was selected *a priori* as the cutoff for defining study arms based on the left-skew distribution of the dataset which showed a small number of facilities treating a large volume of patients each, and many facilities treating a small number of patients each (Supplemental Figure 1). The patient cohort was then divided into more granular groupings (0–49th, 50–89th, 90–98th, and 99th percentiles) for secondary analyses; groupings were selected in a way to ensure an even distribution of patients in each group. Case volumes over the study period for each grouping were 1–4, 4–20, 20–78, and 79–252, respectively.

Covariates examined included gender, age, race, population density of patient residence (classified as metropolitan, urban, or rural), facility type (community, academic, or comprehensive community), patient distance to facility, geographic location of facility, primary insurance coverage, level of educational attainment (defined as percentage of the population in the patient's home ZIP code not achieving a high school degree), income (median income in the patient's home ZIP code), Charlson/Deyo comorbidity score, primary site of tumor, tumor histology, tumor size and grade, type of surgical resection, surgical margin status, radiotherapy sequence (pre-operative vs post-operative), receipt of chemotherapy, and year of treatment.

Endpoints

The primary end-point was OS in patients with STS treated at HV facilities compared to LV facilities. OS was defined as time from the date of diagnosis until death or last follow-up. We also sought to assess nationwide patterns of care and disparities with regards to treatment at HV facilities relative to LV facilities.

Statistical Analysis

Baseline characteristics of patients treated at HV and LV facilities were compared using the Pearson χ^2 test. A multivariable logistic regression model was constructed using all baseline covariates to assess the independent effect of each covariate on the odds of being treated at HV facilities relative to LV facilities.

For the primary survival analysis, a Cox proportional hazards regression model was used incorporating only potential confounding covariates that would have been known prior to initiation of any treatment; as such, treatment associated variables such as type of surgery, surgical margin status, radiotherapy sequence, and receipt of chemotherapy were excluded. This model assessed the independent effect of treatment at HV facilities on OS relative to LV facilities. A secondary Cox regression model was fitted to include all covariates selected for the initial model as well as treatment associated covariates to study the impact of treatment at HV facilities independent of the treatment received; this model allowed for the assessment of potential non-treatment associated factors that confer an OS benefit to treatment at HV facilities. The Kaplan-Meier estimator and the log-rank test were used to compare OS between arms. Proportional hazards assumptions were tested with Schoenfeld's residuals tests and were not violated.

To test the robustness of our findings and to further minimize potential bias, we performed two pre-planned sensitivity analyses. The first sensitivity analysis used 1-to-1 nearest neighbor propensity-score matching¹³ without replacement to identify a matched cohort; only covariates that would have been known prior to initiation of treatment were used to estimate the propensity scores. The propensity score-matched cohort consisted of 3,156 patients – all 1,578 patients from the HV facilities cohort matched to 1,578 patients from the LV facilities cohort. Once cohorts were appropriately matched on baseline covariates (Supplementary Table 1), a Cox proportional hazards survival analysis was repeated using the matched cohorts. The second sensitivity analysis assessed for the presence of a statistically significant interaction between treatment at HV facilities and treatment at academic facilities in the prediction of OS; the purpose of this analysis was to test whether the observed effect of treatment at HV facilities was modified by receipt of treatment at academic facilities.

For all analyses, a two-sided p value of less than 0.05 was considered statistically significant. All analyses were performed using Stata SE, version 14.0 (College Station, TX).

Results

Patient Characteristics

A total of 9,205 patients met study inclusion criteria and received treatment at 973 facilities. Of these patients, 1,578 (17%) were treated at HV facilities while 7,447 (83%) were treated at LV facilities. The median age of the patient cohort was 61 years (interquartile range: 49–73). Baseline characteristics (Table 1) revealed that most patients were male (56%), older than 50 years (73%), white (79%), and were without significant comorbid illness (83%). It was more common for patients to receive treatment at an academic facility (46%) and at a facility >10 miles from their residence (53%). In terms of disease characteristics, patients presented most often with lower extremity (47%) tumors, Grade 3 disease (56%), and tumor size >5cm (52%). The most common histologies overall were undifferentiated/unclassified histology (25%), liposarcoma (23%), and undifferentiated pleomorphic sarcoma (16%). Most patients underwent radical resection (98%) rather than an amputation, received post-operative rather than preoperative radiotherapy (77%), and did not receive chemotherapy (82%).

Compared to patients treated at LV facilities, patients at HV facilities were statistically significantly more likely to be treated at academic facilities, travel longer distances for treatment, have larger and higher grade tumors, and be treated with pre-operative radiotherapy and chemotherapy. Despite the greater proportion of higher risk tumors, patients treated at HV facilities more commonly had negative surgical margins. There were no differences in baseline comorbidity status (Table 1).

Factors Associated With Treatment at HV Facilities

On multivariable analysis (Table 2), receiving treatment at an academic facility relative to a community facility (OR = 4.58, 95% CI: 3.59–5.85, $p < 0.001$), higher educational attainment (highest versus lowest quartiles, OR = 1.77, 95% CI: 1.31–2.40, $p < 0.001$), tumor size 5 to 10cm versus less than 5cm (OR = 1.22, 95% CI: 1.03–1.45, $p = 0.021$), and grade 3 versus grade 1 disease (OR = 1.57, 95% CI: 1.25–1.97, $p < 0.001$) predicted for increased likelihood of treatment at HV facilities. Treatment at HV facilities was associated with a decreased likelihood of having positive surgical margins (OR = 0.72, 95% CI: 0.60–0.87, $p < 0.001$) and receipt of post-operative versus pre-operative radiotherapy (OR = 0.72, 95% CI: 0.60–0.87, $p < 0.001$), but an increased likelihood of receipt of chemotherapy (OR = 1.33, 95% CI: 1.11–1.59, $p = 0.002$).

Conversely, factors that predicted for decreased likelihood of treatment at HV facilities were black compared to white race (OR = 0.74, 95% CI: 0.58–0.94, $p = 0.013$), being uninsured relative to having commercial insurance (OR = 0.65, 95% CI: 0.45–0.95, $p = 0.024$), and non-metropolitan residence (rural vs metropolitan, OR = 0.42, 95% CI: 0.26–0.67, $p < 0.001$). Baseline patient comorbidity and primary site of disease did not influence likelihood of treatment at HV versus LV facilities. Rates of treatment over time at HV facilities remained stable over the study period.

Overall Survival (OS)

The median follow-up time was 47.9 months (range 2.3 to 142.6) overall. On multivariable analysis, treatment at HV facilities was associated with a statistically significant improvement in OS relative to treatment at LV facilities (HR = 0.81, 95% CI: 0.72 – 0.90, $p = 0.001$) (Table 3). This corresponded to a median survival of 11.6 years in the HV facilities arm and 9.8 years in the LV facilities arm, and to 5- and 10-year OS estimates of 72.2% versus 57.1% and 67.4% versus 49.0%, respectively (Figure 2). The HR and associated confidence interval remained identical when using the secondary Cox regression model adjusting for treatment associated covariates. Other factors associated with improved OS were female gender, high educational attainment, and non-head and neck primary site versus head and neck site.

Factors associated with decreased OS were larger tumor size (>5cm vs <5cm, HR = 1.62, 95% CI: 1.47–1.79, $p = 0.001$), higher grade disease (grade 3 vs grade 1, HR = 2.58, 95% CI: 2.20–3.02, $p = 0.001$) and positive surgical margins (HR = 1.39, 95% CI: 1.27–1.51, $p = 0.001$). Other factors associated with decreased OS were older age, being uninsured compared to having commercial insurance, and greater levels of comorbidity. Radiotherapy sequence and receipt of chemotherapy were not associated with OS.

On sensitivity analysis using the propensity-score matched cohort, treatment at HV facilities remained similarly associated with an improved OS relative to treatment at LV facilities (HR = 0.87, 95% CI: 0.80–0.95, $p = 0.001$) (Table 3).

An analysis of facility volume categorized into 4 groups consisting of facilities ranked at the 0–49th percentiles, 50–89th percentiles, 90–98th percentiles, and 99th and higher percentile for over the study period was also performed. Relative to facilities in the 0–49th percentiles, receipt of treatment at facilities at the 99th or higher percentile (HR = 0.70, 95% CI: 0.61–0.83, $p = 0.001$), 90–98th percentiles (HR = 0.87, 95% CI: 0.76–0.98, $p = 0.023$), and 50–89th percentiles (HR = 0.87, 95% CI: 0.77–0.97, $p = 0.014$) was associated with improved OS on multivariable analysis (Figure 3).

Finally, a test for interaction between treatment at HV facilities and treatment at academic facilities was not statistically significant (HR = 0.93, 95% CI: 0.66–1.32, $p = 0.70$), indicating that the OS benefit associated with HV facilities was not modified by treatment at academic facilities.

Discussion

In this observational study of 9,025 patients with non-metastatic STS using a national cancer registry, we demonstrate an improved OS associated with receipt of surgery and radiotherapy at HV facilities compared to LV facilities. We support this association using both multivariable regression and propensity score-matched models adjusted for multiple potential confounders. To the best of our knowledge, this is the most comprehensive study to examine the association between facility case volume and OS in a nationally representative sample of patients with STS. Our findings suggest that patients with STS, a rare and

heterogeneous group of cancers, benefit from receiving treatment at a facility with robust STS experience.

A patterns of care assessment revealed striking disparities in access to care at HV facilities – black patients, those with low educational attainment, those from non-metropolitan areas, and the uninsured were less likely to receive care at HV facilities. Overall, there appears to be an awareness of the need for expert care particularly in STS cases with high-risk features, as patients with larger and higher grade tumors were more likely to receive care at HV facilities. Patients treated at HV facilities were more likely to have negative surgical margins, an important prognostic factor for disease recurrence,¹⁴ potentially indicating the presence of greater surgical expertise at HV facilities. These superior surgical outcomes, however, may only partly explain the OS benefit associated with treatment at HV facilities; as the overall treatment effect remained unchanged following adjustment for treatment associated variables such as margin status, there are likely other factors besides quality of treatment that lead to superior outcomes at HV facilities. Our findings also suggest that the benefit of treatment at HV facilities is independent of facility academic status; patients may derive similar degree benefit from treatment at experienced, HV community or academic facilities. Finally, this study highlights the concentrated nature of STS treatment in the United States with the top 1 percentile of facilities treating almost one-fifth of all patients, and the top 10 percentile treating almost one-half of all patients.

The association between high facility case volume and improved patient outcomes is a well-documented concept in medicine.^{15–17} This volume-outcomes relationship was first described in the surgical literature where studies demonstrated improved OS in patients undergoing procedures such as cardiac interventions¹⁸ and colectomies¹⁹ at HV facilities. Greater physician skill, fewer surgical complications, and more robust perioperative care are cited as drivers for the improved outcomes.^{15,16} More recently, the volume-outcomes relationship has been studied in oncology, a specialty that frequently delivers complex multimodality care. Prior work has revealed an association between high facility volume and improved OS in solid cancers, such as head and neck,²⁰ lung,²¹ prostate,²² cervical,²³ and rectal cancer,²⁴ and hematologic cancers such as lymphomas²⁵ and multiple myeloma;²⁶ improved outcomes have also been shown with facility surgical volume and radiotherapy/chemotherapy volume.^{27,28}

Volume-outcomes studies in patients with STS are limited, even though patients with such rare diseases arguably stand to benefit most as findings may increase understanding and improvements in access and referrals to specialized care. Gutierrez et al. reported that surgery for STS at high volume surgical centers was an independent predictor of OS in 4,205 patients treated from 1981 to 2001 in Florida.⁹ The generalizability of this study to current practice is limited as it utilized a state cancer registry and it included patients treated almost three decades ago, since which time there have been significant advancements in the management of STS. A recent study by Maurice et al. of patients with retroperitoneal sarcoma showed that high facility surgical volume was associated with improved surgical outcomes.²⁹ By comparison, our study investigates the relationship between both facility surgical and radiotherapy case volume, and OS in a nationally representative modern day cohort of more than 9000 patients with STS.

Our finding of improved OS associated with high facility case volume in patients with STS is not surprising considering the rarity of sarcomas and the complexity of care involved. While high case volume is directly proportional to a facility's treatment experience, it may also be a surrogate measure of the providers' expertise, practice paradigms, ability to manage complications, and the availability of a supportive infrastructure to navigate patients through treatment. Besides greater surgical expertise, we postulate that there are other factors driving the improved OS outcomes at HV facilities, such as greater fidelity to national care guidelines,³⁰ established facility care pathways,³¹ multidisciplinary tumor boards to discuss complex cases,³² availability of clinical trials,³³ and superior compliance with clinical trial protocols, all of which have been correlated with improved patient outcomes.^{34,35,36,37} Such systems' qualities specific to sarcoma care are less likely to be available at facilities seeing only a small number of patients with STS. Finally, it is possible that improved outcomes at HV facilities are influenced by patient-related factors such as socioeconomic status and patient willingness to seek treatment at specific facilities. This factors may be reflected in our analysis by long travel distance to treatment being associated with treatment at HV facilities.

Our study is subject to certain limitations. Given its non-randomized, retrospective design, there is likely selection bias that influences the receipt of treatment at HV facilities versus LV facilities, and this bias may have affected the observed results. If present, however, such a selection bias might favor the LV facilities arm as patients receiving treatment at HV facilities were more likely to have more advanced disease such as larger tumors and higher grade disease, factors associated with poorer survival outcomes in STS.³⁸ Nevertheless, we attempted to limit selection bias by performing a secondary survival analysis using cohorts matched by propensity-score. While propensity-score matching accounts for measured confounders, our analysis may still subject to unmeasured confounding. Finally, we are limited by the variables recorded by the NCDB and we are therefore unable to study endpoints such as STS-specific survival, recurrence-free survival, and toxicity outcomes. Despite these shortcomings, our conclusions are concordant with studies of other malignancies demonstrating an association between high facility case volume and improved OS.^{20–28}

In summary, this observational study using the NCDB demonstrates that receipt of surgery and radiotherapy at HV facilities is associated with improved OS compared to receipt of treatment at LV facilities for patients with STS. These results may be reflective of greater physician expertise, increased resource availability, and delivery of highly coordinated care for STS at HV facilities. Additionally, disparities may limit certain populations from receiving care at HV facilities. Our findings underscore the importance of receipt of STS care at facilities with the highest case volumes, and may warrant further study into finding ways to improve access to care at HV facilities for patients with STS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Summary

Patients with soft tissue sarcomas, a group of rare malignancies that require complex management, may benefit from care at high-volume treatment facilities as such facilities may offer greater physician expertise, superior resource availability, and delivery of highly coordinated care. Using the National Cancer Database, we demonstrate an association between high facility case volume and overall survival in patients with soft tissue sarcomas; these findings support centralization of care for sarcomas.

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Figure 1.
Consolidated Standards of Reporting Trials (CONSORT) diagram.

Figure 2.

Overall survival in high-volume facilities and low-volume facilities arms (log rank $p < 0.001$).

HV: High-volume. *LV*: Low-volume

Figure 3.
Overall survival according to percentiles of facility case volume (log rank $p < 0.001$).

Table 1

Baseline characteristics

	Low Volume Facilities (%)	High Volume Facilities (%)	Total	p-value (chi2)
Total no.	7447 (83)	1578 (17)	9025 (100)	
Sex				0.82
Male	4181 (56)	891 (56)	5072 (56)	
Female	3266 (44)	687 (44)	3953 (44)	
Age, y				<0.001
49	1938 (26)	452 (29)	2390 (26)	
50–69	2999 (40)	708 (45)	3707 (41)	
70	2510 (34)	418 (26)	2928 (32)	
Race				<0.001
Non-Hispanic White	5819 (78)	1346 (85)	7165 (79)	
Non-Hispanic Black	769 (10)	125 (8)	894 (10)	
Hispanic	478 (6)	51 (3)	529 (6)	
Other	381 (5)	56 (4)	437 (5)	
County size				<0.001
Metropolitan	6110 (82)	1204 (76)	7314 (81)	
Urban	972 (13)	258 (16)	1230 (14)	
Rural	129 (2)	43 (3)	172 (2)	
Unknown	236 (3)	73 (5)	309 (3)	
Facility Location				<0.001
East	1568 (21)	197 (12)	1765 (20)	
South	1930 (26)	627 (40)	2557 (28)	
Central	1653 (22)	506 (32)	2159 (24)	
West	1369 (18)	18 (1)	1387 (15)	
Unknown	927 (13)	230 (15)	1157 (13)	
Facility type				<0.001
Community	1069 (14)	106 (7)	1175 (13)	
Academic	2961 (40)	1175 (74)	4136 (46)	
Comprehensive Community	2490 (33)	67 (4)	2557 (28)	
Unknown	927 (12)	230 (15)	1157 (13)	
Distance to Treatment				<0.001
10 miles	3848 (52)	282 (18)	4130 (46)	
>10–50 miles	2817 (38)	618 (39)	3435 (38)	
>50 miles	698 (9)	648 (41)	1346 (15)	
Unknown	84 (1)	30 (2)	114 (1)	
Insurance status				<0.001
Commercial Insurance	3686 (49)	844 (53)	4530 (50)	

	Low Volume Facilities (%)	High Volume Facilities (%)	Total	p-value (chi2)
Medicare	2890 (39)	566 (36)	3456 (38)	
Medicaid	404 (5)	57 (4)	461 (5)	
Uninsured	276 (4)	51 (3)	327 (4)	
Other Government/Unknown	191 (3)	60 (4)	251 (3)	
Education				0.004
29%	1024 (14)	169 (11)	1193 (13)	
20%–28.9%	1511 (20)	335 (21)	1846 (20)	
14%–19.9%	1679 (23)	361 (23)	2040 (23)	
<14%	2951 (40)	633 (40)	3584 (40)	
Unknown	282 (4)	80 (5)	362 (4)	
Income (\$)				0.002
<30,000	774 (10)	164 (10)	938 (10)	
30,000–35,000	1182 (16)	254 (16)	1436 (16)	
35,000–45,999	1917 (26)	454 (29)	2371 (26)	
>46,000	3294 (44)	626 (40)	3920 (43)	
Unknown	280 (4)	80 (5)	360 (4)	
Charlson/Deyo Comorbidity Score				0.72
0	6220 (84)	1308 (83)	7528 (83)	
1	1001 (13)	224 (14)	1225 (14)	
2	226 (3)	46 (3)	272 (3)	
Primary Site				<0.001
Head and Neck	510 (7)	80 (5)	590 (7)	
Upper Extremity	1195 (16)	256 (16)	1451 (16)	
Lower Extremity	3341 (45)	868 (55)	4209 (47)	
Thorax/Trunk	1038 (14)	167 (11)	1205 (13)	
Abdomen/Pelvis	1169 (16)	178 (11)	1347 (15)	
Other/NOS	194 (3)	29 (2)	223 (2)	
Histology				<0.001
Undifferentiated/Unclassified	1822 (25)	452 (29)	2274 (25)	
Undifferentiated Pleomorphic Sarcoma	1242 (17)	185 (12)	1427 (16)	
Fibrosarcoma/Fibromyxosarcoma	969 (13)	253 (16)	1222 (14)	
Liposarcoma	1748 (23)	345 (22)	2093 (23)	
Leiomyosarcoma	994 (13)	172 (11)	1166 (13)	
Synovial Sarcoma	416 (6)	126 (8)	542 (6)	
Angiosarcoma	256 (3)	45 (3)	301 (3)	
Size				<0.001
<5cm	2437 (33)	413 (26)	2850 (33)	
5.1–10cm	2507 (34)	578 (37)	2085 (23)	
10cm	2085 (28)	522 (33)	2607 (29)	

	Low Volume Facilities (%)	High Volume Facilities (%)	Total	p-value (chi2)
Unknown	418 (6)	65 (4)	483 (5)	
Grade				<0.001
1	955 (13)	163 (10)	1118 (12)	
2	1069 (14)	193 (12)	1262 (14)	
3	3981 (54)	1071 (68)	5052 (56)	
Unknown	1442 (19)	151 (10)	1593 (18)	
Surgery				0.44
Limb Salvage/Radical Resection	7318 (98)	1555 (99)	8873 (98)	
Amputation	129 (2)	23 (1)	152 (2)	
Surgical Margins				<0.001
Negative	5360 (72)	1285 (81)	6645 (74)	
Positive	1660 (22)	224 (14)	1884 (21)	
Unknown	427 (6)	69 (4)	496 (5)	
Radiation Therapy				<0.001
Pre-Op RT	1442 (19)	591 (37)	2033 (23)	
Post-Op RT	6005 (81)	987 (63)	6992 (77)	
Chemotherapy				<0.001
No	6244 (84)	1187 (75)	7431 (82)	
Yes	981 (13)	355 (23)	1336 (15)	
Unknown	222 (3)	36 (2)	258 (3)	
Year				0.002
2004–2006	2296 (31)	431 (27)	2727 (30)	
2007–2009	2623 (35)	544 (35)	3167 (35)	
2010–2013	2528 (34)	603 (38)	3131 (35)	

Table 2

Factors associated with treatment at High Volume Facilities

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Sex				
Male	–	–	–	–
Female	0.99 [0.88, 1.10]	0.82	0.96 [0.84, 1.10]	0.58
Age, y				
49	–	–	–	–
50–69	1.01 [0.89, 1.15]	0.86	1.06 [0.86, 1.30]	0.60
70	0.71 [0.62, 0.83]	<0.001	0.87 [0.66, 1.14]	0.31
Race				
Non-Hispanic White	–	–	–	–
Non-Hispanic Black	0.70 [0.58, 0.86]	<0.001	0.74 [0.58, 0.94]	0.013
Hispanic	0.46 [0.34, 0.62]	<0.001	0.73 [0.52, 1.03]	0.075
Other	0.64 [0.48, 0.85]	0.002	0.94 [0.67, 1.33]	0.74
County size				
Metropolitan	–	–	–	–
Urban	1.35 [1.16, 1.57]	<0.001	0.51 [0.41, 0.63]	<0.001
Rural	1.69 [1.19, 2.40]	0.003	0.42 [0.27, 0.67]	<0.001
Unknown	1.57 [1.20, 2.06]	0.001	1.14 [0.75, 1.74]	0.53
Location				
East	–	–	–	–
South	1.27 [1.07, 1.50]	0.006	3.29 [2.68, 4.05]	<0.001
Central	1.02 [0.86, 1.21]	0.81	2.86 [2.32, 3.52]	<0.001
West	0.05 [0.03, 0.09]	<0.001	0.10 [0.06, 0.16]	<0.001
Unknown	omitted	–	6.28 [4.33, 9.12]	<0.001
Facility type				
Community Center	–	–	–	–
Academic Center	4.00 [3.24, 4.94]	<0.001	4.58 [3.59, 5.85]	<0.001
Comprehensive Community Center	0.27 [0.20, 0.37]	<0.001	0.48 [0.34, 0.68]	<0.001
Unknown	2.50 [1.96, 3.20]	<0.001	6.18 [4.26, 8.98]	<0.001
Distance to Treatment				
10 miles	–	–	–	–
>10–50 miles	2.99 [2.58, 3.47]	<0.001	2.58 [2.19, 3.05]	<0.001
>50 miles	12.7 [10.8, 14.9]	<0.001	11.4 [9.24, 14.0]	<0.001
Unknown	4.87 [3.16, 7.52]	<0.001	2.20 [1.08, 4.51]	0.031
Insurance status				
Commercial Insurance	–	–	–	–
Medicare	0.86 [0.76, 0.96]	0.009	1.15 [0.94, 1.40]	0.17

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Medicaid	0.62 [0.46, 0.82]	0.001	0.73 [0.52, 1.02]	0.063
Uninsured	0.81 [0.59, 1.10]	0.17	0.65 [0.45, 0.95]	0.024
Other Government/Unknown	1.37 [1.02, 1.85]	0.039	1.22 [0.84, 1.76]	0.29
Education				
29%	–	–	–	–
20%–28.9%	1.34 [1.10, 1.64]	0.004	1.40 [1.08, 1.82]	0.011
14%–19.9%	1.30 [1.07, 1.59]	0.009	1.53 [1.15, 2.04]	0.003
<14%	1.30 [1.08, 1.56]	0.005	1.77 [1.31, 2.40]	<0.001
Unknown	1.72 [1.28, 2.31]	<0.001	2.40 [0.17, 34.5]	0.99
Income (\$)				
<30,000	–	–	–	–
30,000–35,000	1.01 [0.82, 1.26]	0.90	0.80 [0.61, 1.06]	0.12
35,000–45,999	1.12 [0.92, 1.36]	0.27	0.92 [0.69, 1.22]	0.54
>46,000	0.90 [0.74, 1.08]	0.26	0.73 [0.53, 1.01]	0.052
Unknown	1.35 [1.00, 1.82]	0.051	0.73 [0.05, 9.76]	0.99
Charlson/Deyo Comorbidity Score				
0	–	–	–	–
1	1.06 [0.91, 1.24]	0.44	1.08 [0.89, 1.31]	0.42
2	0.97 [0.70, 1.34]	0.84	1.10 [0.75, 1.63]	0.62
Primary Site				
Head and Neck	–	–	–	–
Upper Extremity	1.37 [1.04, 1.79]	0.025	1.37 [0.98, 1.92]	0.065
Lower Extremity	1.66 [1.29, 2.12]	<0.001	1.30 [0.95, 1.79]	0.100
Thorax/Trunk	1.03 [0.77, 1.37]	0.86	1.01 [0.71, 1.44]	0.95
Abdomen/Pelvis	0.97 [0.73, 1.29]	0.84	0.80 [0.56, 1.14]	0.21
Other/NOS	0.95 [0.60, 1.50]	0.84	0.92 [0.53, 1.59]	0.76
Histology				
Undifferentiated/Unclassified	–	–	–	–
Undifferentiated Pleomorphic Sarcoma	0.60 [0.50, 0.72]	<0.001	0.80 [0.64, 1.00]	0.049
Fibrosarcoma/Fibromyxosarcoma	1.05 [0.89, 1.25]	0.56	1.56 [1.25, 1.93]	<0.001
Liposarcoma	0.80 [0.68, 0.93]	0.004	1.19 [0.97, 1.46]	0.099
Leiomyosarcoma	0.70 [0.58, 0.85]	<0.001	0.85 [0.67, 1.08]	0.18
Synovial Sarcoma	1.22 [0.98, 1.53]	0.081	1.23 [0.93, 1.63]	0.16
Angiosarcoma	0.71 [0.51, 0.99]	0.043	1.18 [0.77, 1.80]	0.44
Size				
<5cm	–	–	–	–
5.1–10cm	1.36 [1.19, 1.56]	<0.001	1.22 [1.03, 1.45]	0.021
10cm	1.48 [1.28, 1.70]	<0.001	1.10 [0.90, 1.33]	0.35

	Univariable		Multivariable	
	OR [95% CI]	p-value	OR [95% CI]	p-value
Unknown	0.92 [0.69, 1.22]	0.55	0.81 [0.58, 1.13]	0.21
Grade				
1	–	–	–	–
2	1.06 [0.84, 1.33]	0.63	1.00 [0.76, 1.31]	0.99
3	1.58 [1.32, 1.89]	<0.001	1.57 [1.25, 1.97]	<0.001
Unknown	0.61 [0.48, 0.78]	<0.001	0.55 [0.41, 0.73]	<0.001
Surgery				
Limb Salvage/Radical Resection	–	–	–	–
Amputation	0.84 [0.54, 1.31]	0.44	0.75 [0.45, 1.27]	0.29
Surgical Margins				
Negative	–	–	–	–
Positive	0.56 [0.48, 0.66]	<0.001	0.72 [0.60, 0.87]	0.001
Unknown	0.67 [0.52, 0.88]	0.003	1.01 [0.74, 1.37]	0.96
Radiation Therapy				
Pre-Op RT	–	–	–	–
Post-Op RT	0.40 [0.36, 0.45]	<0.001	0.82 [0.70, 0.95]	0.009
Chemotherapy				
No	–	–	–	–
Yes	1.90 [1.66, 2.18]	<0.001	1.33 [1.11, 1.59]	0.002
Unknown	0.85 [0.60, 1.22]	0.38	1.22 [0.80, 1.85]	0.36
Year				
2004–2006	–	–	–	–
2007–2009	1.10 [0.96, 1.27]	0.16	0.91 [0.77, 1.08]	0.30
2010–2013	1.27 [1.11, 1.46]	<0.001	0.99 [0.84, 1.18]	0.95

Table 3

Factors associated with overall survival

	Multivariable (Pre-Treatment Variables Only)		Multivariable (Pre- and Post-Treatment Variables)		Propensity-Score Matched Cohort	
	HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Treatment Center Volume						
Low Volume Facilities	–	–	–	–	–	–
High Volume Facilities	0.81 [0.72, 0.90]	<0.001	0.81 [0.72, 0.90]	<0.001	0.87 [0.80, 0.95]	0.001
Sex						
Male	–	–	–	–		
Female	0.87 [0.81, 0.94]	<0.001	0.87 [0.81, 0.94]	0.001		
Age, y						
49	–	–	–	–		
50–69	1.13 [0.99, 1.30]	0.077	1.13 [0.99, 1.30]	0.081		
70	2.09 [1.79, 2.45]	<0.001	2.05 [1.75, 2.40]	<0.001		
Race						
Non-Hispanic White	–	–	–	–		
Non-Hispanic Black	0.92 [0.80, 1.05]	0.22	0.93 [0.81, 1.07]	0.28		
Hispanic	0.86 [0.71, 1.04]	0.13	0.88 [0.73, 1.07]	0.19		
Other	0.91 [0.75, 1.10]	0.34	0.92 [0.76, 1.12]	0.40		
County size						
Metropolitan	–	–	–	–		
Urban	1.07 [0.96, 1.20]	0.21	1.07 [0.96, 1.20]	0.21		
Rural	1.04 [0.80, 1.35]	0.77	1.02 [0.79, 1.32]	0.17		
Unknown	1.08 [0.88, 1.33]	0.44	0.69 [0.55, 0.87]	0.002		
Location						
East	–	–	–	–		
South	0.95 [0.85, 1.07]	0.57	0.97 [0.86, 1.08]	0.57		
Central	1.03 [0.92, 1.15]	0.41	1.04 [0.93, 1.16]	0.41		
West	1.00 [0.89, 1.13]	0.89	0.99 [0.88, 1.12]	0.89		
Unknown	omitted	–	omitted	–		

	Multivariable (Pre-Treatment Variables Only)		Multivariable (Pre- and Post-Treatment Variables)		Propensity-Score Matched Cohort	
	HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Facility type						
Community Center	–	–	–	–		
Academic Center	0.92 [0.83, 1.03]	0.23	0.93 [0.83, 1.04]	0.21		
Comprehensive Community Center	0.92 [0.82, 1.03]	0.13	0.92 [0.82, 1.04]	0.13		
Unknown	0.68 [0.54, 0.85]	0.001	0.69 [0.55, 0.87]	0.002		
Insurance status						
Commercial Insurance	–	–	–	–		
Medicare	1.34 [1.20, 1.49]	<0.001	1.33 [1.19, 1.47]	<0.001		
Medicaid	1.18 [0.97, 1.44]	0.093	1.18 [0.97, 1.44]	0.095		
Uninsured	1.50 [1.20, 1.88]	<0.001	1.44 [1.15, 1.80]	0.002		
Other Government/Unknown	1.34 [1.06, 1.70]	0.015	1.33 [1.05, 1.69]	0.018		
Education						
29%	–	–	–	–		
20%–28.9%	0.98 [0.86, 1.12]	0.76	0.98 [0.86, 1.12]	0.78		
14%–19.9%	0.85 [0.73, 0.98]	0.028	0.85 [0.73, 0.98]	0.030		
<14%	0.76 [0.65, 0.89]	<0.001	0.76 [0.65, 0.89]	<0.001		
Unknown	4.20 [0.58, 30.1]	0.15	4.09 [0.57, 29.3]	0.16		
Income (\$)						
<30,000	–	–	–	–		
30,000–35,000	1.06 [0.92, 1.23]	0.43	1.05 [0.91, 1.22]	0.50		
35,000–45,999	1.06 [0.91, 1.23]	0.47	1.06 [0.91, 1.24]	0.43		
>46,000	1.08 [0.91, 1.27]	0.37	1.08 [0.92, 1.28]	0.35		
Unknown	0.26 [0.04, 1.88]	0.18	0.26 [0.04, 1.89]	0.19		
Charlson/Deyo Comorbidity Score						
0	–	–	–	–		
1	1.27 [1.15, 1.40]	<0.001	1.27 [1.15, 1.40]	<0.001		
2	1.59 [1.33, 1.90]	<0.001	1.57 [1.31, 1.88]	<0.001		
Primary Site						

	Multivariable (Pre-Treatment Variables Only)		Multivariable (Pre- and Post-Treatment Variables)		Propensity-Score Matched Cohort	
	HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Head and Neck	–	–	–	–		
Upper Extremity	0.63 [0.53, 0.75]	<0.001	0.65 [0.55, 0.77]	<0.001		
Lower Extremity	0.62 [0.53, 0.73]	<0.001	0.65 [0.56, 0.77]	<0.001		
Thorax/Trunk	0.73 [0.61, 0.86]	<0.001	0.76 [0.64, 0.90]	0.001		
Abdomen/Pelvis	0.75 [0.63, 0.90]	0.001	0.75 [0.63, 0.89]	0.001		
Other/NOS	0.89 [0.70, 1.14]	0.36	0.89 [0.69, 1.13]	0.34		
Histology						
Undifferentiated/Unclassified	–	–	–	–		
UPS	0.87 [0.78, 0.97]	0.012	0.88 [0.79, 0.98]	0.019		
Fibrosarcoma/Fibromyxosarcoma	0.74 [0.65, 0.85]	<0.001	0.74 [0.64, 0.85]	<0.001		
Liposarcoma	0.68 [0.60, 0.76]	<0.001	0.68 [0.60, 0.76]	<0.001		
Leiomyosarcoma	0.95 [0.84, 1.08]	0.43	0.96 [0.85, 1.09]	0.56		
Synovial Sarcoma	1.07 [0.88, 1.30]	0.48	1.05 [0.86, 1.27]	0.63		
Angiosarcoma	1.88 [1.56, 2.26]	<0.001	1.87 [1.55, 2.25]	<0.001		
Size						
<5cm	–	–	–	–		
5.1–10cm	1.67 [1.51, 1.84]	<0.001	1.62 [1.47, 1.79]	<0.001		
10cm	2.70 [2.43, 3.01]	<0.001	2.55 [2.29, 2.84]	<0.001		
Unknown	1.45 [1.22, 1.72]	<0.001	1.39 [1.17, 1.65]	<0.001		
Grade						
1	–	–	–	–		
2	1.61 [1.34, 1.95]	<0.001	1.65 [1.36, 1.99]	<0.001		
3	2.58 [2.20, 3.02]	<0.001	2.65 [2.26, 3.12]	<0.001		
Unknown	2.08 [1.75, 2.49]	<0.001	2.13 [1.78, 2.55]	<0.001		
Surgery						
Limb Salvage/Radical Resection	–	–	–	–		
Amputation	–	–	1.60 [1.27, 2.02]	<0.001		
Surgical Margins						

	Multivariable (Pre-Treatment Variables Only)		Multivariable (Pre- and Post-Treatment Variables)		Propensity-Score Matched Cohort	
	HR [95% CI]	p-value	HR [95% CI]	p-value	HR [95% CI]	p-value
Negative	–	–	–	–		
Positive	–	–	1.39 [1.27, 1.51]	<0.001		
Unknown	–	–	1.46 [1.27, 1.69]	<0.001		
Radiation Therapy						
Pre-Op RT	–	–	–	–		
Post-Op RT	–	–	0.89 [0.81, 1.01]	0.063		
Chemotherapy						
No	–	–	–	–		
Yes	–	–	1.02 [0.91, 1.14]	0.74		
Unknown	–	–	0.73 [0.57, 0.94]	0.016		

UPS: Undifferentiated Pleomorphic Sarcoma