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Chondrosarcoma of the Osseous Spine:

An Analysis of Epidemiology, Patient Outcomes, and Prognostic Factors Using the SEER Registry From 1973 to 2012

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Abstract

Study Design—Retrospective analysis.

Objective—To determine the epidemiology and prognostic indicators in patients with chondrosarcoma of the osseous spine.

Summary of Background Data—Chondrosarcoma of the spine is rare, with limited data on its epidemiology, clinicopathologic features, and treatment outcomes. Therapy centers on complete *en bloc* resection with radiotherapy reserved for subtotal resection or advanced disease.

Methods—The Surveillance, Epidemiology, and End Results Registry was queried for patients with chondrosarcoma of the osseous spine from 1973 to 2012. Study variables included age, sex, race, year of diagnosis, size, grade, extent of disease, and treatment modality.

Results—The search identified 973 cases of spinal chondrosarcoma. Mean age at diagnosis was 51.6 years, and 627% of patients were males. Surgical resection and radiotherapy were performed in 75.2% and 21.3% of cases, respectively. Kaplan-Meier analysis demonstrated overall survival (OS) and disease-specific survival (DSS) of 53% and 64%, respectively, at 5 years. Multivariate Cox regression analysis showed that age (OS, $P < 0.001$; DSS, $P = 0.007$), grade (OS, $P < 0.001$; DSS, $P < 0.001$), surgical resection (OS, $P < 0.001$; DSS, $P < 0.001$), and extent of disease (OS, $P < 0.001$; DSS, $P < 0.001$) were independent survival determinants; tumor size was an independent predictor of OS ($P = 0.006$). For confined disease, age ($P = 0.013$), decade of diagnosis ($P = 0.023$), and surgery ($P = 0.017$) were independent determinants of OS. For locally invasive disease, grade (OS, $P < 0.001$; DSS, $P = 0.003$), surgery (OS, $P = 0.013$; DSS, $P = 0.046$), and size (OS, $P = 0.001$, DSS, $P = 0.002$) were independent determinants of OS and DSS. Radiotherapy was an independent indicator of worse OS for both confined ($P = 0.004$) and locally invasive disease ($P = 0.002$). For metastatic disease, grade (OS, $P = 0.021$; DSS, $P = 0.012$) and surgery (OS, $P = 0.007$; DSS, $P = 0.004$) were survival determinants for both OS and DSS, whereas radiotherapy predicted improved OS ($P = 0.039$).

Conclusion—Surgical resection confers survival benefit in patients with chondrosarcoma of the spine independent of extent of disease. Radiotherapy improves survival in patients with metastatic disease and worsens outcomes in patients with confined and locally invasive disease.

Keywords

chondrosarcoma; dedifferentiated; epidemiology; mesenchymal; radiation therapy; spine; surgery; survival

Malignant primary osseous tumors of the spine are rare, accounting for 5% of all osseous neoplasms.[1] Chondrosarcoma is a malignant tumor comprised of transformed cells producing a cartilaginous matrix without tumor osteoid.[2] Its estimated annual incidence is 1 in 200,000,[3] with 6.5% to 10% of cases arising within the mobile spine and 5% located within the sacrum.[4–7] Chondrosarcoma may arise *de novo* in normal bone or may undergo malignant transformation from a previously benign cartilaginous tumor (*e.g.,* enchondroma or osteochondroma).[2,7] Within the osseous spine, chondrosarcoma has a predilection for the thoracic vertebrae, but can arise anywhere along the length from cervical spine to sacrum.[5] It typically develops in the posterior elements with extension into the vertebral body (45% of cases) or confined to the posterior elements (40%), with some cases (15%) confined to the vertebral body.[8]

Despite occurring uncommonly in the spine,[2] chondrosarcoma is estimated to comprise 26% of primary osseous spinal tumors[9] and when present, carries with it significant risk of morbidity and mortality secondary to local invasion and destruction of adjacent structures and metastasis to distant sites.[10] Treatment has typically involved a surgical approach centered on complete *en bloc* resection with adjuvant radiotherapy reserved for subtotal resection or advanced disease.[6,11–14] Unlike other primary osseous tumors such as osteosarcoma or Ewing sarcoma for which multimodal therapy is more often utilized, chondrosarcoma has been shown to be relatively resistant to radiation and chemotherapy.[14–17] One notable exception to this are the mesenchymal and dedifferentiated subtypes, wherein a low grade tumor reverts to a primitive cell type and loses its characteristic chondroid features. Here, chemotherapy and sometimes radiation therapy are used a last resort where surgical resection alone is ineffective for such aggressive tumors.[18,19] For these reasons, the optimal treatment for chondrosarcoma of the spine remains controversial.

Small case series of treatment outcomes for patients with spinal chondrosarcoma at individual institutions have been reported,[4,5,11,12,20–22] but partially because of the rarity of this malignancy, reports have been limited in terms of number of patients despite data spanning several decades. The Surveillance, Epidemiology, and End Results (SEER) registry began collecting cancer-related information in 1973 and today represents 30% of the total US population, serving as the only comprehensive source of population-level cancer data.[23] Advantages of utilizing such a database includes multiinstitutional data with a large patient pool for greater statistical power. The SEER database has been queried in a series of reports in the past to include all malignant tumors of the osseous spine, including chondrosarcoma from 1973 to 2003.[1,9,10,24] However, analysis of treatment modalities have not been

performed using multivariate regression to account for confounding factors and identify independent prognostic indicators in the treatment of spinal chondrosarcoma to date. The purpose of this study is to report updated data on demographics and clinicopathologic features, and to use multivariate regression modeling to determine specific prognostic indicators and treatment outcomes for patients with chondrosarcoma of the osseous spine from 1973 to 2012.

MATERIALS AND METHODS

A population-based search for patients diagnosed with chondrosarcoma of the spine was performed using the case-listing session protocol of the National Cancer Institute's SEER 18 databases [www.seer.cancer.gov]. No Internal Review Board approval was required in this study because the database uses publicly available information with no personal identifiers. The SEER database is widely used and has been validated independently for analysis of primary osseous tumors of the spine.[1,9,10,24]

Patients diagnosed with chondrosarcoma of the spine from 1973 to 2012, the widest date ranges available in the latest version of the software were reviewed. Site specific codes were first used to identify all primary tumors that originated in the osseous spine: C41.2 (vertebral column) and C41.4 (pelvic bones, sacrum, coccyx, and associated joints). Histologic ICD-0–3 codes were then reviewed for all cases to identify the following histological subtypes with at least one case: "chondrosarcoma not otherwise specified," "juxtacortical chondrosarcoma," "myxoid chondrosarcoma," "mesenchymal chondrosarcoma," "clear cell chondrosarcoma," and "dedifferentiated chondrosarcoma." The following primary data were extracted for analysis: patient age, year of diagnosis, sex, race, histologic subtype (ICD), tumor extent, and tumor size from both extent of disease (EOD) and collaborative stage (CS) coding methods, tumor grade, treatment with surgery and/or radiation therapy, cause of death, and survival months. Tumor grade was reclassified as either low grade for well- or moderately-differentiated histology, or high grade for poorly differentiated or undifferentiated histology. EOD was manually reclassified using EOD and CS coding into three main categories as previously established in the literature[24]: confined (defined as tumor encasement within the periosteum), locally invasive (defined as further contiguous extension beyond the periosteum without distant involvement), and metastatic.

Primary outcome was defined as time in months from diagnosis to death from any cause for overall survival (OS), and time from diagnosis to death specific to the cancer-related diagnosis for disease-specific survival (DSS). Descriptive epidemiological and survival statistics were calculated for all variables. OS and DSS curves were calculated using the Kaplan-Meier method. Differences in survival were inferentially tested using the log-rank test. Covariates were assessed for predictive performance with multivariate Cox proportional hazards regression models,[25] using hazard ratios (HR) with corresponding 95% confidence intervals (CI), with regard to OS and DSS. Comparisons between groups were deemed statistically significant at the $P<0.05$ threshold. Statistical analyses were performed using SPSS 21 software (IBM Corp., Armonk, NY). For all comparisons of therapy as separate variables, no therapy was the reference category. Differences in baseline characteristics between groups were analyzed using one-way ANOVA for continuous variables (age and

size) and Pearson χ^2 test or Fisher exact test for categorical variables (sex, race, decade of diagnosis, grade, extent of disease, and histologic subtype).

RESULTS

The search identified 973 patients with primary chondrosarcoma of the osseous spine from 1973 to 2012. Among these, myxoid (5.8%), dedifferentiated (3.5%), and mesenchymal (2.1%) were the most common histologic variants with the majority of cases being listed as chondrosarcoma, not otherwise specified (Table 1). Demographically, 62.7% of patients were males and 86.6% were White (Table 1). The mean and median age of diagnosis was 51.6 and 51 years, respectively. At diagnosis, 61.2% of cases were from the year 2000 and beyond. Histologically, 63.4% of cases were of low grade, 16.8% were high grade, and 19.7% were of unknown tumor grade. Extent of disease was known in 81.8% of cases, with the majority of cases presenting as locally invasive disease (58.6%). The mean and median tumor size at the time of diagnosis was 8.7 and 7.5 cm, respectively. After diagnosis, 12.3% of patients received both surgery and radiation, 57.9% underwent surgery alone, and 9.0% underwent radiation alone, whereas 16.2% received neither and 4.5% had an unknown treatment regimen.

Survival analysis from Kaplan-Meier curves (Figure 1A, B) revealed that the 5-year OS and DSS for all patients with chondrosarcoma of the spine was 53% and 64%, respectively (Table 2); the median OS was 6.9 years. Demographically, the Kaplan-Meier univariate survival analysis revealed that greater age was associated with worse survival (OS log-rank P <0.001, DSS log-rank P<0.001) (Table 3). As a cohort, White patients had significantly better outcomes than Black patients (OS log-rank P = 0.031, DSS log-rank P = 0.026). Both OS and DSS showed a statistically significant difference in survival based on extent of disease at presentation (OS log-rank P<0.001, DSS log-rank P<0.001) (Figure 2A, B) with metastatic disease portending a dismal prognosis (OS 0.9 years, DSS 1.0 years) (Table 2). High tumor grade was also associated with worse survival prognosis (Figure 2C, D, Table 3) compared with low tumor grade in both OS and DSS (OS log-rank P<0.001, DSS log-rank P<0.001). Similarly, increasing tumor size was associated with worse survival (OS log-rank P<0.001, DSS log-rank P<0.001). For both OS and DSS, sex and decade of diagnosis were not associated with significant differences in survival. Among histologies, mesenchymal (OS 2.0 years, DSS 2.0 years) and dedifferentiated (OS 2.4 years, DSS 3.0 years) chondrosarcomas had particularly dismal prognoses compared with the rest of the cohort (Table 2 and 3). Decade of diagnosis was not associated with improved survival for the entire cohort, nor for any of the three most common histologic variants (myxoid, mesenchymal, and dedifferentiated).

Therapeutically, patients who underwent surgical resection of the chondrosarcoma had significant improved survival (OS log-rank P<0.001, DSS log-rank P<0.001) on univariate Kaplan-Meier analysis, whereas patients who received radiation therapy had a worse prognosis (OS log-rank P<0.001, DSS log-rank P<0.001). Kaplan-Meier analysis was also used to determine the relative survival curves for patients receiving surgical resection, radiation therapy, both or neither (Figure 3A, B, Table 3). As a cohort, patients who underwent surgery alone had greater OS and DSS than patients who underwent both surgery

and radiation therapy (log-rank P<0.001, log-rank P<0.001, respectively). All other pair-wise comparisons achieved statistical significance, except for DSS when comparing radiation therapy and no therapy (Figure 3A, B, Table 3). In addition, patients with histological variants did not receive radiation therapy at a significantly higher frequency than their counterparts (P= 0.357 for myxoid, P= 0.464 for mesenchymal, and P= 0.201 for dedifferentiated). To account for potential confounding baseline characteristics for patients receiving a particular treatment regimen, an analysis of baseline characteristics was performed and revealed age, race, grade, and extent of disease as potential confounders in assessing therapeutic benefit using univariate analysis (Table 4).

On our multivariate analysis model (Table 5), age at diagnosis (HR 1.03, CI 1.02–1.04, P <0.001), tumor grade (HR 2.86, CI 2.08–3.93, P<0.001), surgical resection (HR 0.44, CI 0.29–0.67, P<0.001), tumor size (HR 1.03, CI 1.01–1.06, P= 0.021), and EOD (HR 2.54, CI 1.77–3.66, P<0.001) were found to be independent predictors of OS. Age (HR 1.02, CI 1.01–1.03, P= 0.007), tumor grade (HR 3.21, CI 2.14–4.82, P<0.001), surgical resection (HR 0.37, CI 0.22–0.63, P<0.001), and EOD were found to be independent predictors of DSS (HR 4.61, CI 2.89–7.36, P<0.001). The multivariate analysis model was next used to ascertain the independent effects of these variables on survival in patients with confined, locally invasive disease and patients with metastatic disease as separate cohorts. For cases presenting with confined disease, age (HR 1.08, CI 1.02–1.14, P= 0.013), decade of diagnosis (HR 19.50, CI 1.50–253.85, P= 0.023), and surgical resection (HR 0.06, CI 0.01–0.61, P= 0.017) were independent OS determinants. For cases presenting with locally invasive disease, age (HR 1.03, CI 1.02–1.05, P<0.001), tumor grade (HR 2.70, CI 1.88–3.88, P<0.001), surgical resection (HR 0.52, CI 0.31–0.87, P= 0.013), radiation therapy (HR 1.70, CI 1.13–2.56, P= 0.001), and tumor size (HR 1.05, CI 1.02–1.08, P= 0.001) were independent determinants of OS. In addition, age (HR 1.02, CI 1.01–1.04, P= 0.003), tumor grade (HR 3.43, CI 2.17–5.41, P<0.001), surgical resection (HR 0.48, CI 0.23–0.99, P= 0.046), and size (HR 1.06, CI 1.01–1.09, P= 0.002) were determinants of DSS. For cases presenting with meta-static disease, tumor grade (HR 3.08, CI 1.19–7.98, P= 0.021), surgical resection (HR 0.23, CI 0.08–0.67, P= 0.007), and radiation therapy (HR 0.37, CI 0.14–0.95, P= 0.039) were independent determinants of OS, whereas tumor grade (HR 4.09, CI 1.37–12.20, P= 0.012) and surgical resection (HR 0.16, CI 0.05–0.56, P= 0.004) were independent determinants of DSS. It was noted that although radiation therapy was an independent predictor of improved OS in metastatic disease (HR 0.37, CI 0.14–0.95, P= 0.039), it predicted worse OS in patients with confined (HR 69.43, CI 3.79–1272.92, P= 0.004) and locally invasive disease (HR 1.70, CI 1.13–2.56, P= 0.011).

To account for the potential of newer radiotherapy influencing survival, we additionally performed multivariate analysis on patients treated after the year 2000. We found no difference in outcomes from the cohort for all years with respect to radiotherapy (OS HR 1.44, CI 0.93–2.25, P= 0.107; DSS HR 1.41, CI 0.80–2.48, P= 0.231). This held true for the differential effect of radiotherapy in both confined/locally invasive where it predicted worse outcome (OS HR 2.18, CI 1.36–3.51, P= 0.001; DSS HR 2.44, CI 1.28–4.67, P= 0.007) and metastatic disease (OS HR 0.31, CI 0.10–0.97, P= 0.044; DSS (HR 0.37, CI 0.12–1.18, P= 0.092) where it improved survival.

DISCUSSION

Chondrosarcoma of the osseous spine is considered to be a rare malignancy, and has the potential for both locally invasive destruction and systemic metastasis. Although previous investigations have reported on demographics and prognostic determinants of primary osseous neoplasms of the spine using the SEER registry,[1,10] this study is the first to analyze population-level data on the role and outcomes of surgical resection and radiation therapy for spinal chondrosarcoma, an entity that is frequently resistant to chemotherapy. Furthermore, this study uses multivariate regression analysis to more confidently report on treatment outcomes in the presence of multiple known confounders.[25,26]

Our study found the average age at diagnosis of chondrosarcoma of the spine to be 51 years. We also found that there was a 3:2 predilection of males to females, which has been previously supported in smaller studies.[21,27] In the pathology literature, the reported estimates for each of the histological variants of chondrosarcoma is <5% for all chondrosarcomas.[28] However, to our knowledge there have been no epidemiologic studies reporting on their incidence in the spine. Our study is the first to demonstrate that the frequency of these variants is comparable to those found for the appendicular skeleton (myxoid 5.8%, mesenchymal 2.1%, dedifferentiated 3.5%, and clear cell 0.5%). In terms of survival outcomes, patients had an overall median survival of 6.9 years, and a 5-year OS and DSS of 53% and 64%, respectively. This is by-in-large consistent with prior case series[4,5,11,12,20–22] and prior SEER database reports of primary osseous tumors.[1,9,10,24] In general, the prognosis of chondrosarcoma of the axial skeleton appears to be less favorable than disease affecting the long bones, which has an estimated 5-year survival ranging from 50% to 80% in the literature.[3,29] The findings of this study are congruent with these prior estimates, and implicate that the complexities of the spine anatomy may make curative treatment more difficult than in the extremities. Previous studies have found that high-grade chondrosarcomas of the axial skeleton have significantly worse long-term (at 10 years and beyond) conditional survival compared with high-grade disease of the extremity which further underscores this point.[30,31]

Among tumor histologies, we found that mesenchymal and dedifferentiated chondrosarcomas portended a comparatively dismal prognosis in the spine. These are recognized in the literature as particularly aggressive tumors and frequently necessitate chemotherapy in addition to primary surgery for treatment in the long bones.[18,19] In congruence with prior literature, we also found tumor grade and extent of disease to be independent prognostic indicators of both OS and DSS. Given that the majority of the cases were poorly differentiated or anaplastic on histology and presented with at least local invasion at the time of diagnosis, this association stands to reason when considering that a 5% to 20% chondrosarcomas are high-grade (16.4% in this study), aggressive malignancies with significant soft tissue extension, particularly in the spine.[3,11,29] Notably, tumor size was found to be an independent survival determinant, particularly for confined and locally invasive disease. Though this trend has not been exclusively reported for chondrosarcoma of the spine, it has been reported in other sarcomas, including chondrosarcomas of the appendicular skeleton and skull base.[32,33]

This study also found that patient age at presentation portended worse outcomes in both OS and DSS. This trend is understandable given the aggressive therapies needed to treat such a disease, and has been reported in other sarcomas, and chondrosarcoma in particular.[34] In context, this finding is consistent with children tolerating higher doses of chemotherapy, which is used in instances of advanced disease in mesenchymal and dedifferentiated chondrosarcoma, that may be otherwise intolerable in older patients for therapeutic effect.[18,19,35] Although there was an observed trend, the decade of diagnosis was not found to be associated with a statistically significant improvement in survival in either univariate or multivariate analysis, or for chondrosarcoma variants. Contextually, this may suggest that advances in radiation therapy and chemotherapy regimens have not been as successful for chondrosarcoma as for other bone tumors.[2,3,36] Despite the male predilection for this disease, we also noted differences in survival based on sex.

With regards to treatment outcomes, the multivariate regression model used in this study assesses the effect of surgery and radiation independent of possibly confounding covariates such as age, tumor grade, and extent of disease. In our univariate Kaplan-Meier analysis of treatment modalities, we found that patients who underwent surgical resection of chondrosarcoma had significantly improved survival, whereas patients who received radiation therapy had an overall worse prognosis. When accounting for extent of disease in our multivariate model, the differential survival impact of radiation therapy was more clearly elucidated. The multivariate analysis suggests that surgical resection benefited patients with both metastatic and nonmetastatic disease, in terms of both OS and DSS. However, for patients with confined and locally invasive tumors, radiotherapy portended a poorer OS whereas it conferred an improvement in OS for metastatic disease. This result suggests that radiotherapy may be more effective if restricted to patients with metastatic or otherwise advanced disease burden. It is well established in the literature that chondrosarcomas are as an entity resistant to radiation,[14–17] requiring doses in excess of 50 Gy, a threshold above which there has been an identifiable risk of paralysis and other neurological side effects because of nearby spine and nerve root anatomy.[14,37] This is consistent with the finding that decade of diagnosis, and the contemporary improvement in radiotherapy technology, was not found to be associated with improved survival. However, we acknowledge that such a database study cannot clearly elucidate an explanation for such a differential effect of radiation therapy in survival. This observation may be caused by tumor dedifferentiation with radiotherapy.[38] It may also be because of the fact that early radiation therapy may preclude a patient from being eligible for surgery. Future multiinstitutional studies may be warranted to delineate this as well the role of advances in targeted radiotherapy and chemotherapy regimens, particularly in the treatment of chondrosarcoma variants.

Surgical treatment for spinal chondrosarcoma has traditionally included both *en bloc* resection and curettage. Although *en bloc* resection is preferred, the inherent proximity of the neoplasm with neurovascular structures as well as the need for structural stabilization may make *en bloc* resection difficult, making curettage with a cytotoxic adjuvant more appropriate in some cases.[7] However, results after curettage are inferior to those after *en bloc* therapy.[22,39] Of note, his study found that patients with confined disease are the lone subgroup where survival has improved in the last several decades, which may reflect the improvement of surgical management of this disease. Although the SEER database reports

whether surgical intervention was performed, it is limited in its ability to retrospectively analyze certain other variables, such as margin status, extent of surgical resection, and postoperative tumor recurrence. Similarly, no data on chemotherapy are available in the database. However, the effect of this shortcoming in terms of the current analysis is thought to be lessened by chondrosarcoma's generally accepted lack of response to chemotherapy, except in advanced mesenchymal and dedifferentiated chondrosarcoma.[7]

Acknowledgments

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Key Points

- We reviewed the SEER registry for patients with chondrosarcoma of the spine to determine patient outcomes and survival determinants.

- The median OS was 6.9 years; greater age at diagnosis, increasing tumor size, Black race, tumors of high grade, greater extent of disease, and dedifferentiated and mesenchymal variants of the disease were associated with worse prognosis.

- Surgical resection was an independent predictor of improved survival for both confined/locally invasive and metastatic disease.

- Radiation therapy portended worse prognosis in patients with confined/locally invasive disease and portended better prognosis in metastatic disease.
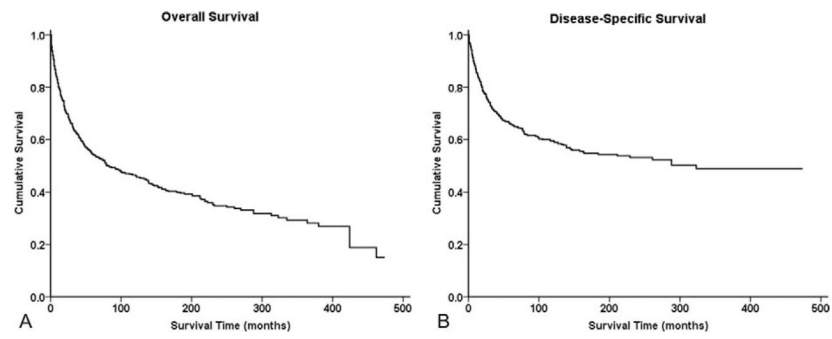
Figure 1.
Survival analysis of patients with chondrosarcoma of the spine using Kaplan-Meier analysis.
(**A**) Kaplan-Meier estimates of overall survival and (**B**) disease-specific survival are shown
for all patients.
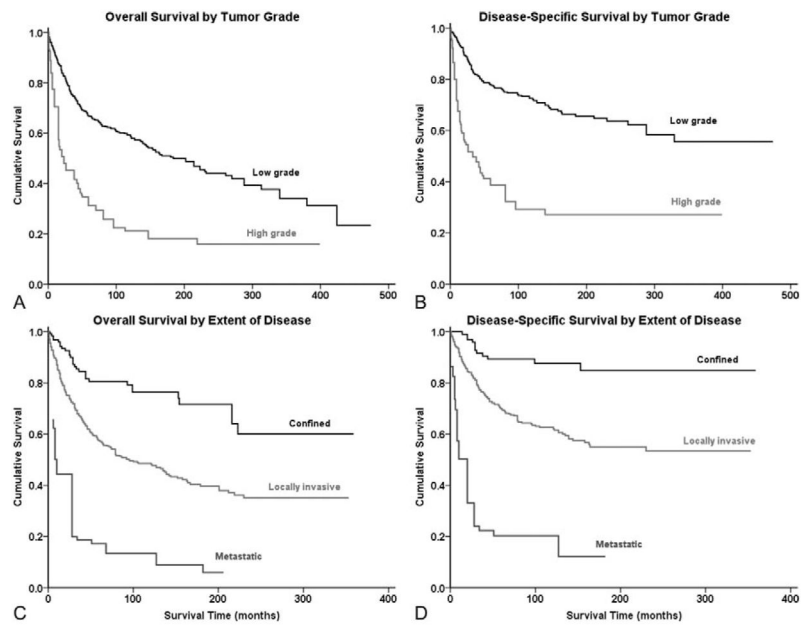
Figure 2.
Kaplan-Meier analyses of patients with chondrosarcoma of the spine for overall survival and disease-specific survival by **(A, B)** tumor grade and extent of disease **(C, D)**.

Figure 3.
Kaplan-Meier analyses of patients with chondrosarcoma of the spine by treatment modality.
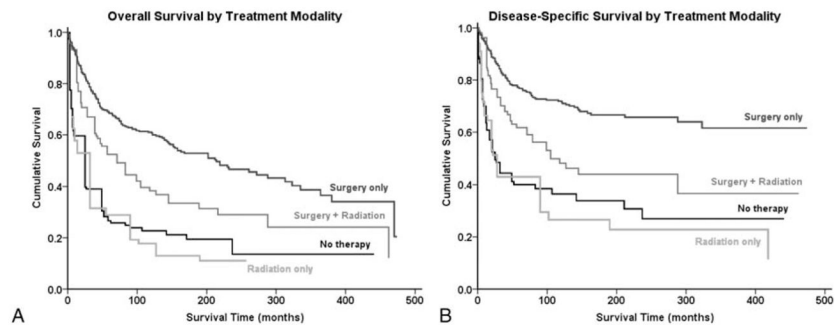**(A)** Kaplan-Meier estimates of overall survival and **(B)** disease-specific survival are depicted for patients who underwent bimodal surgery and radiation therapy, surgery alone, radiation alone, or no therapy.

TABLE 1

Demographics and Clinicopathologic Features (n = 973)

Age	Years
Mean	51.6 ± 18.8
Median	51
Minimum	8
Maximum	93
Characteristic	Percentage (n)
Sex	
Female	37.3 (363)
Male	62.7% (610)
Race/Ethnicity	
White	86.6 (843)
Black	7.4 (72)
Other	4.9 (49)
Unknown	1.0 (10)
Decade	
1970s	8.2 (80)
1980s	11.2 (109)
1990s	19.4 (189)
2000s	61.2 (595)
Tumor grade	
Low grade	63.4 (617)
High grade	16.9 (164)
Unknown	19.7 (192)
Histologic subtype	
Chondrosarcoma, not otherwise specified	87.5 (851)
Juxtacortical chondrosarcoma	0.7 (7)
Myxoid chondrosarcoma	5.8 (56)
Mesenchymal chondrosarcoma	2.1 (20)
Clear cell chondrosarcoma	0.5 (5)
Dedifferentiated chondrosarcoma	3.5 (34)
Extent of disease	
Confined	13.6 (132)
Locally invasive	58.6 (570)
Metastasis	9.7 (94)
Unknown	18.2 (177)
Surgical resection	
Yes	75.2 (732)
No	22.1 (215)

Unknown	2.7 (26)
Radiation therapy performed	
Yes	21.3 (207)
No	76.4 (743)
Unknown	2.4 (23)
Treatment modality	
Surgery + radiation	12.3 (120)
Surgery only	57.9 (563)
Radiation only	9.0 (88)
No therapy	16.2 (158)
Unknown	4.5 (44)
Size (cm)	
Mean	8.7 ± 6.2
Median	7.5

TABLE 2

Survival Data

Median Survival (Years)	OS	(DSS)
Overall	6.9	N/A
Subtype		
Chondrosar coma, NOS	8.2	N/A
Juxtacortical chondrosarcoma	N/A	N/A
Myxoid chondrosarcoma	6.3	9.1
Mesenchymal chondrosarcoma	2.0	2.0
Clear cell chondrosarcoma	N/A	N/A
Dedifferentiated chondrosarcoma	2.4	3.0
Decade of diagnosis		
1970s	4.5	11.1
1980s	4.3	15.1
1990s	11.6	N/A
2000s	6.9	N/A
Tumor grade		
Low grade	15.3	N/A
High grade	1.9	2.8
Extent of disease		
Confined	N/A	N/A
Locally invasive	7.9	N/A
Metastatic	0.9	1.0
Treatment modality		
Surgery + radiation therapy	5.7	9.0
Surgery only	17.6	N/A
Radiation only	1.4	2.0
No therapy	1.4	2.2
Percent survival (%)		
at 2 years	63	72
at 5 years	53	64
at 10 years	45	58

N/A signifies where median survival time incalculable because of death event occurring in fewer than 50% of cases in the cohort.

TABLE 3

Univariate Analysis of Variables Using Kaplan-Meier Method

Characteristic	OS (Log-rank *P*)	DSS (Log-rank *P*)
Age at diagnosis	<0.001	<0.001
Race/Ethnicity		
White *vs.* Black	0.031	0.026
Black *vs.* Other	0.113	0.078
White *vs.* Other	0.703	0.604
Sex	0.073	0.065
Decade of diagnosis	0.100	0.146
Tumor grade	<0.001	<0.001
Subtypes		
NOS *vs.* myxoid	0.356	0.302
NOS *vs.* mesenchymal	0.074	0.003
NOS *vs.* dedifferentiated	0.001	<0.001
Myxoid *vs.* mesenchymal	0.203	0.044
Myxoid *vs.* dedifferentiated	0.004	0.001
Mesenchymal *vs.* dedifferentiated	0.725	0.836
Surgical resection	<0.001	<0.001
Radiation therapy performed	<0.001	<0.001
Treatment modality	<0.001	<0.001
Surgery + radiation *vs.* surgery only	<0.001	<0.001
Surgery + radiation *vs.* radiation only	<0.001	<0.001
Surgery + radiation *vs.* no therapy	<0.001	0.001
Surgery *vs.* radiation only	<0.001	<0.001
Surgery *vs.* no therapy	<0.001	<0.001
Radiation *vs.* no therapy	<0.001	0.659
Extent of disease	<0.001	<0.001
Size (cm)	<0.001	<0.001

DSS indicates disease-specific survival; OS, overall survival.

TABLE 4

Analyses of Baseline Characteristics by Treatment Group

Characteristic	Surgery + Radiation	Surgery Only	Radiation Only	No Therapy	P
Age (yrs, mean)	51.1 ± 18.5	48.3 ± 17.0	61.5 ± 19.9	58.5 ± 20.4	<0.001
Tumor size (cm, mean)*	7.3 ± 4.4	8.9 ± 6.3	9.2 ± 5.5	9.1 ± 8.2	0.205
Sex†					0.893
% Male	65.0	62.2	64.8	61.4	
Race†					0.011
% White	82.5	91.0	86.2	81.0	
% Black	9.2	5.2	9.2	12.0	
% Other	8.3	3.8	4.6	7.0	
Decade of diagnosis†					0.276
% 1970s	7.5	6.7	13.6	10.8	
% 1980s	12.5	9.2	13.6	10.8	
% 1990s	23.3	20.1	19.3	18.4	
% 2000s	56.7	63.9	53.4	60.1	
Grade†					0.001
% High grade	29.4	16.8	26.8	31.4	
Extent of Disease†					<0.001
% Confined	10.6	21.4	6.1	9.0	
% Locally invasive	79.8	73.7	56.1	64.9	
% Metastatic	9.6	4.9	37.9	26.1	

*Differences in age and tumor size distributions among treatment groups were assessed using one-way ANOVA.

†Differences in sex, race, decade, grade, and extent of disease distributions among treatment groups were assessed using χ^2 analysis.

TABLE 5

Cox Proportional Hazards Model for Multivariate Analysis

	OS		DSS	
Characteristic	**HR (95% CI)**	**P**	**HR (95% CI)**	**P**
Overall (n = 974)				
Age	1.03 (1.02–1.04)	<0.001	1.02 (1.01–1.03)	0.007
Race/Ethnicity	1.14 (0.85–1.52)	0.385	1.01 (0.68–1.50)	0.967
Sex	0.96 (0.70–1.31)	0.779	1.04 (0.70–1.55)	0.849
Decade of diagnosis	1.16 (0.84–1.60)	0.363	1.15 (0.78–1.72)	0.479
Grade	2.86 (2.08–3.93)	<0.001	3.21 (2.14–4.82)	<0.001
Surgical resection	0.44 (0.29–0.67)	<0.001	0.37 (0.22–0.63)	<0.001
Radiation therapy	1.30 (0.90–1.86)	0.163	1.18 (0.74–1.88)	0.494
Size (cm)	1.03 (1.01–1.06)	0.021	1.03 (1.00–1.06)	0.053
Extent of disease	2.54 (1.77–3.66)	<0.001	4.61 (2.89–7.36)	<0.001
Confined disease (n = 132)				
Age	1.08 (1.02–1.14)	0.013	–	–
Race/Ethnicity	1.28 (0.45–3.65)	0.643	–	–
Sex	0.98 (0.25–3.84)	0.978	–	–
Decade of diagnosis	19.50 (1.50–253.85)	0.023	–	–
Grade	1.84 (0.28–12.03)	0.527	–	–
Surgical resection	0.06 (0.01–0.61)	0.017	–	–
Radiation therapy performed	69.43 (3.79–1272.92)	0.004	–	–
Size (cm)	0.88 (0.69–1.11)	0.287	–	–
Locally-invasive disease (n = 570)				
Age	1.03 (1.02–1.05)	<0.001	1.02 (1.01–1.04)	0.003
Race/Ethnicity	0.90 (0.62–1.32)	0.595	0.85 (0.51–1.43)	0.546
Sex	0.95 (0.66–1.37)	0.792	0.94 (0.59–1.50)	0.808
Decade of diagnosis	1.19 (0.84–1.69)	0.320	1.29 (0.83–1.99)	0.257
Grade	2.70 (1.88–3.88)	<0.001	3.43 (2.17–5.41)	<0.001
Surgical resection	0.52 (0.31–0.87)	0.013	0.48 (0.23–0.99)	0.046
Radiation therapy performed	1.70 (1.13–2.56)	0.011	1.60 (0.92–2.77)	0.094
Size (cm)	1.05 (1.02–1.08)	0.001	1.06 (1.02–1.09)	0.002
Metastatic disease (n = 94)				
Age	1.03 (0.99–1.06)	0.127	1.02 (0.99–1.06)	0.224
Race/Ethnicity	1.47 (0.59–3.64)	0.404	0.96 (0.35–2.66)	0.938
Sex	1.60 (0.64–3.96)	0.314	1.80 (0.72–4.53)	0.210
Decade of diagnosis	1.29 (0.38–4.34)	0.680	1.35 (0.32–5.70)	0.682
Grade	3.08 (1.19–7.98)	0.021	4.09 (1.37–12.20)	0.012
Surgical resection	0.23 (0.08–0.67)	0.007	0.16 (0.05–0.56)	0.004
Radiation therapy performed	0.37 (0.14–0.95)	0.039	0.49 (0.18–1.31)	0.156

Characteristic	OS		DSS	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Size (cm)	1.01 (0.97–1.04)	0.670	0.97 (0.90–1.05)	0.424

CI indicates confidence interval; DSS, disease-specific survival; HR, hazard ratio; OS, overall survival.