Cohort Study

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Impact of nodal involvement on survival outcomes in chondrosarcoma: retrospective cohort analysis of Surveillance, Epidemiology, and End Results (SEER) database (2004–2015)

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Objectives: Factors associated with nodal involvement in chondrosarcoma and outcomes based on treatment modality were analyzed using the Surveillance, Epidemiology, and End Results (SEER) database.

Methods: Chondrosarcomas involving axial and appendicular parts of the body diagnosed from 2004 to 2015 were identified in SEER. Clinical, pathologic, and treatment parameters were compared with respect to nodal status at initial diagnosis by Fisher's exact or Student's t-test. Disease-specific survival (DSS) and overall survival (OS) were evaluated by Kaplan-Meier analyses, and by Cox regression models.

Results: Synchronous regional nodal metastases were present in 1.3% of chondrosarcoma patients. Lymph node involvement was associated with primary tumor location in extraskeletal tissue and the pelvis, and with distant metastasis and larger primary tumor size at diagnosis. Patients with nodal involvement had 5-year DSS of 48% [95% confidence interval (CI): 28%–65%], versus 82% (95% CI: 80%–84%) for those without (log-rank $P < 0.001$). 5-year OS with and without nodal involvement were 38% (95% CI: 21%–55%) and 73% (95% CI: 71%–75%), respectively (log-rank $P < 0.001$). Surgical excision of nodes was associated with improved DSS and OS. Radiation and chemotherapy were not associated with improved DSS/OS.

Conclusions: The nodal disease is uncommon at presentation in chondrosarcoma. Greater clinical vigilance for regional nodal metastases may be warranted for those with specific risk factors, including extraskeletal or pelvic primary sites, myxoid, mesenchymal, or dedifferentiated histologies, and large size. Surgical excision of regional nodes is associated with improved DSS/OS. This analysis suggests a therapeutic effect of surgical treatment, rather than selection for favorable underlying biological factors.

Keywords: Chemotherapy, Radiotherapy, Adjuvant, Neoadjuvant, Surgery, Prognosis, Outcome, Survival, Cartilage, Myxoid, Mesenchymal

Chondrosarcoma is the second most common primary solid malignancy of bone, comprising 25% of all bone sarcomas[1]. The mainstay of management for patients with the localized disease remains surgery. For most tumors, wide excisions are preferred[2,3]. Low-grade chondrosarcomas of the extremities can be managed with more conservative surgical approaches, including intralesional excision with local adjuvant treatments[4–6]. Radiotherapy is used for patients with unresectable or symptomatic lesions, with most published studies focusing on chondrosarcoma of the spine and skull base[7,8].

High-grade chondrosarcoma (grade III) is associated with a 32%–71% risk of regionally advanced or metastatic disease[9,10]. Chondrosarcomas, like other sarcomas, are generally viewed as having a hematologic route of dissemination, reflected by their propensity for pulmonary metastases. As a result, there is a paucity of data to guide the treatment of patients with uncommon clinical presentations, such as regional lymph node involvement at primary diagnosis.

Chondrosarcoma metastasis to regional lymph nodes is rare, with limited case reports reported in the literature (**Fig. 1**)[11–14]. There have been several reports of chondrosarcomas with lymph node involvement in nonhuman mammals[15–17]. The rarity of lymph node involvement from primary bone tumors may be attributed to the lack of lymphatic vessels in association with bones[18]. Nevertheless, Wan et al recently published an analysis of the Surveillance, Epidemiology, and End Results program (SEER) database, reporting that regional nodal involvement among chondrosarcoma cases occurred in 1.3% of cases, and was associated with inferior survival [hazard ratio (HR): 2.20, 95% confidence interval (CI): 1.50–3.24][19]. This study did not assess the impact of treatment

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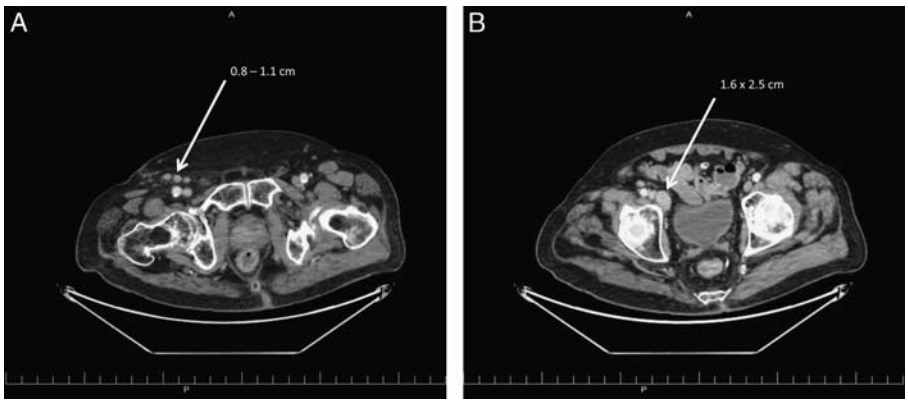

Figure 1. Computed tomographic images of pelvis. Male with right tibial dedifferentiated chondrosarcoma. Biopsy confirmed recurrence ~4 years after initial diagnosis. A, 3 right inguinal lymph nodes (0.8–1.1 cm maximal dimension). B, Right external iliac lymph node (1.6 × 2.5 cm maximal dimension). Arrows indicate the locations of the index lesions within the respective image.

on outcome. In addition, the patients included in the study represented a 27-year timespan, from 1988 to 2015, in which treatment may have changed significantly.

This analysis sought to investigate this high-risk subpopulation of patients further, with specific attention toward the relationship between treatment modality and survival, focusing on those treated more recently. These findings will hopefully help guide management of this challenging subset of chondrosarcoma patients.

Methods

Cohort

For this retrospective cohort analysis, chondrosarcoma cases were extracted from the 1973 to 2016 SEER database. SEER is a publicly accessible database of de-identified data, for which human subjects review is not required. This research project has been registered with the Research Registry (http://www.researchregistry.com) and the unique identifying number is researchregistry5162. This research adheres to the guidelines of the STROCSS Group in regard to the reporting of cohort studies in surgery[20].

A total of 6526 chondrosarcoma cases were identified. Cases were excluded if diagnosed before 2004, due to our interest in patients diagnosed and treated more recently. Cases were also excluded from 2016, due to a change in variable coding in the SEER database, making direct comparisons with patient records from 2004 to 2015 unclear. In addition, cases were excluded if they had duplicate entries (identified using the SEER patient identification number), lacked information regarding survival, had tumor primary location in the head and neck (see Supplemental Materials Table 1 for list of primary tumor sites included, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13), or reported an unknown lymph node status. A total of 2399 unique cases diagnosed between the years 2004 and 2015 met inclusion criteria (**Fig. 2**).

Variables

Demographic and clinical characteristics evaluated in this study included: age at diagnosis, sex, race, year of diagnosis, tumor location, histologic type, distant metastasis, grade, and treatment modalities. Treatment modalities of interest were: surgery of the primary site, lymph node surgery, receipt of radiation, and receipt of chemotherapy. An orthopedic oncologic surgeon categorized primary tumor location, primary tissue origin, and primary bone site for our analysis, based on the primary tumor site listed in SEER. Tumor size was dichotomized according to the American Joint Committee on Cancer (AJCC) guidelines for bone cancer staging as being <8.0 cm or ≥ 8.0 cm[21].

Disease-specific survival (DSS) was the timespan from the time of diagnosis to death from chondrosarcoma. Patients dying from

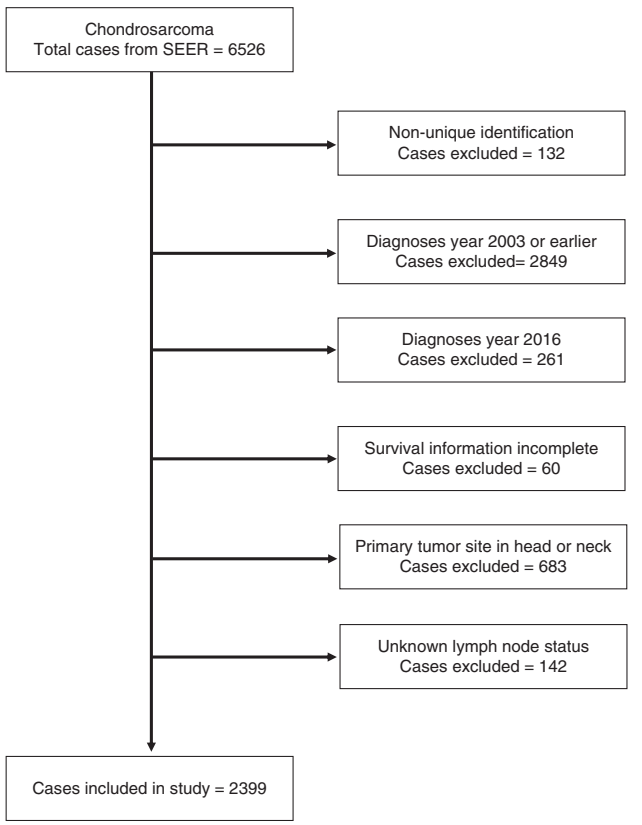

Figure 2. Selection process for inclusion of cases. SEER indicates Surveillance, Epidemiology, and End Results Program.

Table 1

Comparison of demographic, clinical, and pathologic characteristic in patients with or without nodal involvement.

Characteristic	No Nodal Involvement, N = 2367 (%)	Nodal Involvement, N = 32 (%)	*P*
Age at diagnosis			
Mean ± SD (age range)	53 ± 18 (4–98)	57 ± 14 (28–82)	0.2688
Sex			
Male	1335 (56)	20 (62.5)	0.591
Female	1032 (44)	12 (37.5)	
Race			
Black	183 (8)	2 (6)	0.925
White	2031 (86)	29 (91)	
Other/unknown	153 (6)	1 (3)	
Year of diagnosis			
2004–2009	1121 (47)	16 (50)	0.859
2010–2015	1246 (53)	16 (50)	
Primary tumor location			
Appendicular	1423 (60)	17 (53)	0.044
Axial	923 (39)	13 (41)	
Other/unknown	21 (1)	2 (6)	
Primary tissue origin			
Extraskeletal	244 (10)	10 (31)	0.001
Skeletal	2123 (90)	22 (69)	
Primary bone site*			
Upper extremity	437 (21)	3 (14)	< 0.001
Lower extremity	736 (35)	4 (18)	
Ribs/sternum	413 (20)	1 (5)	
Spine	102 (5)	0	
Pelvis	397 (19)	12 (55)	
Bone, NOS	21 (.1)	2 (9)	
Histologic type			
Chondrosarcoma	1731 (73)	14 (44)	0.002
Juxtacortical chondrosarcoma	30 (1)	0	
Chondroblastoma, malignant	26 (1)	0	
Myxoid chondrosarcoma	293 (12)	12 (38)	
Mesenchymal chondrosarcoma	50 (2)	2 (6)	
Clear cell chondrosarcoma	38 (2)	0	
Dedifferentiated chondrosarcoma	199 (8)	4 (13)	
Distant metastasis			
No	2189 (92)	19 (59)	< 0.001
Yes	163 (7)	13 (41)	
Unknown	15 (1)	0 (0)	
Grade			
Grade I	736 (31)	1 (3)	< 0.001
Grade II	817 (35)	7(22)	
Grade III	261 (11)	8 (25)	
Grade IV	192 (8)	5 (16)	
Unknown	361 (15)	11 (34)	
Size			
0.0–8.0 cm	1136 (48)	5 (16)	< 0.001
≥ 8.0 cm	873 (37)	25 (78)	
No mass/tumor found/ unknown	358 (15)	2 (6)	
Lymph node surgery			
No	2257 (95)	17 (53)	< 0.001
Yes	110 (5)	15 (47)	
Surgery			
No	294 (12)	14 (44)	< 0.001
Yes	2070 (87)	18 (56)	
Missing	3 (0)	0 (0)	
Radiation			
No/unknown	2042 (86)	21 (66)	0.003
Yes	325 (14)	11(34)	
Chemotherapy			
No/unknown	2158 (91)	22 (69)	< 0.001
Yes	209 (9)	10 (31)	

*Excludes primary tumors not located on bones. No nodal involvement n = 2106, nodal involvement n = 22.
NOS indicates not otherwise specified.

other causes were censored at the time of death in analyses of DSS. Overall survival (OS) was the timespan from diagnosis to death from any cause. In both DSS and OS analyses, patients lost to follow-up were censored at the last follow-up date indicated in SEER.

Statistical analyses

Baseline characteristics of lymph node positive cases were compared with lymph node negative and lymph node unknown cases using Fisher's exact or Student's t-tests. A Bonferroni correction accounted for multiple comparisons. DSS and OS were estimated using univariable Cox proportional hazards models and evaluated by subpopulation with the Kaplan-Meier method and log-rank test.

Multivariable Cox proportional hazards analyses were limited to 2 independent variables among those lymph node positive cases, due to the limited number of such cases and events for each outcome (DSS: 15 events/32 cases; OS 22 events/32 cases)[22]. The likelihood ratio (LR) test was used to compare the full and reduced Cox regression models. A value of $P \leq 0.05$ was designated for rejection of null hypotheses, with correction (ie, Bonferroni), if appropriate. Statistical analyses were conducted with Stata version 12.1 (StataCorp, College Station, TX).

Results

Baseline characteristics

Of the 2399 included cases, the majority were males with a mean age of 54 years and the median year of diagnosis in 2010. Thirty-two (1.3%) cases were lymph node positive (LN +), while 2367 cases were lymph node negative (LN –) (**Table 1**). The appendicular parts of the body were the most common anatomic sites of the primary tumor (60% of the total population; 53% LN + and 60% LN–). Tumors originated primarily in skeleton irrespective of nodal status (89% of the total population).

Factors associated with nodal involvement

Several clinical and pathologic variables were disproportionately represented in the 32 LN + patients: extraskeletal tumor location, presence of distant metastasis at diagnosis, higher tumor grade, and increased primary tumor size (**Table 1**). Among those with a skeletal primary site, LN + patients were most likely to have the pelvis as primary site (12/22, 55%). Myxoid, mesenchymal, and

Table 2

Univariable Cox analyses of DSS and OS.

	n	DSS HR (95% CI)	DSS 5-Year (95% CI)	OS HR (95% CI)	OS 5-Year (95% CI)
Entire Study Population, n = 2399					
Lymph node status					
No	2367	Referent	82% (80%–84%)	Referent	73% (71%–75%)
Yes	32	4.22 (2.52–7.06)	48% (28%–65%)	3.74 (2.44–5.72)	38% (21%–55%)
Lymph node positive population, n = 32					
Lymph node surgery					
No	17	Referent	19% (3%–45%)	Referent	16% (3%–39%)
Yes	15	0.19 (0.06–0.61)	76% (42%–92%)	0.42 (0.17–1.00)	60% (32%–80%)
Surgery					
No	14	Referent	16% (1%–47%)	Referent	13% (1%–40%)
Yes	18	0.16 (0.05–0.50)	68% (39%–85%)	0.26 (0.10–0.67)	56% (31%–75%)
Radiation					
No/unknown	21	Referent	49% (22%–71%)	Referent	34% (14%–55%)
Yes	11	1.32 (0.47–3.68)	45% (17%–71%)	0.67 (0.27–1.67)	45% (17%–71%)
Chemotherapy					
No/unknown	22	Referent	45% (22%–66%)	Referent	38% (18%–58%)
Yes	10	0.64 (0.20–2.02)	53% (17%–79%)	0.65 (0.25–1.68)	40% (12%–67%)

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

dedifferentiated histologic subtypes were more common among LN+ versus LN− patients.

LN+ patients were more likely to have received early multimodality treatment with lymph node surgery, radiation therapy, and chemotherapy as part of their primary treatment. In contrast, such patients were less likely to have received surgery of the primary site than LN− chondrosarcoma patients. Among those with lymph node involvement, 18 received any type of surgery, 15 received lymph node surgery, and 14 patients did not undergo any type of surgical treatment.

Survival outcomes relative to nodal status

The 5-year DSS and OS of all chondrosarcoma cases included were 82% (95% CI: 80%–83%) and 72% (95% CI: 70%–74%), respectively. In univariable analyses, nodal involvement was associated with inferior DSS and OS (DSS HR: 4.22, 95% CI: 2.52–7.06 and OS HR: 3.74, 95% CI: 2.44–5.72, **Table 2**). Five-year DSS rate for LN+ and LN− cases were 48% (95% CI: 28%–65%) and 82% (95% CI: 80%–84%), respectively (log-rank $P < 0.001$, **Fig. 3A**). The 5-year OS rates were 38% (95% CI: 21%–55%) for LN+ cases and 73% (95% CI: 71%–75%) for those without nodal involvement (log-rank $P < 0.001$, **Fig. 3B**).

Survival outcomes in LN+ patients relative to treatment modality

Receipt of lymph node surgery was associated with superior survival among LN+ cases (DSS HR: 0.19, 95% CI: 0.06–0.61and OS HR: 0.42, 95% CI: 0.17–1.00) (**Table 2; Fig. 4**). The median DSS was 110 months (95% CI: 44 mo–NA) for those who received lymph node surgery and 8 months (95% CI: 2–29 mo) for cases that did not. Receipt of any surgery was also associated with superior DSS and OS

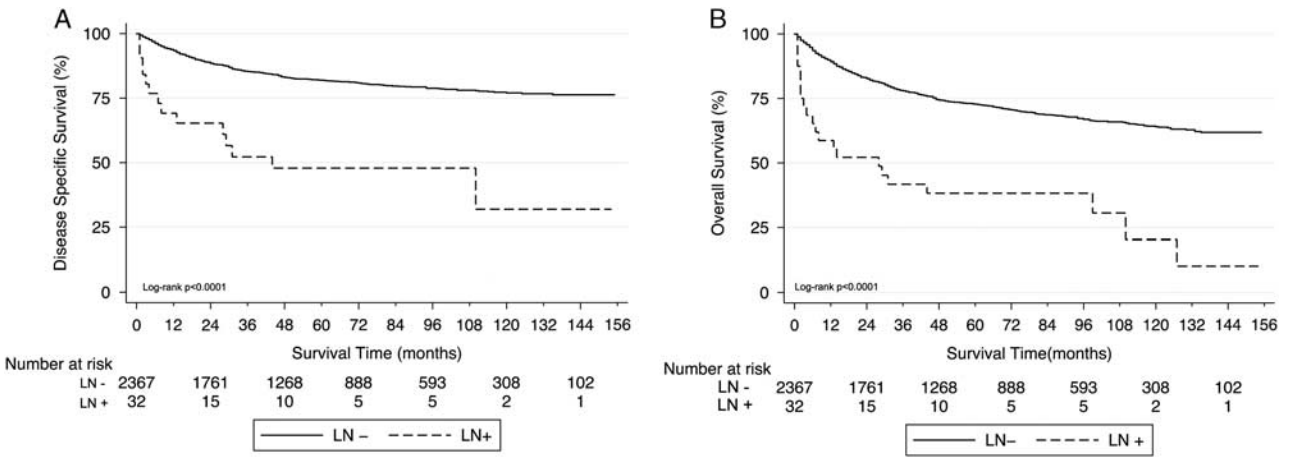

Figure 3. Survival outcomes by status of lymph nodes at initial diagnosis. A, Disease-specific survival. B, Overall survival. LN+ indicates lymph node positive; LN−, lymph node negative.

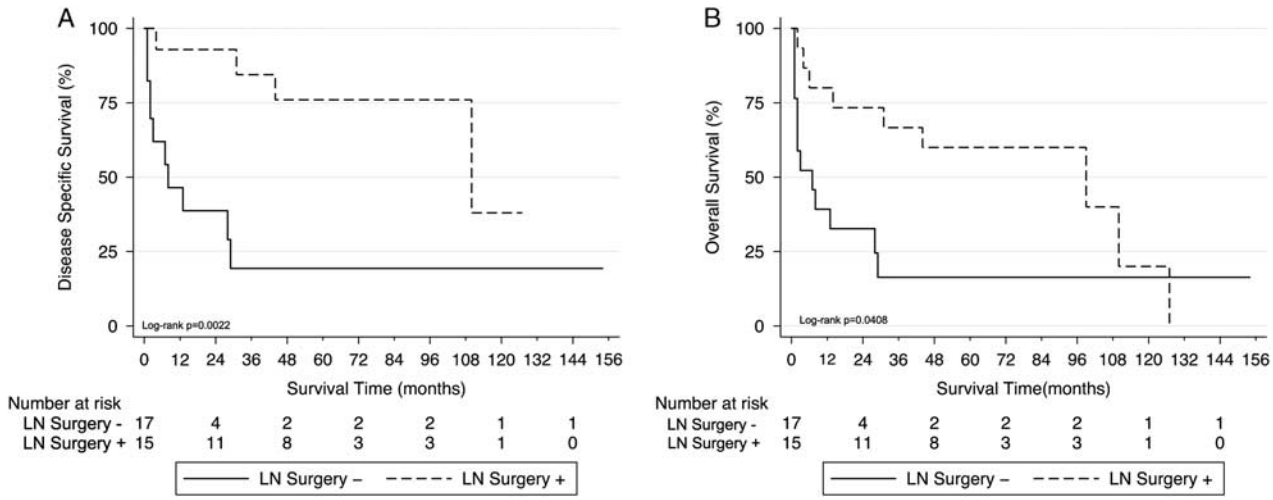

Figure 4. Survival outcomes by receipt of lymph node surgery in patients with lymph nodes involved by chondrosarcoma at initial diagnosis. A, Disease-specific survival. B, Overall survival. LN Surgery + indicates treated with lymph node surgery; LN Surgery – , not treated with lymph node surgery.

survival among those with positive nodal involvement (DSS HR: 0.16, 95% CI: 0.05–0.50 and OS HR: 0.26, 95% CI: 0.10–0.67, **Table 2**).

Patients with distant metastases at diagnosis were less likely to receive surgical treatment than those without distant metastases (Supplemental Materials Table 2, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13). This was true both for the entire study population ($P < 0.0001$) and for the LN + cohort ($P = 0.029$). In LN + patients, lymph node surgery was less likely in those with distant metastases at diagnosis ($P = 0.005$; Supplemental Materials Table 3, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13). Among the entire study population, the likelihood of lymph node surgery was not associated with the presence of distant metastases ($P = 0.375$).

Multivariable Cox analyses were conducted to assess the impact of surgical treatment and the presence of distant metastases at diagnosis among LN + patients (**Table 3**). For both DSS and OS, receipt of surgery was associated with improved survival outcomes. In contrast, the presence of distant metastases was not significantly associated with DSS or OS. The LR test indicated that the inclusion of distant metastasis status in the model did not improve the model fit versus surgery status alone.

Table 3

Multivariable Cox analyses of DSS and OS.

	DSS HR (95% CI)	OS HR (95% CI)
Surgery		
No	Referent	Referent
Yes	0.20 (0.05–0.71)	0.27 (0.09–0.76)
Distant metastases		
No	Referent	Referent
Yes	1.59 (0.49-5.14)	1.01 (0.38-2.68)
LR test vs. surgery alone*	$P = 0.43$	$P = 0.99$

Lymph node positive population, n = 32.

*LR test with one degree of freedom.

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

Treatment with radiation therapy or chemotherapy was not associated with improved DSS or OS compared with those not receiving these modalities or with unknown treatment status. Receipt of chemotherapy and radiation therapy were not associated with one another among all patients with distant metastases at diagnosis (n = 176, $P = 0.516$, Supplemental Materials Table 4A, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13) or among those LN + patients (n = 32, $P = 0.703$, Supplemental Materials Table 4B, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13). LN + patients receiving chemotherapy (n = 10) included those in 4 major histologic subclassifications (Supplementary Materials Table 5, Supplemental Digital Content 1, http://links.lww.com/IJSO/A13).

Discussion

We used the SEER database to explore lymph node involvement in the primary diagnosis of chondrosarcoma. As anticipated, regional lymph node involvement was uncommon, being evident in only 1.3% of cases in the SEER database. These findings are consistent with prior reports[19]. The subset of patients presenting with such involvement was distinct from those lacking lymph node involvement. Specifically, cases with lymph node involvement were more commonly extraskeletal, larger, higher grade, arising in the axial skeleton, of myxoid or dedifferentiated histologic subtypes, and more commonly metastatic at initial presentation.

Collectively, these data suggest that lymph node involvement is associated with more aggressive and more advanced disease at initial presentation. Consistent with this, the presence of lymph node involvement was associated with inferior DSS and OS (**Fig. 3**). Biologic variation in histologic type may be one explanatory factor, with myxoid, mesenchymal, and dedifferentiated chondrosarcomas representing a greater proportion of those with lymph node involvement. Indeed, myxoid chondrosarcomas have been known to behave differently than other types of chondrosarcomas, including conventional chondrosarcomas[23].

A key objective of this analysis was the identification of recommendations for treatment in LN+ patients. Only primary tumor surgery and lymph node surgery were associated with improved outcomes among LN+ patients. Surgery was more commonly undertaken in those without metastatic disease at presentation. The beneficial association of surgery seen in multivariable Cox analyses, after controlling for distant metastasis status, supports a protective effect of surgical treatment itself, rather than simply selecting for those with inherently better prognoses.

Receipt of lymph node surgery was inversely associated with distant metastasis status in those with lymph node involvement, again potentially indicating selection for lymph node surgery those with an inherently better prognosis. That improved survival outcomes were associated specifically with lymph node surgery is important, as such therapy is intended to treat directly the clinical scenario of interest herein, lymph node involvement. This beneficial effect was detectable despite receipt of lymph node surgery by less than half (47%, 15/32) of LN+ patients. Taken together, these data support an actual therapeutic effect of lymph node surgery in those chondrosarcoma patients with lymph node involvement. The limited sample size of LN+ patients and limited selection of explanatory variables in SEER prevent a more detailed analysis of other potential confounders.

Neither radiation therapy nor chemotherapy was associated with improved DSS or OS. It was possible that radiation therapy and chemotherapy might be administered preferentially in conjunction to those with advanced disease. However, there was no association between the use of these 2 treatment modalities among all patients with distant metastases at presentation, or among LN+ patients. It is therefore less likely that these treatments are being selectively administered to those with a poor prognosis.

The guidelines of the National Comprehensive Cancer Network (NCCN) recognize the potential utility of radiation therapy in the management of chondrosarcoma, especially those with limited surgical resectability[21]. Our results do not exclude benefit. Instead, our results suggest that its use be adapted to the clinical situation of a particular patient.

In contrast, NCCN guidelines state "[t]here is no established chemotherapy regimens for conventional chondrosarcoma (grades 1-3)" (see page MS-8)[21]. Other chondrosarcoma subtypes reputedly display some sensitivity to chemotherapy, with mesenchymal chondrosarcoma more responsive to Ewing sarcoma regimens and dedifferentiated chondrosarcoma more responsive to osteosarcoma regimens[21,24,25]. Sirolimus and cyclophosphamide[26] or dasatinib[27] have modest activity in high-grade chondrosarcomas and are used clinically. Recently, a potential role for immunotherapy has been reported[28]. Again, while our analysis does not indicate benefit for the use of chemotherapy in chondrosarcoma patients generally, there may be specific clinical situations justifying such use. The histologic subtype may be one such criterion that clinicians use to select patients for chemotherapy treatment.

This analysis must be interpreted in light of its limitations. First, the number of LN+ chondrosarcoma patients is small. As a result, we are unable to distinguish the independent effect of lymph node positivity in the absence of further metastatic disease. The limited sample size also prevented stratification by histologic subtypes. The subtypes included are recognized as having differential sensitivity to radiation and chemotherapy, as noted above. Therefore the statistical power to detect beneficial effects for radiation therapy or chemotherapy is further limited. That being said, surgical therapy was associated with improved outcomes, serving effectively as a positive control. If radiation therapy or chemotherapy have any beneficial effects when applied generally to LN+ chondrosarcoma patients, the effect size is significantly less then that of surgical treatment.

Second, these anlyses are retrospective, reflecting cases diagnosed in 2004–2015. This time frame was selected because (1) treatment patterns and modalities during that period likely reflect current practice; and (2) changes in SEER classifications of cases and covariates outside this interval might introduce greater variability into the analyses. Changes in treatment patterns could affect the applicability of the results, but we are unaware of breakthrough insights that might alter the conclusions.

Another significant limitation of SEER is the granularity of treatment information available. For radiation therapy, information regarding the mode of treatment administrations is available, but the limited number of LN+ chondrosarcoma cases did not allow us to consider different radiation treatment protocols. For chemotherapy, only receipt or nonreceipt/unknown are coded. Thus, despite the broad potential meaning of "radiation therapy" or "chemotherapy," these data do not allow more granular exploration of such treatments.

SEER classifies both radiation therapy and chemotherapy treatment as "yes" versus "no/unknown." Concerns have been raised regarding the investigation of radiation therapy and chemotherapy using data from SEER[29]. This relates to questions regarding misclassification, with a comparison between SEER and a Medicare claims database (the latter acting as a "gold standard") indicating up to 10% of cases are misclassified with respect to receipt of either radiation therapy or chemotherapy. This study was conducted in patients with cancer of the bladder, female breast, colorectal, lung, ovarian pancreatic, and prostate. There are several compelling reasons to undertake analyses such as this using SEER data.

First, primary regional lymph node involvement is an uncommon presentation of an uncommon type of disease (chondrosarcoma). Opportunities to explore clinical parameters, outcomes, and treatment are therefore limited. Even a large sarcoma treatment center is unlikely to see enough LN+ chondrosarcoma patients to undertake meaningful investigations. Thus, these data allow such exploration, even with limitations.

Second, the concerns raised regarding the misclassification of SEER treatment data were raised in a study using insurance claims data as a gold standard comparator[29]. However, there exist reports of significant misclassification associated with insurance claims databases[30]. Thus, the comparator used as "gold standard" may not be as reliable as hoped. That 90% of cases in the study were classified correctly implies that significant information exists within the SEER radiation therapy and chemotherapy classifications.

In the current study, neither radiation nor chemotherapy was associated with improved survival. Lack of association may be explained by 3 potential reasons: there is actually no benefit; there is a benefit, but misclassification prevented its detection; or there is benefit from certain types of therapy in certain subsets of patients, with inadequate numbers of cases available to detect a modest treatment effect. The last 2 explanations are not mutually exclusive. A modest treatment effect might have existed, but either the total number of cases receiving particular treatments

were inadequate or misclassification tended to minimize the differences between groups receiving or not receiving the particular treatment. Both effects would tend to lead to an underpowered assessment of these modalities. Both limitations could be overcome with a considerable increase in the number of patients receiving treatment for nodal involvement. On the basis of the rarity of this circumstance, such data are unlikely to become available.

In conclusion, lymph node involvement in patients with chondrosarcomas is uncommon, but does occur disproportionately in patients with large tumors, high grade, and nonconventional disease histologies, including myxoid, mesenchymal, and dedifferentiated. Synchronous distant metastases are more common in node-positive patients, likely reflecting more aggressive disease biology. The presence of regional node involvement in those with chondrosarcoma is associated with inferior DSS and OS versus those without such involvement.

It is the practice at our center to investigate for lymph node metastasis only when concerns for such lesions are raised by suggestive clinical or radiological evidence. Given the low frequency of lymph node involvement in chondrosarcoma, additional measures, such as sentinel lymph node biopsy, do not appear to be warranted. The utility of further measures to risk-stratify patients for lymph node involvement would require additional investigation.

In those with nodal involvement at presentation, surgical treatment, including lymph node surgery, is associated with improved survival outcomes. The results of this analysis suggest this is an actual effect of surgical treatment, rather than selecting for those with inherently better prognosis. In contrast, no beneficial effects were detected from either radiation therapy or chemotherapy, although a small benefit cannot be excluded. In the uncommon circumstance of chondrosarcoma patients presenting with lymph node involvement, surgical intervention should be the mainstay of treatment. Radiation therapy and chemotherapy should be tailored to the unique needs of specific patients.

Ethical approval

All research described herein was undertaken using data from SEER (https://seer.cancer.gov). SEER is a publicly accessible database of de-identified data, for which human subjects review and ethical approval are not required.

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No specific funding source was used in the conduct of this research project.

Author contribution

L.D.C., B.C., and G.J.P.: conception and design, data acquisition. L.D.C., B.C., M.J.T., E.T.L., S.M.P., M.J.W., T.S.K., E.Y.K., G.M.K., and G.J.P.: analysis and interpretation of data. L.D.C., B.C., M.J.T., E.T.L., S.M.P., M.J.W., T.S.K., E.Y.K., G.M.K., and G.J.P.: drafting, revision, and final approval of manuscript.

Conflict of interest disclosure

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