

## ORIGINAL RESEARCH

# Impact of Prior Cancer on the Prognosis of Patients with Chondrosarcoma: A Population-Based Study of the SEER Database

Jun Qian, MM; Shijie Dai, MM; Haoyu Wang, MM

### ABSTRACT

**Background** • Patients with prior cancer are generally exempt from cancer experiments. This research aims to describe the prevalence, clinical features, and effects of past malignancy among patients with chondrosarcoma.

**Methods** • Chondrosarcoma patients diagnosed between 2010 to 2015 were collected from the SEER database. The propensity score matching method was used to reconcile the disparity in baseline attributes. Kaplan–Meier analysis was employed to explore the outcomes of prior cancer on overall survival. The proportional hazards assumption was used to certain whether the covariate matched the Cox regression model. The potential outliers were estimated by deviance residuals type.

**Results** • A total of 1,721 unique individuals were collected, of those 284 (16.50%) patients had a history of

cancer, with prostate cancer being commonly documented ( $n = 49$ , 17.25%). Approximately half of the previous tumors are diagnosed within 5 years before the diagnosis of chondrosarcoma. Chondrosarcoma patients with prior cancers have a lower survival rate than those without prior malignancy ( $P < .001$ ). A multivariable Cox analysis reveals that past cancer is a distinct risk factor for lifespan (hazard ratio = 2.489,  $P < .001$ ).

**Conclusion** • This study initially discovered that chondrosarcoma patients with past cancer have a bad prognosis. Different types of past cancer have varying effects on survival. We urgently propose that cancer trial exclusion criteria be set specifically by cancer classification, rather than accepting the unchangeable criterion for default. (*Altern Ther Health Med.* 2023;29(8):674-679).

**Jun Qian**, MM, Department of Orthopaedics, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou, Zhejiang, China. **Shijie Dai**, MM, College of Pharmacy, Hangzhou Medical College. **Haoyu Wang**, MM, Department of Orthopaedics, The Quzhou Affiliated Hospital of Wenzhou Medical University, Quzhou People's Hospital, Quzhou, Zhejiang, China.

Corresponding author: Haoyu Wang, MM  
E-mail: [why870102@163.com](mailto:why870102@163.com)

### INTRODUCTION

Chondrosarcoma, with the capability to promote cartilage production, is the second most frequent malignancy of skeletal system cancers, accounting for 20-30% of cases.<sup>1-3</sup> Unlike osteosarcoma, which is commonly recorded in adolescents, chondrosarcoma is the most common bone tumor in aging populations. The main therapeutic regimens for chondrosarcoma are surgery, optimization of chemotherapy, and radiotherapy. However, chondrosarcoma is generally considered chemo- and radioresistant.<sup>4-6</sup> The 5-year overall survival (OS) of different subtypes of chondrosarcoma varied from 11.3% to 68.1%.<sup>7</sup>

Given that, to further improve the survival of patients with chondrosarcoma, a set of clinical trials was conducted worldwide to identify the optimum comprehensive therapy.

Although clinical trials are vital to ameliorating survival for chondrosarcoma patients, under 5% of cases are enrolled in cancer trials.<sup>8</sup> Increasingly restrictive eligibility criteria is one of the most major obstacles. Based on the commonly held notion that prior cancer diagnosis and treatment could interfere with survival, about one-quarter of patients recently diagnosed with lung cancer are excluded from malignancies trials.<sup>9</sup> Nevertheless, not every incidence of past cancers is detrimental to survival.<sup>10</sup>

The total number of cancer survivors is quickly expanding, with a four-fold increase over the three decades, in the United States.<sup>9</sup> Owing to the improvement in treatment, more than 60% of the cancer survivors population has survived more than 5 years after being first diagnosed with cancer.<sup>11</sup> For the expanding number of cancer survivors, such stringent criteria resulted in some qualified volunteers being denied enrollment in clinical studies, reducing the credibility and universality of studies on cancer.

The effects of past malignancy on chondrosarcoma patients remain unknown. Consequently, we performed an investigation to first analyze the incidence, clinical

characteristics, and consequences of prior cancer on chondrosarcoma individuals by utilizing the SEER database.

## MATERIAL AND METHODS

### Data extraction

Complete information was gathered from the SEER database. The following were the exclusion criteria: (1) Patients whose ages at diagnosis were unknown; (2) patients identified through autopsies or death certificates; (3) Patients with unclear survival and subsequent data. The inclusion criteria for this study involved including the remaining chondrosarcoma patients after excluding those who met the exclusion criteria. The following 16 covariates were collected from SEER, including marital status, gender, race, age, diagnosed year, primary sites, Seer stage, TNM stage, pathology grade, histology, T stage, N stage, M stage, radiation, chemotherapy, and surgery.

### Statistical methods

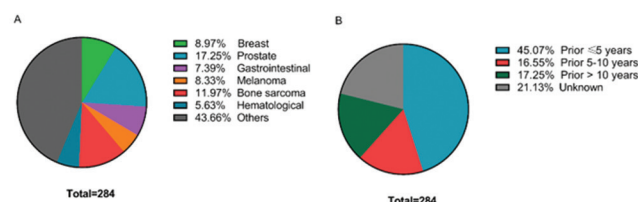
Participants with chondrosarcoma were divided into two groups based on their prior malignancy history. The differences in the characteristics of patients in these two groups were tested by Pearson  $\chi^2$  analysis. The propensity score matching (PSM) method was employed to decrease the bias of heterogeneous variables.<sup>12</sup> Subsequent analyses were performed by the balanced PSM pairs. The Kaplan-Meier curves were used to compare the difference in the overall survival (OS) between the two groups. The proportional hazards (PH) models were used to find independent prognostic risk variables. We meticulously chose eligible factors for multivariate Cox analysis to improve the dependability of the outcomes. The statistical significance level was chosen at  $P < .05$ .

## RESULTS

### Study characteristics

Information about a total of 1,721 unique chondrosarcoma patients were collected from the SEER database. Among them, 284 (16.50%) individuals are with prior cancer history. The group of patients with prior cancer consist higher percentage of elderly people together with lower levels of early-stage, early T stage (T1-2), N0 stage, M0 stage, and chemotherapy, as shown in Table 1. The discrepancy between these two groups is balanced after adjustment for propensity score (Table 1, Matched data set). A detailed characteristic of eligible chondrosarcoma patients is presented in Table 1. Figure 1A demonstrates the proportions of different prior cancer types. The most common type of cancer is prostate cancer (17.25%), followed by bone sarcoma (11.79%), breast cancer (8.79%), melanoma (8.33%), gastrointestinal cancer (7.39%), and hematological cancer (5.63%). Notably, some prior cancer types are recorded as unknown, which are combined with those less reported cancers into the others group. Hence, we need to interpret carefully the implication of the others group. Figure 1B exhibits the relative time of diagnosis of prior cancer.

**Figure 1.** Type (A) and Interval Time of Diagnosis (B) of Prior Cancer



**Table 1.** Baseline Characteristics of Chondrosarcoma in the Original and Matched Datasets (N = 1721)

Characteristics	Original data set			Matched data set		
	No prior cancer, n = 1437 (%)	With prior cancer, n = 284 (%)	P value	No prior cancer, n = 284 (%)	With prior cancer, n = 284 (%)	P value
<b>Age</b>			<.001			.620
≤50	615 (42.8)	64 (22.5)		69 (24.3)	64 (22.5)	
>50	822 (57.2)	220 (77.5)		215 (75.7)	220 (77.5)	
<b>Gender</b>			.811			.732
Female	603 (42.0)	117 (41.2)		113 (39.8)	117 (41.2)	
Male	834 (58.0)	167 (58.8)		171 (60.2)	167 (58.8)	
<b>Race</b>			.504			.356
White	1230 (85.6)	249 (87.7)		238 (83.8)	249 (87.7)	
Black	109 (7.6)	16 (5.6)		24 (8.5)	16 (5.6)	
Others	98 (6.8)	19 (6.7)		22 (7.7)	19 (6.7)	
<b>Marital status</b>			.006			.387
Married	737 (51.3)	171 (60.2)		181 (63.7)	171 (60.2)	
Unmarried	700 (48.7)	113 (39.8)		103 (36.3)	113 (39.8)	
<b>Diagnosed year</b>			.674			.355
2010-2012	709 (49.3)	144 (50.7)		155 (54.6)	144 (50.7)	
2013-2015	728 (51.7)	140 (49.3)		129 (45.4)	140 (49.3)	
<b>Primary site</b>			.002			.692
Extremity	670 (46.6)	122 (43.0)		122 (43.0)	122 (43.0)	
Trunk	682 (47.5)	129 (45.4)		135 (47.5)	129 (45.4)	
Other	85 (5.9)	33 (11.6)		27 (9.5)	33 (11.6)	
<b>SEER stage</b>			.028			.731
Local	770 (53.6)	137 (48.2)		141 (49.6)	137 (48.2)	
Regional	404 (28.1)	83 (29.2)		79 (27.8)	83 (29.2)	
Distant	147 (10.2)	26 (9.2)		32 (11.3)	26 (9.2)	
Unknown	116 (8.1)	38 (13.4)		32 (11.3)	38 (13.4)	
<b>TNM stage</b>			.004			.234
I-II	1034 (72.0)	188 (66.2)		183 (64.4)	188 (66.2)	
III-IV	152 (10.6)	23 (8.1)		35 (12.3)	23 (8.1)	
Unknown	251 (17.4)	73 (25.7)		66 (23.2)	73 (25.7)	
<b>Grade</b>			.541			.696
Grade I-II	882 (61.4)	168 (59.2)		164 (57.7)	168 (59.2)	
Grade III-IV	268 (18.6)	61 (21.5)		57 (20.1)	61 (21.5)	
Unknown	287 (20.0)	55 (19.4)		63 (22.2)	55 (19.4)	
<b>Histology</b>			.365			.254
Chondrosarcoma	1058 (73.6)	216 (76.0)		210 (73.9)	216 (76.0)	
Myxoid chondrosarcoma	189 (13.2)	26 (9.2)		42 (14.8)	26 (9.2)	
Dedifferentiated chondrosarcoma	118 (8.2)	26 (9.2)		22 (7.7)	26 (9.2)	
Mesenchymal chondrosarcoma	46 (3.2)	8 (2.8)		7 (2.5)	8 (2.8)	
Clear cell chondrosarcoma	16 (1.1)	6 (2.1)		2 (0.7)	6 (2.1)	
Juxtacortical chondrosarcoma	10 (0.7)	2 (0.7)		1 (0.4)	2 (0.7)	
<b>T stage</b>			.007			.902
T1-2	1141 (79.4)	203 (71.5)		203 (71.5)	203 (71.5)	
T3-4	15 (1.0)	2 (0.7)		3 (1.0)	2 (0.7)	
Unknown	281 (19.6)	79 (27.8)		78 (27.5)	79 (27.8)	
<b>N stage</b>			.032			.386
N0	1268 (88.3)	237 (83.5)		238 (83.8)	237 (83.5)	
N1	22 (1.5)	3 (1.0)		7 (2.5)	3 (1.0)	
Unknown	147 (10.2)	44 (15.5)		39 (13.7)	44 (15.5)	
<b>M stage</b>			.002			.078
M0	1246 (86.7)	240 (84.5)		231 (81.3)	240 (84.5)	
M1	117 (8.1)	15 (5.3)		29 (10.2)	15 (5.3)	
Unknown	74 (5.2)	29 (10.2)		24 (8.5)	29 (10.2)	
<b>Radiation</b>			.346			.316
No/unknown	1181 (82.2)	240 (84.5)		231 (81.3)	240 (84.5)	
Yes	256 (17.8)	44 (15.5)		53 (18.7)	44 (15.5)	
<b>Chemotherapy</b>			.018			.383
No/unknown	1298 (90.3)	269 (94.7)		264 (93.0)	269 (94.7)	
Yes	139 (9.7)	15 (5.3)		20 (7.0)	15 (5.3)	
<b>Surgery</b>			.054			.831
No/unknown	204 (14.2)	53 (18.7)		55 (19.4)	53 (18.7)	
Yes	1233 (85.8)	231 (81.3)		229 (80.6)	231 (81.3)	

## OS of chondrosarcoma patients with prior cancer

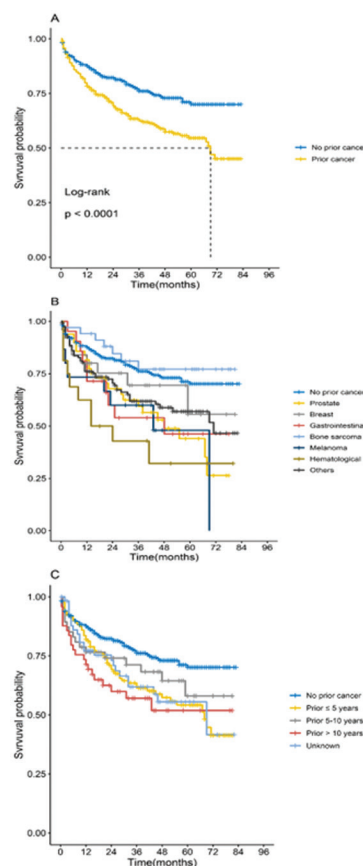
Figure 2A reveals the result of Kaplan–Meier analysis for the effects of prior cancer on OS. Chondrosarcoma patients with prior cancer are significantly associated with poor OS. Figure 2B demonstrates the effects of different prior cancer types on OS. Chondrosarcoma patients with prior prostate, melanoma, and hematological cancer have a worse OS ( $P < .05$ ). However, there have been no statistically significant changes in OS in patients with prior bone sarcoma, breast, and gastrointestinal cancer. Patients with prior cancer whose diagnosis interval time is  $\leq 5$  years or  $> 10$  years have a worse OS ( $P < .05$ ) (Figure 2C).

Subgroup analysis was constructed to yield a comprehensive insight into the effects of clinical characteristics of chondrosarcoma patients with prior cancer. Figure 3A–I demonstrates the effects of the following factors on the OS of chondrosarcoma patients: gender, age, TNM stage, histology, grade, Seer stage, radiation, surgery, and chemotherapy. Chondrosarcoma patients with prior cancer are remarkably associated with a poor OS in both the male and female populations ( $P < 0.01$ ) (Figure 3A). The same tendency is found in both the radiation and no radiation groups, in both the grade I–II and grade III–IV groups (Figure 3E, 3G). Additionally, chondrosarcoma patients with prior cancer have an inferior OS in the age  $> 50$  years group, TNM stage I–II group, chondrosarcoma group, myxoid chondrosarcoma group, local stage group, regional stage group, surgery group, and no chemotherapy group (Figure 3B–D, 3F, 3H–I). Beyond that, the result of other factors, including diagnosed year, race, marital status, primary site, T stage, N stage, and M stage have been displayed in the Supplement Figure 1A–G.

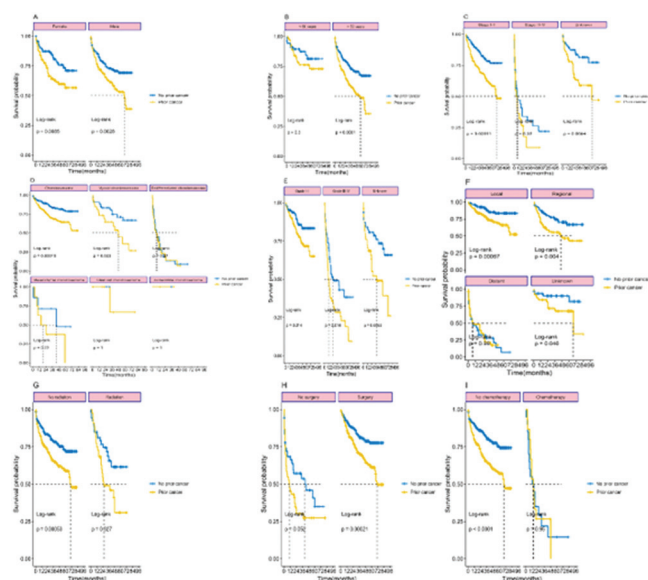
## Cox analysis

As for the univariate Cox analysis, the results reveal that the OS is observably lower in the prior cancer group [hazard ratio (HR): 1.812, 95% CI: 1.346–2.439,  $P < 0.001$ ], lower in the  $> 50$  years group (HR: 2.093, 95% CI: 1.373–3.190,  $P < .001$ ), lower in the Black group than the White group (HR: 2.059, 95% CI: 1.305–3.251,  $P = 0.002$ ), lower in the unmarried group (HR: 1.360, 95% CI: 1.016–1.821,  $P = .039$ ), lower in the regional and distant group than local group (HR: 1.998, 95% CI: 1.405–2.843,  $P < .001$ , HR: 7.469, 95% CI: 5.049–11.049,  $P < .001$ , respectively), lower in the TNM stage III–IV group (HR: 5.610, 95% CI: 3.911–8.046,  $P < .001$ ), lower in the grade III–IV group (HR: 5.431, 95% CI: 3.890–7.582,  $P < .001$ ), lower in the dedifferentiated chondrosarcoma and mesenchymal chondrosarcoma group than reference group (HR: 7.959, 95% CI: 5.524–11.467,  $P < .001$ , HR: 3.064, 95% CI: 1.551–6.055,  $P = .001$ , respectively), lower in the N1 stage group (HR: 3.423, 95% CI: 1.512–7.746,  $P = .003$ ), lower in the M1 stage group (HR: 7.547, 95% CI: 5.200–10.954,  $P < .001$ ), lower in the radiation group (HR: 1.575, 95% CI: 1.115–2.224,  $P = .010$ ), lower in the chemotherapy group (HR: 4.168, 95% CI: 2.773–6.265,  $P < .001$ ), and lower in the no surgery group (HR: 0.273, 95% CI: 0.201–0.371,  $P < .001$ ). However, there is no significant discrepancy in the gender, year of diagnosis, primary site, and T stage groups (Table 2).

**Figure 2.** Kaplan–Meier Survival Curves (A), Subgroup Analysis Stratified by the Prior Cancer Type (B), and Interval Time (C) of Prior Cancer Effects on OS in Patients With Chondrosarcoma



**Figure 3.** Subgroup Analysis Stratified by the Sex (A), Age (B), TNM Stage (C), Histology (D), Pathologic Grade (E), SEER Stage (F), Radiation (G), Surgery (H), and Chemotherapy (I) of the Effects on Overall Survival in Chondrosarcoma Patients





We merely selected variables with a value of  $P < .05$  in univariate Cox analysis and matched with PH assumption for multivariate Cox analysis, including age, race, a history of prior cancer, pathology grade, Seer stage, N stage, M stage, radiation, and chemotherapy. Importantly, prior cancer history is an independent risk factor based on multivariate Cox analysis (HR: 2.489, 95% CI: 1.811-3.419,  $P < .001$ ) (Figure 4A).

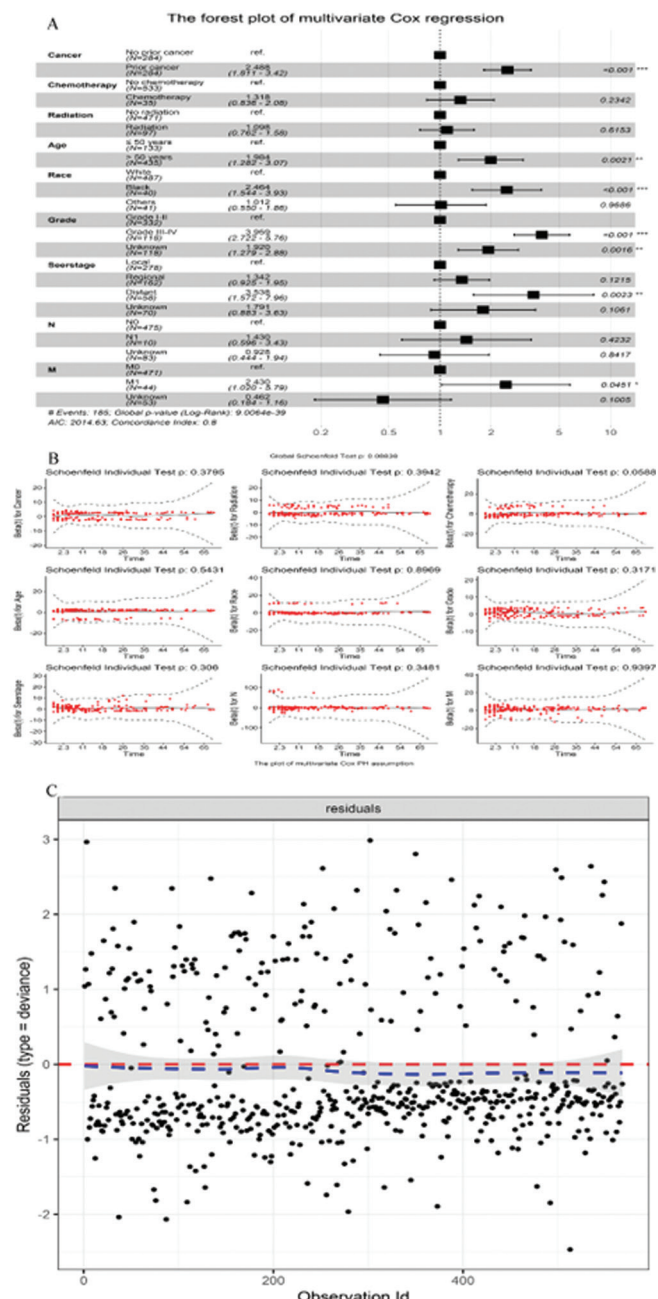
**Table 2.** Cox Regression Analysis of Prior Cancer History Effects on Patients With Chondrosarcoma

Variables	Univariate Cox regression		Multivariate Cox regression	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
<b>Age</b>				
≤50	Reference		Reference	
>50	2.093 (1.373-3.190)	<0.001	1.984 (1.282-3.071)	.002
<b>Gender</b>				
Female	Reference		NA	NA
Male	1.234 (0.914-1.665)	0.170	NA	NA
<b>Race</b>				
White	Reference		Reference	
Black	2.059 (1.305-3.251)	0.002	2.464 (1.544-3.934)	<.001
Others	1.073 (0.596-1.932)	0.815	1.012 (0.550-1.865)	.969
<b>Marital status</b>				
Married	Reference		NA	NA
Unmarried	1.360 (1.016-1.821)	0.039	NA	NA
<b>Diagnosed year</b>				
2010-2012	Reference		NA	NA
2013-2015	1.106 (0.814-1.504)	0.519	NA	NA
<b>Prior cancer</b>				
No	Reference		Reference	
Yes	1.812 (1.346-2.439)	<0.001	2.489 (1.811-3.419)	<.001
<b>Primary site</b>				
Extremity	Reference		NA	NA
Trunk	1.144 (0.845-1.548)	0.384	NA	NA
Other	0.833 (0.487-1.427)	0.507	NA	NA
<b>Seer stage</b>				
Local	Reference		Reference	
Regional	1.998 (1.405-2.843)	<0.001	1.342 (0.925-1.948)	.121
Distant	7.469 (5.049-11.049)	<0.001	3.538 (1.572-7.961)	.002
Unknown	1.123 (0.648-1.948)	0.679	1.791 (0.883-3.629)	.106
<b>TNM stage</b>				
I-II	Reference		NA	NA
III-IV	5.610 (3.911-8.046)	<0.001	NA	NA
Unknown	1.096 (0.760-1.580)	0.623	NA	NA
<b>Grade</b>				
Grade I-II	Reference		Reference	
Grade III-IV	5.431 (3.890-7.582)	<.001	3.959 (2.722-5.758)	<.001
Unknown	2.357 (1.599-3.475)	<.001	1.920 (1.279-2.883)	.002
<b>Histology</b>				
Chondrosarcoma	Reference		NA	NA
Myxoid chondrosarcoma	1.510 (0.983-2.320)	.060	NA	NA
Dedifferentiated chondrosarcoma	7.959 (5.524-11.467)	<.001	NA	NA
Mesenchymal chondrosarcoma	3.064 (1.551-6.055)	.001	NA	NA
Clear cell chondrosarcoma	0.583 (0.081-4.182)	.592	NA	NA
Juxtacortical chondrosarcoma	NA	NA	NA	NA
<b>T stage</b>				
T1-2	Reference		NA	NA
T3-4	2.598 (0.825-8.179)	.103	NA	NA
Unknown	1.229 (0.895-1.686)	.202	NA	NA
<b>N stage</b>				
N0	Reference		Reference	
N1	3.423 (1.512-7.746)	.003	1.430 (0.596-3.429)	.423
Unknown	0.737 (0.463-1.173)	.198	0.928 (0.444-1.937)	.842
<b>M stage</b>				
M0	Reference		Reference	
M1	7.547 (5.200-10.954)	<.001	2.430 (1.020-5.793)	.045
Unknown	0.622 (0.327-1.182)	0.147	0.462 (0.184-1.161)	.100
<b>Radiation</b>				
No/unknown	Reference		Reference	
Yes	1.575 (1.115-2.224)	.010	1.098 (0.762-1.584)	.615
<b>Chemotherapy</b>				
No/unknown	Reference		Reference	
Yes	4.168 (2.773-6.265)	<.001	1.318 (0.836-2.077)	.234
<b>Surgery</b>				
No/unknown	Reference		NA	NA
Yes	0.273 (0.201-0.371)	<.001	NA	NA

## Cox proportional hazards model: assumption and evaluation of potential outliers

The premise of using Cox analysis is that the covariate satisfied the PH assumption. Schoenfeld individual test and the global Schoenfeld test are not statistically significant ( $P > .05$ ), as shown in Figure 4B. Furthermore, as shown in Figure 4C, the deviance residuals are usually symmetrically dispersed around zero with a deviation from the mean within one, meaning that no exceptional cases occurred in this study.

**Figure 4.** Forest Plot of Multivariate Cox Regression (A). Plot of Multivariate Cox PH Assumption (B). Schoenfeld Residuals are Independent of Time. Influence Plot of Potential Outliers (C). The Deviance Residuals are Symmetrically Distributed About Zero with a Standard Deviation Within 1.



## DISCUSSION

This is a specialized study focusing on a specific cancer called “chondrosarcoma” rather than overall bone tumors. We provide the incidence of prior cancer in chondrosarcoma patients, their clinical characteristics, and elaborate on the impact of prior cancer history on survival, along with further subgroup analysis. The results of this study found that 16.50% of chondrosarcoma patients have a history of past malignancy. Prostate cancer is commonly documented as a prior cancer type. Approximately half of the previous tumors are diagnosed within 5 years before the diagnosis of chondrosarcoma. Chondrosarcoma patients with prior cancers have a lower survival rate than those without prior malignancy ( $P < .001$ ). The different types of previous tumors and the interval between the diagnosis of previous tumors and the diagnosis of chondrosarcoma have varying impacts on the survival of chondrosarcoma patients. A multivariable Cox analysis reveals that prior cancer is a distinct risk factor for lifespan.

This study found that 16.50% of chondrosarcoma patients have a history of previous tumors, which is consistent with Zhou’s findings of 17.16%.<sup>10</sup> Prior prostate cancer and breast cancer are commonly recorded, accounting for 17.25% and 8.97% of all prior cancers. According to the most recent worldwide cancer research, the second prevalent disease in males is prostate cancer, and the first most common cancer in women is breast cancer.<sup>13</sup>

In this study, we discovered that chondrosarcoma patients who previously had cancer have a considerably poorer survival percentage than those who did not, which is consistent with Zhou’s findings that bone and soft tissue cases with prior cancer have a poor survival rate.<sup>10</sup> Notably, the main discrepancy is that our study focuses on particular cancer (chondrosarcoma) instead of whole bone and soft tissue cancer. Another distinction is the varied scales of the research participants and inclusion criteria. Zhou et al. evaluated individuals who suffered bone and soft tissue cases between 2004 and 2009, while we collected individuals diagnosed with chondrosarcoma between 2010 to 2015.

Figure 2B shows that not all past cancers have an effect on chondrosarcoma patients’ survival. Individuals with a history of prostate cancer, melanoma, or hematological cancer (mostly non-Hodgkin’s lymphoma) have a shorter life expectancy than those without a history of cancer. Previous diagnosis of breast cancer, gastrointestinal cancer, and bone sarcoma, on the other hand, have non-inferior survival compared to people without past cancer. These findings demonstrate that different forms of past cancer have varying effects on the clinical prognosis of chondrosarcoma patients. Superior OS groups have a higher 5-year survival rate than non-inferior OS groups.<sup>14</sup> Moreover, T1-2 stage, N0 stage, and M0 stage chondrosarcoma patients with prior cancer have the same tendency (Supplement Figure 1E-G). In accordance with the findings reported above, we offer preliminary proof showing that prior cancers with relatively good prognoses are more likely to cause troubles with chondrosarcoma patients’ surviving, but prior cancers with relatively poor prognoses have no effect on survival.

The duration between earlier cancer diagnoses is an important exclusion criterion in therapeutic trials. The majority of cancer trials set 5-years as the exclusion window based on previous studies.<sup>15,16</sup> In the current study, chondrosarcoma patients with prior cancer have a significantly lower OS in groups with earlier cancer diagnosis time interval of  $\leq 5$  years and  $> 10$  years ( $P = .006$  and  $P = .007$ , respectively). However, the OS is similar in groups whose prior cancer diagnoses ranged from 5 to 10 years ( $P = .431$ ). These interesting findings further support that a 5-year interval time is an important exclusion window. Beyond that, it seemed that the 10-year interval time might be used as another exclusion window. Notably, patients with 5-10 years interval time of prior cancer diagnosis could be enrolled in cancer trials. As a result, an additional study should be conducted on large-scale populations to investigate the association between the period interval of previous cancer diagnosis and survival from chondrosarcoma.

Several studies suggest that females are associated with favorable survival outcome,<sup>17,18</sup> but other research indicate that female gender is not a prognostic factor of good survival outcome.<sup>19</sup> The findings in this investigation demonstrate that chondrosarcoma patients with prior cancer are significantly related to an inferior OS regardless of being male or female, which implies that gender is not needed to be considered as an exclusion index. Consistent with the literature, this research found that older patients are an independent prognostic factor.<sup>18,20,21</sup> In individuals who had prior carcinoma, the OS is considerably lower in the  $> 50$  years group. A possible explanation for this might be that the elderly are more likely to be affected by prior cancers due to their poor basic health. Consequently, 50 years old could be set as an exclusion index. Subsequent studies could consider including patients younger than 50 years old. There are remarkable differences in survival between chondrosarcoma subtypes based on the previous studies.<sup>7,22,23</sup> Compared with dedifferentiated and mesenchymal chondrosarcoma, classic and myxoid chondrosarcoma have a favorable survival. Based on this, we suppose that patients with relatively favorable prognoses are more easily affected by prior cancer history. In accordance with the present results, previous studies demonstrate that patients without radiation or chemotherapy have a better OS than those treated with radiation or chemotherapy.<sup>24,25</sup> One possibility is that chondrosarcoma is generally considered chemo- and radioresistant, receiving treatment might not be beneficial for survival. These findings supported our hypothesis that patients with relatively favorable prognoses are more easily affected by prior cancer history. Intriguingly, there are substantial pieces of evidence to corroborate our hypothesis according to the results of this study. Data from several previous studies show that patients have a favorable prognosis in patients with stage I-II, grade III-IV, local stage, regional stage, T1-2 stage, N0 stage, M0 stage, and surgical treatment.<sup>7,17-19, 26</sup> In addition, Cox analysis found that pre-existing cancer is a distinct risk variable. Taken together,

these findings highlight the role of prior cancer in reducing survival outcomes of chondrosarcoma patients. We used PH assumption testing and probable outlier identification to reduce the influence of bias and confounding factors and boost the study's validity. The results demonstrate that there are no outliers in this sample. In general, this is the first study to examine the prevalence, clinical features, and effects of past malignancy in individuals with chondrosarcoma.

## CONCLUSION

This study firstly yielded an insight into chondrosarcoma patients with prior cancer are associated with poor OS. Furthermore, we hypothesize that patients with comparatively favorable prognoses would be more affected by prior malignancy history. Further research should be undertaken to validate the association according to large-scale populations.

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## AUTHOR DISCLOSURE STATEMENT

The authors have no conflicts of interest to declare.

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**Supplement Figure 1.** Subgroup Analysis Stratified by the Diagnosed Year (A), Race (B), Marital Status (C), Primary Site (D), T Stage (E), N Stage (F), M Stage (G) of the Effects on Overall Survival in Chondrosarcoma Patients With or Without Prior Cancer.

