Clin Orthop Relat Res (2018) 476:987-996
DOI 10.1007/s11999.0000000000000152

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Clinical Research

Can a Nomogram Help to Predict the Overall and Cancer-specific Survival of Patients With Chondrosarcoma?

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Received: 1 August 2017 / Accepted: 7 December 2017 / Published online: 22 February 2018

Abstract

Background Many factors have been reported to be associated with the prognosis of patients with chondrosarcoma, but clinicians have few tools to estimate precisely an individual patient's likelihood of surviving the illness. We therefore sought to develop effective nomograms to better estimate the survival of patients with chondrosarcoma.

Questions/purposes (1) Which clinicopathologic features are independent prognostic factors for patients with chondrosarcoma? (2) Can we develop a nomogram to predict 3- and 5-year overall and cancer-specific survival of individual patients with chondrosarcoma based on personalized information?

Methods We collected information on patients diagnosed with chondrosarcoma between 1988 and 2011 from the Surveillance, Epidemiology, and End Results (SEER) database. The SEER database consists of 18 cancer registries and covers approximately 30% of the total United States population. One thousand thirty-four adult patients with grade II or III chondrosarcoma were included in the cohort (patients with grade I chondrosarcoma were not evaluated in this study), while 327 patients were excluded from the study owing to missing data regarding tumor size or metastasis. Nine hundred nineteen patients (89%) in the cohort had complete followup for at least 1 year. The X-tile program was used to determine optimal cutoff points. Univariate and multivariate analyses were applied to identify independent factors that were further included in the nomograms predicting 3- and 5-year overall survival and cancer-specific survival. Records of 1034 patients were collected and randomly divided into training (n = 517) and validation (n = 517) cohorts. The nomograms were developed based on training cohort. Data for the training cohort were obtained for internal validation of the nomograms, whereas data for the validation cohort were obtained for external validation of the nomograms. Bootstrapped validation, which used a resample with 500 iterations, was applied to validate the nomograms internally and externally.

Results Six independent prognostic factors for overall survival and six for cancer-specific survival were identified and incorporated to construct nomograms for 3- and 5-year overall and cancer-specific survival. These nomograms can easily be used by providers in the office to estimate a patient's prognosis; the only clinical details a provider

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needs to use these nomograms effectively are age, histologic subtype, tumor grade, whether surgery was performed, tumor size, and the presence or absence of metastases. Internal and external calibration plots for the probability of 3- and 5-year overall survival and cancer-specific survival showed good agreement between nomogram prediction and observed outcomes. The concordance indices (C-indices) for internal validation of overall survival and cancer-specific survival prediction were 0.803 and 0.829, respectively, whereas the C-indices for external validation were 0.753 and 0.759, respectively.

Conclusions We were able to develop effective nomograms to predict overall survival and cancer-specific survival for patients with chondrosarcoma; these nomograms require only basic information, which should be available to all providers in the office setting. If these observations can be validated in different registries or databases, the nomograms can assist clinicians in counseling patients regarding therapeutic choices.

Level of Evidence Level III, prognostic study.

Introduction

In the United States (US), there were an estimated 3260 patients diagnosed with primary bone cancers and an estimated 1550 deaths attributed to those tumors in 2017 [31]. Chondrosarcoma accounts for 30% of primary malignancies of the skeletal system, making it the second-most-common histologic type after osteosarcoma [4], and many patients die from this disease. Surgical resection is the most widely accepted treatment modality for chondrosarcoma [25, 27, 30], most commonly without radiation or chemotherapy [16, 20, 23].

As with any malignancy, it is important to identify prognostic factors for patients with chondrosarcoma, as these factors can guide therapeutic choices. Tumor grade and tumor size have been reported to be independent prognostic factors for survival for patients with chondrosarcoma [12, 21, 25, 28], as have tumor site [5], local recurrence [11], patient age [32], and metastasis [7]. Nevertheless, as survival is undoubtedly multifactorial, influenced by many such factors, finding ways to use all available information to arrive at a more-precise estimate of prognosis seems important. Nomograms have been used as user-friendly and convenient statistical tools to predict the overall probability of a specific outcome in other cancers by incorporating numerous prognostic factors [9, 22, 37]. However, to the best of our knowledge, comprehensive nomograms predicting survival of patients with chondrosarcoma have not been reported.

Therefore, in this study, we aimed to develop comprehensive and effective nomograms to better predict survival of individual patients with chondrosarcoma based on a large population with long-term followup. We asked: (1) Which clinicopathologic features are independent prognostic factors for patients with chondrosarcoma? (2) Can we develop a nomogram to predict 3- and 5-year overall and cancer-specific survival of individual patients with chondrosarcoma based on personalized information?

Materials and Methods

Patient information was obtained from the Surveillance, Epidemiology, and End Results (SEER) database [24], which consists of 18 cancer registries and covers approximately 30% of the total US population. SEER*Stat software (Version 8.3.2; National Cancer Institute, Bethesda, MD, USA) was used to extract information from the database. Two types of data were entered in SEER, one was from autopsy reports and the other was from patients with complete followup. However, we excluded data obtained from autopsy reports, and included only data obtained from patients with complete followup.

The inclusion criteria were: (1) patient age of 18 years at diagnosis; (2) diagnosed between 1988 and 2011 to ensure an adequate length of followup; (3) diagnosis of grade II or III chondrosarcoma as the primary malignancy; (4) diagnosis acquired in a living patient, not from a death certificate or autopsy; (5) confirmation of histologic type of chondrosarcoma; (6) site limited to a bone only, excluding soft tissue chondrosarcoma; (7) known months of survival after diagnosis and cause of death; and (8) complete followup without missing data.

Because the primary site information in the SEER database did not indicate the exact location of the bone (eg, humerus, radius, and ulna were recorded as long bones of the upper extremities without distinction) or have sufficient patient numbers with chondrosarcoma of short bones, the primary sites were categorized in three groups, which were the extremities (long and short bones of the upper and lower extremities), axial bones (spine, ribs, and pelvic bones), and other bones (mandible and bones of the skull or face).

Patient Baseline Characteristics

From 1988 to 2011, data for a total of 1428 patients with chondrosarcoma who met the inclusion criteria were collected from the SEER database. Among these patients, 43 patients who were younger than 18 years were excluded. We then excluded 315 patients and 12 patients whose data were missing with respect to tumor size and metastasis, respectively. Because there were only nine and 15 patients

in the clear cell and mesenchymal histologic subgroups, these patients also were excluded from the cohort. Finally, we included 1034 patients in the study and randomly allocated 517 patients to the training cohort and the other 517 patients to the validation cohort. Among these 1034 adult patients with grade II or III chondrosarcoma, 919 (88.9%) had complete followup for at least 1 year, 112 (10.8%) died within the 1-year followup period, and only three (0.3%) were alive at the time of the last followup and had a followup less than 1 year.

Although this study was retrospective, because we divided the group into training and validation cohorts, we use the terms "predict", "prediction", and "prognostic factors" which normally are associated with prospective studies. We recognize that true predictions can only be made from prospective datasets, but we are using these terms as shorthand to simplify communication because of the training and validation approach to nomogram development.

Of the 1034 patients in the cohort, 600 (58%) were male and 434 (42%) were female. Among the patients included, 727 (70%) were diagnosed with grade II chondrosarcoma, and 307 (30%) were diagnosed with grade III chondrosarcoma. Most patients (95%) in the cohort had cancer-directed surgery as primary treatment, while only 53 patients, which represented 5% of the cohort, did not have surgery for treatment (Table 1). For the training cohort, the median age at diagnosis was 52 years (range, 18-87 years) and the median survival was 65 months (range, 0-301 months). For the validation cohort, the median age at diagnosis was 52 years (range, 18-90 years) and the median survival was 66 months (range, 0-311 months). Of these 1034 patients, 303 (29%) had died from primary cancer and 99 (10%) had died from other causes by the end of the last followup.

Table 1. Baseline demographics and clinical characteristics of the patients

Characteristic	All patients (n = 1034) Number (%)	Training cohort (n = 517) Number (%)	Validation cohort (n = 517) Number (%)
Categorical variables			
Race			
White	915 (89)	457 (88)	458 (89)
Black	67 (6)	31 (6)	36 (7)
Other*	52 (5)	29 (6)	23 (4)
Sex			
Male	600 (58)	305 (59)	295 (57)
Female	434 (42)	212 (41)	222 (43)
Primary site			
Extremity	529 (51)	271 (51)	258 (50)
Axial	426 (41)	209 (42)	217 (42)
Other†	79 (8)	37 (7)	42 (8)
Histologic subtype			
Conventional chondrosarcoma	854 (82)	417 (81)	437 (84)
Dedifferentiated chondrosarcoma	92 (9)	52 (10)	40 (8)
Myxoid chondrosarcoma	88 (9)	48 (9)	40 (8)
Grade			
II	727 (70)	358 (69)	369 (71)
III	307 (30)	159 (31)	148 (29)
Cancer-directed surgery			
No	53 (5)	27 (5)	26 (5)
Yes	981 (95)	490 (95)	491 (95)
Distant metastasis			
No	948 (92)	466 (90)	482 (93)
Yes	86 (8)	51 (10)	35 (7)
Continuous variables			
Age at diagnosis (years)			
Median (range)	52 (18-90)	52 (18-87)	52 (18-90)
Tumor size (cm)			
Median (range)	7.0 (0.1-50.0)	7.0 (0.1-50.0)	7.0 (0.6-43.0)
Outcome			
Survival (months)			
Median (range)	66 (0-311)	65 (0-301)	66 (0-311)

*Including Native American/Alaska Native, Asian/Pacific Islander.
†including mandible and bones of the skull or face.

Statistical Analysis

The entire database of patients (n = 1034) was randomly divided into a training cohort (n = 517) and a validation cohort (n = 517) to construct and validate the nomograms. Nine important clinicopathologic factors were included in the univariate analysis. The optimal cutoff values of tumor size were identified using the X-tile program (Yale University, New Haven, CT, USA), which was first introduced to determine the best cutoff values of several prognostic factors in cohorts of patients with breast cancer [8]. The X-tile program could divide tumor size into three subgroups for all possible divisions. A chi-square value then was calculated for every possible division of tumor size. Finally, the X-tile program selected the optimal division of tumor size by selecting the highest chi-square value. In the training cohort, the X-tile program identified optimal cutoff values of tumor size as 5.9 and 14.5 cm based on overall survival (Fig. 1). We then rounded the cutoff values to 6.0 and 14.0 cm. Therefore, the entire training cohort was

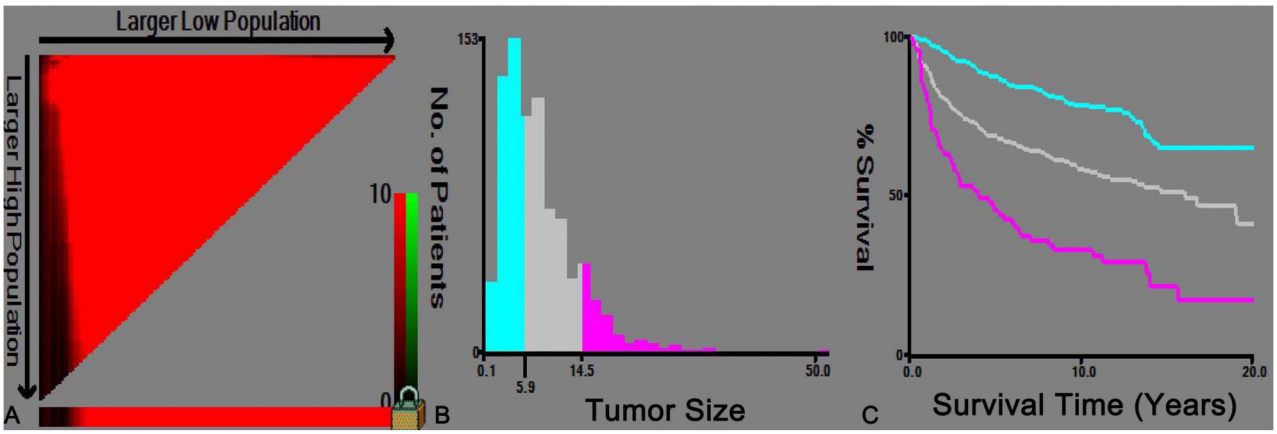

Fig. 1A-C The graphs show identification of optimal cutoff values of tumor size using X-tile analysis. X-tile analysis was conducted on the training cohort (n = 517). **(A)** The X-tile analysis of the training cohort is shown with the "lock" symbol indicating that optimal cutoff values of tumor size have been identified. **(B)** A histogram and **(C)** Kaplan-Meier analysis were developed based on these cutoff values. Optimal cutoff values of tumor size were identified as 5.9 cm and 14.5 cm based on overall survival.

divided into three groups, which were less than 6.0 cm, 6.0 to 14.0 cm, and greater than 14.0 cm by tumor size (Table 2). Another continuous variable, age at diagnosis, was stratified into six groups by 10-year intervals.

Overall survival was one of the primary endpoints of interest, which was measured as the time from diagnosis to death from all possible causes. Patients who were alive at the time of last followup were considered censored observations. Cancer-specific survival was another primary endpoint of interest, which was measured as the time from diagnosis to death attributed to chondrosarcoma. Patients who were alive at the time of last followup were considered censored observations. Missing data were excluded from our study.

Table 2. Baseline information on age and tumor size after stratification

Characteristic	All patients (n = 1034) Number (%)	Training cohort (n = 517) Number (%)	Validation cohort (n = 517) Number (%)
Age at diagnosis (years)			
< 30	100 (10)	47 (9)	53 (10)
30-39	150 (15)	85 (16)	65 (13)
40-49	208 (20)	94 (18)	114 (22)
50-59	208 (20)	104 (20)	104 (20)
60-69	179 (17)	89 (17)	90 (17)
≥ 70	189 (18)	98 (19)	91 (18)
Tumor size (cm)			
< 6.0	376 (36)	181 (35)	195 (38)
6.0-14.0	525 (51)	271 (52)	254 (49)
> 14.0	133 (13)	65 (13)	68 (13)

Kaplan-Meier analyses and log-rank tests were applied to select significant prognostic factors associated with overall survival or cancer-specific survival in the univariate analysis. For the training cohort, data regarding age at diagnosis, race, sex, primary site, histologic subtype, grade, surgery, tumor size, and distant metastasis were included in the univariate analysis. Radiation and chemotherapy were excluded from univariate analysis, because both therapies exert limited efficacy on most chondrosarcoma subtypes [16, 20, 23]. Age at diagnosis, histologic subtype, grade, surgery, tumor size, and distant metastasis proved to be associated with overall survival in the univariate analysis ($p < 0.05$) (Table 3). Variables associated with cancer-specific survival also were identified in the univariate analysis ($p < 0.05$) (Table 4).

Multivariate Cox proportional hazard models were applied to verify prognostic factors selected in the univariate log-rank test and calculate the hazard ratios of each prognostic factor.

Development and Validation of the Nomograms

To minimize the influence of information loss, we used a backward stepwise method to further sort out prognostic factors verified in the multivariate analysis. The Akaike information criterion (AIC) is widely used as an objective tool for selecting between different competing models, and lower AIC values suggest relative superiority [36, 38]. The backward stepwise method initially included all independent prognostic factors identified in the multivariate analysis to calculate the AIC. Each prognostic factor then was excluded successively to calculate the AIC to see

Table 3. Univariate and multivariate analysis of overall survival in the training cohort

Characteristic	Univariate analysis p value	Multivariate analysis HR (95% CI)	Multivariate analysis p value
Age at diagnosis (years)	< 0.001		
< 30		Reference	
30-39		1.446 (0.629-3.324)	0.385
40-49		1.402 (0.629-3.127)	0.409
50-59		1.961 (0.910-4.227)	0.086
60-69		2.715 (1.256-5.872)	0.011
≥ 70		4.843 (2.317-10.122)	< 0.001
Race	0.662	NI	
White			
Black			
Other			
Sex	0.402	NI	
Male			
Female			
Primary site	0.984	NI	
Extremity			
Axial			
Other			
Histologic subtype	< 0.001		
Conventional		Reference	
Dedifferentiated		3.477 (2.277-5.309)	< 0.001
Myxoid		0.963 (0.586-1.584)	0.883
Grade	< 0.001		
II		Reference	
III		1.854 (1.329-2.586)	< 0.001
Cancer-directed surgery	< 0.001		
No		Reference	
Yes		0.498 (0.286-0.866)	0.014
Tumor size (cm)	< 0.001		
< 6.0		Reference	
6.0-14.0		1.504 (1.049-2.156)	0.026
> 14.0		2.399 (1.529-3.762)	< 0.001
Distant metastasis	< 0.001		
No		Reference	
Yes		4.483 (3.015-6.666)	< 0.001

HR = hazard ratio; NI = not included (n = 517).

Table 4. Univariate and multivariate analysis of cancer-specific survival in the training cohort

Characteristic	Univariate analysis p value	Multivariate analysis HR (95% CI)	Multivariate analysis p value
Age at diagnosis (years)	< 0.001		
< 30		Reference	
30-39		1.421 (0.535-3.770)	0.481
40-49		1.525 (0.613-3.796)	0.365
50-59		1.885 (0.780-4.558)	0.159
60-69		2.479 (1.020-6.024)	0.045
≥ 70		3.318 (1.402-7.849)	0.006
Race	0.152	NI	
White			
Black			
Other			
Sex	0.401	NI	
Male			
Female			
Primary site	0.489	NI	
Extremity			
Axial			
Other			
Histologic subtype	< 0.001		
Conventional		Reference	
Dedifferentiated		3.613 (2.272-5.747)	< 0.001
Myxoid		1.077 (0.611-1.896)	0.798
Grade	< 0.001		
II		Reference	
III		2.500 (1.689-3.700)	< 0.001
Cancer-directed surgery	< 0.001		
No		Reference	
Yes		0.510 (0.271-0.959)	0.037
Tumor size (cm)	< 0.001		
< 6.0		Reference	
6.0-14.0		1.813 (1.150-2.861)	0.010
> 14.0		2.695 (1.551-4.684)	< 0.001
Distant metastasis	< 0.001		
No		Reference	
Yes		5.367 (3.469-8.302)	< 0.001

HR = hazard ratio; NI = not included (n = 517).

whether a smaller AIC was achieved. Finally, the smallest AIC was achieved and therefore prognostic factors to be incorporated in the nomograms were determined. Nomograms incorporating sorted prognostic factors were developed to predict 3- and 5-year overall survival and cancer-specific survival.

Bootstrapped validation, which used a resample with 500 iterations, was applied to validate the nomograms internally and externally. Harrell's concordance index (C-index) was applied to evaluate predictive ability of the nomograms. The value of the C-index ranges from 0.5 to 1.0, whereas 0.5 indicates total chance and 1.0 indicates

perfect matching [33]. Calibration plots also were used to validate the nomograms by comparing nomogram predictions with actual outcomes.

Univariate analysis and multivariate Cox regression were conducted using SPSS Version 22.0 (IBM Corporation, Armonk, NY, USA). Development and validation of the nomograms were performed using R version 3.3.1 (http://www.r-project.org/) with rms [15] and cmprsk [13] packages. All p values were two-sided and a probability less than 0.05 was considered statistically significant.

Results

Independent Prognostic Factors for Patients With Chondrosarcoma

After controlling for potentially confounding variables such as race, sex, and primary site, we found that age at diagnosis, histologic subtype, grade, surgery, tumor size, and distant metastasis proved to be associated with overall survival (Table 3). Similarly, these six variables still proved to be independently associated with cancer-specific survival after controlling for confounding variables (Table 4).

Nomograms for 3- and 5-Year Survival

The six independent prognostic factors for overall survival and for cancer-specific survival were identified and incorporated to construct nomograms for 3- and 5-year overall and cancer-specific survival, respectively (Fig. 2). These nomograms can easily be used by providers in the office to estimate a patient's prognosis; the only clinical details a provider needs to use these nomograms effectively are age, histologic subtype, tumor grade, whether surgery was performed, tumor size, and the presence or absence of metastases. Independent prognostic factors in the multivariate analysis were further sorted by a backward stepwise method with the AIC to minimize information loss and arrive at the nomograms.

To use the nomograms, one can add the points of each predictor (Table 5) based on personalized information and correlate the total points with the event probability that we want to predict. For example, a 55-year-old man was diagnosed with grade III conventional chondrosarcoma with a primary tumor of 6.0 cm; he then underwent surgery and had no signs of metastasis. By adding the points, he ended up with 11.1 and 12.6 points in overall survival and cancer-specific survival nomograms, respectively. Eventually, his estimated 5-year overall survival and cancer-specific survival rates were 67% and 70%, respectively, according to the nomograms.

The nomograms were validated internally and externally. In the training cohort for internal validation, the concordance indices (C-index) for overall survival and cancer-specific survival prediction were 0.803 (95% CI, 0.773-0.833) and 0.829 (95% CI, 0.796-0.862), respectively. In the validation cohort for external validation,

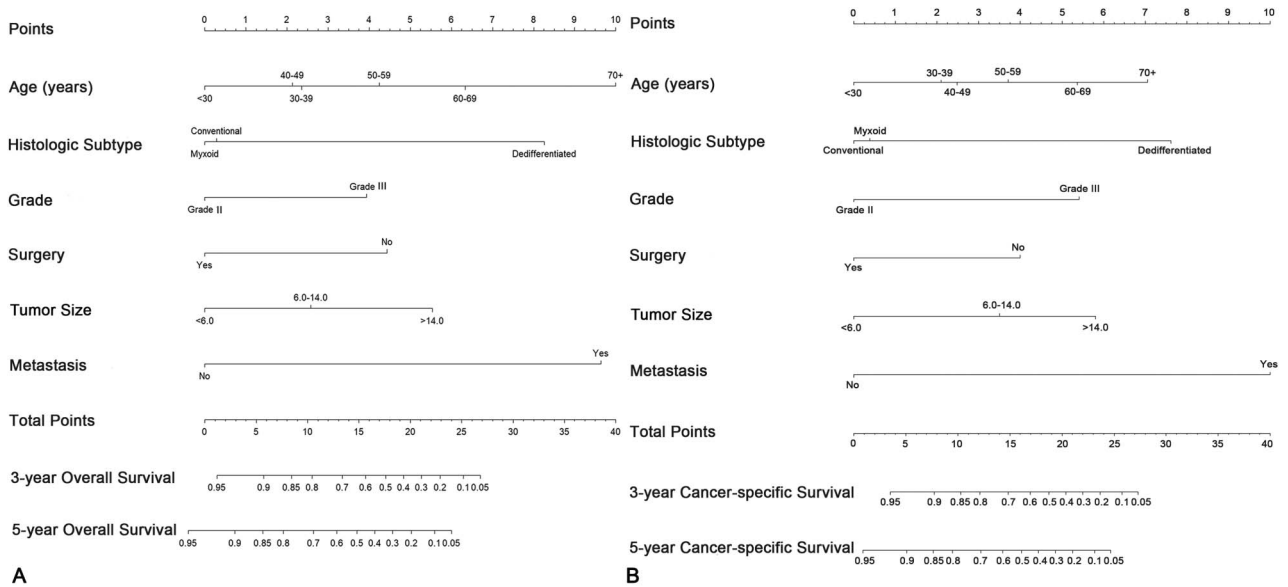

Fig. 2A-B The graphs show the nomograms predicting 3- and 5-year **(A)** overall survival and **(B)** cancer-specific survival of patients with chondrosarcoma. To use the nomograms, first acquire personalized information including all the predictors in the nomograms. Then draw a vertical line from each variable to the point scale to obtain the points of each predictor. Next, add the points of each predictor to obtain the total points. Finally, draw a vertical line from the total point scale to the overall survival or cancer-specific survival scale to obtain the predicted probabilities of survival.

Table 5. Detailed scores of each predictor in the nomograms

Characteristic	Overall survival nomogram	Cancer-specific survival nomogram
Age at diagnosis (years)		
< 30	0.0	0.0
30-39	2.4	2.1
40-49	2.1	2.5
50-59	4.3	3.7
60-69	6.3	5.4
≥ 70	10.0	7.1
Histologic type		
Conventional	0.3	0.0
Dedifferentiated	8.3	7.6
Myxoid	0.0	0.4
Grade		
II	0.0	0.0
III	3.9	5.4
Surgery		
No	4.4	4.0
Yes	0.0	0.0
Tumor size (cm)		
< 6.0	0.0	0.0
6.0-14.0	2.6	3.5
> 14.0	5.5	5.8
Distant metastasis		
No	0.0	0.0
Yes	9.6	10.0

the C-indices for overall survival and cancer-specific survival prediction were 0.753 (95% CI, 0.714-0.792) and 0.759 (95% CI, 0.720-0.798), respectively. Internal and external calibration plots for 3- and 5-year overall survival and cancer-specific survival showed excellent agreement between nomogram prediction and observed outcomes (Fig. 3).

Discussion

Chondrosarcoma is the second-most-common malignancy of the skeleton, and although numerous factors—including patient age, tumor size, tumor grade, and metastasis—have been individually identified as having prognostic value by prior studies [7, 12, 21, 25, 28, 32], using those factors in combination in a practical way is impossible without a nomogram. A well-validated nomogram can help the clinician anticipate a patient's prognosis, as has been shown for osteosarcoma, prostate cancer, gastric cancer, lung cancer, and breast cancer [3, 9, 18, 19, 22, 26, 29, 33, 34]. However, to our knowledge, there is no prognostic nomogram for chondrosarcoma. Based on the SEER database [24], which consists of 18 cancer registries covering approximately 30% of the total US population, we therefore constructed comprehensive and novel nomograms for predicting 3- and 5-year overall survival and cancer-specific survival of patients with chondrosarcoma (Fig. 2), which can be used in the clinical setting using patient-specific information likely to be available to the orthopaedic oncologist.

Several limitations should be considered in our study. First, 327 patients with chondrosarcoma, which represented nearly ⅓ of the cohort, were excluded from the study because of missing data. Although age, histologic subtype, grade, surgery, and distant metastasis still proved to be independently associated with survival after including patients with missing data on tumor size (see Tables, Supplemental Digital Content 1 and Supplemental Digital Content 2), potential bias still existed because the scores of each predictor in the nomograms might change if we included patients with missing data. Second, we did not include some known prognostic factors such as margin status [25] and pathologic fracture [6], which might improve predictive ability if incorporated. The reason was that the SEER database did not collect information regarding these variables. Third, since the SEER database does not collect information for local recurrence, we were not able to develop the nomogram predicting local recurrence for patients with chondrosarcoma. Fourth, we developed and validated the nomograms from the same retrospective dataset. To really know the predictive ability of the nomograms, prospective validation is needed, or at least, validation with another database. Fifth, results of a backward selection process might be sample-specific as selection depends on statistical criteria that may vary from sample to sample. This may result in some bias; for example, the C-index is likely lower if the nomograms are applied to non-SEER registry data. Moreover, owing to the insufficient sample of patients with chondrosarcoma of short bones, we combined patients with chondrosarcoma of long bones and short bones in the extremity subgroup, which may result in bias. Finally, although we used multivariate analysis to control for the influence of confounding variables on a single variable, it was still difficult to eliminate such influence between variables; for example, metastasis is associated with tumor grade and such correlation could not be eradicated in the study.

After controlling for confounding variables, we identified six independent prognostic factors for overall survival (Table 3) and cancer-specific survival (Table 4). Regarding cancer-specific survival, it is noteworthy that a small overestimation of mortality is expected owing to the existence of competing risks [10]. The cumulative incidence function is a robust method for analyzing cause-specific incidence when competing events exist. However, in

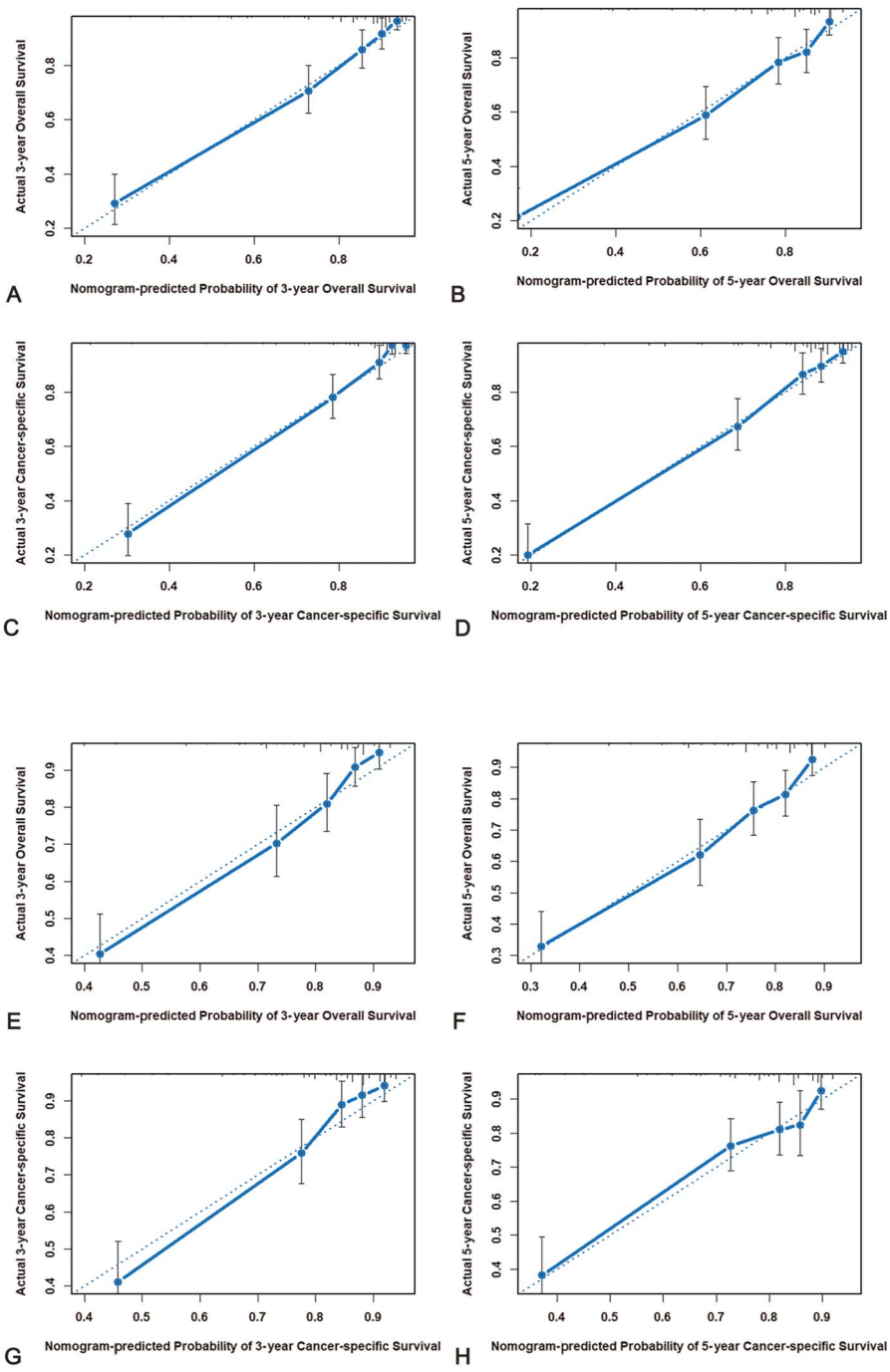

Fig. 3A-H The graphs show the internal calibration plots for **(A)** actual 3-year and **(B)** 5-year overall survival; **(C)** actual 3-year and **(D)** actual 5-year cancer-specific survival; and external calibration plots for **(E)** actual 3-year and **(F)** 5-year overall survival; and **(G)** actual 3-year and **(H)** 5-year cancer-specific survival. The dashed line in each plot shows good agreement between nomogram prediction (X-axis) and observed outcomes (Y-axis). For internal and external validation, the cohort was divided into five groups with equivalent sample sizes, respectively. The vertical bars around each point represent the 95% CI of the observed survival probability. Closer distances between the points and the dashed line indicate better agreement between nomogram prediction and observed outcomes.

consideration of better comparability with previous studies [14, 34, 39], we still used the Cox model rather than the competing risk model for multivariate analysis of cancer-specific survival. Verification of age, grade, tumor size, surgery, and distant metastasis as independent prognostic factors for overall survival and cancer-specific survival is in line with previous studies [12, 17, 25, 28, 32, 35]. We are not aware of any studies that used multivariate analysis to identify histologic type as an independent prognostic factor, although Giuffrida et al. [12] calculated survival rates based on different histologic types. According to our research, histologic type showed a substantial effect on prognosis and patients with conventional chondrosarcoma were found to have relatively better survival than those with dedifferentiated chondrosarcoma. Regarding primary tumor site, Andreou et al. [1] reported that patients with chondrosarcoma of the axial skeleton and pelvic girdle had poorer prognoses than patients with chondrosarcoma of the extremities. Another study showed that appendicular chondrosarcoma was associated with better survival than axial chondrosarcoma only in patients with grade III disease [2]. Based on an analysis of 2890 patients with chondrosarcoma, Giuffrida et al. [12] concluded that patients with appendicular chondrosarcoma had better overall survival than patients with axial chondrosarcoma in univariate analysis, but the multivariate analysis showed that site was not a significant prognostic factor for overall survival. However, in our study, primary tumor site was not identified as a prognostic factor for either overall survival or cancer-specific survival in the univariate analysis. Giuffrida et al. [12] first reported that female sex was correlated with better survival in univariate analysis but not in multivariate analysis, meaning that attributing improved survival to sex is likely to instead be a function of confounding variables; in our study, we did not find sex to be associated with survival in patients with grade II and grade III chondrosarcoma.

We also created a nomogram, based on the independent predictors of overall and cancer-specific survival that we identified; this nomogram can be easily used in practice to estimate a patient's prognosis (Fig. 2). To our knowledge, no other nomogram of this sort exists for patients with chondrosarcoma. An effective nomogram can increase the surgeon's ability to provide patients with precise estimates of the likelihood of survival at particular time intervals, and to help the surgeon identify patients at higher risk of early death. To use the nomograms, one adds the points of each predictor (Table 5) and correlates the total points with the event probability that we seek to predict. For example, a 65-year-old woman was diagnosed with grade II conventional chondrosarcoma with a primary tumor of 8.0 cm; she then underwent surgery and had signs of metastasis. Totaling the points for this patient, we see that she had 18.8 and 18.9 points in the overall-survival and cancer-specific survival nomograms, respectively. This results in estimated 3-year overall survival and cancer-specific survival rates of 43% and 49%, respectively, according to the nomograms. Because development and validation of the nomograms are based on the SEER database [24], future studies should investigate whether the nomograms apply well to patients from other registries and evaluate the accuracy of the predictions one can make using the nomograms we have developed.

We developed and preliminarily validated nomograms predicting 3- and 5-year overall survival and cancer-specific survival of patients with chondrosarcoma based on the SEER database [24]. The nomograms seemed accurate when tested in validation cohorts, and they require only basic information, which should be available to all providers in the office setting. If our findings can be validated by others using other databases or in prospective studies, this may prove to be a useful tool for clinicians and patients. Another potential use of our nomogram would be to identify patients at high risk of death so they could be invited to participate in studies evaluating novel treatments for patients with an extremely poor prognosis. Currently, no such strategies are in standard use, but we hope that such treatments might be forthcoming.

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