Original Article

Individualized estimation of conditional survival for patients with spinal chordoma

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Background: Unlike traditional survival analysis methods, conditional survival (CS) provides enhanced insight by offering a personalized prognosis estimation as time advances for tumor patients. This study aimed to estimate CS and devised a novel CS-nomogram for real-time prediction of 10-year CS for patients with spinal chordoma.

Methods: Patients diagnosed with spinal chordoma from 2000 to 2019, as documented in the Surveillance, Epidemiology, and End Results (SEER) database, were included in this study. CS represents the likelihood of surviving an additional y years given that the patient has already survived x years. It is computed using the equation $CS(x|y) = S(x + y)/S(x)$, where S(x) denotes the patient's survival rate at x years. The univariate Cox hazard regression, least absolute shrinkage and selection operator (LASSO) analysis and best subset regression (BSR) methods were employed for variable selection. Based on these selected factors, the CS-based nomogram and a risk classification system were developed. Finally, several approaches were used to validate the performance of our model.

Results: Between 2000 and 2019, the SEER database identified 730 patients with spinal chordoma, distributed into 510 in the training group and 220 in the validation group. CS analysis showed that patients experienced a gradual augmentation in their 10-year survival rates over the course of each additional year post-diagnosis. We also successfully created a CS-based nomogram model for forecasting 3-, 5-, and 10-year overall survival, along with 10-year CS. The CS-based nomogram incorporating age, tumor size, tumor extension, multiple primary tumors, and surgery demonstrated robust predictive capabilities. Moreover, a novel risk classification system was constructed to aid in tailored management strategies and personalized treatment decisions for spinal chordoma patients.

Conclusions: In contrast to traditional survival assessment methods, our analysis of CS yielded more dynamic and real-time outcomes for spinal chordoma patients. Via our CS-based nomogram model and risk classification system, we have provided more precise prognostic insights for these patients, aiding in treatment planning and follow-up strategy formulation in clinical settings.

Keywords: Spinal chordoma; conditional survival (CS); nomogram; risk classification system; Surveillance, Epidemiology, and End Results (SEER)

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Introduction

Chordoma, originating from notochordal remnants, is a comparatively uncommon malignant tumor, representing approximately 3–4% of all primary bone tumors (1-3). Chordomas are primarily located in the sacrum (50%), followed by the skull base (30%), and the mobile spine (20%) (4-6). In the United States, the reported incidence of chordoma is 0.08 per 100,000 individuals (7). Despite being classified as a malignancy of low-to-moderate grade, it is crucial to emphasize that chordomas originating in the sacrococcygeal and spinal regions exhibit a more aggressive behavior compared to those originating in the skull area (8,9). As a result of their localized aggressiveness, patients may experience significant deterioration in both survival and quality of life. The overall 5-year survival rate is estimated to be approximately 65% (10-12), underscoring the importance of conducting further in-depth research specifically targeting the spinal tumor population.

Considering the low morbidity but aggressive character of spinal chordomas, patients harbor significant concerns regarding their prognosis following diagnosis (13). To address this concern, conditional survival (CS) emerges as a preferable alternative to accrued survival (14-17). CS(x/y) refers to the likelihood of surviving for an additional y years, provided that a patient has already survived for x years following the diagnosis of spinal chordomas. Hence, unlike conventional survival analysis methods, CS could offer enhanced insight by furnishing a personalized prognosis estimation as time advances (17). Presently, prognostic assessment of spinal chordomas is largely confined to traditional overall survival (OS), with the CS trajectory of these patients remaining unexplored.

The nomogram, typically depicted graphically, correlates each predictive factor with a corresponding score, which is then combined to calculate the probability of a specific event, making it widely employed in tumor prognosis prediction (18-20). Therefore, in this study, we attempted to integrate CS analysis into the nomogram model, thus combining their respective strengths to create a convenient tool for clinical use in predicting CS prognosis. Moreover, in light of the uncommon occurrence of this tumor, we utilized the vast sample cohorts provided by the Surveillance, Epidemiology, and End Results (SEER) public database. This allowed us to analyze the CS profile tailored to this specific tumor type and to train and validate a relatively large-scale CS-nomogram model. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1912/rc).

Highlight box

Key findings

- Create a convenient tool for clinical use in predicting conditional survival (CS) prognosis of spinal chordoma patients.

What is known and what is new?

- Nomogram is widely employed in tumor prognosis prediction.
- The CS-nomogram of spinal chordoma is more dynamic and real-time.

What is the implication, and what should change now?

- CS-based nomogram model and a risk classification system may provide more precise prognostic insights for spinal chordoma patients. Our clinical tool will further facilitate the development of treatment plans and the formulation of follow-up strategies in clinical practice.

Methods

Patient

This retrospective cohort study extracted patients diagnosed with chordoma from the SEER database, which gathers clinical cancer data from 18 different cancer registries spanning since 1973, encompassing around 30% of the total U.S. population. The data for this observational study was exclusively sourced from the freely accessible SEER database, and patient consent was waived accordingly. Subject selection criteria were established as follows: (I) diagnosis of chordoma (9370/3, 9371/3, 9372/3) based on International Classification of Disease for Oncology, version 3, histological codes; (II) diagnosis between 2000 and 2019 to ensure adequate follow-up time; (III) primary site of vertebral column (C41.2) or pelvis, sacrum, or coccyx (C41.4); (IV) diagnosis obtained from a living patient rather than from a death certificate or autopsy; (V) complete follow-up duration without missing data. Exclusion criteria encompassed: (I) unknown race and tumor extension; (II) undisclosed treatment approach. In this study, we use the term 'spinal chordoma' to refer to both spinal and sacrococcygeal chordomas. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Variable selection and outcomes

Patient clinical characteristics were delineated as follows:

age at diagnosis, race, sex, marital status, household income and treatment modalities encompassing surgery, radiotherapy and chemotherapy. Tumor-specific attributes such as tumor site, tumor size, tumor extension and number of primary tumors were also considered. Tumor extension was categorized into localized (tumor encasement within the periosteum), regional (further contiguous extension beyond the periosteum without distant involvement), and distant metastasis. Surgical procedures were identified based on the "RX Summ-Surg Prim Site (1998+)" field and subsequently grouped into three distinct categories: no surgery, subtotal resection (STR) and gross total resection (GTR). OS was defined as the duration from the diagnosis of spinal and pelvic chordoma to either death from any cause or censoring.

CS analysis

The concept of CS delves into the probability of a patient surviving an additional y years given they have already survived for x years. This statistical representation can be succinctly expressed as the CS $(x|y) = S(x+y)/S(x)$, where S (x) denotes the cumulative survival rate over x years. To calculate the CS, we utilized life table survival data, enabling a comprehensive understanding of survival dynamics over time. This methodological approach not only offers insight into immediate survival prospects but also accounts for the evolving nature of disease prognosis over extended periods (21).

CS-nomogram construction and validation

The cohort of all patients was divided into training and validation sets at a ratio of 7:3 for CS-nomogram construction and validation (22). To initiate preliminary variable selection, the training group underwent assessment via three distinct methodologies: univariate Cox hazard regression, least absolute shrinkage and selection operator (LASSO) analysis and best subset regression (BSR) (23-25). Subsequently, a backward stepwise multivariable Cox regression analysis was conducted to ascertain the ultimate significant independent prognostic factors. During the univariate Cox hazard regression analysis, variables with a P value <0.05 were identified for potential inclusion in the ensuing multivariable Cox regression analysis. The LASSO method was employed to mitigate severe multicollinearity, achieving this by implementing a penalty function to shrink variable coefficients, thus averting overfitting. Similarly, the BSR method facilitated the selection of an optimal model given prevailing variable conditions, guided by the criterion of adjusted R^2 (25). Ultimately, the optimal predictive model was determined through a comprehensive comparison of receiver operating characteristic (ROC) curves and Akaike information criterion (AIC) values, ensuring robustness and accuracy in prognostic modeling (26). The AIC serves as a versatile tool for assessing and comparing the relative quality of various models, aiding in the selection of the most suitable one. Lower AIC values signify models that strike a superior balance between fit and parsimony, thereby indicating their superiority in capturing essential patterns within the data while avoiding unnecessary complexity.

Following the identification of variables, a comprehensive multivariable Cox regression analysis was performed to validate the prognostic significance of these selected factors. Ultimately, a comprehensive CS-nomogram was constructed to facilitate the prediction of survival outcomes, encompassing 3-, 5-, and 10-year OS, as well as 10-year CS. This nomogram was developed utilizing the refined multivariable Cox regression model, incorporating key prognostic factors to provide a practical and user-friendly tool for estimating survival probabilities across various time horizons.

The validation group was employed to validate the CS-nomogram model, ensuring its reliability and generalizability across different patient cohorts. The evaluation of the nomogram's predictive performance involved multiple methodologies. Calibration curves were employed to gauge the agreement between predicted and observed outcomes, providing insights into the nomogram's calibration capability. Concordance index (C-index) and the ROC curve, along with its associated area under the curve (AUC), served as primary metrics for assessing predictive accuracy (27). Furthermore, decision curve analysis (DCA) was conducted to appraise the clinical utility of the nomogram, shedding light on its practical value in informing clinical decision-making (28). Through these comprehensive analyses, the nomogram's effectiveness in real-world clinical settings were thoroughly examined.

Risk system classification development

We utilized the CS-nomogram to generate risk scores for each patient. Subsequently, based on the optimal risk stratification cutoff values determined by restricted cubic spline (RCS) curve (29,30), patients were stratified into distinct risk groups, namely low- and high-risk categories. Kaplan-Meier curves, together with the log-rank tests,

were employed to visually depict and compare the survival outcomes among patients stratified into different risk categories. This stratification process facilitated a nuanced understanding of patients' prognostic profiles, aiding in tailored management strategies and personalized treatment decisions.

Statistical analyses

Categorical variables were presented as counts and proportions. All statistical analyses were performed with use of R (www.r-project.org). A statistical significance threshold is typically set at a two-tailed P value of less than 0.05.

Results

Baseline characteristics

Between 2000 and 2019, the SEER database identified a total of 730 patients diagnosed with spinal chordoma. Following random assignment facilitated by R software, the training group encompassed 510 patients, while the validation group comprised 220 individuals. Across the entire cohort, a notable majority of patients were aged over 60 years (57.9%), male (60.0%), and White ethnicity (87.1%). The primary site of tumors was predominantly within pelvic bones (58.1%), with a sizable proportion being localized (46.2%). And patients with this type of tumor concurrently have other tumors, accounting for 27.4%. Treatment modalities varied, with 73.7% of patients undergoing surgery, 49.7% receiving radiotherapy, and only 4.8% undergoing chemotherapy. Regarding the extent of surgical resection, 35.6% of patients underwent STR, while 38.1% underwent GTR. A comprehensive overview of patient clinical characteristics is provided in *Table 1*.

CS

Utilizing the Kaplan-Meier method, we derived estimates of OS rates for patients diagnosed with spinal chordoma, projecting rates of 81%, 70%, and 45% at 3, 5, and 10 years, respectively. Interestingly, there was a discernible upward trajectory observed in the 10-year CS survival. Over the course of each additional year post-diagnosis, patients experienced a gradual augmentation in their 10-year survival rates, advancing from an initial rate of 45% to subsequent rates of 49%, 53%, 56%, 60%, 65%, 71%, 76%, 84%, and 91% after surviving for 1 to 9 years, respectively. This progression underscores the evolving nature of survival outcomes for spinal chordoma patients over time. A graphical representation of the 10-year CS rates at various intervals is provided in *Figure 1*, offering a visual depiction of these dynamic trends.

Variable selection

To initiate variable selection, we employed univariate Cox hazard regression, LASSO, and BSR methods. Univariate Cox hazard regression identified six variables with P values <0.05, encompassing age, tumor size, tumor extension, multiple primary tumors, surgery, and marital status, as illustrated in *Figure 2A*. Subsequently, the BSR analysis finalized a set of five variables, including age, tumor size, tumor extension, multiple primary tumors, and surgery (*Figure 2B*). In the LASSO regression analysis, four variables associated with the lambda.1se value were identified: age, tumor size, tumor extension, and surgery (*Figure 2C,2D*). Following this initial selection process, the variables derived from each regression approach underwent a backward stepwise multivariable Cox regression analysis. This iterative process led to the formulation of three predictive models, as detailed in *Table 2*. Upon analysis using R software, the predictive model established through multivariate Cox regression, incorporating variables selected by univariate Cox regression and BSR, exhibited the lowest AIC value (AIC =2,029.2, *Figure 2E*). Furthermore, it yielded the highest AUC values for the ROC curves (*Figure 2F*). Consequently, the final predictive model included the following variables: age, tumor size, tumor extension, multiple primary tumors, and surgery. And we further illustrated the significant prognostic relevance of the selected variables through a forest plot generated by multivariable regression analysis (*Figure 3*).

CS-nomogram construction and validation

We introduced an innovative approach by integrating CS analysis into the nomogram model, thus creating a CS-based survival prediction model. Utilizing the multivariable Cox model, we formulated the CS-nomogram for forecasting 3-, 5-, and 10-year OS, along with 10-year CS (*Figure 4*).

Then, multiple methods were employed to assess the performance of our predictive model in both the training and validation cohorts. The calibration plots indicated strong concordance between the model's predictions and the

Table 1 Baseline clinicopathological characteristics

Characteristics	Total cohort (N=730), n (%)	Training group (N=510), n (%)	Validation group (N=220), n (%)
Age at diagnosis, years			
<60	307 (42.1)	218 (42.7)	89 (40.5)
60–69	161 (22.1)	112 (22.0)	49 (22.3)
70–79	152 (20.8)	108 (21.2)	44 (20.0)
≥80	110 (15.1)	72 (14.1)	38 (17.3)
Sex			
Male	438 (60.0)	298 (58.4)	140 (63.6)
Female	292 (40.0)	212 (41.6)	80 (36.4)
Race			
White	636 (87.1)	444 (87.1)	192 (87.3)
Non-White	94 (12.9)	66 (12.9)	28 (12.7)
Tumor size			
≤65 mm	280 (38.4)	195 (38.2)	85 (38.6)
>65 mm	282 (38.6)	199 (39.0)	83 (37.7)
Unknown	168 (23.0)	116 (22.7)	52 (23.6)
Primary site			
Vertebral column	306 (41.9)	202 (39.6)	104 (47.3)
Pelvic bones	424 (58.1)	308 (60.4)	116 (52.7)
Tumor extension			
Localized	337 (46.2)	237 (46.5)	100 (45.5)
Regional	313 (42.9)	219 (42.9)	94 (42.7)
Distant	80 (11.0)	54 (10.6)	26 (11.8)
Multiple primary tumors			
No	530 (72.6)	369 (72.4)	161 (73.2)
Yes	200 (27.4)	141 (27.6)	59 (26.8)
Surgery			
No surgery	192 (26.3)	139 (27.3)	53 (24.1)
STR	260 (35.6)	176 (34.5)	84 (38.2)
GTR	278 (38.1)	195 (38.2)	83 (37.7)
Radiotherapy			
No	367 (50.3)	259 (50.8)	108 (49.1)
Yes	363 (49.7)	251 (49.2)	112 (50.9)
Chemotherapy			
No	695 (95.2)	488 (95.7)	207 (94.1)
Yes	35 (4.8)	22 (4.3)	13 (5.9)

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Total cohort (N=730), n (%)	Training group (N=510), n (%)	Validation group (N=220), n (%)
Marital status			
Single	276 (37.8)	193 (37.8)	83 (37.7)
Married	422 (57.8)	295 (57.8)	127 (57.7)
Unknown	32 (4.4)	22 (4.3)	10 (4.5)
Household income, USD			
<70,000	380 (52.1)	257 (50.4)	123 (55.9)
≥70,000	350 (47.9)	253 (49.6)	97 (44.1)

STR, subtotal resection; GTR, gross total resection; USD, United States dollar.

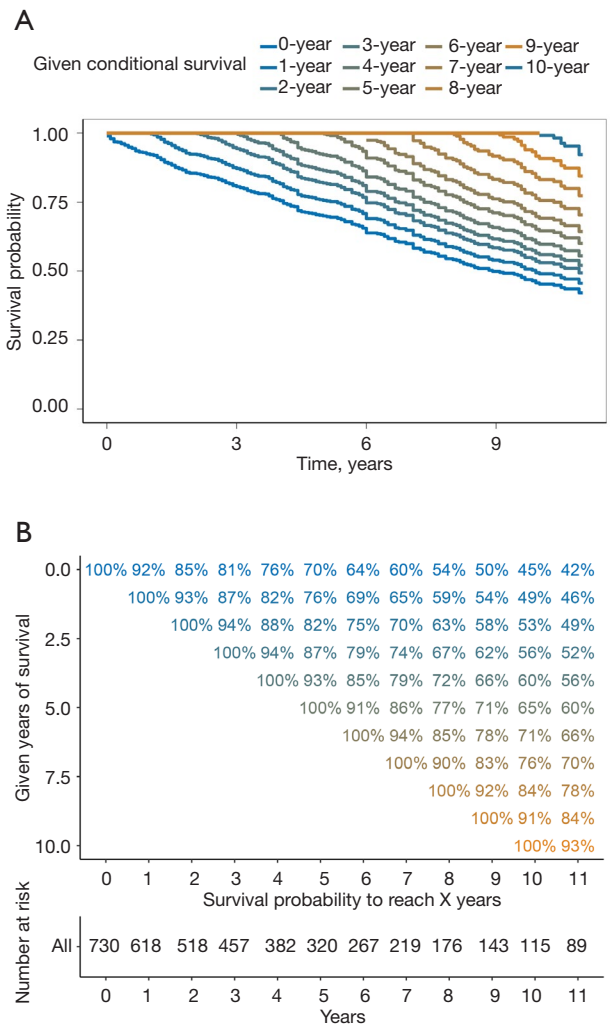

Figure 1 CS of spinal chordoma patients. (A) CS curves adjusted for survival duration. (B) Updated survival data incorporated into the survival analysis. CS, conditional survival.

observed outcomes, with the 3-, 5- and 10-year predictive calibration curves closely resembling the ideal curve (*Figure 5A*,*5B*). The C-index values for the predictive model in the training and validation cohorts were 0.757 and 0.748, respectively. To assess the discriminative performance of the nomogram in predicting the endpoint event, we utilized ROC curves. The AUC values for predicting 3-, 5-, and 10-year OS were found to be 0.756, 0.730 and 0.725 in training cohort (*Figure 5C*). Upon validation, the corresponding AUC values in the validation cohort were 0.716, 0.733, and 0.665 (*Figure 5D*). Furthermore, the analysis conducted on DCA curves revealed compelling evidence supporting the potential utility of the CS-nomogram as a valuable tool for guiding medical interventions, resulting in a significant net benefit in both training and validation cohorts (*Figure 6A*,*6B*). These results indicated the robustness and consistency of the nomogram's predictive performance.

Development of nomogram-based risk stratification system

The risk stratification prediction model was formulated by utilizing the points assigned to each patient in the training cohort, computed through the nomogram. Subsequently, RCS analysis was performed to explore the correlation between the risk score and all-cause mortality, and to determine the optimal cutoff point for the risk score. The RCS analysis unveiled that the risk of mortality remained relatively stable until approximately 114.5 score, after which it began to escalate rapidly (*Figure 7A*). This method enabled the classification of all patients into low- and high-risk groups based on their respective risk scores. The Kaplan-Meier survival curves demonstrated a clear

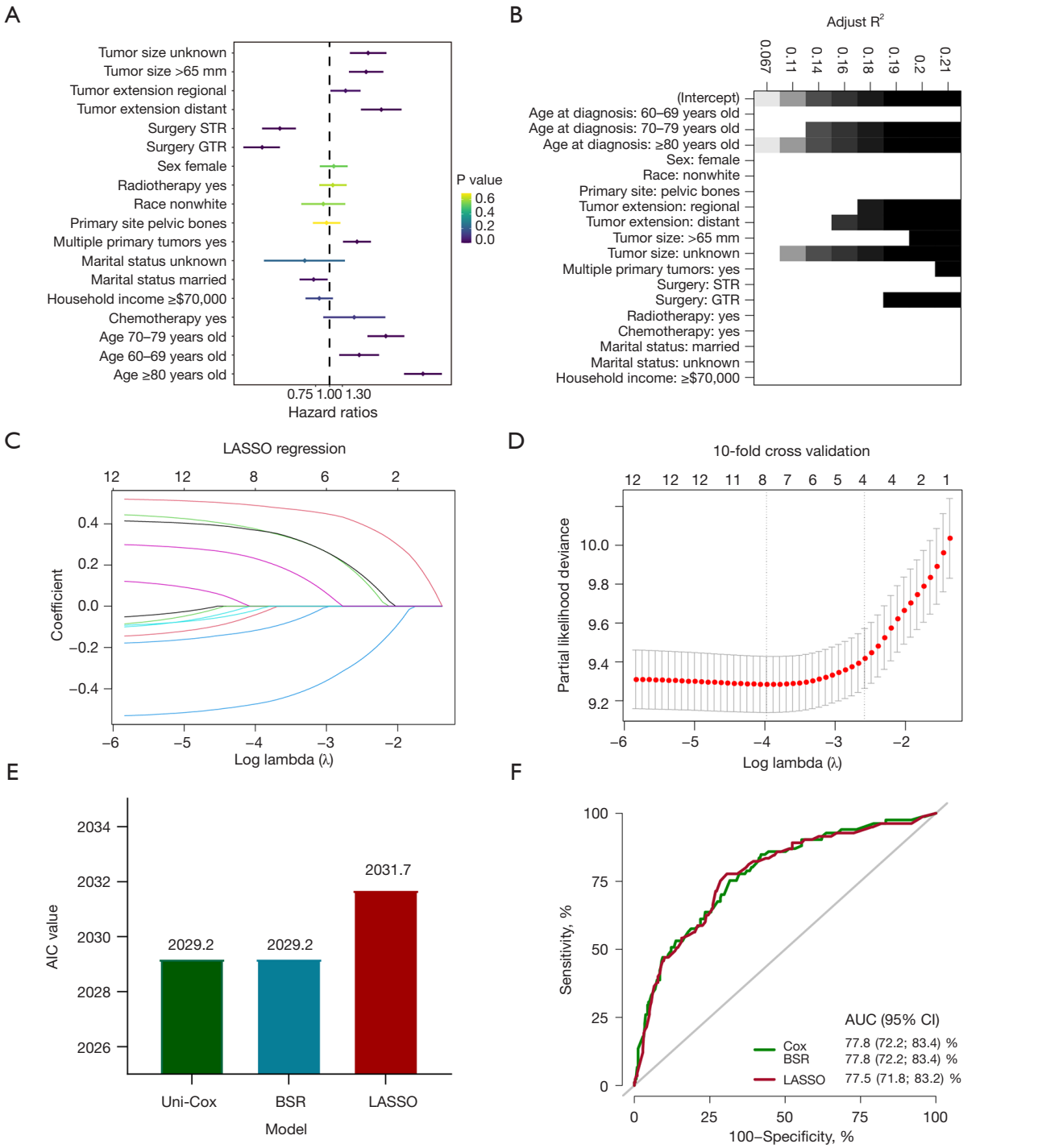

Figure 2 Three methods of screening predictors. Univariate Cox regression analysis (A), BSR (B), and LASSO regression (C,D); comparison AIC (E) and ROC curves with AUC values (F) among different models. BSR, best subset regression; LASSO, least absolute shrinkage and selection operator; ROC, receiver operating characteristic; AUC, area under the curve; AIC, Akaike information criterion; GTR, gross total resection; STR, subtotal resection; CI, confidence interval.

differentiation in OS among patients across various risk groups in both training and validation groups, as predicted by the risk stratification prediction model (P<0.005, *Figure 7B*,*7C*). This highlighted the model's ability to accurately discern survival outcomes based on individual risk profiles.

Discussion

Traditional survival analysis in clinical research typically examines the distribution of patients' survival time from the date of diagnosis or treatment initiation. However, estimates of survival based on fixed time points may be affected by changes in the mortality rate and could potentially mislead both physicians and patients. Therefore, it is crucial to understand how prognosis evolves over time, accounting for the duration of patient survival. Additionally, considering the elevated risk of recurrence and the difficulties associated with achieving complete resection in spinal conventional chordoma cases (2,31,32), there is a need for a concise and accurate nomogram developed on a population-based cohort with sufficient follow-up duration. Therefore, in this study, by integrating CS analysis into the nomogram model (21,33,34), we amalgamated the advantages of both methodologies, resulting in the development of a user-friendly tool for clinical application in predicting CS prognosis. This integration enabled a more comprehensive and accurate assessment of CS outcomes, enhancing its utility in clinical practice.

In our retrospective cohort study, we firstly analyzed data from the population-based SEER database to investigate the dynamic survival trends in patients with spinal chordoma. We found that with the progression of each successive year following diagnosis, patients observed a steady increase in their 10-year CS rates, with the initial rate of 45% evolving to subsequent rates of 49%, 53%, 56%, 60%, 65%, 71%, 76%, 84%, and 91% after surviving for 1 to 9 years, respectively, indicating that the residual risk of death

Table 2 Variable selection results via three methods

Model	Variable selection
Uni-Cox	Age, tumor size, tumor extension, multiple primary tumors, surgery
BSR	Age, tumor size, tumor extension, multiple primary tumors, surgery
LASSO	Age, tumor size, tumor extension, surgery

BSR, best subset regression; LASSO, least absolute shrinkage and selection operator.

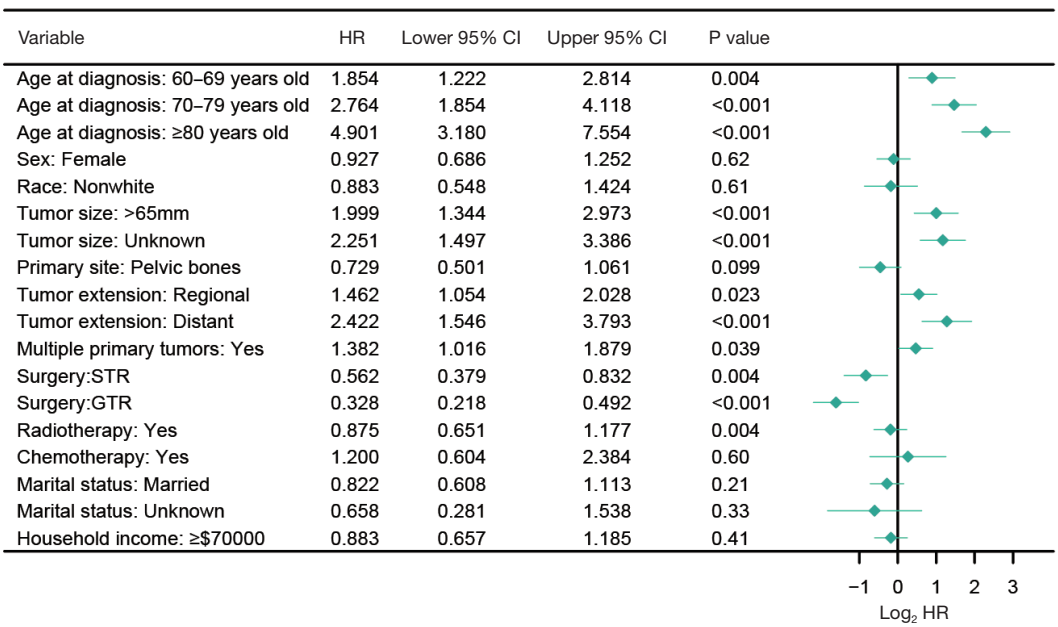

Figure 3 The forest plot of multivariate Cox hazard regression in the training cohort. STR, subtotal resection; GTR, gross total resection; CI, confidence interval; HR, hazard ratio.

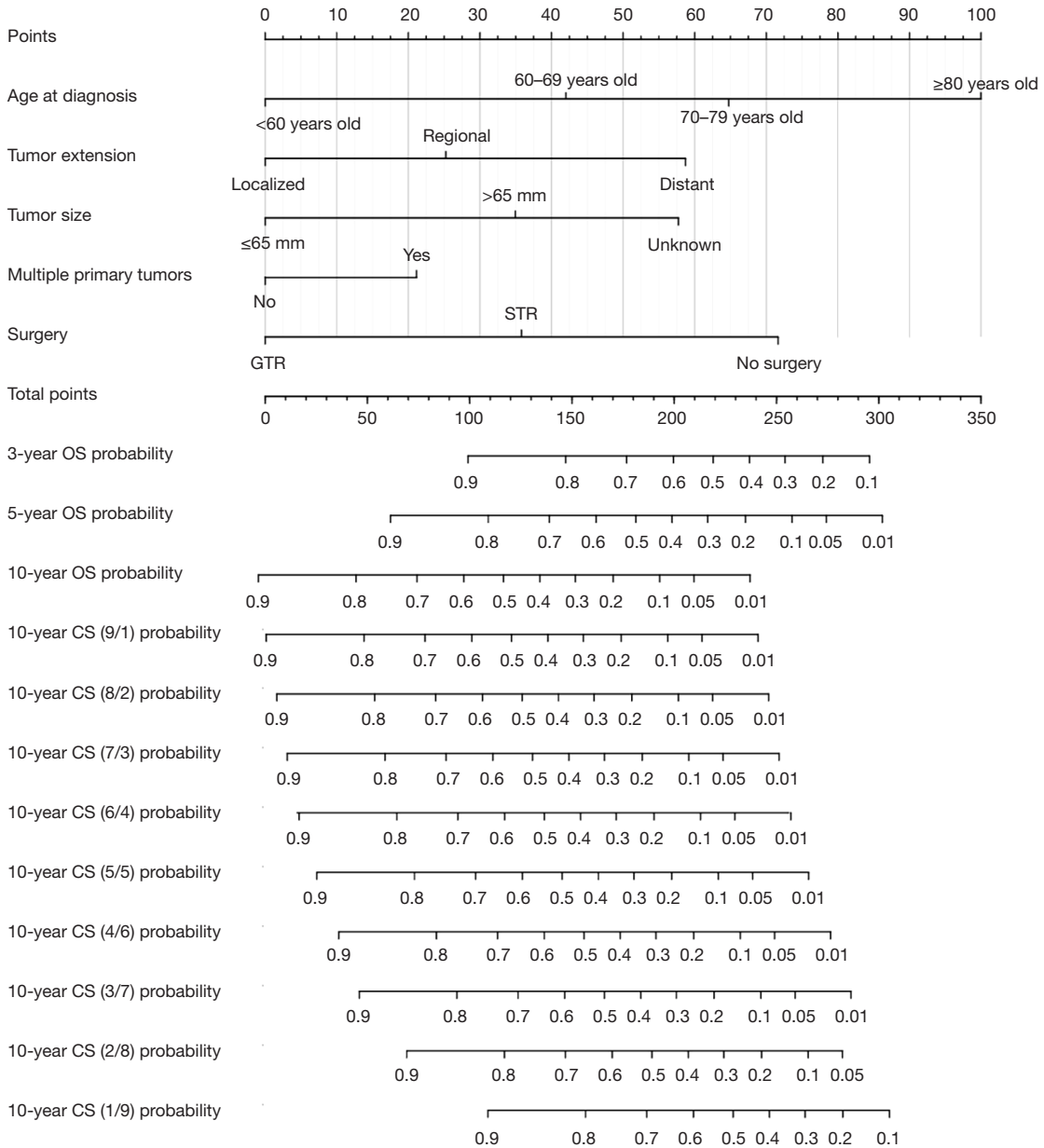

Figure 4 CS-based nomogram to predict 3-, 5-, and 10-year OS and 10-year CS for spinal chordoma patients. CS, conditional survival; OS, overall survival; GTR, gross total resection; STR, subtotal resection.

substantially diminished over time. These encouraging results could alleviate patients' concerns, enhance their resilience in battling cancer, and elevate their overall well-being.

Then, we utilized a combination of three approaches: univariate Cox regression, BSR, and LASSO, in a stepwise manner to construct a multivariable Cox regression model, with the objective of mitigating the risks of overfitting and underfitting. Following a comprehensive evaluation of the AUC and AIC values across different models, we proceeded to develop a predictive model utilizing the variables that were identified during the comparison process. Ultimately, we successfully established the CS-based nomogram model to provide real-time dynamic predictions of the prognosis

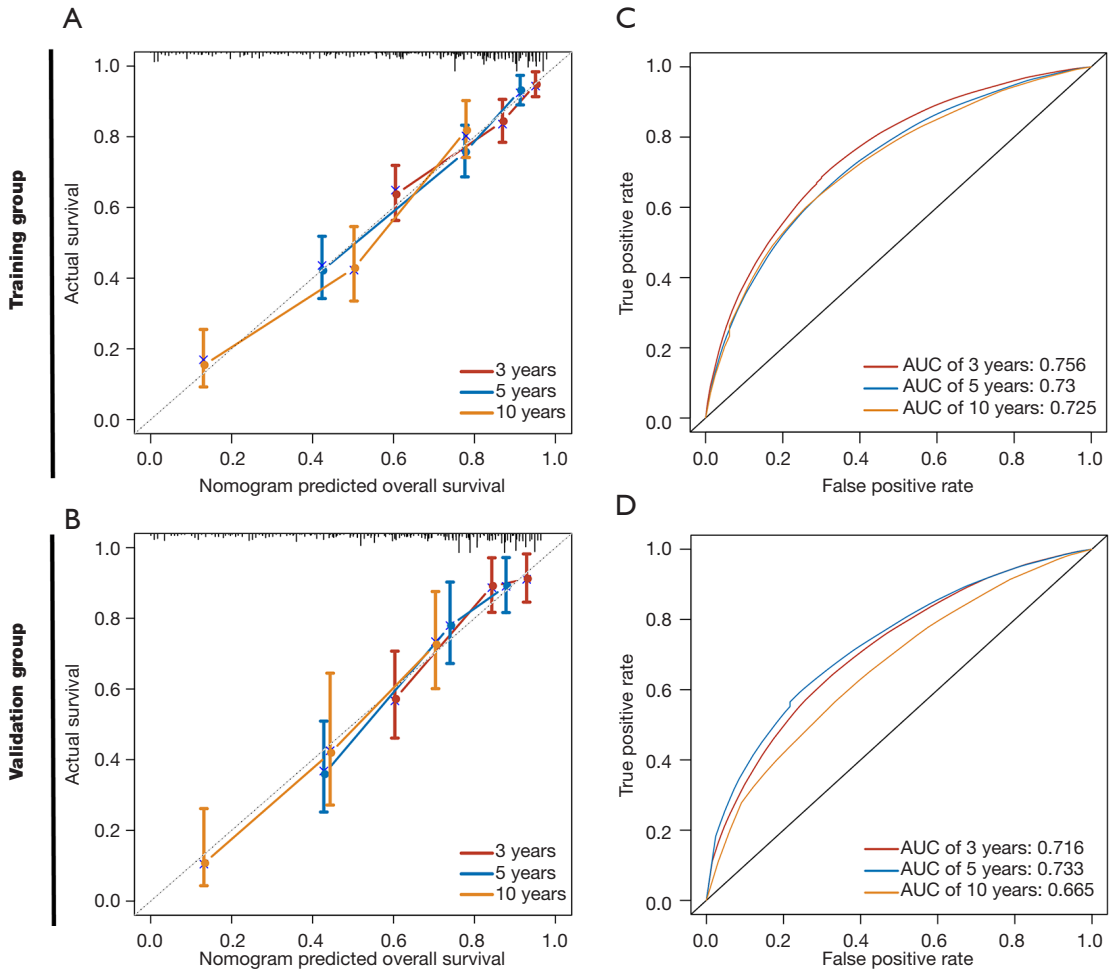

Figure 5 Model performance evaluation. The calibration curves of the nomogram in training (A) and validation (B) groups. The time-dependent ROC curves of the nomogram in training (C) and validation (D) groups, respectively. ROC, receiver operating characteristic; AUC, area under the curve.

for patients with spinal chordoma. Then, we rigorously validated this model using various statistical methods, and the results demonstrated excellent predictive performance. In addition to the CS-nomogram, this study also designed a risk stratification system that categorized the target population into low- and high-risk groups. This prognostic risk prediction model can assist physicians in formulating personalized treatment and follow-up strategies, enhancing doctor-patient communication, and optimizing clinical management processes.

In our nomogram model, we ultimately included five variables: age, tumor size, tumor extension, multiple primary tumors, and surgery. Besides age, surgery appeared to exert the most significant influence on prognosis (35). Despite the inherent risks accompanying surgical intervention, it persists as a viable and dependable treatment modality for individuals diagnosed with spinal chordoma (9,32,36). Additionally, our findings suggested that extensive resection leads to better long-term prognostic outcomes, which is consistent with previous research findings (8,35,37). Several studies have highlighted that incomplete surgical resection can result in significant morbidity and high recurrence rates, particularly when adjuvant therapies are not applied. Grouping all surgical patients together without considering additional treatments, morbidity, and recurrence creates challenges, as it overlooks the variability in outcomes and fails to account for the distinct treatment approaches needed for patients who are not surgical candidates. To address this, future studies should aim to separate surgical and non-surgical patients in their analysis

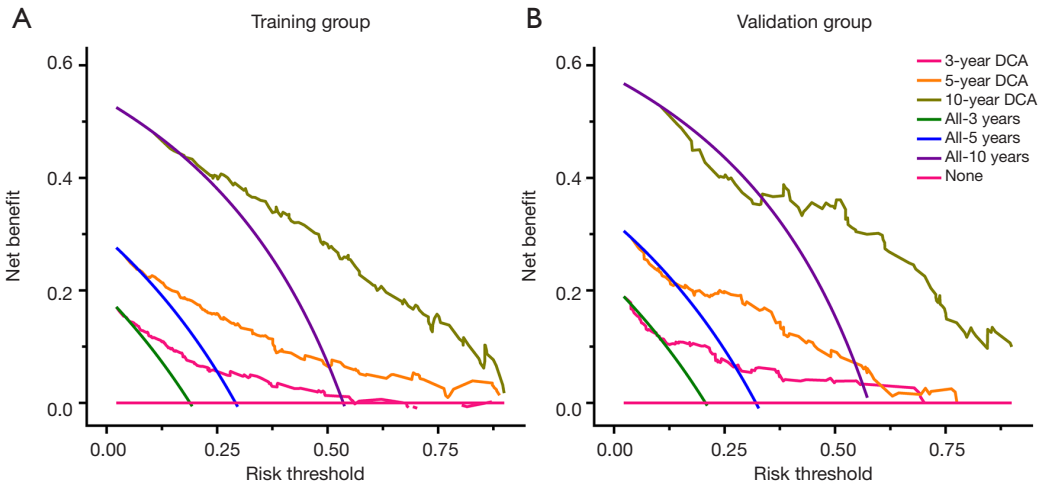

Figure 6 The decision curve analysis of the nomogram for predicting 3-, 5-, and 10-year survival of the training (A) and validation (B) groups. DCA, decision curve analysis.

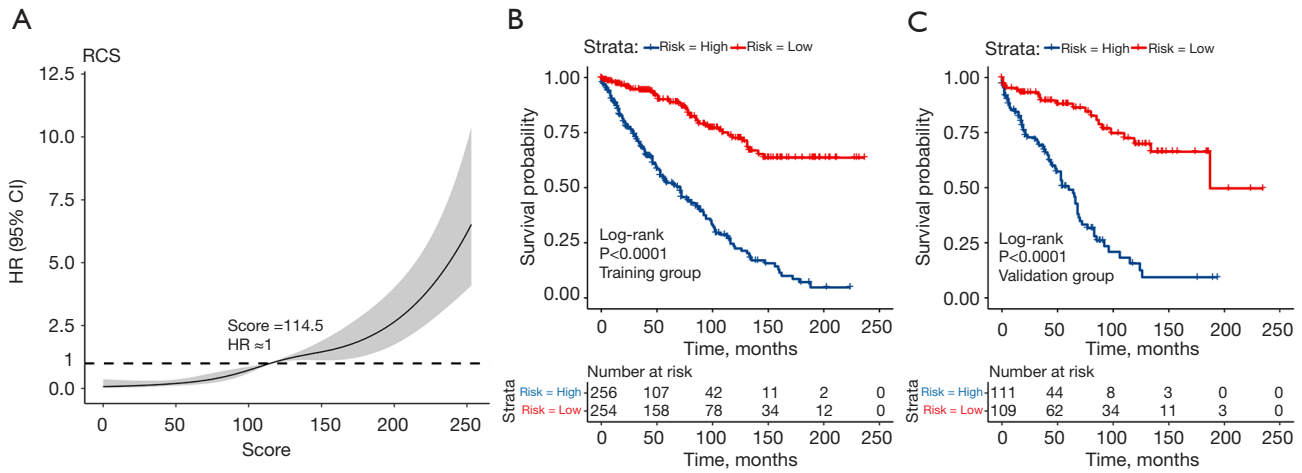

Figure 7 Risk classification system development. Results of restricted cubic spline of risk score in training cohort (A). Kaplan-Meier curves with log-rank tests by different risk groups in both training (B) and validation (C) cohorts. HR, hazard ratio; CI confidence interval; RCS, restricted cubic spline.

and include detailed information on additional treatments and outcomes. This approach would allow for more accurate assessments of treatment efficacy and better reflect the complexity of clinical decision-making.

Due to the resistance of chordomas to chemotherapy, radiation is commonly used as an adjunctive treatment to support surgical excision of these tumors (9,38,39). Advancements in technology have led to increased interest in focused radiation modalities, such as photon therapy, proton beam therapy, and carbon ion therapy. Of these, focused photon therapy is the most accessible and commonly used (9). Current consensus suggests radiation should be used as an adjuvant or neoadjuvant to improve local control after chordoma resection. Recent studies have also indicated that patients who receive radiotherapy immediately after surgery experience prolonged progression-free survival (40-43). However, our research did not demonstrate a strong correlation between radiotherapy and OS. In one regard, the SEER database lacks detailed information on the provision of radiotherapy, which may have led to result bias. On the other hand, some studies have indicated that radiotherapy did not improve

the prognosis of patients who underwent complete tumor resection. However, these studies also relied on database analyses, which share similar limitations to those in the current study (44,45). Zhou *et al.* also found no significant association between survival outcomes and radiation therapy in their study involving 682 spinal chordoma patients (13). Our study, which aggregated all case analyses without stratifying patients, may have resulted in an underestimation of the benefits of radiotherapy. Moreover, due to limitations in the SEER database, information on tumor recurrence was not available for further analysis. Therefore, further research is needed to clarify the survival benefits of radiotherapy, identify patient characteristics that would benefit most from this treatment, and establish appropriate radiotherapy protocols. Additionally, in the implementation of radiotherapy plans, due to the potential toxicity and side effects of radiation, a more precise, safe, and effective approach is required in the delineation of the primary clinical target volume, fractionation schedule, and total dose to be administered.

Chemotherapy's role in the treatment of spinal chordomas is relatively limited. However, for some patients who cannot undergo surgical resection or experience recurrence after radiation therapy, chemotherapy may be used as an alternative treatment option. And several small molecule tyrosine kinase inhibitors have been explored, including sunitinib, lapatinib, imatinib, sorafenib, and erlotinib. Among these, promising early results have been reported for the PDGFR inhibitor imatinib and the EGFR inhibitor erlotinib (9). Additionally, immunotherapies such as the anti-PD-1 antibody nivolumab (NCT02989636 and NCT03173950) and the anti-CTLA4 antibody ipilimumab (NCT02834013) are currently under investigation in clinical trials (9,46).

Due to the SEER database's use of binary yes/no coding for treatments such as surgery, chemotherapy, and radiotherapy, it lacks detailed information on treatment regimens, dosages, and schedules. This simplification may lead to incomplete or inaccurate data, introducing potential bias and selection errors. The absence of detailed treatment data makes it difficult to control for confounding factors. However, the large sample size and long follow-up data provided by the database offer valuable insights into the prognosis of the tumor. The simple categorization of treatment information should be interpreted with caution, but it can highlight the potential clinical value of these treatments, thereby laying the foundation for more in-depth and detailed research.

Our study encountered several limitations. Firstly, due to its retrospective nature, inherent biases may have been present, as is common in such studies. And information bias is also a concern, as the data are derived from clinical records that may not always be complete or consistently recorded. Due to the low incidence of this disease, we selected patients with a broader time span to ensure an adequate number of cases for sufficient statistical power. However, the rapid advancements in diagnostics and treatments over the past decade may introduce some level of heterogeneity. Variability in documentation practices across different registrations could lead to discrepancies in key variables. Secondly, it also does not provide detailed information on radiotherapy and chemotherapy plans, including mode, dosage, and so on. The absence of detailed treatment analysis may obscure potential interactions between therapies, which could be critical for understanding how combinations of treatments influence outcomes. Some complications occurring during the follow-up period, as well as recurrence status, are also unavailable. These factors should be considered to correct for the impact of covariates on outcomes and thus enhance the performance of the model. Moreover, our model requires further validation with external cohorts to enhance its generalizability. However, it is undeniable that the SEER database stands as a well-recognized national repository, offering both a sizable cohort and extensive longitudinal follow-up, which are essential prerequisites for investigating CS of spinal chordomas.

Conclusions

The CS of spinal chordoma exhibited a dynamic pattern, showing an increase with each additional year survived. In contrast to traditional survival assessment methods, our analysis of CS yielded more dynamic and real-time outcomes. By developing our CS-based nomogram model and a risk classification system, we have provided more precise prognostic insights for these patients. Our clinical tool will further facilitate the development of treatment plans and the formulation of follow-up strategies in clinical practice.

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can be found in the SEER database: https://seer.cancer.gov/data-software/.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1912/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Walcott BP, Nahed BV, Mohyeldin A, et al. Chordoma: current concepts, management, and future directions. Lancet Oncol 2012;13:e69-76.
2. Huang JF, Chen D, Sang CM, et al. Nomogram for Individualized Prediction and Prognostic Factors for Survival in Patients with Primary Spinal Chordoma: A Population-Based Longitudinal Cohort Study. World Neurosurg 2019;128:e603-14.
3. Wedekind MF, Widemann BC, Cote G. Chordoma: Current status, problems, and future directions. Curr Probl Cancer 2021;45:100771.
4. Zuckerman SL, Bilsky MH, Laufer I. Chordomas of the Skull Base, Mobile Spine, and Sacrum: An Epidemiologic Investigation of Presentation, Treatment, and Survival. World Neurosurg 2018;113:e618-27.
5. Lin K, Song K, Wang S, et al. Predict overall survival of spinal conventional chordoma: Development and assessment of a new predictive nomogram. Clin Neurol Neurosurg 2020;197:106174.
6. Smoll NR, Gautschi OP, Radovanovic I, et al. Incidence and relative survival of chordomas: the standardized mortality ratio and the impact of chordomas on a population. Cancer 2013;119:2029-37.
7. Stacchiotti S, Casali PG, Lo Vullo S, et al. Chordoma of the mobile spine and sacrum: a retrospective analysis of a series of patients surgically treated at two referral centers. Ann Surg Oncol 2010;17:211-9.
8. Li J, Ma C, Yuan X, et al. Competing risk nomogram for predicting prognosis of patients with spinal and pelvic chordoma: A SEER-based retrospective study. Eur Spine J 2023;32:1334-44.
9. Pennington Z, Ehresman J, McCarthy EF, et al. Chordoma of the sacrum and mobile spine: a narrative review. Spine J 2021;21:500-17.
10. Mukherjee D, Chaichana KL, Gokaslan ZL, et al. Survival of patients with malignant primary osseous spinal neoplasms: results from the Surveillance, Epidemiology, and End Results (SEER) database from 1973 to 2003. J Neurosurg Spine 2011;14:143-50.
11. McMaster ML, Goldstein AM, Bromley CM, et al. Chordoma: incidence and survival patterns in the United States, 1973-1995. Cancer Causes Control 2001;12:1-11.
12. Hui-Hui S, Xin H, Bing L, et al. Survival analysis of patients with spinal chordomas. 2018;42:
13. Zhou J, Sun J, Bai HX, et al. Prognostic Factors in Patients With Spinal Chordoma: An Integrative Analysis of 682 Patients. Neurosurgery 2017;81:812-23.
14. Abdallah NH, Smith AN, Geyer S, et al. Conditional survival in multiple myeloma and impact of prognostic factors over time. Blood Cancer J 2023;13:78.
15. Meng X, Chang X, Qin P, et al. Risk-dependent conditional survival analysis and annual hazard rate of inflammatory breast cancer. Eur J Surg Oncol 2023;49:106957.
16. Latenstein AEJ, van Roessel S, van der Geest LGM, et al. Conditional Survival After Resection for Pancreatic Cancer: A Population-Based Study and Prediction Model.

Ann Surg Oncol 2020;27:2516-24.
17. Liu X, Wu T, Zhu SY, et al. Risk-Dependent Conditional Survival and Failure Hazard After Radiotherapy for Early-Stage Extranodal Natural Killer/T-Cell Lymphoma. JAMA Netw Open 2019;2:e190194.
18. Tao M, Luo S, Wang X, et al. A Nomogram Predicting the Overall Survival and Cancer-Specific Survival in Patients with Parathyroid Cancer: A Retrospective Study. Front Endocrinol (Lausanne) 2022;13:850457.
19. van der Gaag NA, Kloek JJ, de Bakker JK, et al. Survival analysis and prognostic nomogram for patients undergoing resection of extrahepatic cholangiocarcinoma. Ann Oncol 2012;23:2642-9.
20. Gittleman H, Sloan AE, Barnholtz-Sloan JS. An independently validated survival nomogram for lower-grade glioma. Neuro Oncol 2020;22:665-74.
21. Meng X, Cai Y, Chang X, et al. A novel conditional survival nomogram for monitoring real-time prognosis of non-metastatic triple-negative breast cancer. Front Endocrinol (Lausanne) 2023;14:1119105.
22. Dong W, Okamoto T, Ji X, et al. Conditional Survival Rate Estimates for Anaplastic Thyroid Cancer Beyond the First Year: An Analysis of SEER Data (2004-2019). Thyroid 2023;33:523-6.
23. Incesu RB, Barletta F, Tappero S, et al. Conditional survival of stage III non-seminoma testis cancer patients. Urol Oncol 2023;41:435.e11-8.
24. Huang X, Luo Z, Liang W, et al. Survival Nomogram for Young Breast Cancer Patients Based on the SEER Database and an External Validation Cohort. Ann Surg Oncol 2022;29:5772-81.
25. Zhao J, Bian S, Di X, et al. A Nomogram and Risk Classification System Predicting the Prognosis of Patients with De Novo Metastatic Breast Cancer Undergoing Immediate Breast Reconstruction: A Surveillance, Epidemiology, and End Results Population-Based Study. Curr Oncol 2023;31:115-31.
26. Yang XL, Huang H, Kou LN, et al. Construction and validation of a prognostic model for stage IIIC endometrial cancer patients after surgery. Eur J Surg Oncol 2022;48:1173-80.
27. Wang J, Zhanghuang C, Tan X, et al. A Nomogram for Predicting Cancer-Specific Survival of Osteosarcoma and Ewing's Sarcoma in Children: A SEER Database Analysis. Front Public Health 2022;10:837506.
28. Yu C, Zhang Y. Establishment of prognostic nomogram for elderly colorectal cancer patients: a SEER database analysis. BMC Gastroenterol 2020;20:347.
29. Wu J, Wang H, Yin X, et al. Normalization weighted combination scores re-evaluate TNM staging of gastric cancer: a retrospective cohort study based on a multicenter database. Int J Surg 2024;110:11-22.
30. Feng H, Zheng J, Zheng C, et al. The probability of Lymph node metastasis with a tumor size larger than and smaller than 4 cm is different in stages T1-T3 of Siewert type II adenocarcinoma of esophagogastric junction: A Population-Based Study. J Cancer 2021;12:6873-82.
31. Zhong N, Yang X, Yang J, et al. Surgical Consideration for Adolescents and Young Adults With Cervical Chordoma. Spine (Phila Pa 1976) 2017;42:E609-16.
32. Passer JZ, Alvarez-Breckenridge C, Rhines L, et al. Surgical Management of Skull Base and Spine Chordomas. Curr Treat Options Oncol 2021;22:40.
33. Luo J, Hu X, Ge X. Conditional survival nomogram for monitoring real-time survival of young non-metastatic nasopharyngeal cancer survivors. J Cancer Res Clin Oncol 2023;149:10181-8.
34. Meng X, Jiang Y, Chang X, et al. Conditional survival analysis and real-time prognosis prediction for cervical cancer patients below the age of 65 years. Front Oncol 2023;12:1049531.
35. Pham J, Shaaya E, Rhee B, et al. Gross total resection and survival outcomes in elderly patients with spinal chordoma: a SEER-based analysis. Front Oncol 2024;13:1327330.
36. Michiel E R B, Nicolas D, Christopher P A, et al. Surgical Strategies for Chordoma. 2020;31:
37. Pan Y, Lu L, Chen J, et al. Analysis of prognostic factors for survival in patients with primary spinal chordoma using the SEER Registry from 1973 to 2014. J Orthop Surg Res 2018;13:76.
38. Redmond KJ, Schaub SK, Lo SL, et al. Radiotherapy for Mobile Spine and Sacral Chordoma: A Critical Review and Practical Guide from the Spine Tumor Academy. Cancers (Basel) 2023;15:2359.
39. Konieczkowski DJ, DeLaney TF, Yamada YJ. Radiation Strategies for Spine Chordoma: Proton Beam, Carbon Ions, and Stereotactic Body Radiation Therapy. Neurosurg Clin N Am 2020;31:263-88.
40. Sherry AD, Maroongroge S, De B, et al. Management of chordoma and chondrosarcoma with definitive dose-escalated single-fraction spine stereotactic radiosurgery. J Neurooncol 2023;164:377-86.
41. Tobert DG, Kelly SP, Xiong GX, et al. The impact of radiotherapy on survival after surgical resection of chordoma with minimum five-year follow-up. Spine J 2023;23:34-41.

42. Yolcu YU, Zreik J, Wahood W, et al. Comparison of Oncologic Outcomes and Treatment-Related Toxicity of Carbon Ion Radiotherapy and En Bloc Resection for Sacral Chordoma. JAMA Netw Open 2022;5:e2141927.
43. Fujiwara T, Tsuda Y, Stevenson J, et al. Sacral chordoma: do the width of surgical margin and the use of photon/proton radiotherapy affect local disease control? Int Orthop 2020;44:381-9.
44. Gendreau J, Kuo CC, Mehkri Y, et al. Radiotherapy after gross-total resection and subtotal resection of spinal chordoma: a SEER database analysis of overall survival outcomes. J Neurosurg Spine 2023;39:411-8.
45. Muhonen EG, Yasaka TM, Lehrich BM, et al. Impact of Treatment Modalities upon Survival Outcomes in Skull Base and Clival Chordoma: An NCDB Analysis. J Neurol Surg B Skull Base 2022;84:60-8.
46. Meng T, Jin J, Jiang C, et al. Molecular Targeted Therapy in the Treatment of Chordoma: A Systematic Review. Front Oncol 2019;9:30.

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