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Prognostic factors of chondroblastic osteosarcoma and nomogram development for prediction

A population-based, STROBE-compliant study

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Abstract

The present study aimed to develop nomograms to predict survival in patients with chondroblastic osteosarcoma (COS).

An analysis was conducted of 320 cases of COS collected from the surveillance, epidemiology, and end results (SEER) database between 2004 and 2015. Independent prognostic factors were screened using univariate and multivariate Cox analyses. Subsequently, nomograms were established to predict the patients' cancer-specific survival (CSS) and overall survival (OS) rates. The prediction accuracy and discriminative ability of the nomograms were examined using calibration curves and the concordance index (*C*-index).

As revealed in the univariate and multivariate Cox regression analysis, age, tumor size, the primary site, the presence of metastasis, a history of having undergone surgery, and a history of having received radiotherapy were found to be independent prognostic factors associated with survival in patients with COS (all $P < .05$). Furthermore, age >39 years, the presence of distant metastasis, no history of having undergone any surgery, and tumor size >103 mm were found to be associated with poor prognosis in patients, while the primary site of the mandible and no history of having undergone radiotherapy showed associations with a more favorable prognosis in patients. Next, nomograms were constructed to predict the OS and CSS in patients with COS.

We constructed nomograms that can provide accurate survival predictions in patients with chondroblastic osteosarcoma. These nomograms can help surgeons customize the treatment strategies for patients with chondroblastic osteosarcoma.

Abbreviations: CI = confidence interval, *C*-index = concordance index, COS = chondroblastic osteosarcoma, CSS = cancer-specific survival, HR = hazard ratio, OS = overall survival, SEER = surveillance, epidemiology, and end results.

Keywords: chondroblastic osteosarcoma, nomogram, prognostic factors, surveillance, epidemiology, and end results, survival

1. Introduction

Chondroblastic osteosarcoma (COS) is the most common subtype of osteosarcoma, accounting for approximately 25% of osteosarcoma cases. It is defined as a high-grade bone tumor exhibiting a substantial volume of tumor tissue with a chondrosarcomatous phenotype adjacent to osteoid-forming areas.[1–3] The incidence rate in men is higher than that in women, with a man to woman ratio of about 1.5 to 1.[4] It is primarily detected in the metaphysis of the long bones. From a histological perspective, COS largely consists of lobules of malignant cartilage cells with improved cellularity and sheets of peripheral spindle cells.[5–8]

It is generally known that although osteosarcoma exhibits a low incidence, about 5 cases per million, it remains the most common bone malignant tumor, accounting for 45.3% of all bone tumors; moreover, each subtype has unique gene expression characteristics, sensitive treatments, and prognoses.[9–14] COS is the most occurring subtype of osteosarcoma; thus, the prognostic factors associated with survival in patients with COS should be explored. However, due to the low incidence, the existing studies of COS are mostly case reports, and few population-based studies have analyzed the prognostic factors of COS. In addition, a complete evaluation system has not yet been established for accurate prognosis prediction in patients with COS. As a simple statistical prediction tool, a nomogram is capable of more accurately predicting survival and prognosis in patients with

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Ethical review: The data extracted from the SEER database do not require individual informed consent. The patient data in this study was anonymously managed in all stages, including stages of data cleaning and statistical analyses. This study was conducted in accordance with the Declaration of Helsinki.

Data availability statement: The raw data underlying this paper is available upon request from the corresponding author.

The datasets generated during and/or analyzed during the current study are publicly available.

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visual results, thereby further facilitating treatment in patients.[15] This study adopted a retrospective research method to collect patients with COS from the surveillance, epidemiology, and end results (SEER) database, analyzed the prognostic factors associated with survival in patients, and generated nomograms to help clinicians accurately predict survival in patients, in an attempt to potentially guide clinicians in treating patients with COS.

2. Materials and methods

2.1. Data resources

All cases involved in the present study originated from the SEER database of the National Cancer Institute, presenting a comprehensive population-based source of information (http://seer.cancer.gov/). It has been collecting data regarding cancer cases since 1973, accounting for approximately 28% of the total population of 18 regions in the United States.[16] The SEER database presents information regarding tumor statistics, and it is considered the standard for cancer information collection worldwide.

2.2. Study population

Overall, 432 patients with COS diagnosed based on the International Oncology Classification of Diseases between 2004 and 2015 were collected from the SEER database. The recorded information consisted of the patient's race, sex, age, marital status, year of diagnosis, primary site, tumor size, pathological grade, metastasis, surgical treatment, radiation, chemotherapy record, survival time, and survival status. Moreover, after excluding patients with unknown tumor size, non-single primary cancer, unknown metastasis, and unknown primary site, 320 patients were included in the study (Fig. 1). For further analysis, the primary site codes (C40.0, C40.1, C40.3, and C40.4) were classified as limb bones. C41.2 and C41.4 corresponded to the spine and pelvic bone, respectively; C41.1 was set as the mandible; C41.0 and C41.3 were classified as other bones. Pathological grades 1, 2, 3, and 4 represented well-

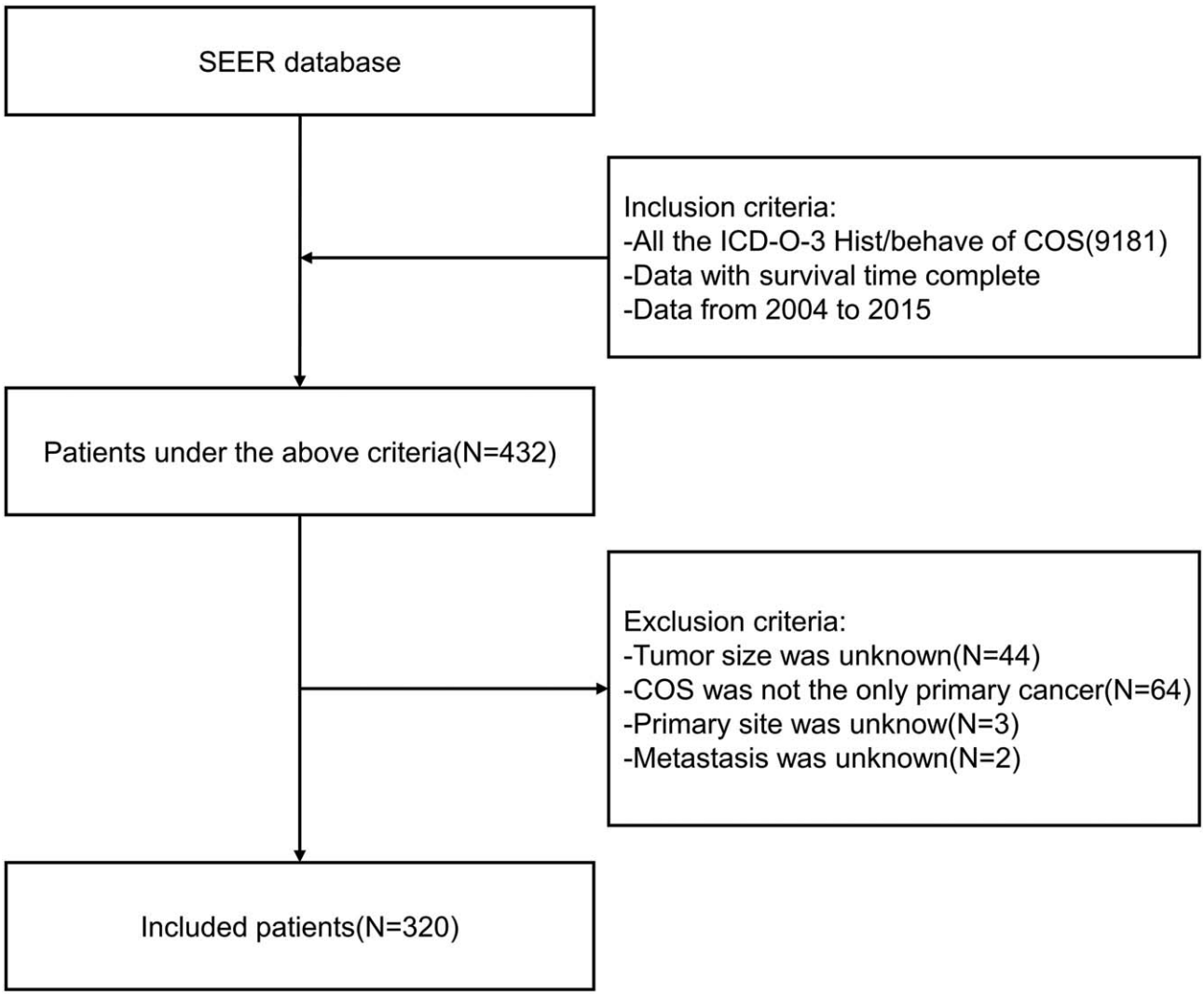

Figure 1. Flowchart of patient cohort selection.

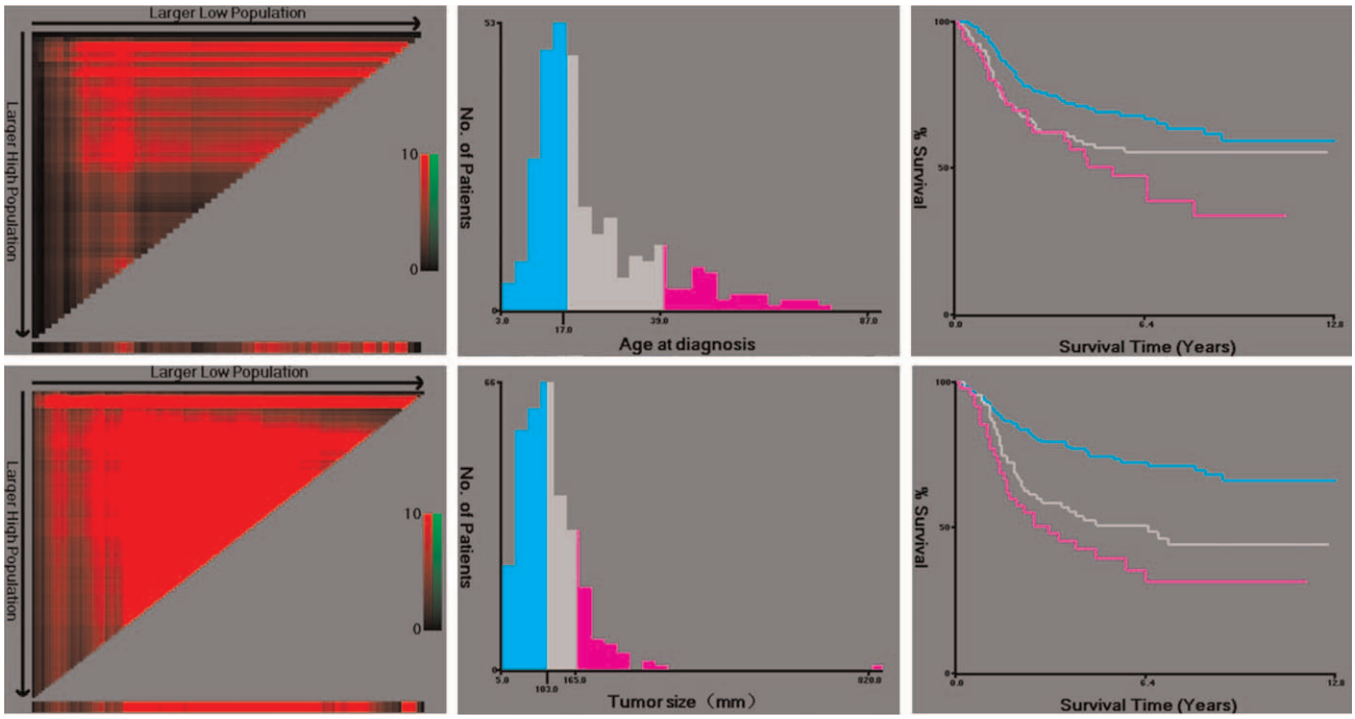

Figure 2. X-tile analysis of the best cut-off values for age and tumor size of COS patients. COS = chondroblastic osteosarcoma.

differentiated, moderately differentiated, poorly differentiated, and undifferentiated and anaplastic, respectively.

2.3. Statistical analysis

X-Tile software (Departments of Pathology and Genetics, Yale University, School of Medicine, New Haven, Connecticut) was used for the correlation analysis to set cut-off points for continuous variables (age and tumor size). It is a bio-informatics tool for outcome-based cut-off points optimization.[17] IBM SPSS Statistics 22.0 (IBM, Inc., Armonk, NY) software was employed to conduct most statistical analyses. For instance, the log-rank test and Kaplan–Meier analysis were conducted to determine the patients' CSS and overall survival (OS) rates based on various clinicopathological factors. Subsequently, using multivariate and univariate Cox proportional hazard regression models, the hazard ratio (HR) with 95% confidence interval (CI) was calculated, and the prognostic factors that affect the OS and CSS rates in patients with COS were determined. The OS and CSS rates were set as the time from diagnosis to death or the end of follow-up and from diagnosis to cancer-related death or the end of follow-up, respectively. Moreover, regarding the CSS rates, patients who died from other causes were considered censored data. $P < .05$ was considered to be of statistical significance.

Next, the independent prognostic factors identified in the multivariate Cox regression analysis were incorporated, and nomograms of OS and CSS were established for patients at 1, 3, and 5 years. An internal verification method was used to verify the nomograms. Finally, the concordance index (*C*-index) was determined, and calibration curves were plotted. As the *C*-index approached 1, the credibility of the model increased. Establishment and internal verification of the nomograms were conducted using R software (version 4.0.2; Institute of Statistics and Mathematics, Vienna, Austria).

3. Results

3.1. Age and tumor size cut-off points

X-Tile data are presented in a right triangular grid where each point represents a different cut-off point. And the software allows the user to move a cursor across the grid and provides an "on-the-fly" histogram of the resulting population subsets along with an associated Kaplan–Meier curve. This type of graphical representation can provide insight into the biological nature. For example, does it show a linear distribution relative to survival.[17]

As revealed from the results analyzed using X-Tile software, the optimal cut-off points for age were 17 and 39 years, and the patients comprised 3 groups according to age (≤17, 18–39, and >39 years); the optimal cut-off points for tumor size were 103 and 165 mm, and the patients were split into 3 groups (≤103, 104–165, and >165 mm) (Fig. 2).

3.2. Patient characteristics

A total of 320 patients with COS were included in the analysis of data between 2004 and 2015. Table 1 presents the patients' basic characteristics. Patients underwent follow-up for 1 to 153 months, with an average of 54.9 months. The incidence in male patients (55.6%) was higher than that in female patients (44.4%). The median age at the time of diagnosis was 18 years, with an average of 23.9 years. The oldest patient was 87 years old, and the youngest patient was only 3 years old. Eighty-six percent of the patients were aged ≤39 years at the time of the diagnosis. COS was more common in limb bones (68.8%), followed by the spine and pelvic bones (12.2%). Regarding the tumor size, most patients had tumors that were <104 mm (56.6%). Furthermore, most patients were diagnosed with regional metastasis (50.3%), and a few showed distant metastasis (21.3%). Patients harboring

Table 1

The characteristics of patients.

Characteristic	Patients(N = 320)	
	N	Percentage
Age		
≤17 yr	143	44.7
18–39 yr	132	41.3
>39 yr	45	14.0
Year of diagnosis		
2004–2010	175	54.7
2011–2015	145	45.3
Gender		
Male	178	55.6
Female	142	44.4
Race		
White	236	73.8
Black	58	18.1
Other	26	8.1
Marital status		
Married	54	16.9
Single	266	83.1
Primary site		
Limb bones	220	68.8
Spine and pelvic bones	39	12.2
Mandible	30	9.4
Other	31	9.7
Tumor size		
≤103 mm	181	56.6
104–165 mm	90	28.1
>165 mm	49	15.3
Pathological grade		
Grade1/2	20	6.3
Grade 3	106	33.1
Grade4	127	39.7
Unknown	67	20.9
Metastasis		
Localized	91	28.4
Regional	161	50.3
Distant	68	21.3
Surgery		
Yes	293	91.6
No	27	8.4
Radiation		
Yes	32	10.0
No/Unknown	288	90.0
Chemotherapy		
Yes	293	91.6
No/Unknown	27	8.4

poorly differentiated and undifferentiated/anaplastic tumors accounted for 33.1% and 39.7%, respectively. Of the patients, 91.6% received chemotherapy, 10% received radiation treatment, and 91.6% underwent surgery.

3.3. Kaplan–Meier analysis

Overall, 117 patients died during the follow-up period, of whom 107 died of COS. In the Kaplan–Meier analysis, the patients' 1-, 3-, and 5-year OS rates were 91.3%, 71.6%, and 66.9%, respectively, while the 1-, 3-, and 5-year CSS rates were 92.2%, 74.1%, and 69.4%, respectively. The log-rank test revealed that the primary site ($P < .001$), history of having undergone surgery ($P < .001$), presence of metastasis ($P < .001$), history of having received radiation treatment ($P = .016$ for CSS; $P = .045$ for OS), the tumor size ($P < .001$), and age ($P < .001$ for OS; $P = .007$ for CSS) were associated with CSS and OS rates in patients with COS. We generated the Kaplan–Meier curves (Figs. 3 and 4) and performed the log-rank test. The results revealed that age >39 years, COS of the spine and pelvic bones, the presence of distant metastasis, tumor size >104 mm, no history of having undergone any surgery, and a history of having received radiation treatment were associated with a low survival rate among patients with COS.

3.4. Univariate and multivariate Cox analyses

Among the 12 factors, univariate Cox regression analysis indicated associations of OS and CSS in patients with the primary site, a history of having undergone surgery, the pathological grade, the presence of metastasis, tumor size, a history of having received radiation treatment, and age ($P < .05$). Multivariate Cox regression analysis further confirmed these 7 factors.

Lastly, the results indicated that age >39 years (HR 5.071 for OS; HR 5.087 for CSS), the presence of distant metastasis (HR 2.856 for OS; HR 3.176 for CSS), no history of having undergone any surgery (HR 2.948 for OS; HR 2.207 for CSS), tumor size between 104 and 165 mm (HR 2.107 for OS; HR 2.314 for CSS), and tumor size >165 mm (HR 2.188 for OS; HR 2.515 for CSS) were independent prognostic factors and exhibited correlations with low survival rates. Primary tumors in the mandible (HR 0.239 for OS; HR 0.261 for CSS) and no history of having received radiation treatment (HR 0.448 for OS; HR 0.368 for CSS) were prognostic factors and correlated with long survival times. Tables 2 and 3 list the results of univariate and multivariate Cox regression analyses, respectively.

3.5. Nomogram analysis

Finally, age, the presence of metastasis, a history of having undergone surgery, a history of having received radiation treatment, tumor size, and primary site were incorporated, and nomograms were established to predict the patients' OS and CSS (Figs. 5 and 6). In the nomograms, each variable axis presented the value of a patient. The number of points received for the respective variable values was calculated based on an upward line. The total points axis represented the sum of the relevant numbers. The likelihood of 1-, 3-, or 5-year survival was determined based on a line downward to the survival axes.[15] The *C*-indexes of the nomograms predicting OS and CSS were 0.748 (95% CI 0.699–0.797) and 0.764 (95% CI 0.714–0.813), respectively. Calibration curves revealed excellent consistency between actual survival and nomogram predictions (Fig. 7).

4. Discussion

In this population-based study of prognostic factors associated with survival in patients with COS, we screened and retrospectively analyzed 320 patients with COS recorded in the SEER database between 2004 and 2015. We found that tumor size, the presence of distant metastasis, a history having undergone surgical treatment, age, a history of having received radiotherapy, and primary site are independent prognostic factors associated with survival in patients with COS. Age >39 years, the presence of distant metastasis, no history of having undergone any

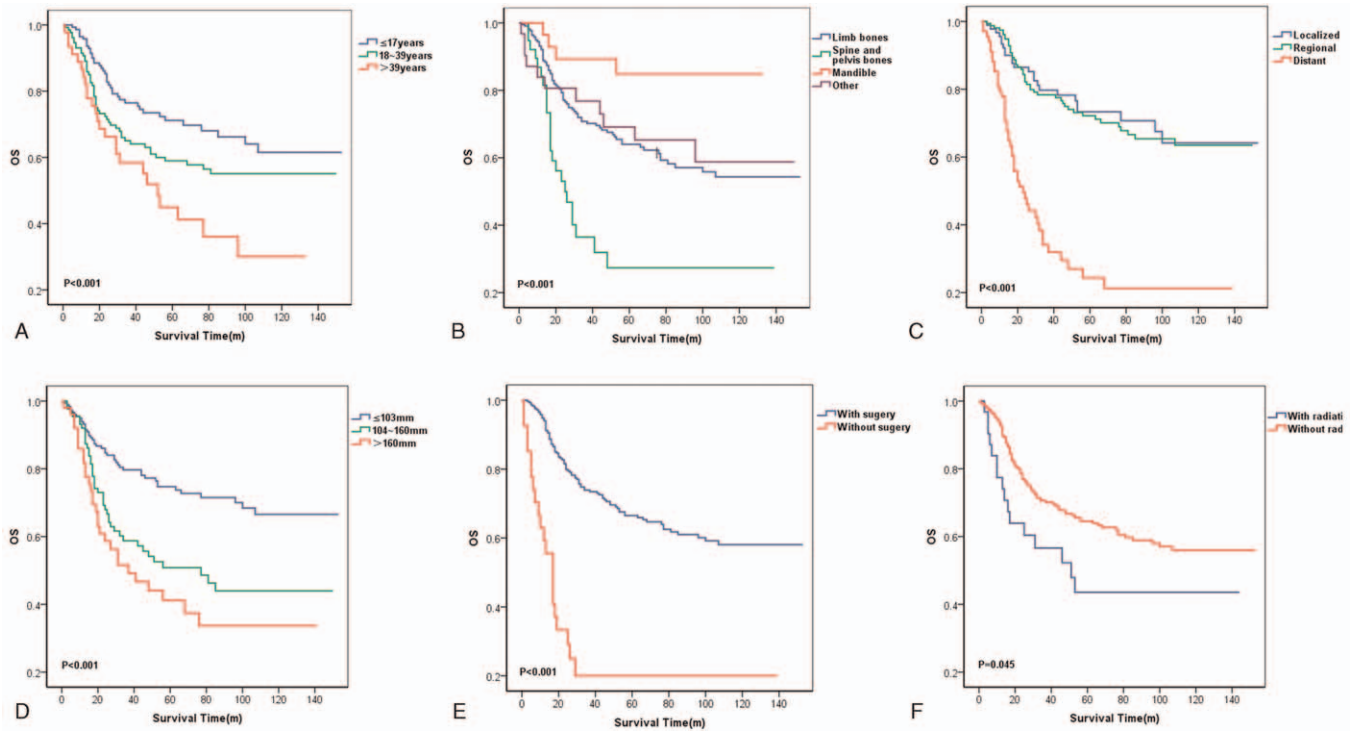

Figure 3. Kaplan–Meier overall survival curve according to age (A), primary site (B), metastasis (C), tumor size (D), surgery (E), and radiation (F). (*P* value, Log-rank test).

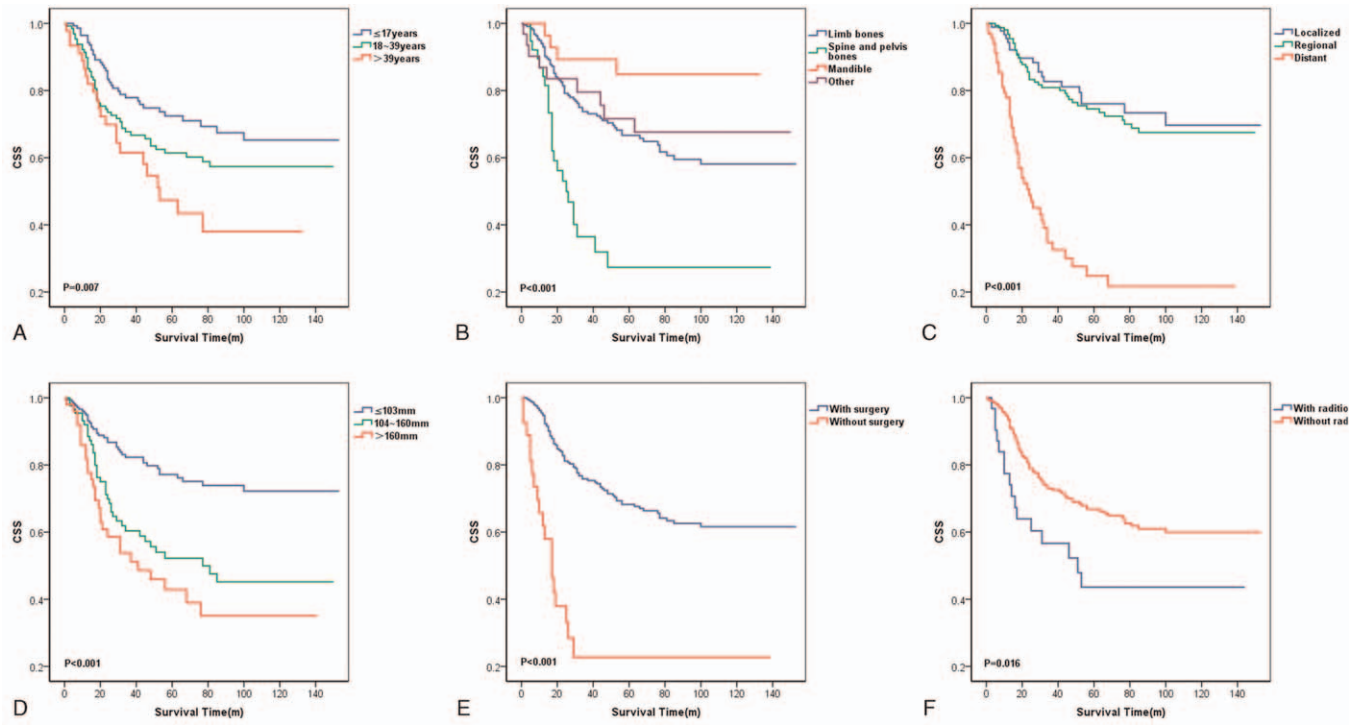

Figure 4. Kaplan–Meier cancer specific survival curve according to age (A), primary site (B), metastasis (C), tumor size (D), surgery (E), and radiation (F). (*P* value, Log-rank test).

Table 2

Univariate and multivariate Cox analysis of demographics and clinicopathologic characteristics for OS of patients.

	Univariate analysis		Multivariate analysis	
Variables	**HR (95% CI)**	***P* value***	**HR (95% CI)**	***P* value***
Age				
≤17 yr	Ref.		Ref.	
18–39 yr	1.524 (1.009–2.302)	*P*=.045	1.489 (0.964–2.299)	*P*=.072
>39 yr	2.378 (1.442–3.921)	*P*=.001	5.071 (2.868–8.968)	*P*<.001
Year of diagnosis				
2004–2010	Ref.			
2011–2015	0.931 (0.629–1.380)	*P*=.723		
Gender				
Male	Ref.			
Female	0.810 (0.560–1.171)	*P*=.263		
Race				
White	Ref.			
Black	1.263 (0.796–2.003)	*P*=.322		
Other	1.217 (0.631–2.344)	*P*=.558		
Marital status				
Married	Ref.			
Single	1.094 (0.676–1.771)	*P*=.714		
Primary site				
Limb bones	Ref.		Ref.	
Spine and pelvic bones	2.494 (1.572–3.955)	*P*<.001	0.675 (0.329–1.383)	*P*=.282
Mandible	0.306 (0.112–0.836)	*P*=.021	0.239 (0.074–0.771)	*P*=.017
Other	0.917 (0.487–1.726)	*P*=.788	0.611 (0.270–1.380)	*P*=.236
Tumor size				
≤103 mm	Ref.		Ref.	
104–165 mm	2.152 (1.416–3.271)	*P*<.001	2.107 (1.294–3.430)	*P*=.003
>165 mm	3.042 (1.905–4.858)	*P*<.001	2.188 (1.286–3.722)	*P*=.004
Pathological grade				
Grade1/2	Ref.		Ref.	
Grade 3	4.467 (1.078–18.510)	*P*=.039	2.747 (0.628–12.108)	*P*=.180
Grade4	5.013 (1.219–20.606)	*P*=.025	3.045 (0.704–13.168)	*P*=.136
Unknown	4.457 (1.055–18.825)	*P*=.042	3.232 (0.734–14.234)	*P*=.121
Metastasis				
Localized	Ref.		Ref.	
Regional	1.104 (0.674–1.809)	*P*=.695	0.946 (0.561–1.594)	*P*=.834
Distant	4.392 (2.670–7.224)	*P*<.001	2.856 (1.654–4.930)	*P*<.001
Surgery				
Yes	Ref.		Ref.	
No	4.511 (2.800–7.268)	*P*<.001	2.948 (1.387–6.265)	*P*=.005
Radiation				
Yes	Ref.		Ref.	
No/Unknown	0.588 (0.347–0.997)	*P*=.049	0.448 (0.234–0.859)	*P*=.016
Chemotherapy				
Yes	Ref.			
No/Unknown	0.618 (0.288–1.329)	*P*=.218		

CI = confidence interval, HR = hazard ratio, OS = overall survival, Ref. = reference.
* Likelihood ratio tests.

surgery, and tumor size >103 mm are associated with poor prognosis. In contrast, primary tumors of the mandible and no history of having received radiotherapy are associated with a more favorable prognosis. Next, the aforementioned independent prognostic factors were used to establish nomograms to predict the 1-, 3-, and 5-year OS and CSS rates in the patients. The calibration curves and *C*-indexes indicated that the nomograms are a reliable tool for estimating survival in patients with COS. For instance, consider a 15-year-old patient whose tumor was 170 mm in the spine that had metastasized at a distant site and who had not undergone radiotherapy or surgery. As indicated by the nomogram, the 1-, 3-, and 5-year OS rates of the patient are 75%, <30%, and <20%, respectively. If he had undergone surgery, the 1-, 3, and 5-year OS rates would rise to nearly 90%, nearly 50%, and nearly 40%, respectively. The nomogram may help doctors more accurately predict survival rates in particular patients and guide further treatment.

Several studies have demonstrated that the 5-year OS rate in patients with COS is 56% to 60%.[9,18,19] Herein, the 5-year OS rate in patients with COS was 66.9%, which was higher than the results previously reported, but still comparable. Sun et al[9] suggested that race, age, pathological differentiation, the

Table 3

Univariate and multivariate Cox analysis of demographics and clinicopathologic characteristics for CSS of patients.

	Univariate analysis		Multivariate analysis	
Variables	**HR (95% CI)**	***P* value***	**HR (95% CI)**	***P* value***
Age				
≤17 yr	Ref.		Ref.	
18–39 yr	1.525 (0.993–2.342)	*P*=.054	1.513 (0.962–2.377)	*P*=.073
>39 yr	2.259 (1.332–3.830)	*P*<.001	5.087 (2.777–9.316)	*P*<.001
Year of diagnosis				
2004–2010	Ref.			
2011–2015	0.986 (0.656–1.481)	*P*=.946		
Gender				
Male	Ref.			
Female	0.845 (0.575–1.240)	*P*=.390		
Race				
White	Ref.			
Black	1.245 (0.769–2.016)	*P*=.373		
Other	1.053 (0.508–2.180)	*P*=.890		
Marital status				
Married	Ref.			
Single	1.283 (0.754–2.183)	*P*=.358		
Primary Site				
Limb bones	Ref.		Ref.	
Spine and pelvis bones	2.818 (1.765–4.498)	*P*<.001	0.846 (0.419–1.711)	*P*=.642
Mandible	0.342 (0.125–0.937)	*P*=.037	0.261 (0.078–0.869)	*P*=.029
Other	0.830 (0.414–1.663)	*P*=.599	0.542 (0.220–1.334)	*P*=.182
Tumor size				
≤103 mm	Ref.		Ref.	
104–165 mm	2.434 (1.565–3.786)	*P*<.001	2.314 (1.378–3.886)	*P*=.002
>165 mm	3.490 (2.139–5.694)	*P*<.001	2.515 (1.435–4.409)	*P*=.001
Pathological grade				
Grade1/2	Ref.		Ref.	
Grade 3	4.106 (0.988–17.062)	*P*=.052	2.246 (0.508–9.923)	*P*=.286
Grade4	4.678 (1.136–19.258)	*P*=.033	2.614 (0.601–11.376)	*P*=.200
Unknown	3.712 (0.870–15.836)	*P*=.076	2.486 (0.557–11.088)	*P*=.233
Metastasis				
Localized	Ref.		Ref.	
Regional	1.182 (0.693–2.018)	*P*=.539	0.965 (0.550–1.694)	*P*=.901
Distant	5.207 (3.062–8.856)	*P*<.001	3.176 (1.778–5.675)	*P*<.001
Surgery				
Yes	Ref.		Ref.	
No	4.525 (2.742–7.468)	*P*<.001	2.207 (1.021–4.772)	*P*=.044
Radiation				
Yes	Ref.		Ref.	
No/Unknown	0.528 (0.311–0.899)	*P*=.019	0.368 (0.189–0.719)	*P*=.003
Chemotherapy				
Yes	Ref.			
No/Unknown	0.678 (0.315–1.460)	*P*=.320		

CI = confidence interval, CSS = cancer-specific survival, HR = hazard ratio, Ref. = reference.
* Likelihood ratio tests.

presence of metastasis, and a history of having undergone surgery are independent prognostic factors correlated with survival in patients with COS. Consistent with their study, the present study found that age, the presence of metastasis, and a history of having undergone surgery are independent prognostic factors associated with survival in patients with COS. However, the difference is that the present study did not reveal independent predictability of race and pathological differentiation. In the present study, the pathological differentiation of tumors was a prognostic factor in univariate Cox analysis. But, by observation, we found that pathological differentiation had an interaction with tumor size and primary site, which might lead to the fact that pathological differentiation has no significant relationship with prognosis in the multivariate Cox analysis. Regarding the factor of race, Sadykova et al[20] found that osteosarcoma is more common in Africa than other continents, with a higher incidence rate detected in African Americans than others, and associated with patient survival. As opposed to the results of their study, other studies have not shown that race is an independent prognostic factor associated with survival in patients with osteosarcoma.[19,21–23] For this reason, whether the factor of race can independently predict survival in patients with COS remains controversial, and further research is required.

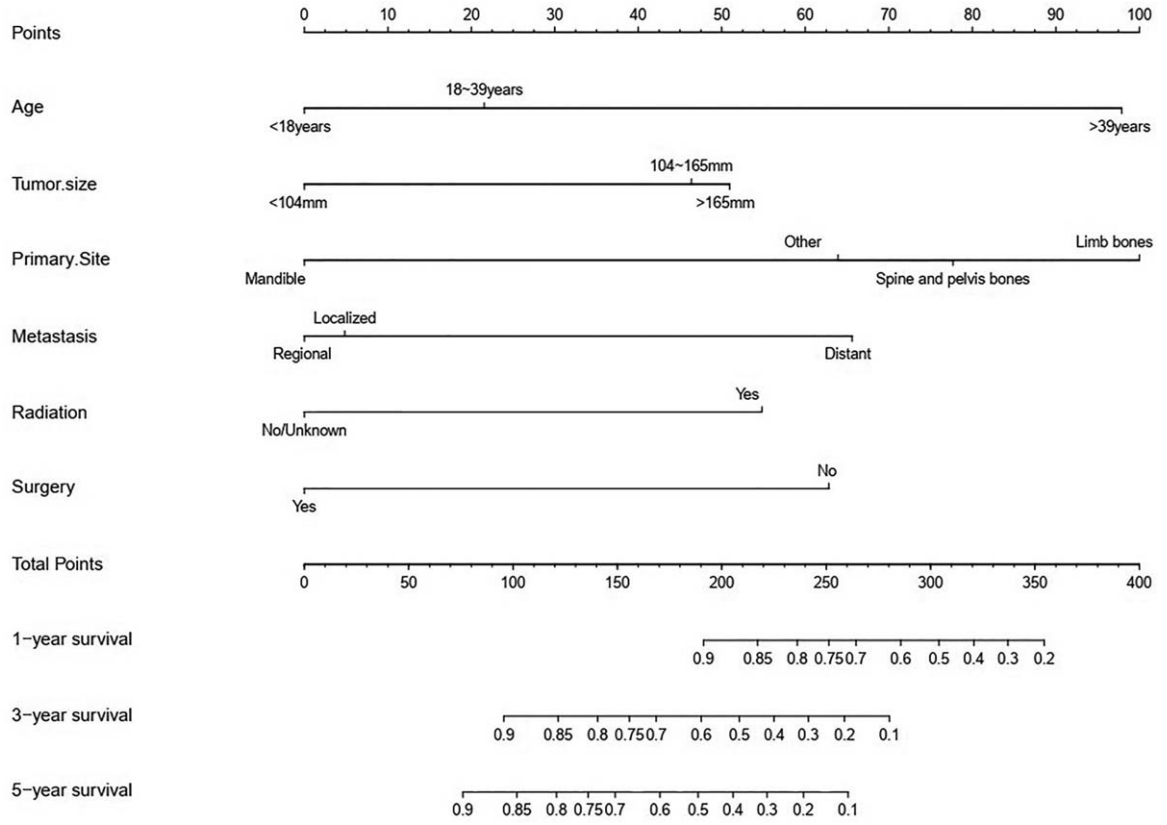

Figure 5. Nomogram predicting 1-, 3-, and 5-year OS for patients with COS. COS = chondroblastic osteosarcoma, OS = overall survival.

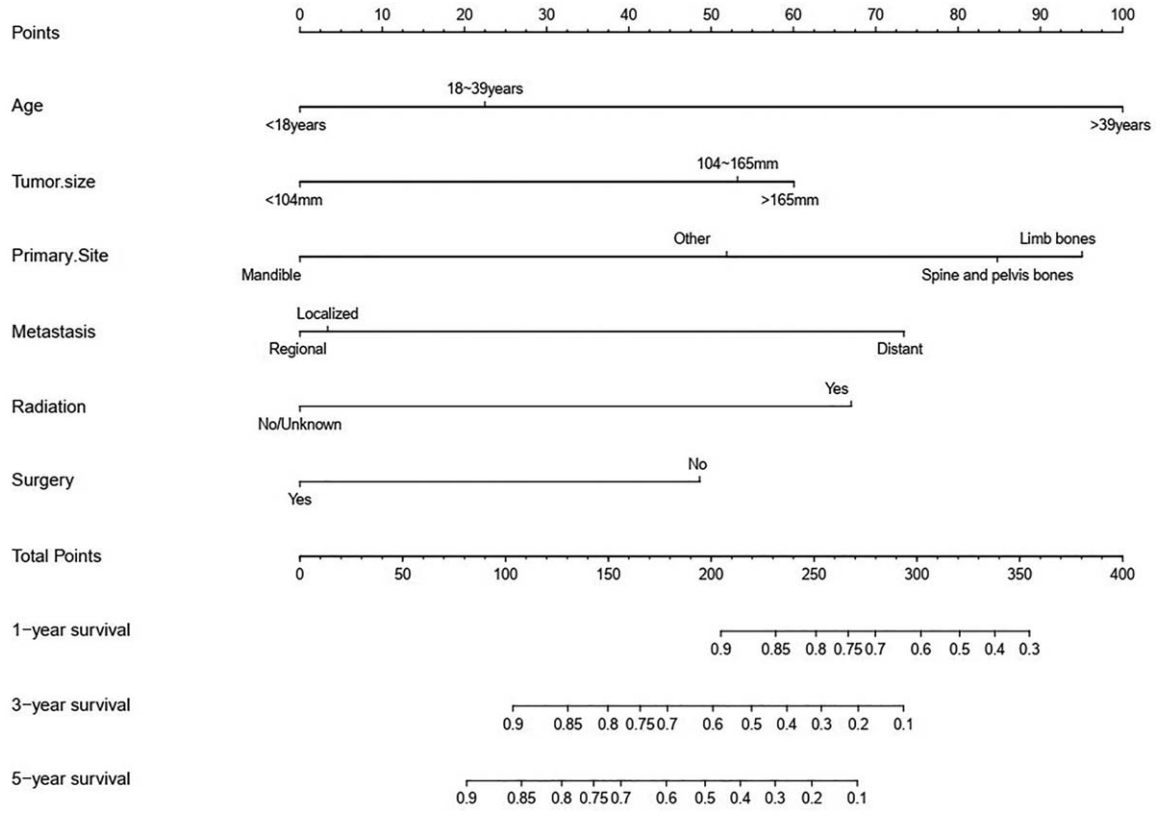

Figure 6. Nomogram predicting 1-, 3-, and 5-year CSS for patients with COS. COS = chondroblastic osteosarcoma, OS = overall survival.

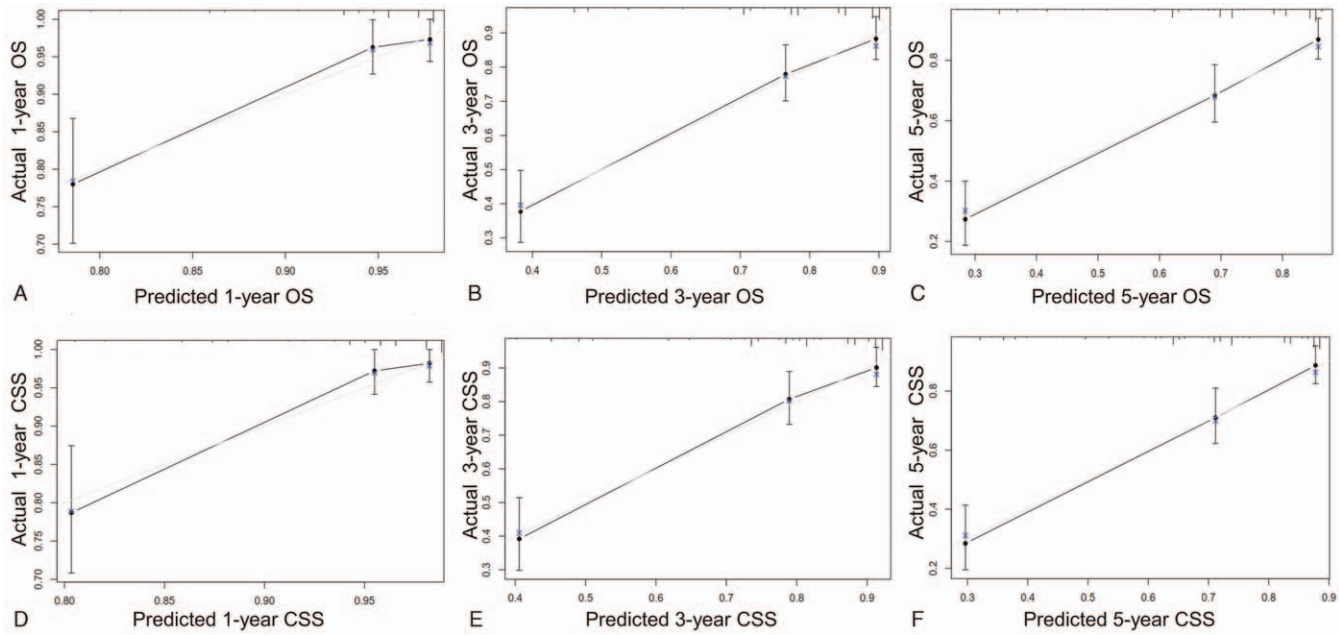

Figure 7. Calibration curves for prediction of patients' 1-year OS (A), 3-year OS (B), and 5-year OS (C), and patients' 1-year CSS (D), 3-year CSS (E), and 5-year CSS (F). Nomogram-predicted OS or CSS is plotted on the *x*-axis; actual OS or CSS is plotted on the *y*-axis. The imaginary line indicates a perfect calibration model in which the predicted probabilities are identical to the actual survival outcomes. CSS = cancer-specific survival, OS = overall survival.

This study revealed that patients aged >39 years had a worse prognosis than that of patients aged ≤17 years, which is consistent with the results of some other studies.[19,24–26] One possible explanation for this is that treatment strategies may be inconsistent among older patients, and older patients may exhibit poorer physical conditions and more complications than those in younger patients. However, it is noteworthy that no significant difference was identified in survival between patients aged ≤17 years and patients aged 18 to 39 years. As shown in previous studies, tumor size is an independent prognostic factor in patients with osteosarcoma, and large tumors are associated with low survival rates in patients with osteosarcoma.[19,27–30] In this most common subtype of osteosarcoma, a consistent conclusion was drawn. Kager et al[31] explained that larger tumors make it rather difficult to obtain adequate surgical margins. Furthermore, larger tumors tend to metastasize, thereby causing low survival rates in patients.[22] In the present study, univariate Cox analysis demonstrated that the survival rate in patients with the primary tumor site in the spine and pelvis was lower than that in patients with the primary site in the bones of the extremities, whereas multivariate Cox analysis revealed that the primary site was not an independent risk factor corresponding to survival in patients. This result is consistent with the results achieved by Sun et al.[9] The difference is that, compared with that of patients who harbored tumors in the bones of the extremities, patients who harbored primary tumors in the mandible were found to have a more favorable prognosis. This may be because patients with tumors in the mandible may undergo surgical resection, develop less metastasis, usually harbor smaller tumors, and exhibit more effective pathological differentiation.[32] These factors are associated with a more favorable prognosis. After multivariate Cox analysis, this study found that after excluding the effect of confounding factors (e.g., history of having undergone surgery, presence of metastasis, tumor size, and pathological differentiation), the primary site of the mandible remained an independent prognostic factor.

Currently, surgical resection and systemic chemotherapy are the standard treatments for osteosarcoma.[33] However, other studies have shown that chemotherapy for osteosarcoma may not be similarly effective for COS, and a history of having received chemotherapy is not a prognostic factor that affects survival in patients.[9] This conforms to the findings of the present study. However, chemotherapy is essential. The Birmingham classification system, considering the response to chemotherapy, is predictive of local recurrence, and research has indicated that the response to chemotherapy is a significant factor in the univariable analysis regarding local control of the disease.[20] In addition, a history of having received radiotherapy predicted a lower survival rate in this study, which is consistent with the results of other similar studies.[9,20] This may be attributed to the radiation resistance of osteosarcoma.[27] For treatment in patients with tumors that occur at unresectable sites or bone metastases, radiotherapy remains a treatment that is capable of prolonging survival and reducing pain intensity.[34,35]

The present study had several limitations. First, as a retrospective study, it may have been subject to unavoidable biases in attribution and selection. Second, because of the low incidence of COS, and because the diagnostic criteria and diagnostic techniques in earlier years may be different from those in recent years, this study only selected patients with COS included in the SEER database between 2004 and 2015, thereby resulting in a small sample size. Lastly, the records of radiotherapy and chemotherapy in the SEER database did not distinguish between unknown and no treatment. Moreover, there were no records of specific radiotherapy and chemotherapy regimens, which is another limitation. Besides, if a nomogram can be externally verified using data from other research centers or databases, we consider that the corresponding test results will be

more credible, and it can also be implemented to verify whether the nomogram exhibits universal applicability. Despite these limitations, this study generated the first known predictive model capable of accurately assessing prognosis in patients with COS. Furthermore, although the sample size was not large enough to analyze the factors of prognosis in patients with cancer and establish predictive models, it remains one of the largest-scale studies to study the factors affecting prognosis in patients with COS.

5. Conclusions

In general, our study suggested that age >39 years, the presence of distant metastasis, no history of having undergone any surgery, and tumor size >103 mm are risk factors that significantly shorten survival in patients with COS, while the primary site of the mandible and no history of having received radiotherapy are associated with a more favorable prognosis. We then used these variables to generate a nomogram for predicting the 1-, 3-, and 5-year OS and CSS rates in patients with COS. The nomogram achieved prognostic prediction in patients with COS with high accuracy, which may potentially guide treatment in patients.

Author contributions

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