Discover Oncology

Analysis

Development and validation of nomogram model predicting overall survival and cancer specific survival in glioblastoma patients

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Abstract

Background Identifying the incidence and risk factors of Glioblastoma (GBM) and establishing effective predictive models will benefit the management of these patients.

Methods Using GBM data from the Surveillance, Epidemiology, and End Results (SEER) database, we used Joinpoint software to assess trends in GBM incidence across populations of different age groups. Subsequently, we identified important prognostic factors by stepwise regression and multivariate Cox regression analysis, and established a Nomogram mathematical model. COX regression model combined with restricted cubic splines (RCS) model was used to analyze the relationship between tumor size and prognosis of GBM patients.

Results The incidence of GBM has been on the rise since 1978, especially in the age group of 65–84 years. 11498 patients with GBM were included in our study. The multivariate Cox analysis revealed that age, tumor size, sex, primary tumor site, laterality, number of primary tumors, surgery, chemotherapy, radiotherapy, systematic therapy, marital status, median household income, first malignant primary indicator were independent prognostic factors of overall survival (OS) for GBMs. For cancer-specific survival (CSS), race is also independent prognostic factors. Additionally, risk of poor prognosis increased significantly with tumor size in patients with tumors smaller than 49 mm. Moreover, our nomogram model showed favorable discriminative ability.

Conclusion At the population level, the incidence of GBM is on the rise. The relationship between tumor size and patient prognosis is still worthy of further study. Moreover, the proposed nomogram with good performance was constructed and verified to predict the OS and CSS of patients with GBM.

Keywords Glioblastoma · Prognostic nomogram · Overall survival · Cancer-specific survival · SEER

1 Introduction

GBM is the most prevalent and aggressive primary brain tumor, associated with poor prognosis [1]. According to the WHO classification, GBM is the highest grade in WHO classification, Grade IV [2]. The median survival time for GBM has been reported to be less than 15 months [3]. The annual incidence is about 5.26 per 100 000 people [4]. Cancer

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incidence, mortality, and the burden of disability-adjusted life years (DALY) vary widely by country, region, and age [5]. The incidence of GBM has been reported to increase with age, with more than 50% of patients older than 65 years of age [6]. Understanding the epidemiology of GBM is essential for improving cancer prevention and management strategies. Despite advancements in cancer treatment, therapeutic outcomes for GBM remain unsatisfactory [7]. The usual treatment for glioblastoma includes surgery, chemotherapy and radiation [8]. However, the limited efficacy of current GBM treatments is attributed to its highly invasive nature, high recurrence rate, and several anatomical and physiological barriers. The blood–brain barrier restricts drug delivery to the tumor site, and tumor localization in critical brain regions further complicates surgical and therapeutic interventions [9–14]. All these contribute to the poor prognosis of GBM. However, the understanding of prognostic factors for GBM is still incomplete.

The Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) (https://seer.cancer.gov/) collects demographic, tumor location, morphology, treatment, and survival data for approximately 30% of cancer patients in the United States since 1973, serving as a valuable resource for oncology research [15, 16]. This study analyzed temporal trends in the incidence of GBM across various age groups from 1975 to 2019 using SEER data. Furthermore, prognostic factors for GBM were identified, and a personalized prognostic model was developed. Nomogram-based prediction models have been increasingly utilized in oncology research [17–24]. These models integrate multiple prognostic factors, provide a visual representation of risk assessment, and support personalized medicine [25]. Furthermore, they offer an accessible tool for clinicians to estimate patient prognosis.

In this study, a large GBM cohort from the SEER database was analyzed to evaluate the incidence of GBM and develop a nomogram for prognostic prediction in GBM patients. This model was designed to estimate Overall Survival (OS) and Cancer-Specific Survival (CSS), thereby assisting in clinical decision-making.

2 Materials and methods

2.1 Patients selection

All patients in this study were recruited from the SEER database, which was established by the National Cancer Institute to conduct comprehensive national clinical investigations [16, 17]. The clinical variables of patients confirmed as GBM between 2006 and 2016 were retrieved by using SEER*Stat software (version 8.3.6). The inclusion criteria: (1) Glioblastoma, NOS (ICD-O-3/WHO 2009); (2) complete information on interested variables. The exclusion criteria were as follows: (1) surgery except no surgery, Local tumor destruction, partial resection of lobe of brain, radical resection of tumor, subtotal resection of tumor; (2) Laterality except paired site and only one side—side unspecified; (3) Radiation and surgery sequence except postoperative radiotherapy, directed surgery, preoperative and postoperative radiotherapy; (4) unknown tumor size, age, race, marital status, income, origin recode NHIA (Non-Hisp/ Hispanic) and total number of in situ/malignant tumors in patient; (5) Survival time unknown; (6) No histological findings. The study population determination protocol is shown in Fig. 1. All GBM patients included in the study were randomly divided into training and validation cohorts in a 7:3 ratio using RStudio software (Fig. 1).

2.2 Study on variable selection

Specific information on tumor size (continuous variable), age (continuous variable), year of diagnosis (continuous variable), race (categorical variable), sex (binary variable), chemotherapy (binary variable), surgery (categorical variable), radiotherapy (binary variable), surgery and radiotherapy sequence (categorical variable), systemic and surgery sequence (categorical variable), primary site (categorical variable), laterality (categorical variable), months from diagnosis to treatment (binary variable), marital status (categorical variable), median household income (categorical variable), origin recode NHIA (binary variable), first malignant primary indicator (binary variable), total number of in situ/malignant tumors in patient (binary variable), causes of death (categorical variable), and survival time (continuous variable) were downloaded from the SEER database. In terms of clinical outcomes, OS was selected as the primary endpoint and CSS as the secondary endpoint.

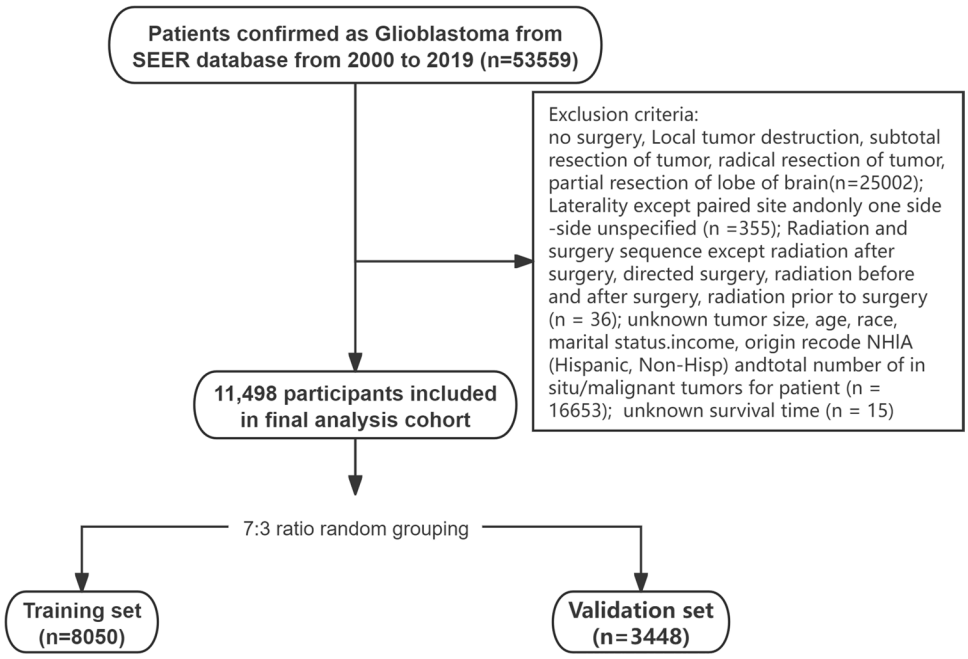

Fig. 1 Flowchart of the inclusion and exclusion criteria for this study

2.3 Statistics

Categorical variables were presented as counts and percentages and compared using the chi-square test. Continuous variables were summarized as medians and interquartile ranges (IQRs) and compared using the Kruskal–Wallis test.

To identify independent prognostic factors, stepwise Cox regression was performed using the Akaike Information Criterion (AIC) minimum principle. The bidirectional selection method was used to select variables for inclusion in the final multivariate Cox model. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated for each factor. Variables with $P < 0.05$ in the stepwise selection were retained in the final model.

A nomogram was developed to predict overall survival (OS) and cancer-specific survival (CSS) in GBM patients. Model construction and validation were conducted using R software (version 4.1.3). The predictive performance of the nomogram was assessed using the calibration curve and concordance index (C-index). Calibration was performed to evaluate the agreement between the predicted and observed survival probabilities at 6 months, 1 year, 2 years, 3 years, 5 years, and 8 years. The C-index, ranging from 0.5 (no discrimination) to 1 (perfect discrimination), was used to quantify the predictive accuracy, with higher values indicating better model performance.

Each patient's total score was calculated based on the nomogram, and patients in both the training and validation cohorts were stratified into high-risk and low-risk groups using the optimal cut-off value. Kaplan–Meier survival analysis was used to estimate OS, and differences between groups were compared using the log-rank test. Cumulative risk curves were plotted at 6 months, 1 year, 2 years, 3 years, 5 years, and 8 years in both cohorts. All evaluations were conducted using bootstrap resampling ($n = 1000$). A two-sided $P < 0.05$ was considered statistically significant.

Additionally, we assessed glioma mortality based on SEER cancer registry data and evaluated glioma incidence trends according to age and calendar year. Joinpoint regression analysis (Joinpoint software, version 4.7.0.0) was used to detect changes in incidence trends over time, modeling piecewise log-linear trends with normalized rates by year.

To explore the association between tumor size and prognosis in GBM patients, we employed a restricted cubic spline (RCS) model to analyze the relationship between tumor size and survival outcomes (OS/CSS). Multivariable Cox proportional hazards regression was performed to adjust for potential confounders. The optimal model was selected based on the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) minimum principle.

3 Results

The analysis of the time trend of the global GBM incidence data from 1975 to 2019 showed that the incidence of GBM was higher in the 65–74 and 75–84 age groups. In the 65–74 age group, the incidence increased rapidly from 1978 to 1992, and slowly increased from 1992 to 2019 without decreasing trend. In the 75–84 age bracket, the GBM morbidity increased rapidly from 1972 to 1998, exceeding the age group of 65–74 in 1004, becoming the age bracket with the highest morbidity of GBM, and then slowly increased and continued to occupy the age bracket with the highest morbidity of GBM. The trend of incidence in the 85 + age bracket was generally consistent with those in the 75–84 age bracket, but the overall incidence was lower than that in the 75–84 age group. In general, since 1999, the incidence of GBM has remained high and is still slowly rising. (Fig. 2).

3.1 Patient baseline characteristics

Finally, a total of 11498 patients diagnosed with GBM from 2000 to 2019 were enrolled and then randomly divided into the training set (8050 cases) and the validation set (3448 cases) (Fig. 1). Among all patients, 59.2% were male and 40.8% were female. White 5.3%, black 5.1%; Unmarried 14.7%, married 67.8%; Surgery 78.5%; Chemotherapy accounted for 76.4%; Radiotherapy accounted for 83.1%; Systematic treatment accounted for 60.7%; The proportion of bilateral hemispheres was 44.7, and the left hemisphere was 42.6%. Only one primary tumor accounted for 89.5%; 71.3% started treatment within 1 month after diagnosis. Age and tumor size were continuous variables, median age was 63 [54–72] (median [IQR]), median tumor size was 45 [33–56]. The median follow-up time was 10 month [4–19]. Deaths accounted

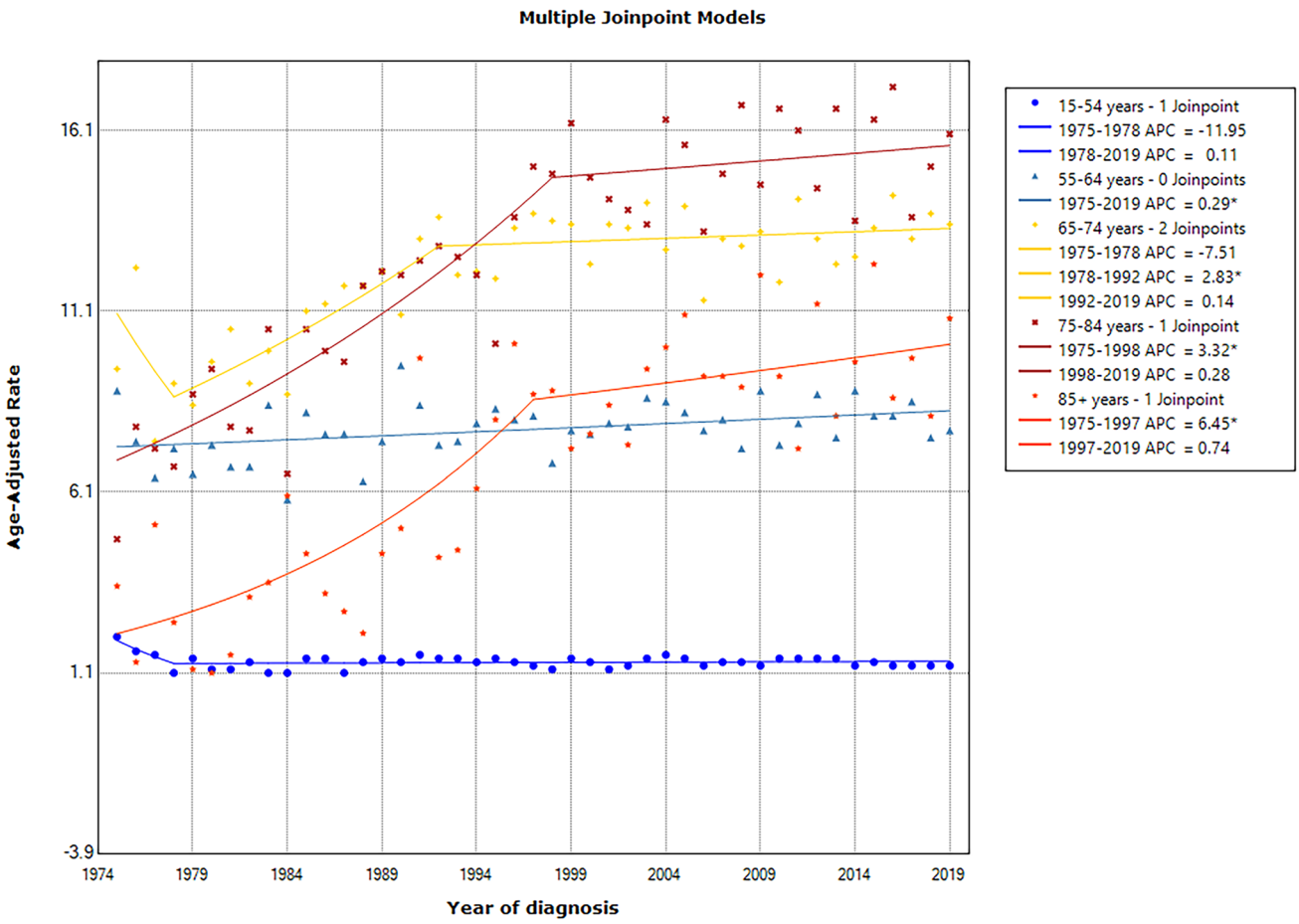

Fig. 2 Joinpoint analysis of the incidence rates of glioblastoma in the U.S. between 1975 and 2019. (*) Indicates the annual percent change (APC) that is significantly different from zero ($P < 0.05$)

for 95.8 percent (Table 1). There were no significant differences in each of the included variables between the training and validation groups.

3.2 Identification of independent factors of GBM in training cohort

The prognostic factors associated with OS and CSS in GBM patients were analyzed by stepwise regression and then multivariate Cox regression. Stepwise Cox regression analysis revealed that age, tumor size, sex, primary site and Laterality, number of primary tumors, surgery, chemotherapy, radiotherapy, systematic treatment, marital status, median household income, and first malignant primary indicator were the related factors of OS in GBM patients. Multivariate Cox regression analysis showed that all the above were independent risk factors for OS in GBM patients (Table 2).

For CSS, stepwise Cox regression analysis showed that demographic and clinicopathological factors associated with CSS added race compared with OS.All the above factors were included in multivariate Cox proportional hazards regression analysis, and all were independent prognostic factors for CSS except systematic treatment and race (Table 2). Thus, OS and CSS nomogram models for 0.5, 1-, 2-, 3-, 5 -, and 8-years were established respectively. (Fig. 3A and B).

3.3 Development of a prognostic nomogram for OS and CSS

Prognostic nomogram were constructed based on multivariate Cox regression results. In the nomogram, each variable subtype corresponds to the value of a points scale, that was, the contribution to OS and CSS results. The total score of each GBM individual was obtained by adding the scores of each subtype corresponding to each variable. A line was drawn at the corresponding position of the total Points scale. The individual OS and CSS probabilities of 0.5, 1, 2, 3, 5, and 8 years were obtained. (Fig. 3A, B).

3.4 Validation of the prognostic nomogram

The accuracy of the Nomogram was evaluated by internal and external validation of the C-index and calibration chart. In training cohort, the C index of Nomogram OS was 0.724 (95% CI 0.718–0.730) and that of CSS was 0.720 (95% CI 0.714–0.726). In the validation cohort, the C index of the Nomogram OS and CSS was 0.718 (95% CI 0.708–0.728) and 0.719 (95% CI 0.713–0.725), respectively. Calibration curves were also made to compare the nomogram prediction curve with the perfect curve. The results showed that the 0.5-, 1-, 2-, 3-, 5- and 8-year OS (Fig. 4A) and CSS (Fig. 4B) nomograms of the training cohort were in good agreement with the actual observation results, which was also reflected in the validation cohort. (Fig. 4C, D) The above results show that the predicted values of nomogram are in good agreement with the measured values on the training and validation cohorts.

In addition, we calculated the individual score (PI score) based on the Nomogram, and then used the score to predict the survival of patients at 0.5-, 1-, 2-, 3-, 5- and 8 years. ROC curves were drawn to evaluate the predictive performance of the Nomogram in different cohorts. The AUC value ranges from 0.5 (no predictive effect) to 1 (complete prediction), and the higher the value, the stronger the nomogram resolution will be. The results showed that PIscore had a good ability to distinguish the survival conditions of OS and CCS at different time points in both the training cohort and the validation cohort, and the AUC was greater than or equal to 0.75 (Fig. 5).

Moreover, KM survival curves were constructed to assess the associations between the PIscore and OS/CCS in training cohort and validation cohort, the cutoff points were used to divided patients in high-risk and low-risk subgroups, and the results indicated that the high-risk subgroup had a worse prognosis (All log-rank $P < 0.001$, Fig. 6 and Supplementary Fig. 1) and a heightened risk of mortality (All log-rank $P < 0.001$, Fig. 7 and Supplementary Fig. 2).

3.5 Association between tumor size and prognosis in GBM patients

The relationship between tumor size and survival outcomes (OS/CSS) in GBM patients was analyzed using a RCS model. After adjusting for potential confounders with multivariable Cox regression, the resulting curve is shown in the Fig. 8. The optimal model was selected based on the minimum AIC and BIC values, and the final model included three knots. The overall association test ($P < 0.001$) and the non-linearity test ($P < 0.001$) indicated a significant non-linear dose–response relationship between tumor size and GBM survival outcomes. Compared to patients with tumor size > 49 mm, those with tumor size ≤ 49 mm exhibited a steeper increase in risk. The results demonstrated that when tumor size < 49 mm, the

Table 1 Baseline characteristics of total study population

Baseline characteristics	Level	Overall cohort	training cohort	validation cohort	*P*
n		11498	8050	3448	
Year of diagnosis (median [IQR])		2012 [2010, 2014]	2012 [2010, 2014]	2012 [2010, 2014]	0.055
Sex n (%)	Male	6804 (59.2)	4767 (59.2)	2037 (59.1)	0.905
	Female	4694 (40.8)	3283 (40.8)	1411 (40.9)	
Primary Site (%)	C71.0-Cerebrum	415 (3.6)	300 (3.7)	115 (3.3)	0.780
	C71.1-Frontal lobe	3304 (28.7)	2321 (28.8)	983 (28.5)	
	C71.2-Temporal lobe	2922 (25.4)	2019 (25.1)	903 (26.2)	
	C71.3-Parietal lobe	1894 (16.5)	1339 (16.6)	555 (16.1)	
	C71.4-Occipital lobe	493 (4.3)	338 (4.2)	155 (4.5)	
	C71.5-Ventricle, NOS	43 (0.4)	26 (0.3)	17 (0.5)	
	C71.6-Cerebellum, NOS	96 (0.8)	65 (0.8)	31 (0.9)	
	C71.7-Brain stem	78 (0.7)	55 (0.7)	23 (0.7)	
	C71.8-Overlapping lesion of brain	1687 (14.7)	1191 (14.8)	496 (14.4)	
	C71.9-Brain, NOS	566 (4.9)	396 (4.9)	170 (4.9)	
Laterality (%)	Bilateral	5141 (44.7)	3602 (44.7)	1539 (44.6)	0.612
	Left	4899 (42.6)	3415 (42.4)	1484 (43.0)	
	Notpaired	1294 (11.3)	911 (11.3)	383 (11.1)	
	Right	164 (1.4)	122 (1.5)	42 (1.2)	
surgery (%)	No	2467 (21.5)	1729 (21.5)	738 (21.4)	0.217
	Local tumor destruction	9 (0.1)	8 (0.1)	1 (0.0)	
	subtotal resection of tumor	3307 (28.8)	2293 (28.5)	1014 (29.4)	
	radical resection of tumor	3669 (31.9)	2551 (31.7)	1118 (32.4)	
	partial resection of lobe of brain	2046 (17.8)	1469 (18.2)	577 (16.7)	
Surgery and Radiation Sequence (%)	No radiation and/or cancer-directed surgery	4195 (36.5)	2957 (36.7)	1238 (35.9)	0.759
	Radiation after to surgery	7225 (62.8)	5040 (62.6)	2185 (63.4)	
	Radiation before and after surgery	40 (0.3)	26 (0.3)	14 (0.4)	
	Radiation prior to surgery	38 (0.3)	27 (0.3)	11 (0.3)	
Radiation (%)	None/Unknown	1938 (16.9)	1375 (17.1)	563 (16.3)	0.337
	Yes	9560 (83.1)	6675 (82.9)	2885 (83.7)	
Chemotherapy (%)	No/Unknown	2719 (23.6)	1921 (23.9)	798 (23.1)	0.419
	Yes	8779 (76.4)	6129 (76.1)	2650 (76.9)	
Systemic therapy(%)	No	4522 (39.3)	3187 (39.6)	1335 (38.7)	0.392
	Yes	6976 (60.7)	4863 (60.4)	2113 (61.3)	
Systemic and Surgery Sequence (%)	Intraoperative systemic therapy with other therapy administered before and/or after surgery	102 (0.9)	67 (0.8)	35 (1.0)	0.388
	Intraoperative systemic therapy	63 (0.5)	47 (0.6)	16 (0.5)	

Table 1 (continued)

Baseline characteristics	Level	Overall cohort	training cohort	validation cohort	*P*
	No systemic therapy and/or surgical procedures	4522 (39.3)	3187 (39.6)	1335 (38.7)	
	Systemic therapy after surgery	6650 (57.8)	4639 (57.6)	2011 (58.3)	
	Systemic therapy before surgery	59 (0.5)	45 (0.6)	14 (0.4)	
	Systemic therapy both before and after surgery	102 (0.9)	65 (0.8)	37 (1.1)	
Months from diagnosis to treatment (%)	< = 1 month	8199 (71.3)	5736 (71.3)	2463 (71.4)	0.864
	> 1 month	3299 (28.7)	2314 (28.7)	985 (28.6)	
Tumor size (median [IQR])	(mm)	45.0 [33.0, 56.0]	45.0 [33.0, 56.0]	45.0 [33.0, 56.0]	0.768
months (median [IQR])		10.0 [4.0, 19.0]	10.0 [4.0, 19.0]	10.0 [4.0, 19.0]	0.642
Dead (%)	No	482 (4.2)	344 (4.3)	138 (4.0)	0.540
	Yes	11,016 (95.8)	7706 (95.7)	3310 (96.0)	
Race (%)	Black	582 (5.1)	399 (5.0)	183 (5.3)	0.403
	Other	10,304 (89.6)	7210 (89.6)	3094 (89.7)	
	White	612 (5.3)	441 (5.5)	171 (5.0)	
Age (median [IQR])	(year)	63.0 [54.0, 72.0]	63.0 [54.0, 72.0]	64.0 [55.0, 72.0]	0.076
Marital status (%)	Divorced/Widowed/Separated	2005 (17.4)	1397 (17.4)	608 (17.6)	0.511
	Married	7801 (67.8)	5486 (68.1)	2315 (67.1)	
	Unmarried	1692 (14.7)	1167 (14.5)	525 (15.2)	
Income (%)	< $35,000	172 (1.5)	117 (1.5)	55 (1.6)	0.995
	$35,000–$39,999	297 (2.6)	209 (2.6)	88 (2.6)	
	$40,000–$44,999	480 (4.2)	338 (4.2)	142 (4.1)	
	$45,000–$49,999	704 (6.1)	488 (6.1)	216 (6.3)	
	$50,000–$54,999	1010 (8.8)	699 (8.7)	311 (9.0)	
	$55,000–$59,999	910 (7.9)	641 (8.0)	269 (7.8)	
	$60,000–$64,999	2016 (17.5)	1422 (17.7)	594 (17.2)	
	$65,000–$69,999	1590 (13.8)	1102 (13.7)	488 (14.2)	
	$70,000–$74,999	897 (7.8)	632 (7.9)	265 (7.7)	
	$75,000 +	3422 (29.8)	2402 (29.8)	1020 (29.6)	
Origin (%)	Non-Spanish	10292 (89.5)	7243 (90.0)	3049 (88.4)	0.014
	Spanish	1206 (10.5)	807 (10.0)	399 (11.6)	
First malignant primary indicator (%)	No	1650 (14.4)	1139 (14.1)	511 (14.8)	0.362
	Yes	9848 (85.6)	6911 (85.9)	2937 (85.2)	
Total number of in situ/malignant tumors for patient (%)	1	9590 (83.4)	6730 (83.6)	2860 (82.9)	0.402
	> 1	1908 (16.6)	1320 (16.4)	588 (17.1)	

Table 2 Multivariate analysis of overall survival (OS) AND cancer-specific survival (CSS) rates in the training cohort

Characteristic	Category	OS		CSS	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age		1.0320 (1.0299–1.0340)	< 0.001	1.0289 (1.0268–1.0310)	< 0.001
Tumor size		1.0013 (1.0008–1.0019)	< 0.001	1.0014 (1.0008–1.0019)	< 0.001
Sex (Female)		0.8883 (0.8474–0.9311)	< 0.001	1.0753 (1.0247–1.1285)	0.003
Primary Site					
	C71.0-Cerebrum	Reference		Reference	
	C71.1-Frontal lobe	0.7467 (0.6566–0.8491)	< 0.001	0.7463 (0.6541–0.8515)	< 0.001
	C71.2-Temporal lobe	0.6675 (0.5855–0.7610)	< 0.001	0.6546 (0.5722–0.7489)	< 0.001
	C71.3-Parietal lobe	0.7499 (0.6560–0.8571)	< 0.001	0.7155 (0.6235–0.8210)	< 0.001
	C71.4-Occipital lobe	0.6948 (0.5890–0.8195)	< 0.001	0.6628 (0.5606–0.7836)	< 0.001
	C71.5-Ventricle, NOS	0.7063 (0.4584–1.0884)	0.115	0.8840 (0.6080–1.2854)	0.519
	C71.6-Cerebellum, NOS	0.6199 (0.4668–0.8231)	< 0.001	0.6778 (0.5094–0.9018)	0.008
	C71.7-Brain stem	1.3024 (0.9621–1.7631)	0.087	0.8538 (0.6292–1.1586)	0.310
	C71.8-Overlapping lesion of brain	0.7665 (0.6650–0.8835)	< 0.001	0.8263 (0.7205–0.9475)	0.006
	C71.9-Brain, NOS	0.8605 (0.7285–1.0165)	0.077	0.9600 (0.8187–1.1257	0.616
Laterality					
	Bilateral	Reference		Reference	
	Left	0.9523 (0.9074–0.9994)	0.047	0.9447 (0.8990–0.9927)	0.024
	Notpaired	1.1546 (1.0438–1.2773)	0.005	1.1326 (1.0218–1.2555)	0.018
	Right	1.2762 (1.0613–1.5347)	0.010	1.2745 (1.0541–1.5410)	0.012
Surgery					
	No	Reference		Reference	
	Local tumor destruction	1.0699 (0.5302–2.1593)	0.85	0.4656 (0.1499–1.4466)	0.186
	subtotal resection of tumor	0.7561 (0.6719–0.8508)	< 0.001	0.6507 (0.6059–0.6989)	< 0.001
	radical resection of tumor	0.5719 (0.5084–0.6433)	< 0.001	0.4826 (0.4493–0.5184)	< 0.001
	partial resection of lobe of brain	0.7826 (0.6939–0.8827)	< 0.001	0.6613 (0.6107–0.7159)	< 0.001
	Radiation (Yes)	0.5941 (0.5495–0.6423)	< 0.001	0.5876 (0.5447–0.6339)	< 0.001
	Chemotherapy (Yes)	0.5991 (0.5386–0.6664)	< 0.001	0.5329 (0.4984–0.5698)	< 0.001
	Systemic therapy (Yes)	0.8653 (0.7652–0.9784)	0.021		
Marital status					
	married	Reference		Reference	
	Unmarried	1.1443 (1.0686–1.2253)	< 0.001	1.2002 (1.1264–1.2789)	< 0.001
	Divorced/Widowed/Separated	1.2229 (1.1489–1.3017)	< 0.001	1.1133 (0.9508–1.2183)	0.088
Income					
	< $35,000	Reference		Reference	
	$35,000–$39,999	1.0469 (0.8312–1.3187)	0.697	1.0473 (0.8260–1.3280)	0.703

Table 2 (continued)

Characteristic	Category		OS		CSS
	$40,000–$44,999	1.0271 (0.8292–1.2723)	0.806	1.0158 (0.8148–1.2664)	0.889
	$45,000–$49,999	0.9285 (0.7558–1.1407)	0.480	0.9142 (0.7396–1.1299)	0.406
	$50,000–$54,999	0.8903 (0.7289–1.0875)	0.255	0.9057 (0.7376–1.1121)	0.344
	$55,000–$59,999	0.8945 (0.7314–1.0939)	0.278	0.9155 (0.7447–1.1256)	0.402
	$60,000–$64,999	0.7765 (0.6406–0.9414)	0.010	0.7784 (0.6387–0.9486)	0.013
	$65,000–$69,999	0.8842 (0.7279–1.0742)	0.215	0.8996 (0.7366–1.0985)	0.299
	$70,000–$74,999	0.8888 (0.7267–1.0871)	0.251	0.8924 (0.7256–1.0976)	0.281
	$75,000+	0.8027 (0.6641–0.9701)	0.023	0.8223 (0.6769–0.9988)	0.049
First malignant primary indicator (No)		0.6391 (0.5423–0.7531)	<0.001	0.5894 (0.4937–0.7037)	<0.001
Total number of in situ/malignant tumors for patient (>1)		0.6469 (0.5539–0.7554)	<0.001	0.5863 (0.4957–0.6936)	<0.001
Months from diagnosis to treatment (>1)				0.9363 (0.9085–0.9651)	<0.001

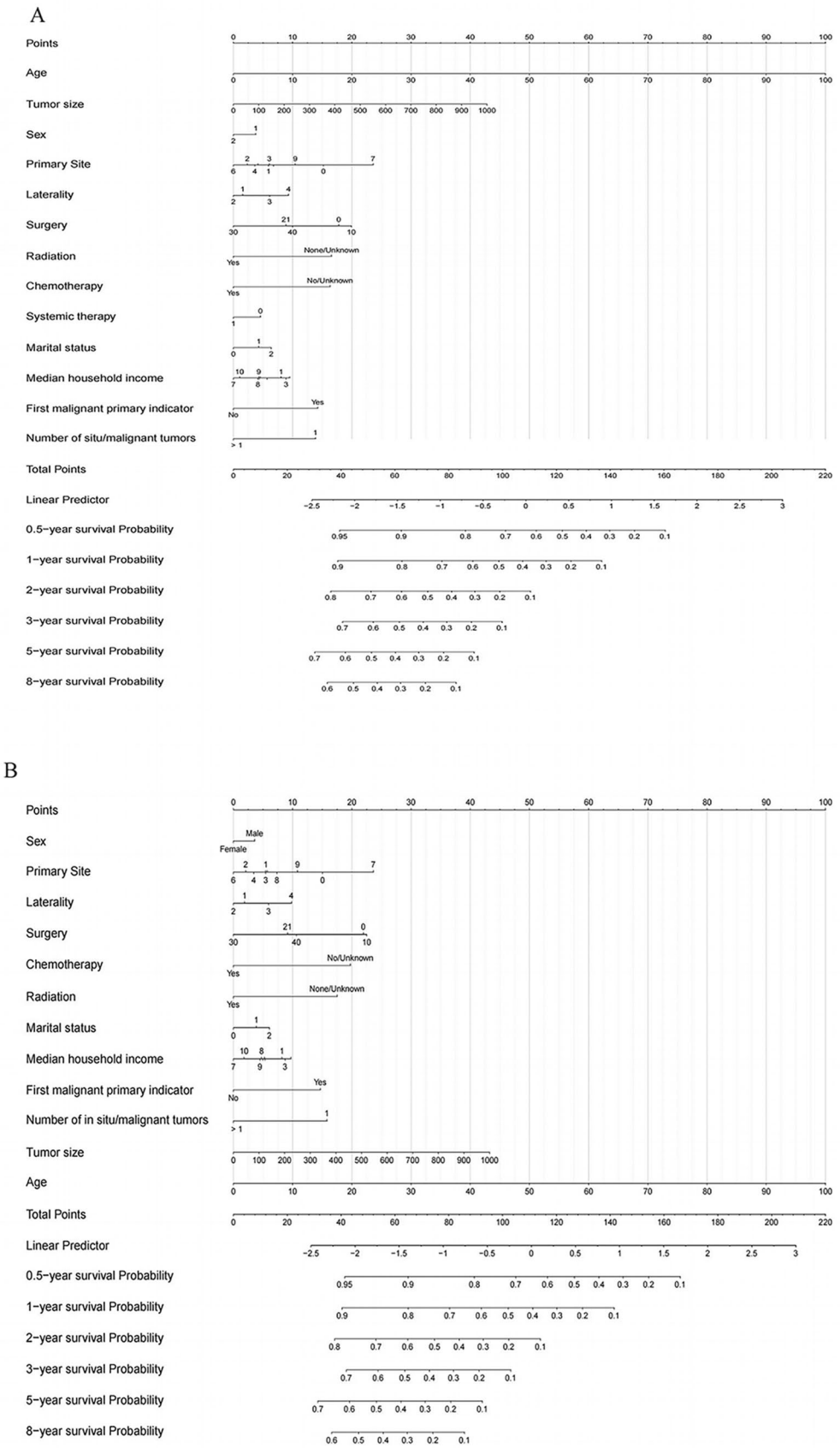

Fig. 3 Establishment of overall survival (OS) and cancer-specific survival (CSS) nomograms. **A** Construction of OS nomogram; **B** construction of CSS nomogram

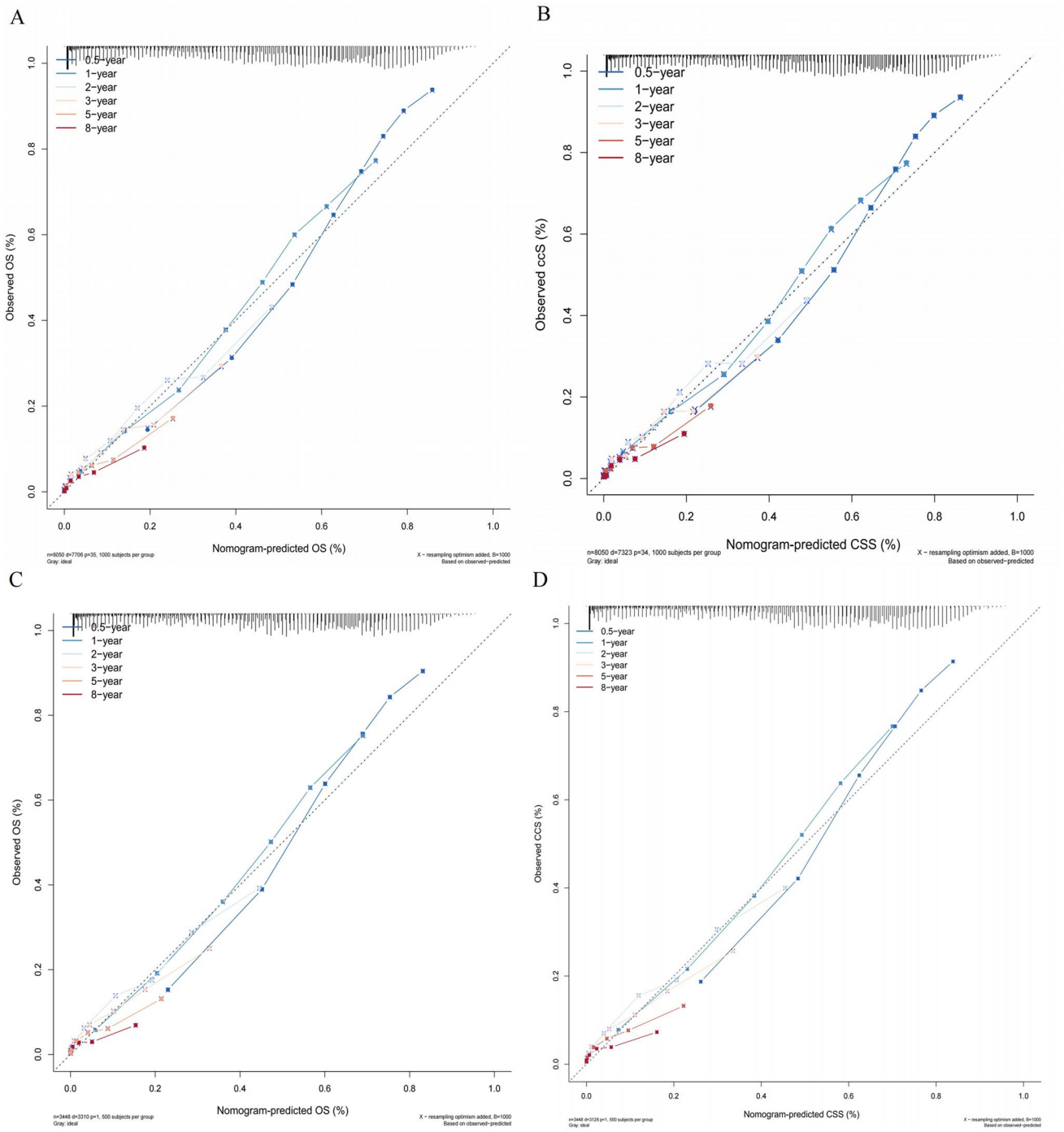

Fig. 4 Calibration plot of the nomogram for predicting 0.5-,1-, 2-, 3-, 5- and 8-year overall survival (OS) and cancer-specific survival (CSS) in training cohort and validation cohort, respectively. **A** 0.5-,1-, 2-, 3-, 5- and 8-year OS in training cohort; **B** 0.5-,1-, 2-, 3-, 5- and 8-year CSS in training cohort; **C** 0.5-,1-, 2-, 3-, 5- and 8-year OS in validation cohort; **D** 0.5-,1-, 2-, 3-, 5- and 8-year CSS in validation cohort

risk of adverse clinical events increased rapidly with tumor size. However, when tumor size > 49 mm, the risk of all-cause mortality continued to rise but at a slower rate.

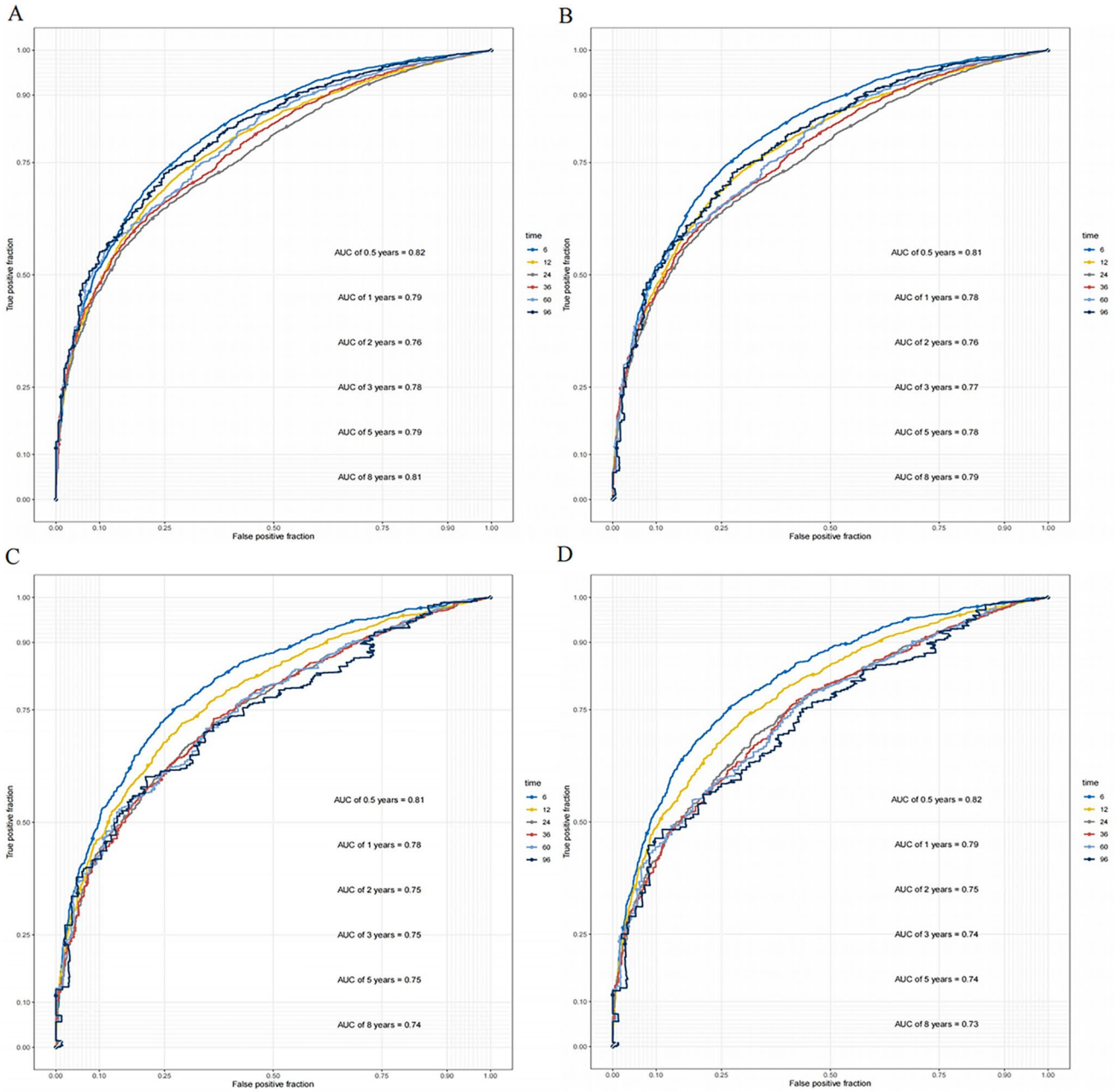

Fig. 5 Receiver operating characteristics curve (ROC) comparison of overall survival (OS) and cancer-specific survival (CSS) nomogram in training cohort and validation cohort, respectively. **A** 0.5-,1-, 2-, 3-, 5- and 8-year ROC of OS nomogram using training cohort; **B** 0.5-,1-, 2-, 3-, 5- and 8-year ROC of CSS nomogram using training cohort; **C** 0.5-,1-, 2-, 3-, 5- and 8-year ROC of OS nomogram using validation cohort; **D** 0.5-,1-, 2-, 3-, 5- and 8-year ROC of CSS nomogram using validation cohort

4 Discussion

GBM is a highly malignant tumor with a poor prognosis. Using the latest data from the SEER database, we found that the incidence of GBM has been increasing since 1978, with a rapid rise before 1992, followed by a slower but continuous increase, particularly among individuals aged 65–74 and 75–84 years. Early diagnosis of GBM remains challenging, and most patients already have a poor prognosis at the time of detection [26]. Additionally, the blood–brain barrier limits the efficacy of chemotherapy and targeted therapies, making treatment outcomes unsatisfactory [27]. Given these challenges, there is a pressing need to enhance GBM awareness, implement preventive strategies, accurately

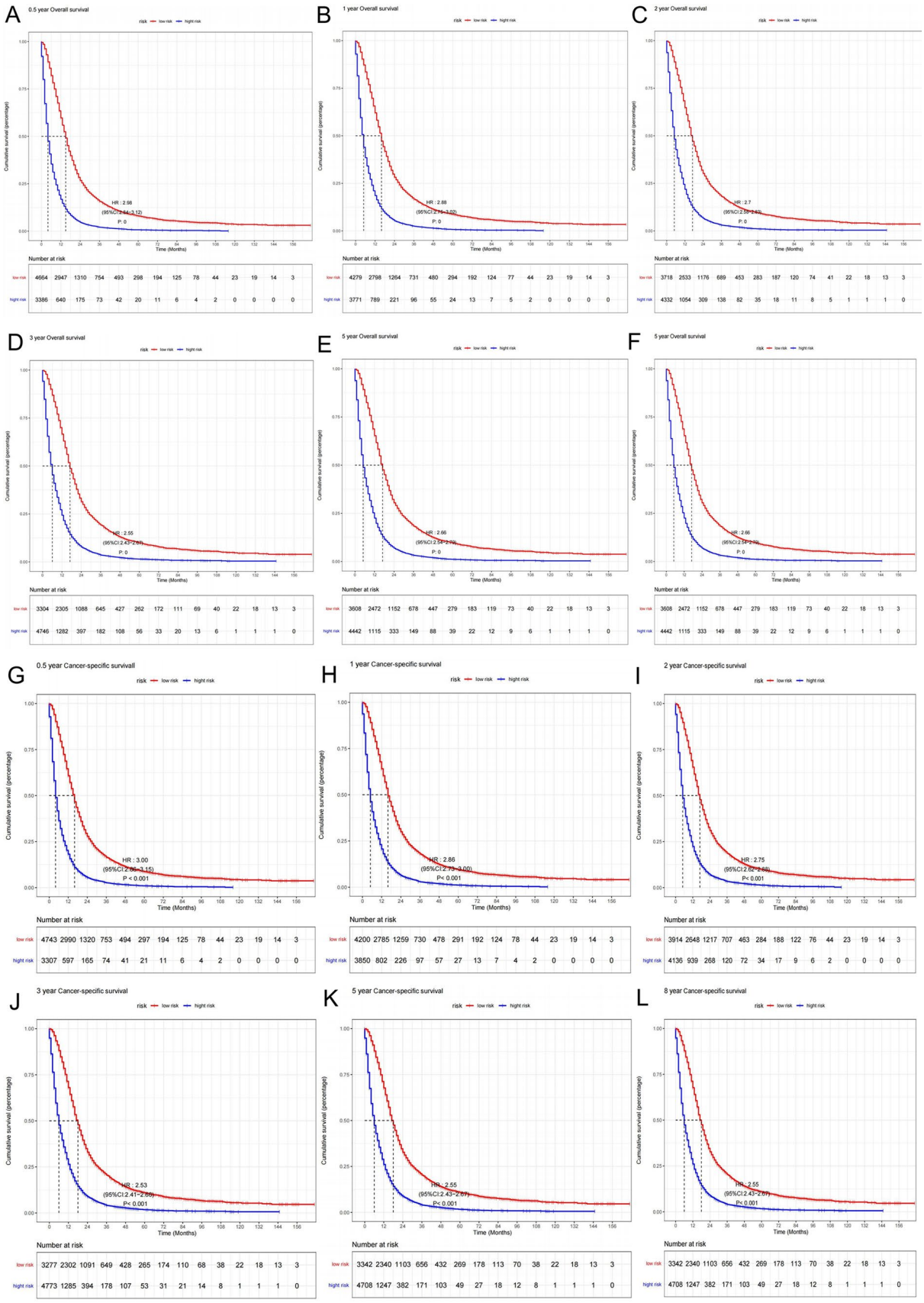

Fig. 6 Kaplan–Meier survival curves for glioblastoma patients. **A–F** 0.5-**A**,1-**b**, 2-**C**, 3-**D**, 5-**E** and 8-**F** year overall survival (OS) in training cohort; **G–L** 0.5-**G**,1-**H**, 2-**I**, 3-**J**, 5-**K** and 8-**L** year cancer-specific survival (CSS) in training cohort

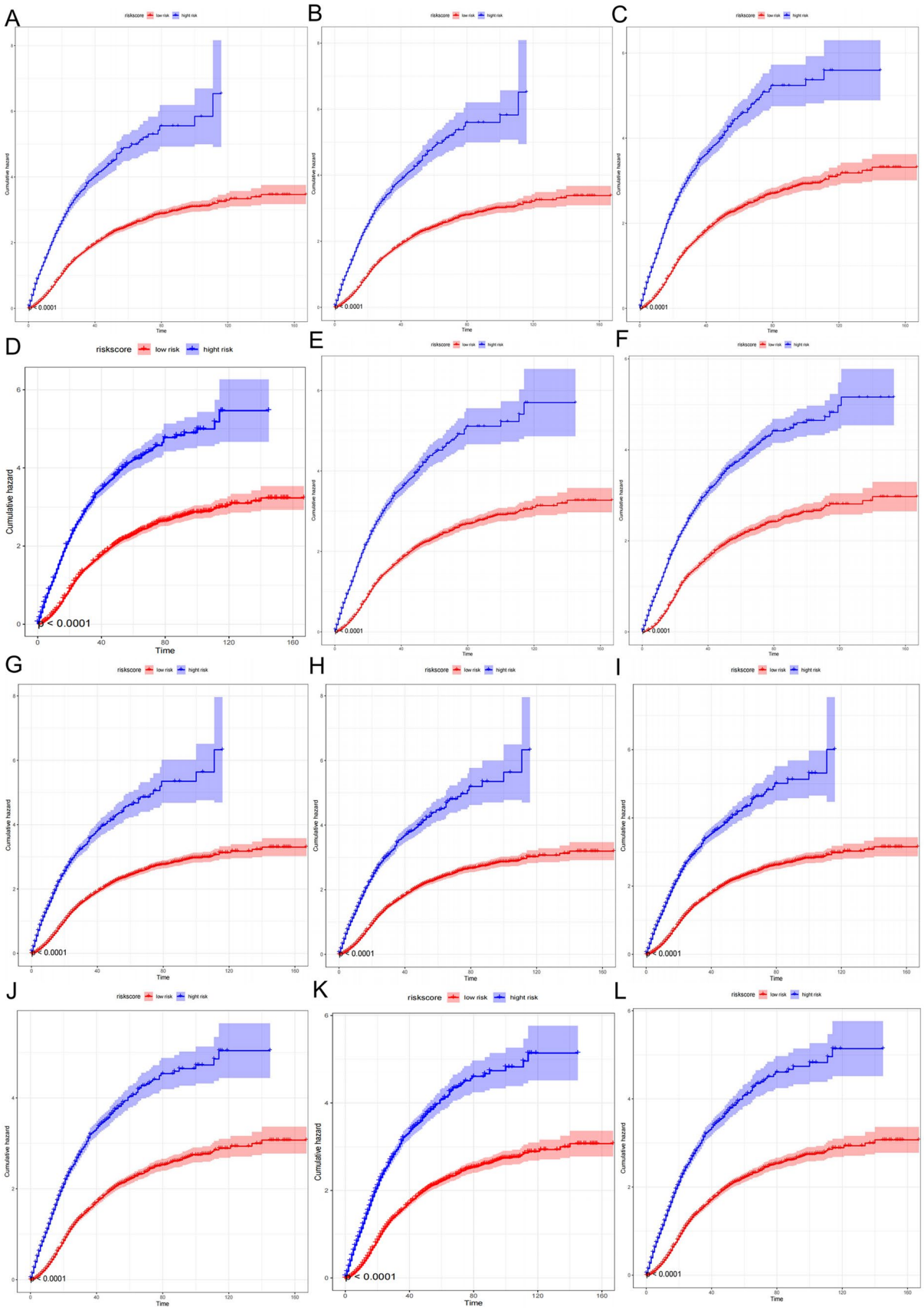

Fig. 7 Cumulative risk curves for glioblastoma patients. **A–F** 0.5-**A**,1-**B**, 2-**C**, 3-**D**, 5-**E** and 8-**F** year overall survival (OS) in training cohort; **G–L** 0.5-**G**,1-**H**, 2-**I**, 3-**J**, 5-**K** and 8-**L** year cancer-specific survival (CSS) in training cohort

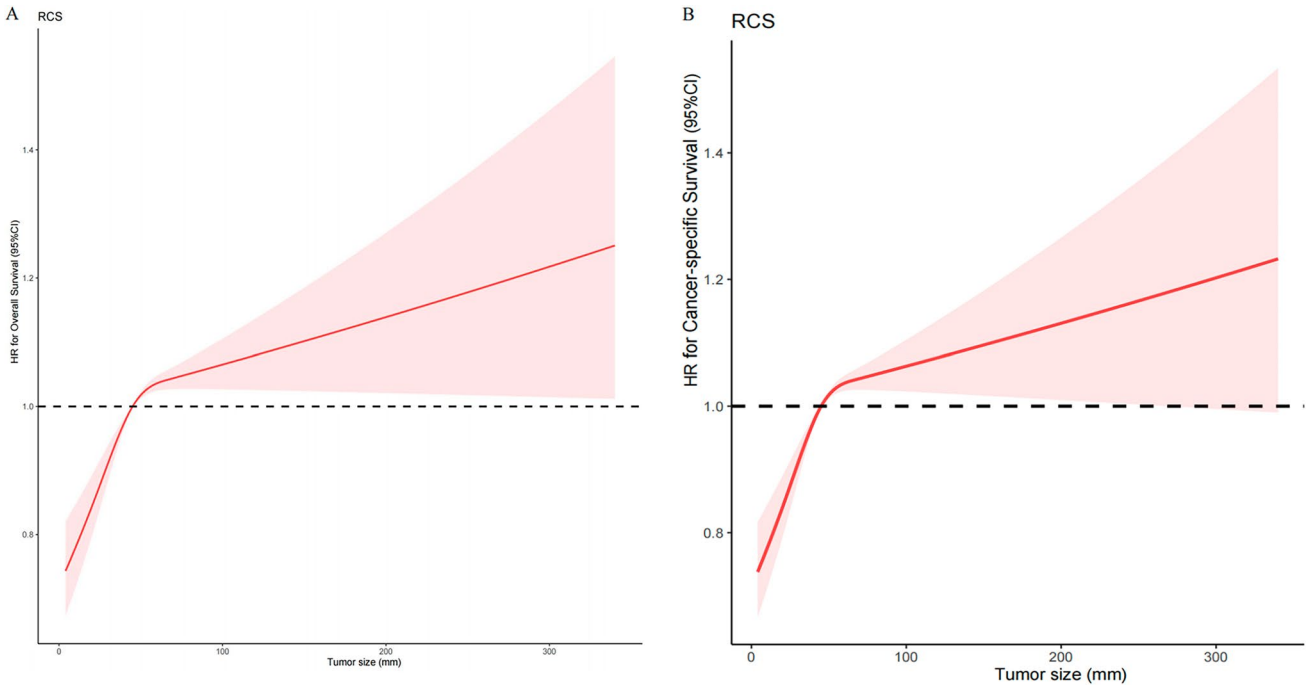

Fig. 8 Adjusted cubic spline models showing association between tumor size and hazard ratio for overall survival (**A**) and cancer-specific survival (**B**). The solid line and red zone represent the estimated odds ratio and its 95% confidence interval

predict patient prognosis, and develop individualized treatment plans to improve disease management. Nomograms serve as valuable statistical tools for prognostic assessment by integrating multiple risk factors, assigning weighted scores to each variable, and visualizing individualized survival probabilities, thereby aiding clinicians in decision-making [28, 29]. Previously, numerous studies have developed nomograms to predict survival in various cancers, including intrahepatic cholangiocarcinoma [30], invasive lung adenocarcinoma [31], colorectal cancer [32], and hepatocellular carcinoma with lung metastasis [33]. The SEER database, which collects high-quality data on approximately 450,000 cancer cases annually, provides a robust foundation for oncological research. In this study, leveraging the SEER database, we comprehensively analyzed the demographic and clinical characteristics of GBM, identified key prognostic factors, and developed a validated predictive model for individualized survival estimation.

By analyzing GBM data from the SEER database, our study found that male sex, lower median household income, brainstem involvement, and multiple tumor locations were associated with worse prognosis. In contrast, being married, undergoing chemotherapy, radiotherapy, and particularly tumor excision, were protective factors for GBM. The number and location of tumors significantly influence surgical feasibility and treatment decisions. For instance, tumors located in the brainstem are often challenging to resect due to their critical anatomical position, contributing to poorer prognosis. Our findings also indicate that the risk of death increases with age, aligning with previous research [34]. Statistically, older patients exhibit higher hazard ratios (HRs) and worse survival outcomes, with the mortality risk for GBM patients over 65 years old being approximately seven times higher than that of patients under 65 [35]. This may be attributed to age-related factors such as increased susceptibility to comorbidities and weakened immune function, which may accelerate tumor progression [36]. Moreover, tumor laterality emerged as a significant factor. Our study found that patients with right-sided tumors had significantly worse OS and CSS compared to those with left-sided tumors. Given the brain's functional compartmentalization, clinicians may prioritize functional preservation during treatment planning, potentially impacting surgical and therapeutic choices. The prognostic impact of GBM laterality has also been reported in prior studies [37]. While some studies indicate longer progression-free survival (PFS) in patients with right-hemisphere tumors, no significant difference in OS has been observed between left- and right-sided GBM [38]. Furthermore, our analysis revealed a nonlinear relationship between tumor size and prognosis in GBM patients. Using RCS analysis, we identified three optimal knots. The results demonstrated that for tumors ≤ 49 mm, the risk of adverse outcomes increased rapidly with tumor size. However, for tumors > 49 mm, the risk continued to rise but at a slower rate, suggesting a potential threshold effect. Survival analysis further confirmed a significant difference in OS and CSS between tumors ≤ 49 mm and those > 49 mm. We speculate that in larger tumors, extensive central hypoxia and necrosis may limit further malignant progression,

potentially explaining the attenuated risk increase. These findings emphasize the importance of considering nonlinear effects when evaluating tumor size as a prognostic factor in GBM. Currently, maximal tumor resection, when feasible, remains the cornerstone of GBM treatment, followed by adjuvant radiotherapy and chemotherapy [39]. In our study, all these treatment modalities contributed to prolonged OS and CSS. Radiotherapy has been widely validated as a feasible treatment for GBM [40]. Temozolomide remains the first-line chemotherapy for malignant gliomas [41]. Since Stupp et al. introduced the combination of radiotherapy and adjuvant temozolomide in 2005, the prognosis of GBM patients has significantly improved [42]. Additionally, based on a cohort of 562 elderly patients with GBM, Perry et al. demonstrated that short-term radiotherapy plus temozolomide resulted in longer survival than short-term radiotherapy alone [43].

Based on our findings, we recommend that eligible GBM patients undergo maximal tumor resection, followed by adjuvant radiotherapy and chemotherapy to improve survival outcomes. Additionally, greater attention should be given to elderly patients, as they face a significantly higher risk of mortality. The relationship between tumor size and prognosis requires further investigation to better understand its clinical implications. Given the poor survival outcomes associated with GBM, continued research into effective therapeutic interventions remains a critical priority.

Our study has several limitations. First, as the SEER database is based on retrospective data, our findings only establish correlations rather than causal relationships, which require further validation through prospective studies. Additionally, while certain GBM tumor markers have been identified as prognostic indicators, our dataset lacks genetic information and detailed comorbidity data. A more comprehensive evaluation of individual patient prognosis would require integrating genetic profiles with clinical characteristics. Furthermore, the chemoradiotherapy data in SEER are incomplete—key details such as radiotherapy timing, dosage, and intervals, as well as chemotherapy drug types, dosages, and treatment courses, are unavailable. These factors are critical for predicting patient outcomes, and their absence may limit the accuracy of our prognostic model. Finally, although our model has been internally validated using SEER data, its generalizability requires further validation in external datasets to ensure its applicability across diverse populations.

5 Conclusion

By analyzing the SEER database, we found that GBM incidence has been rising since 1975, particularly in the 65–74 and 75–84 age groups. We developed and validated a nomogram to predict 0.5-, 1-, 2-, 3-, 5-, and 8-year OS and CSS, providing an objective prognostic tool for GBM patients. Additionally, our analysis revealed a nonlinear relationship between tumor size and prognosis, with mortality risk increasing sharply for tumors ≤ 49 mm. These findings underscore the need for early detection and individualized treatment strategies to improve GBM outcomes. Future studies incorporating genetic and molecular data will further refine risk assessment and management.

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Author contributions SY, YT and YMM drafted the manuscript. SY, YMM, JCL and YT performed data analysis. YMM, JHZ, TX, and SY checked the statistical accuracy. SY, YMM, JHL, JQZ and YT performed the literature search and wrote the first draft of the manuscript. SY, YT and YMM revised and edited the final version of the manuscript. All authors read and approved the final manuscript.

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Data availability The data that support the findings of this study are available from SEER database. Data are however available from the authors upon reasonable request and with permission of SEER database. Ethics approval and consent to participate Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors.

Declarations

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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