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Prognostic factors and nomogram prediction of survival probability in primary spinal cord astrocytoma patients

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OBJECTIVE Knowledge on the management of spinal cord astrocytoma (SCA) remains scarce. Here, the authors constructed and validated a predictive nomogram, often used for individualized prognosis and evaluations, to estimate cancer-specific survival (CSS) and overall survival (OS) for patients with SCA.

METHODS Epidemiological characteristics were compared between low-grade SCA (LGSCA) and high-grade SCA (HGSCA) patients from the Surveillance, Epidemiology, and End Results (SEER) database. Risk factors for CSS and OS were determined using univariate and multivariate analyses and Kaplan-Meier curves. A nomogram was developed to individually predict the 3-, 5-, and 10-year CSS and OS rates. The clinical usefulness of the nomogram was assessed using calibration plots, the concordance index (C-index), and time-dependent receiver operating characteristic curves.

RESULTS A total of 468 LGSCA and 165 HGSCA patients were eligible for inclusion. LGSCA and HGSCA patients demonstrated differences in age, tumor extension, insurance status, adjuvant treatment, and survival. Multivariate analysis demonstrated that in the LGSCA group, tumor extension, surgery type, and adjuvant therapy were individually associated with CSS. The distance of tumor extension and WHO grade were individually associated with CSS in the HGSCA group. The prognostic variables were further demonstrated using the Kaplan-Meier method, which also suggested that adjuvant treatment provided no advantage to HGSCA patients. A nomogram was constructed, and the C-index for CSS was 0.84 by internal validation (95% CI 0.79–0.90).

CONCLUSIONS This research suggests that the distance of tumor extension, type of surgery, and adjuvant therapy are significant risk factors for CSS using multivariate analysis in the LGSCA group. Adjuvant treatment provided no advantages for CSS or OS in patients with HGSCAs. The nomogram may be clinically useful to healthcare providers.

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KEYWORDS spinal cord; glioma; astrocytoma; SEER; Surveillance, Epidemiology, and End Results; nomogram; real-world study; oncology

Spinal cord gliomas are a relatively rare type of glioma that account for 4.2% of CNS gliomas, and astrocytoma accounts for 20% of all spinal cord gliomas.[1,2] Some previous studies summarized data analyses of all spinal cord gliomas, which makes it very difficult to distinguish spinal cord astrocytoma (SCA) from other gliomas.

The current knowledge of SCA is ambiguous, and the prognostic factors and optimal management strategies are not clear.[3] There are obvious differences in the biological behaviors and management strategies for primary spinal cord gliomas and brain gliomas.[4,5] Many studies have suggested that the extent of resection (EOR) is associated with worse outcomes in SCA patients,[6–10] but other studies have reported that EOR is associated with better outcomes[4,11–13] in patients with low-grade[12] and high-grade[4,11] astrocytoma. Some studies have suggested that the EOR does not significantly affect outcomes.[4,12,14–16] Findings on the outcome of radiation therapy are inconsistent and have been related to better outcomes,[7,17] no obvious changes in results,[4,6,14,18,19] and worse outcomes[13] across different reports. However, fewer reports have suggested the useful-

ABBREVIATIONS C-index = concordance index; CSS = cancer-specific survival; EOR = extent of resection; GTR = gross-total resection; HGSCA = high-grade SCA; LGSCA = low-grade SCA; OS = overall survival; ROC = receiver operating characteristic; SCA = spinal cord astrocytoma; SEER = Surveillance, Epidemiology, and End Results; STR = subtotal resection.

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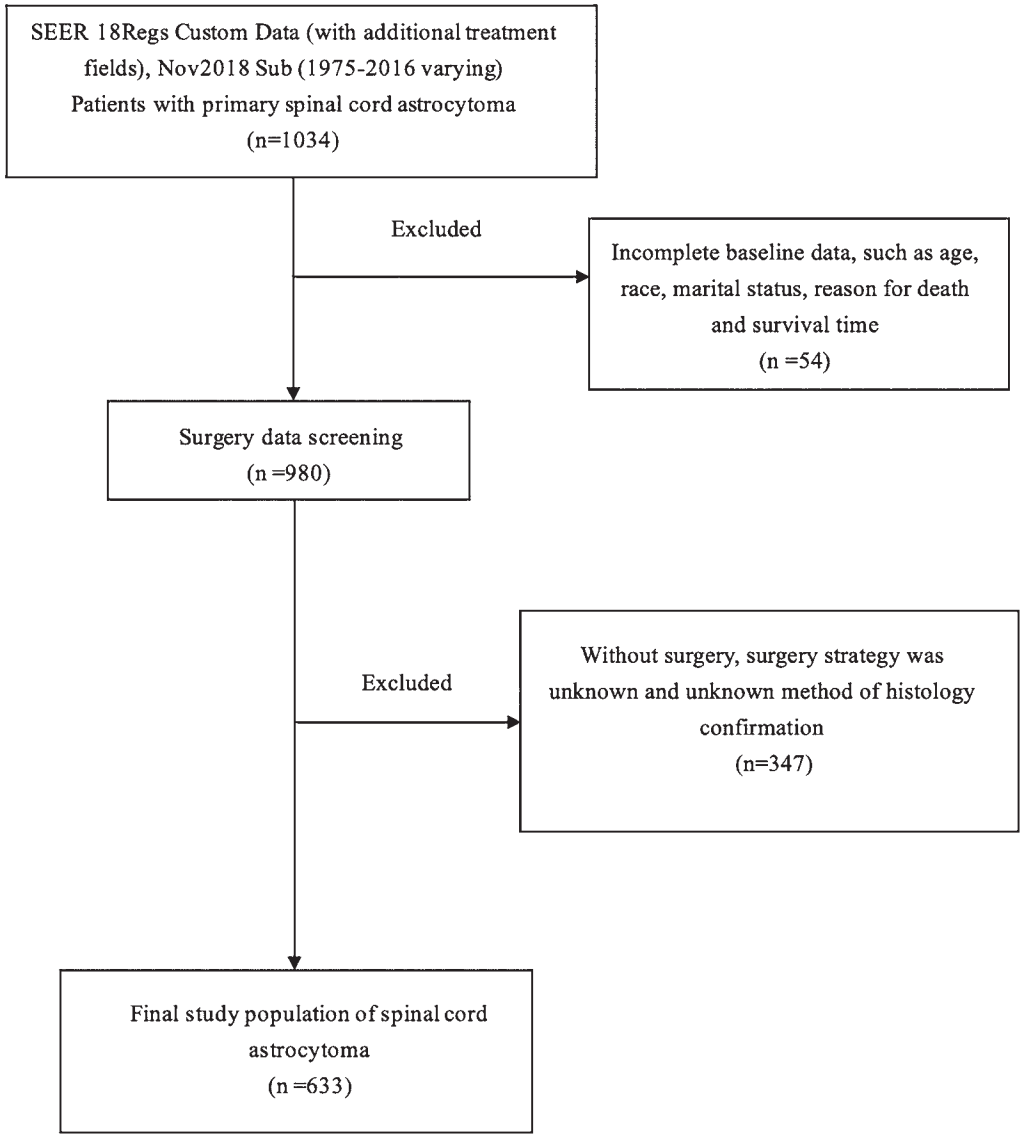

FIG. 1. Flowchart of SCA patient selection.

ness of chemotherapy, with two studies showing no obvious effect on the results.[6,18] The significance of prognostic variables is also inconsistent. However, the WHO grade is consistently associated with outcomes.[7,10,14,20–24] Most of the studies that have focused on the prognostic factors of SCA used small samples or single centers, and treatment plans varied between doctors. Therefore, we summarized the effects of prognostic factors and the associations between the outcomes and treatment strategies for SCA.

Methods

Data Collection and Study Population

The Surveillance, Epidemiology, and End Results (SEER) database provided prospectively collected data. Therefore, the present study did not require approval from the institutional review board.

Data for this study were extracted from the SEER database (1975–2016) using SEER*Stat (version 8.3.8) software. Patients who were diagnosed with a histopathologically confirmed astrocytoma according to the *International Classification of Disease for Oncology 3rd Edition* (ICD-O-3) site record, including low-grade SCA (LGSCA; pilocytic astrocytoma [9421], diffuse astrocytoma [protoplasma, fibrillary; 9420/9410]; astrocytoma, not otherwise specified [9400]; and unique astrocytoma variants [9424]) and high-grade SCA (HGSCA; astrocytoma, anaplastic [9401/9411]; and glioblastoma [9440/9441]) were enrolled in the analysis. Lesions located at the spinal cord (ICD-O-3 code C72.0 for "spinal cord") were included, but lesions located at the cauda equina were not. Only primary intramedullary spinal cord lesions were extracted using the sequence number of one primary only or first of 2 or more primaries, which denote the primary lesion. The detailed screening flowchart is shown in Fig. 1.

The following selected variables were collected: age,

TABLE 1. Demographic characteristics, patient characteristics, and treatment strategies in the cohort

Parameter	Total (n = 633)	LGSCA (n = 468)	HGSCA (n = 165)	p Value
Age group, yrs				**0.004**
≤19	267 (42.2)	213 (45.5)	54 (32.7)	
>19	366 (57.8)	255 (54.5)	111 (67.3)	
Sex				0.66
Male	366 (57.8)	273 (58.3)	93 (56.4)	
Female	267 (42.2)	195 (41.7)	72 (43.6)	
Race				0.715
White	506 (79.9)	373 (79.7)	133 (80.6)	
Black	75 (11.8)	58 (12.4)	17 (10.3)	
Other	52 (8.2)	37 (7.9)	15 (9.1)	
Marital status				0.455
Married	224 (35.4)	159 (34.0)	65 (39.4)	
Single/unmarried	363 (57.3)	274 (58.5)	89 (53.9)	
Divorced/ separated/ widowed	46 (7.3)	35 (7.5)	11 (6.7)	
Insurance status				**0.008**
Insured/insured, NOS	197 (31.1)	140 (29.9)	57 (34.5)	
Medicaid	64 (10.1)	47 (10.0)	17 (10.3)	
Uninsured	4 (0.6)	0 (0)	4 (2.4)	
Unknown	368 (58.1)	281 (60.0)	87 (52.7)	
Tumor size, mm				0.659
<50	159 (25.1)	114 (24.4)	45 (27.3)	
≥50	68 (10.7)	49 (10.5)	19 (11.5)	
Unknown	406 (64.1)	305 (65.2)	101 (61.2)	
Tumor extension				**0.002**
Localized	408 (64.5)	315 (67.3)	93 (56.4)	
Regional	27 (4.3)	13 (2.8)	14 (8.5)	
Distant	23 (3.6)	13 (2.8)	10 (6.1)	
Unstaged	175 (27.6)	127 (27.1)	48 (29.1)	
Metastasis				0.668
No	558 (88.2)	414 (88.5)	144 (87.3)	
Yes	8 (1.3)	5 (1.1)	3 (1.8)	
Unknown	67 (10.6)	49 (10.5)	18 (10.9)	
Type of surgery				0.07
GTR	174 (27.5)	140 (29.9)	34 (20.6)	
STR	334 (52.8)	239 (51.1)	95 (57.6)	
Local excision/ biopsy	125 (19.7)	89 (19.0)	36 (21.8)	
Radiation therapy				**<0.001**
Yes	297 (46.9)	162 (34.6)	135 (81.8)	
No	336 (53.1)	306 (65.4)	30 (18.2)	
Chemotherapy				**<0.001**
Yes	165 (26.1)	67 (14.3)	98 (59.4)	
No	468 (73.9)	401 (85.7)	67 (40.6)	
Year of diagnosis				0.156
1988–1994	101 (16.0)	70 (15.0)	31 (18.8)	
1995–2001	124 (19.6)	95 (20.3)	29 (17.6)	
2002–2008	192 (30.3)	151 (32.3)	41 (24.8)	
2009–2016	216 (34.1)	152 (32.5)	64 (38.8)	
Vital status				**<0.001**
Alive	386 (61.0)	352 (75.2)	34 (20.6)	
Dead	247 (39.0)	116 (24.8)	131 (79.4)	
Cancer-specific death status				**<0.001**
Alive	430 (67.9)	387 (82.7)	43 (26.1)	
Dead	203 (32.1)	81 (17.3)	122 (73.9)	

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TABLE 1. Demographic characteristics, patient characteristics, and treatment strategies in the cohort

NOS = not otherwise specified.
Boldface type indicates statistical significance.

sex, race, marital status, insurance status, WHO grade, surgery type, tumor size, metastasis, tumor extension, radiotherapy and chemotherapy, and year of diagnosis. The cancer-specific survival (CSS) and overall survival (OS) rates were the studied indexes compared between LGSCA and HGSCA in this research.

Statistical Analysis

The baseline data of the two groups of patients were summarized using descriptive statistics and compared using the Student t-test, the Mann-Whitney U-test, the chi-square test, or Fisher's exact test. Statistical analysis was performed using IBM SPSS (version 25.0, IBM Corp.).

Univariate and multivariate Cox regression models were used to identify different prognostic factors in each group. The Kaplan-Meier method and log-rank test were used for survival analyses between the groups by related prognostic factors. A nomogram was constructed from the indexes identified by multivariate analysis using the RMS package in R version 4.0.2. The nomogram was verified in the primary and validation groups and assessed using the concordance index (C-index), calibration plots, and receiver operating characteristic (ROC) curves; $p < 0.05$ was considered statistically significant.

Results

Patient Population and Baseline Characteristics

A total of 468 LGSCA and 165 HGSCA patients met inclusion criteria. Among the patients in the LGSCA group, 213 were children and 255 were adults. The data suggested that LGSCA had a pediatric preponderance (45.5%), which was statistically significant ($p = 0.004$). The sex difference was not statistically significant ($p = 0.660$). Most patients were White (n = 373, 79.7%), 58 (12.4%) were Black, and 37 (7.9%) were Asian/Pacific Islander in the LGSCA group. Most patients were single or unmarried (n = 274, 58.5%),

TABLE 2. Univariate and multivariate analyses to determine prognostic variables of CSS for patients with LGSCA and HGSCA

	LGSCA				HGSCA			
	Univariable		Multivariable		Univariable		Multivariable	
Variable	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Age, yrs								
≤19	Ref		Ref		Ref			
>19	3.607 (2.134–6.097)	**<0.001**	1.889 (0.878–4.061)	0.103	0.778 (0.534–1.133)	0.191		
Sex								
Male	Ref				Ref			
Female	0.991 (0.637–1.542)	0.97			1.326 (0.928–1.895)	0.121		
Race								
White	Ref				Ref			
Black	1.553 (0.867–2.782)	0.139			1.127 (0.641–1.979)	0.678		
Other/unknown	1.409 (0.673–2.950)	0.363			1.705 (0.948–3.067)	0.074		
Marital status								
Married	Ref		Ref		Ref			
Single/ unmarried	0.423 (0.267–0.672)	**<0.001**	0.804 (0.438–1.474)	0.481	1.302 (0.892–1.902)	0.171		
Divorced/ separated/ widowed	1.050 (0.491–2.244)	0.899	1.161 (0.539–2.499)	0.702	0.810 (0.395–1.661)	0.566		
Insurance status								
Insured/insured, NOS	Ref				Ref			
Medicaid	0.956 (0.382–2.396)	0.925			0.915 (0.428–1.955)	0.819		
Uninsured	NA				0.707 (0.170–2.927)	0.633		
Unknown	0.943 (0.551–1.614)	0.832			0.902 (0.611–1.333)	0.606		
Tumor size, mm								
<50	Ref				Ref			
≥50	1.583 (0.647–3.873)	0.314			0.617 (0.313–1.219)	0.165		
Unknown	1.813 (0.975–3.371)	0.06			0.919 (0.614–1.374)	0.68		
Tumor extension								
Localized	Ref		Ref		Ref		Ref	
Regional	1.104 (0.267–4.559)	0.891	0.897 (0.213–3.775)	0.882	0.849 (0.437–1.650)	0.63	0.743 (0.377–1.467)	0.393
Distant	5.001 (2.248–11.122)	**<0.001**	7.118 (2.523–20.081)	**<0.001**	2.431 (1.156–5.111)	**0.019**	2.400 (1.097–5.250)	**0.028**
Unstaged	1.344 (0.827–2.183)	0.232	1.654 (0.932–2.935)	0.085	0.680 (0.444–1.041)	0.075	0.916 (0.436–1.925)	0.817
Metastasis								
No	Ref		Ref		Ref			
Yes	3.878 (1.220–12.32)	**0.021**	1.478 (0.332–6.582)	0.607	1.030 (0.253–4.186)	0.967		
Unknown	1.300 (0.597–2.83)	0.508	0.648 (0.266–1.578)	0.340	0.925 (0.451–1.898)	0.833		
WHO grade								
I	Ref		Ref					
II	3.498 (2.048–5.974)	**<0.001**	2.152 (1.215–3.813)	**0.008**				
III	NA		NA		Ref		Ref	
IV	NA		NA		1.904 (1.325–2.737)	**<0.001**	1.712 (1.150–2.548)	**0.007**
Type of surgery								
GTR	Ref		Ref		Ref			
STR	2.331 (1.238–4.387)	**0.008**	1.743 (0.893–3.403)	0.103	1.234 (0.792–1.920)	0.352		
Local excision/ biopsy	4.995 (2.594–9.616)	**<0.001**	3.863 (1.913–7.798)	**<0.001**	1.367 (0.804–2.323)	0.248		

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TABLE 2. Univariate and multivariate analyses to determine prognostic variables of CSS for patients with LGSCA and HGSCA

	LGSCA				HGSCA			
	Univariable		Multivariable		Univariable		Multivariable	
Variable	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Radiation therapy								
Yes	Ref		Ref		Ref			
No	0.179 (0.111–0.290)	**<0.001**	0.331 (0.191–0.573)	**<0.001**	1.112 (0.686–1.802)	0.665		
Chemotherapy								
Yes	Ref		Ref		Ref			
No	0.422 (0.254–0.702)	**<0.001**	0.529 (0.306–0.917)	**0.02**	1.067 (0.741–1.536)	0.728		
Year of diagnosis								
1988–1994	Ref				Ref		Ref	
1995–2001	0.826 (0.427–1.600)	0.573			1.872 (1.042–3.360)	**0.035**	1.428 (0.688–2.963)	0.338
2002–2008	0.745 (0.396–1.404)	0.364			2.079 (1.203–3.590)	**0.008**	1.628 (0.642–4.126)	0.303
2009–2016	0.974 (0.495–1.915)	0.94			1.582 (0.912–2.744)	0.102	1.077 (0.430–2.695)	0.873

NA = not applicable.
Boldface type indicates statistical significance.

159 (34.0%) were married, and 35 (7.5%) were divorced/separated/widowed in the LGSCA group. However, there may be a clear bias because most children are unmarried. The data suggested that patients in the HGSCA group had some insurance or were insured/not otherwise specified preponderance (34.5%), which was statistically significant ($p = 0.008$). Most patients were diagnosed during 2002–2008 in the LGSCA group compared with 2009–2016 in the HGSCA group (n = 151 [32.3%] vs n = 41 [24.8%], $p = 0.156$). Metastasis occurred in 5 patients (1.0%) in the LGSCA group, which not statistically significant compared with that of the HGSCA group ($p = 0.668$). However, obvious bias may exist because of its sequence number. There was no significant difference in tumor size between the LGSCA and HGSCA groups ($p = 0.659$).

There was an obvious significant difference in tumor extension between the two subgroups ($p = 0.002$). The proportion of patients with distant tumor extension in the HGSCA group was higher than that in the LGSCA group (6.1% vs 2.8%). However, the number of regions or distances was limited. For treatment strategy, the EOR was significantly different between the two groups ($p = 0.002$). Most HGSCA patients received radiation therapy (81.8 vs 34.6%, $p < 0.001$), and fewer HGSCA patients received chemotherapy (59.4 vs 14.3%, $p < 0.001$) (Table 1).

Prognostic Variables of CSS and OS

Univariate analysis suggested that adult patients (HR 3.607, 95% CI 2.134–6.097; $p < 0.001$), distant tumor extension (HR 5.001, 95% CI 2.248–11.122; $p < 0.001$), grade II tumor (HR 3.498, 95% CI 2.048–5.974; $p < 0.001$), and subtotal resection (STR) or biopsy (HR 2.331, 95% CI 1.238–4.387; $p = 0.008$; and HR 4.995, 95% CI 2.594–9.616; $p < 0.001$, respectively) correlated with a decreased CSS rate in the LGSCA group (Table 2). In contrast, a single/unmarried status (HR 0.423, 95% CI 0.267–0.672; $p < 0.001$), no radiation therapy (HR 0.179, 95% CI 0.111–0.290; $p < 0.001$), and no chemotherapy (HR 0.422, 95% CI 0.254–0.702; $p < 0.001$) were significantly associated with an increased CSS rate. In the HGSCA group, distant tumor extension (HR 2.431, 95% CI 1.156–5.111; $p = 0.019$), grade IV disease (HR 1.904, 95% CI 1.325–2.737; $p < 0.001$), and year of diagnosis were associated with a decreased CSS rate.

Multivariate analysis revealed that tumor extension (HR 7.118, 95% CI 2.523–20.081; $p < 0.001$) and biopsy or local excision (HR 3.863, 95% CI 1.913–7.798; $p < 0.001$) were independently associated with a decreased CSS rate in the LGSCA group. Analysis of the surgery type suggested that STR (HR 1.743, 95% CI 0.893–3.403; $p = 0.103$) was not associated with worse CSS compared with gross-total resection (GTR) after controlling for the confounding effects of other variables (Table 2). In contrast, no radiation therapy (HR 0.331, 95% CI 0.191–0.573; $p < 0.001$) and no chemotherapy (HR 0.529, 95% CI 0.306–0.917; $p = 0.02$) were independently associated with an improved CSS rate. However, the multivariate analysis in the HGSCA group only showed that distant tumor extension and grade (HR 2.400, 95% CI 1.097–5.250; $p = 0.028$; and HR 1.712, 95% CI 1.150–2.548; $p = 0.007$, respectively) were associated with a decreased CSS rate (Table 2). The predictive factors of OS were similar to those of CSS on multivariate analysis, with only slight differences in the HR, 95% CI, and p value (Tables S1 and S2).

The Kaplan-Meier method was also used to compare the CSS of SCA patients by different factors. The results suggested that age group ($p < 0.0001$), marital status ($p = 0.006$), insurance ($p = 0.043$), tumor extension ($p < 0.0001$), chemotherapy ($p < 0.001$), radiation therapy ($p < 0.0001$), WHO grade ($p < 0.0001$), surgery ($p < 0.0001$), and histology ($p < 0.0001$) showed significant differences (Fig. 2). According to the different variables in the subgroup, an additional Kaplan-Meier curve showed that age ($p < 0.0001$), tumor extension ($p < 0.0001$), chemotherapy ($p < 0.0001$), radiation therapy ($p < 0.0001$), and surgery

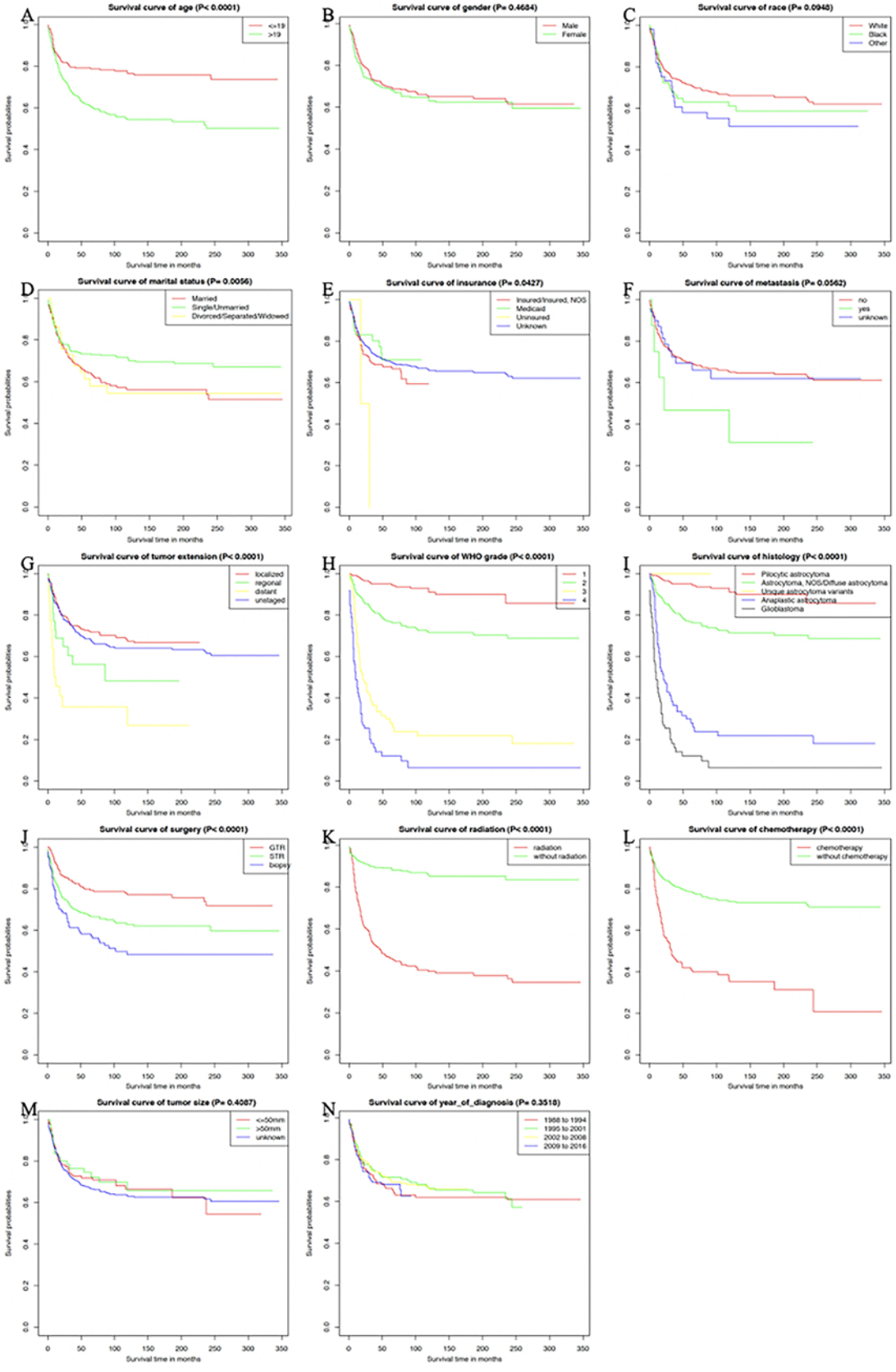

FIG. 2. Kaplan-Meier survival curves for patients with SCA by different factors, including age (**A**), sex (**B**), race (**C**), marital status (**D**), insurance status (**E**), metastasis (**F**), tumor extension (**G**), WHO grade (**H**), histology (**I**), surgery (**J**), radiation therapy (**K**), chemotherapy (**L**), tumor size (**M**), and year of diagnosis (**N**). Figure is available in color online only.

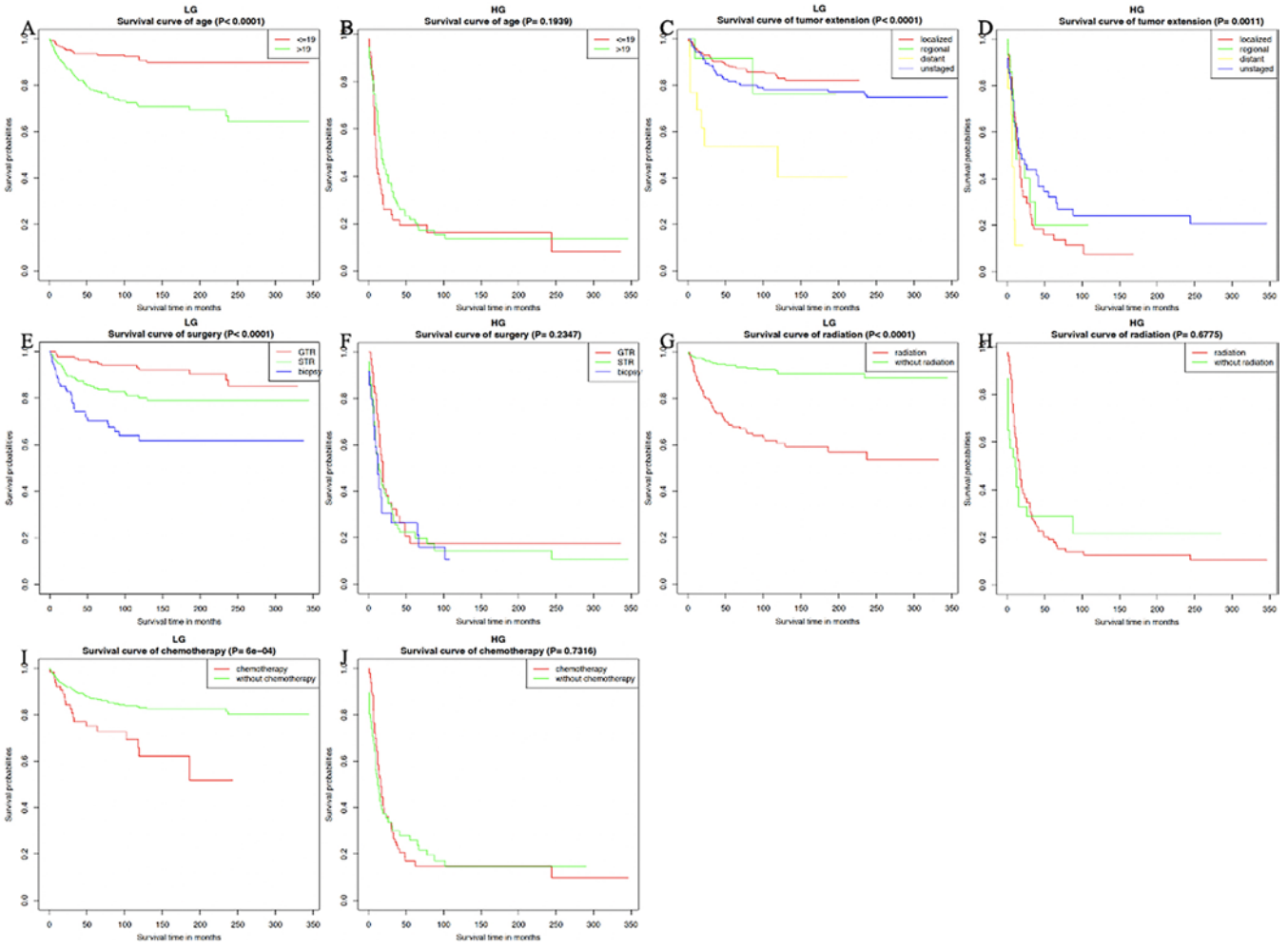

FIG. 3. Kaplan-Meier survival curves for the LGSCA (LG) and HGSCA (HG) subgroups based on different variables, including age (**A and B**), tumor extension (**C and D**), surgery (**E and F**), radiation therapy (**G and H**), and chemotherapy (**I and J**). Figure is available in color online only.

($p < 0.0001$) in the LGSCA group or tumor extension in the HGSCA group ($p = 0.001$) were significantly different (Fig. 3). Additional Kaplan-Meier analyses were used to assess the effectiveness of adjuvant therapy in the GTR and non-GTR groups (Fig. 4). The results suggested that patients who received radiation therapy or chemotherapy had worse survival regardless of the type of surgery performed in the LGSCA group. However, the results also suggested that supplementary adjuvant treatment was not inferior to single surgery, excluding chemotherapy in the GTR group, for HGSCA patients.

Nomogram and Internal Validation

The entire group was randomly separated into a primary cohort (n = 445) and a validation cohort (n = 188) (Table 3). We used the Cox model to obtain statistically significant variables for CSS (Table 3) and OS (Table S3) in the primary group. Tumor extension, surgery, WHO grade, and radiation therapy were entered into the nomogram for CSS (Fig. 5) and OS (Fig. S1). We performed internal validation of the nomograms. The calibration plots for the rates of postoperative CSS (Fig. 5) and OS (Fig. S2) at 3, 5, and 10 years were satisfactory because of good uniformity between the predicted survival rates and the actual survival rates in the primary and validation groups. The corresponding C-indexes for CSS and OS rates were 0.84 (95% CI 0.79–0.90) and 0.82 (95% CI 0.77–0.86), respectively. The areas under the ROC curve values for the CSS (Fig. 5) and OS (Fig. S3) rates at different time points in the training and validation sets were nearly 0.9.

Discussion

We examined the demographics and nationwide treatment results of SCA patients and the risk factors for survival using the large, population-based SEER database. Although SCA patients are rare, this research easily increases our knowledge of the variables associated with survival due to the large study population and sufficient follow-up time. A total of 633 SCA patients satisfied our inclusion criteria and were assessed in detail. Obvious differences were seen between the epidemiological and biological characteristics of LGSCA and HGSCA patients.

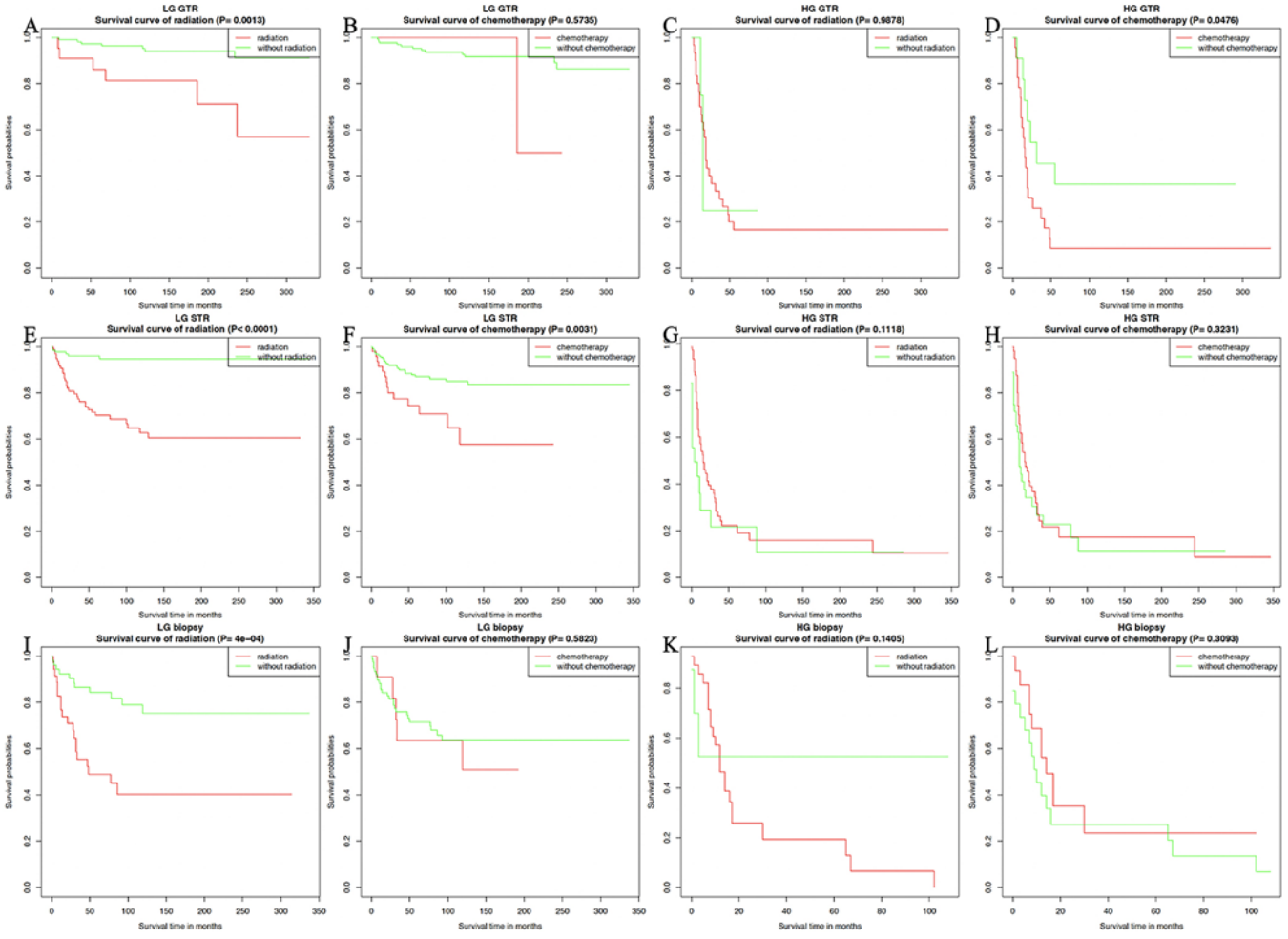

FIG. 4. Kaplan-Meier survival curves for the GTR (**A–D**), STR (**E–H**), and biopsy/local excision (**I–L**) subgroups based on different adjuvant therapies, including radiation therapy (A, C, E, G, I, and K) and chemotherapy (B, D, F, H, J, and L). Figure is available in color online only.

Our research suggested that age and marital status were associated with CSS and OS in LGSCA patients. We also concluded that the WHO grade, distant tumor invasion, EOR, and adjuvant therapy were significantly associated with CSS and OS in these patients. GTR and a lack of adjuvant treatment were significantly associated with better survival in patients with LGSCA but not in those with HGSCA. A higher WHO grade and distant tumor invasion were negatively correlated with CSS and OS in patients with HGSCA. These findings provide a basis of knowledge for evidence-based clinical practices for the management of SCA patients.

Previous large reports of SCA alone that analyzed age as a prognostic variable reported inconsistent outcomes.[4,11,21,25] Minehan et al. suggested that younger age was associated with better results.[7] Santi et al. suggested that age was an obvious risk factor after controlling for other variables.[25] However, age was a categorical variable in their multivariate model. Their findings should be interpreted with caution because of the relatively small sample size. Some smaller studies suggested no obvious prognostic significance for age on survival, but this influence was likely underestimated.[17,23] Age only reached obvious statistical significance in the plotted Kaplan-Meier curves and univariate analysis of the LGSCA group in our study. This finding also suggested that age was a relatively significant risk factor of CSS in LGSCA patients.

Some studies found that histology was not related to survival in HGSCA.[6,25,26] The literature introduced survival rates that varied from 6 to 72 months for anaplastic astrocytoma and 6 to 10 months for glioblastoma.[4,27,28] However, most studies reported the WHO grade as the most obvious risk factor (Table S4).[4,7,14,23,29] These outcomes were also true in pediatric patients.[29,30] Our results are consistent with this insight.

The EOR in LGSCA patients showed an obvious correlation with survival in the univariate and multivariate analyses in our study, but this correlation did not reach significance in the HGSCA group on multivariate analysis. Some studies have suggested that partial resection and GTR of spinal cord tumors should be performed, and the clinical results of these studies improved.[31,32] However, this conclusion is contrary to those in previous studies on brain gliomas.[33,34] For HGSCA patients,[4,12,14,20,25,30,35] only one study suggested

TABLE 3. Primary and validation groups for the nomogram predictions of the 3-, 5-, and 10-year CSS rates of SCA patients and univariate and multivariate analyses to determine prognostic variables of CSS in the primary group

Variable	Primary Cohort (n = 445)	Validation Cohort (n = 188)	Univariable		Multivariable	
			HR (95% CI)	p Value	HR (95% CI)	p Value
Age, yrs						
≤19	181 (40.7)	86 (45.7)	Ref		Ref	
>19	264 (59.3)	102 (57.5)	2.28 (1.604–3.242)	**<0.001**	1.176 (0.709–1.952)	0.528
Sex						
Male	261 (58.7)	105 (54.3)	Ref			
Female	184 (41.3)	83 (42.6)	1.19 (0.869–1.628)	0.277		
Race						
White	350 (78.7)	156 (83.0)	Ref			
Black	54 (12.1)	21 (13.6)	1.411 (0.916–2.174)	0.118		
Other	41 (9.2)	11 (5.9)	1.147 (0.680–1.934)	0.607		
Marital status						
Married	167 (37.5)	57 (30.3)	Ref		Ref	
Single/unmarried	248 (55.7)	115 (61.2)	0.609 (0.440–0.843)	**0.002**	0.911 (0.591–1.405)	0.675
Divorced/separated/widowed	30 (76.7)	16 (8.5)	0.927 (0.503–1.708)	0.809	0.913 (0.479–1.739)	0.781
Insurance status						
Insured/insured, NOS	145 (32.6)	52 (27.7)	Ref			
Medicaid	46 (10.3)	18 (9.6)	0.843 (0.448–1.586)	0.598		
Uninsured	2 (0.4)	2 (1.1)	1.676 (0.231–12.158)	0.609		
Unknown	252 (56.7)	116 (61.7)	0.854 (0.600–1.214)	0.38		
Tumor size, mm						
<50	110 (22.7)	49 (26.1)	Ref			
≥50	51 (11.5)	17 (9.0)	0.855 (0.477–1.535)	0.601		
Unknown	284 (63.8)	122 (64.9)	1.009 (0.695–1.466)	0.959		
Tumor extension						
Localized	293 (65.8)	115 (61.2)	Ref		Ref	
Regional	16 (3.6)	11 (5.9)	2.147 (1.082–4.261)	**0.028**	0.701 (0.340–1.445)	0.336
Distant	18 (4.0)	5 (2.7)	3.967 (2.214–7.107)	**<0.001**	3.108 (1.535–6.292)	**0.001**
Unstaged	118 (26.5)	57 (30.3)	1.058 (0.733–1.526)	0.763	0.794 (0.514–1.227)	0.299
Metastasis						
No	397 (89.2)	161 (85.6)	Ref		Ref	
Yes	5 (1.1)	3 (1.6)	4.376 (1.790–10.70)	**0.001**	1.630 (0.553–4.797)	0.374
Unknown	43 (9.7)	24 (12.8)	0.994 (0.523–1.89)	0.985	1.080 (0.528–2.206)	0.832
WHO grade						
I	145 (32.6)	74 (39.4)	Ref		Ref	
II	173 (38.9)	76 (40.4)	3.168 (1.746–5.749)	**<0.001**	2.598 (1.397–4.832)	**0.002**
III	57 (12.8)	22 (11.7)	12.987 (7.034–23.980)	**<0.001**	9.628 (4.743–19.543)	**<0.001**
IV	70 (15.7)	16 (8.5)	25.764 (14.158–46.884)	**<0.001**	20.446 (10.146–41.202)	**<0.001**
Type of surgery						
GTR	124 (27.8)	50 (26.6)	Ref		Ref	
STR	226 (50.8)	108 (57.4)	2.071 (1.359–3.158)	**<0.001**	1.576 (1.010–2.460)	**0.045**
Local excision/biopsy	95 (21.3)	30 (16.0)	2.854 (1.799–4.526)	**<0.001**	2.759 (1.654–4.601)	**<0.001**
Radiation therapy						
Yes	216 (48.5)	81 (43.1)	Ref		Ref	
No	229 (51.5)	107 (56.9)	0.180 (0.123–0.264)	**<0.001**	0.446 (0.280–0.710)	**<0.001**
Chemotherapy						
Yes	127 (28.5)	38 (20.2)	Ref		Ref	
No	318 (71.5)	150 (79.8)	0.319 (0.232–0.438)	**<0.001**	1.260 (0.824–1.925)	0.285

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TABLE 3. Primary and validation groups for the nomogram predictions of the 3-, 5-, and 10-year CSS rates of SCA patients and univariate and multivariate analyses to determine prognostic variables of CSS in the primary group

Variable	Primary Cohort (n = 445)	Validation Cohort (n = 188)	Univariable		Multivariable	
			HR (95% CI)	p Value	HR (95% CI)	p Value
Year of diagnosis						
1988–1994	71 (16.0)	30 (16.0)	Ref			
1995–2001	85 (19.1)	39 (20.7)	1.015 (0.615–1.676)	0.952		
2002–2008	132 (29.7)	60 (31.9)	0.906 (0.565–1.455)	0.685		
2009–2016	157 (35.3)	59 (31.4)	1.105 (0.686–1.779)	0.68		
Vital status						
Alive	256 (57.5)	130 (69.1)				
Dead	189 (42.5)	58 (30.9)				
Cancer-specific death event						
Alive	287 (64.5)	143 (76.1)				
Dead	158 (35.5)	45 (23.9)				

Boldface type indicates statistical significance.

that aggressive resection was associated with survival.[4] Although great progress has been made in neurosurgery, the prognosis of HGSCA has not changed in past decades, and the prognosis of HGSCA patients remains disappointing.[31]

The adjuvant protocol for SCA is primarily derived from the management strategies for patients with brain glioma. Radiation therapy has an obvious vigorous effect on CSS for all brain glioma patients, but chemotherapy has an obvious survival effect only for glioblastoma patients.[33,34] The efficacy of adjuvant treatment for SCA is heterogeneous.[23,24,32,36,37] Previous research suggested no significant association between radiation therapy and survival.[14,23,30] However, some studies concluded that radiation therapy improved survival results for HGSCA.[24,26] Other studies suggested that it did not have a beneficial effect.[25] An adjuvant protocol is not suitable for LGSCA, especially radiotherapy. However, some of the patients who needed radiation therapy were at higher risk and not suitable for surgery. Few studies suggested a survival benefit from chemotherapy.[23] The impact of a chemotherapy protocol on the survival rate was not realized in some studies because the sample size was too small[7,30] or there were no relevant data.[11,17] Generally, an adjuvant protocol is not suitable for SCA, especially LGSCA. Because there is a potential selection bias toward adjuvant therapy in higher-grade tumors, and patients who clearly underwent STR may undergo radiation therapy, the outcome of radiotherapy or chemotherapy may be easily skewed.

Strengths and Limitations

The SEER database lacks other important information, although it includes a large amount of information, such as data about the concrete tumor position; vertebral segments of the tumor; functional status; neurological function; the surgical approach; method of tumor size measurement; lack of confirmation of the pathological stage; molecular diagnostic criteria; and the category, type, and dose of adjuvant protocol as well as the time span.

The present study is the largest population-based, real-world study of SCA, which used the SEER database. The results of this research are consistent with those of many previous conclusions of other small-sample, clinical research studies, but they are more robust and have less bias. This research demonstrated, for the first time, the clinical characteristics, such as marital status and insurance status, of SCA patients and risk factors for survival and compared them between LGSCA and HGSCA patients. A clinically useful nomogram was also introduced to predict the CSS and OS rates of SCA patients.

Conclusions

This study of 633 SCA patients demonstrated obvious differences between the LGSCA and HGSCA groups. Our findings strongly recommend safe maximal resection as a useful treatment for LGSCA patients. Safe resection is the first choice, especially for HGSCA patients. Adjuvant therapy is not recommended for LGSCA, especially radiotherapy. Observation may be a reasonable choice for HGSCA patients after incomplete resection because radiation and chemotherapy showed no improvement in CSS or OS.

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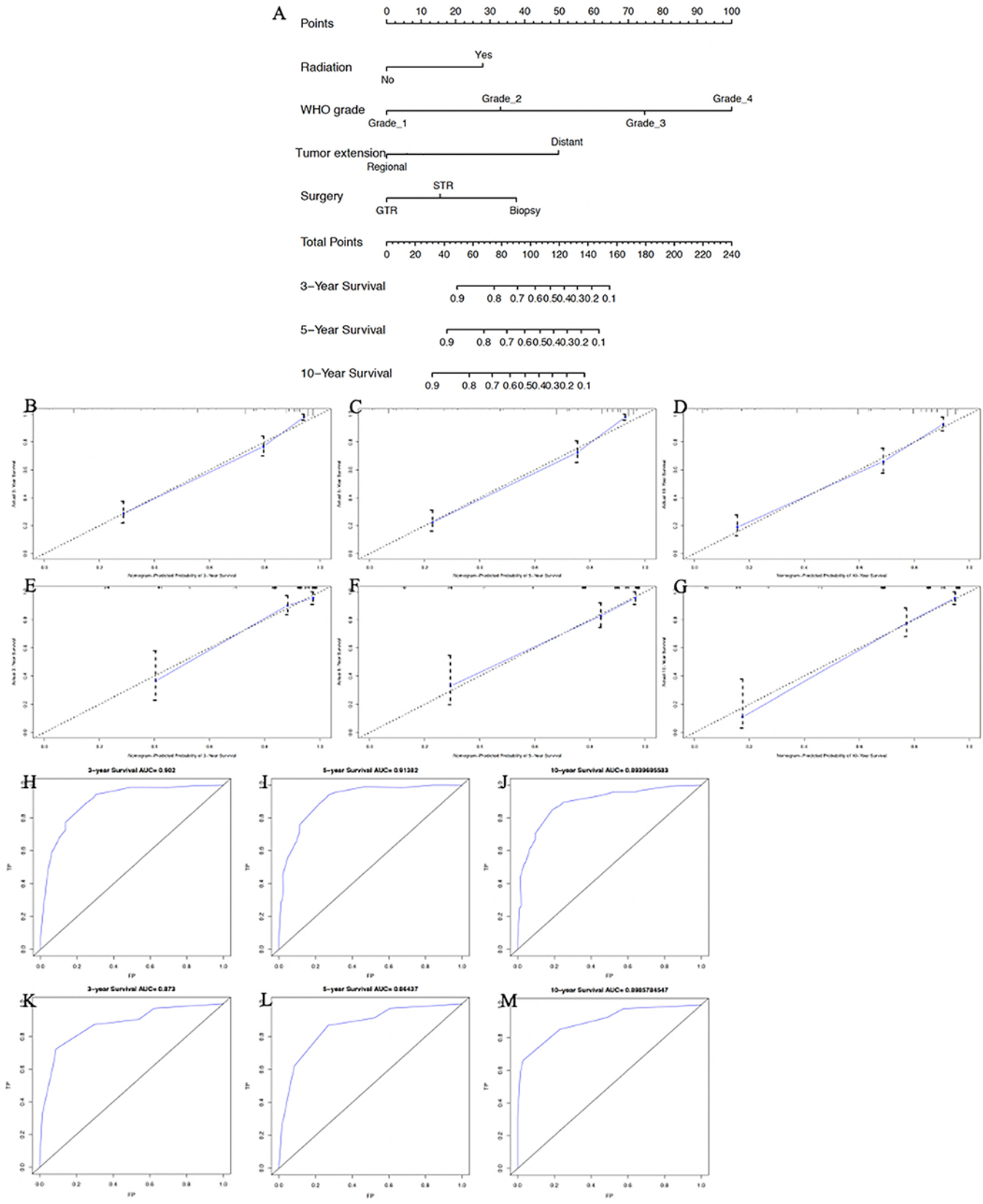

FIG. 5. A: SCA nomogram for CSS. **B–G:** The internal calibration plots to predict the 3-year CSS rate in the primary group (B) and validation group (C), the 5-year CSS rate in the primary group (D) and validation group (E), and the 10-year CSS rate in the primary group (F) and validation group (G). **H–M:** Area under the ROC curve (AUC) of the 3-, 5-, and 10-year CSS rates in the primary group (H, I, and J) and in the validation group (K, L, and M). FP = 1 − specificity; TP = sensitivity. Figure is available in color online only.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Jian, Yuan, Yao. Acquisition of data: Yuan, Yao, Cheng, Zhang, Ma. Analysis and interpretation of data: Yuan, Yao, Cheng, Zhang, Ma. Drafting the article: Yuan. Critically revising the article: Yao, Ma, Guan. Reviewed submitted version of manuscript: Jian, Zhang, Guan. Approved the final version of the manuscript on behalf of all authors: Jian. Statistical analysis: Yuan, Yao, Cheng, Zhang, Ma. Administrative/technical/material support: Jian. Study supervision: Jian.

Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

Figs. S1–S3 and Tables S1–S4. https://thejns.org/doi/suppl/10.3171/2021.1.SPINE202017.

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