Original Article

Epidemiological characteristics and prognostic factors of high-grade brainstem glioma for all ages and the establishment of a nomogram

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Background: High-grade brainstem gliomas (HGBSGs) are aggressive tumors with dismal prognoses. Large-scale studies across all ages are needed to clarify their characteristics and identify predictors of cancer-specific mortality. This study sought to use data from the Surveillance Epidemiology and End Results (SEER) database to conduct a population-based analysis of HGBSG patients of all ages, identify factors influencing cancer-specific survival (CSS), and develop nomograms for prognostic prediction.

Methods: We retrospectively analyzed patients with pathologically confirmed brainstem high-grade gliomas using the SEER database from 2000 to 2018. Univariate and multivariate Cox regression, which included patient demographics, tumor characteristics, and treatments were used to identify risk factors that affected CSS in high-grade glioma patients of all ages. In addition, we evaluated nomograms that were developed using these patient cohorts.

Results: A total of 300 patients were selected for this study, which included 179 adults and 121 pediatric patients. The median survival time was longer in pediatric (11 months) than in adult patients (7 months; P=0.041). Multivariate analysis showed that anaplastic astrocytoma (AA) [hazard ratio (HR), 0.66; 95% confidence interval (CI): 0.50–0.89; P=0.006] and chemotherapy (HR, 0.57; 95% CI: 0.42–0.77; P<0.001) significantly increased patient's CSS. In contrast, being single (HR, 1.70; 95% CI: 1.08–2.66; P=0.02) significantly reduced patient's CSS. Multivariate analysis and Kaplan-Meier curves demonstrated that the extent of resection and radiotherapy (RT) were not independent factors that affected patient prognosis.

Conclusions: Overall survival was poor. However, the survival time of pediatric patients was significantly longer compared to adult patients. In HGBSG patients, the extent of resection may not have a significant effect on prognosis. Chemotherapy was found to significantly improve patient prognosis. The effect of RT on patient prognosis requires further study.

Keywords: Brainstem gliomas; prognostic factors; nomogram; Surveillance Epidemiology and End Results database (SEER database)

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Introduction

Brainstem glioma (BSG) is a very rare intracranial tumor and accounts for about 1–2% of intracranial tumors in adults (1) and 20% of intracranial tumors in children (2). The age-adjusted incidence rate was 0.311 cases per 100,000 person-years between 2004 and 2016 in the United States (3) and is the leading cause of morbidity and mortality among all central nervous system tumors (4). Brainstem tumors are defined as lesions occurring in the midbrain, the pons, or the medulla oblongata. The natural history of these tumors is one of debilitating clinical progression and poor survival (5). In pediatric patients, they are broadly grouped into two main entities: diffuse intrinsic pontine glioma (DIPG), which comprises 80% of patients, and focal brainstem glioma (FBSG), which constitutes 20% (6). Guillamo *et al.* identified three major types of adult BSG, namely, high-grade gliomas, diffuse infiltrating low-grade gliomas (LGGs), and tectal gliomas. They all have marked differences in life expectancy (7). Based on pathology, brainstem gliomas can be divided into low grade [World Health Organization (WHO) grade 1 and 2] and high grade (WHO grade 3 and 4). Previous studies have demonstrated a shorter median survival time for patients with high-grade brainstem gliomas (HGBSGs) and a more prolonged survival time for patients with LGG (8,9). In recent years, there have been numerous studies on the prognostic factors for patients with low-grade brainstem gliomas. These findings suggest that total resection could significantly improve patient prognosis (10,11). A study involving 305 patients with low-grade brainstem glioma (LGBSG) found that total resection was effective, but postoperative adjuvant radiotherapy (RT) and chemotherapy had no significant effect on residual tumors (12). To date, there have been no specific studies dealing with HGBSG patient prognosis for all age groups.

We conducted a population-based study using data obtained using the Surveillance Epidemiology and End Results (SEER) database to investigate the characteristics of patients with HGBSG. We aimed to identify risk factors that affected cancer-specific survival (CSS) in HGBSG patients and to develop and evaluate nomograms. This could help improve the management of patients with HGBSG. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1030/rc).

Highlight box

Key findings

- This study analyzed 300 patients with high-grade brainstem glioma (HGBSG) (179 adults, 121 pediatric patients) using the Surveillance Epidemiology and End Results database. Pediatric patients had significantly longer median survival (11 months) than adults (7 months, P=0.041). Anaplastic astrocytoma [hazard ratio (HR) =0.66, 95% confidence interval (CI): 0.50–0.89, P=0.006] and chemotherapy (HR =0.57, 95% CI: 0.42–0.77, P=0.001) improved cancer-specific survival (CSS), while single marital status (HR =1.70, 95% CI: 1.08–2.66, P=0.02) reduced CSS. Resection extent and radiotherapy (RT) were not independent prognostic factors. A nomogram based on 6 factors (race, pathology, gender, chemotherapy, age, marital status) predicting 6-month, 1-year and 2-year CSS achieved areas under the curve of 0.75, 0.724 and 0.727.

What is known and what is new?

- HGBSG is aggressive with poor prognosis, but data on all-age HGBSG prognostic factors and nomograms is lacking.
- We present the first population-based nomogram spanning all ages, quantify the independent benefit of chemotherapy, and reveal marital status as a novel prognostic factor.

What is the implication, and what should change now?

- The nomogram enables clinicians to individualize HGBSG prognosis across ages. Chemotherapy should be prioritized in treatment, while resection extent may not need overemphasis. RT's role requires further research.
- Future HGBSG studies should integrate molecular markers (e.g., H3K27M) and tumor location (midbrain/pons/medulla) to refine prognostic models; clinical practice should consider marital support as a potential adjunct to improve patient outcomes.

Methods

Study population

Patient data for this study were extracted from the SEER database, which is a National Cancer Institute maintained, nationwide cancer registry that contains prospective data on patient demographics, tumor characteristics, and survival outcomes. SEER has been approved for public use by the local ethics committee, hence our study did not require a local ethics approval or statement. This study screened patients of all age groups from 2000 to 2018 using the SEER database who met the following criteria. First and primary lesions are located within the brainstem (primary site code C71.7). Histologically confirmed anaplastic astrocytoma (AA) (International Classification of Diseases for Oncology, Third Edition (ICD-O-3) code 9401/3), anaplastic oligodendroglioma (AO) (ICD-O-3 code 9451/3), glioblastoma (GBM) (ICD-O-3 code 9440/3). Giant cell

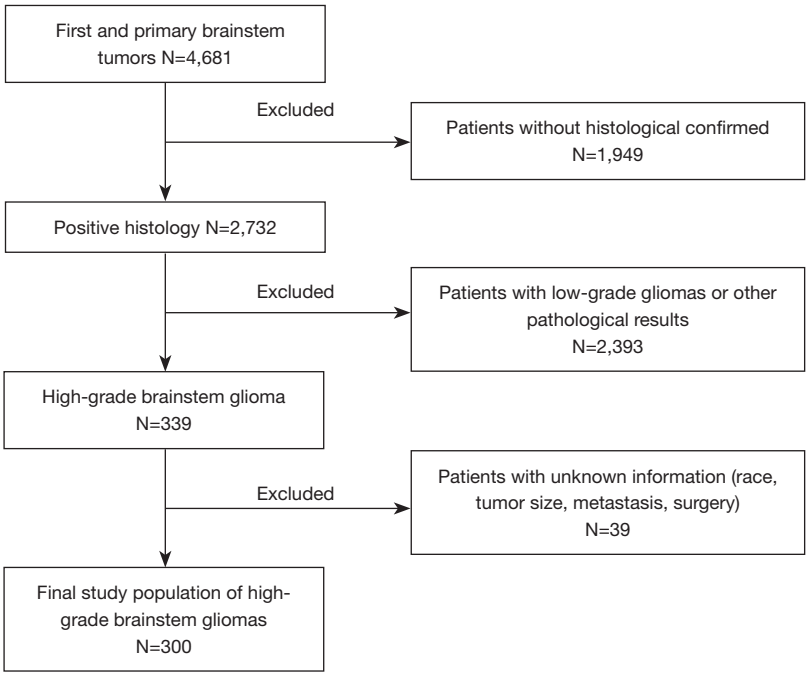

Figure 1 Flowchart of high-grade brainstem glioma patient.

GBM (ICD-O-3 code 9441/3) and gliosarcoma cases (ICD-O-3 code 9442/3) were grouped with the GBM cases. Patients without biopsy or surgery, whose information (race, tumor size, metastasis, surgery) was unknown were excluded from the analysis (*Figure 1*). This study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

Variable definitions

Collected variables included age at diagnosis (patients aged <20 years were assigned to the pediatric group, and those aged ≥20 years were assigned to the adult group), survival month, sex (male, female), race (White, Black, Asian/Pacific islander), year of diagnosis (2000–2009, 2010–2018), marital status (married, divorced, single, widowed, unknown), and size (maximum diameter ≤15 mm, 16–40 mm, >40 mm). We divided the histological types into GBM, AO, and AA according to the 2021 WHO classification of tumors of the central nervous system. The extent of surgical resection was categorized as gross total resection (GTR), subtotal or partial resection (STR), biopsy or not otherwise specified (NOS) (a surgical procedure was done, but no information on the type of surgical procedure was provided), metastasis (no, yes), chemotherapy (no/unknown, yes), radiation (no/unknown, yes), specific death (alive, dead), and vital status (alive, dead).

Statistical analyses

We analyzed and compared patient demographics, tumor characteristics, and treatment course. The patient population was divided into the adult and pediatric groups based on age. The survival time was represented by the median (range). An independent sample *t*-test was used for comparison between the groups. Parameters were expressed using n (%). The Chi-squared test was used for group comparison. Cox proportional hazards regression models were constructed to evaluate factors that affected patient survival time. Significant factors from univariate Cox regression analyses were included in multivariate Cox regression. Kaplan-Meier curve and log-rank test were used to provide different variables for visualization of survival.

The nomograms were constructed to predict the survival rate of patients at 6 months, 1 year, and 2 years using the six indexes. These indexes were meaningful in multivariate Cox regression. The constructed nomograms were evaluated using calibration plots, and receiver operating characteristic (ROC) curve, including the degree of differentiation between the predicted value and the true value. We used

R 4.1.0 version for data analysis. P<0.05 was considered statistically significant.

Results

Baseline demographic and clinical information

This study included 300 patients with pathologically proven HGBSG from the SEER database and consisted of 179 adult and 121 pediatric patients. The median survival time for adults was 7 (0–130) months, and the median survival time for pediatric patients was 11 (0–221) months, which was significantly longer compared to adult patients (P=0.041). There were 104 males (58.1%) in the adult group and 60 males (49.6%) in the pediatric group (P=0.15). Compared to patients in the adult group (49.2%), more patients in the pediatric group (64.5%) were diagnosed during 2000–2008 (P=0.009). There were 233 (77.7%) White patients, 36 (12.0%) Black patients, and 31 (10.3%) Asian/Pacific patients. Among adult patients, 108 (60.3%) were married, 14 (7.8%) were divorced, 46 (25.7%) were single, and 6 (3.4%) were widowed. There were 21 (7.0%) patients with maximum diameter lesions ≤15 mm, 212 (70.7%) patients had lesions between 16–40 mm and 67 (22.3%) patients had lesions with diameter >40 mm. Based on pathology, there were 122 (68.2%) cases with GBM, 3 (1.7%) cases with AO, and 54 (30.2%) cases with AA in the adult group. In the pediatric group, there were 67 (55.4%) cases with GBM, 1 (0.8%) case with AO, and 53 (43.8%) cases with AA. Statistical significant differences were observed between the two groups (P=0.049). Among adult patients, there were 13 (7.3%) cases with GTR, 33 (18.4%) cases with STR, 40 (22.3%) cases with biopsies, and 93 (52.0%) patients who lacked specific surgical method. In the pediatric group, there were 8 (6.6%) cases with GTR, 34 (28.1%) cases with STR, 19 (15.7%) cases with biopsy, and 60 (49.6%) cases with NOS. There was no significant difference with regards to the extent of resection between the two groups. There were 110 (61.5%) and 81 (66.9%) patients who received chemotherapy in the adult and pediatric groups, respectively. No significant difference between the groups was observed. The number of patients with tumor metastasis in the adult group was 4, which was 3 more than the number of tumor metastases in the pediatric group, however, there was no significant difference between the groups. Of the 300 patients evaluated, 259 (86.3%) patients died, and 245 (81.7%) died of brainstem glioma (*Table 1*).

Predictors of CSS

Univariate Cox regression analyses showed that 40–59 years old [hazard ratio (HR), 0.53; 95% confidence interval (CI): 0.36–0.79; P=0.002], 20–39 years old (HR, 0.47; 95% CI:

Table 1 Patient demographics, tumor characteristics, and treatment options of 300 high-grade brainstem glioma patients

Characteristic	Overall (N=300)	Adult (N=179)	Pediatric (N=121)	P
Survival month				0.041
Median (range)	9 (0–221)	7 (0–130)	11 (0–221)	
Sex				0.15
Male	164 (54.7)	104 (58.1)	60 (49.6)	
Female	136 (45.3)	75 (41.9)	61 (50.4)	
Year of diagnosis				0.009
2000–2009	134 (44.7)	91 (50.8)	43 (35.5)	
2010–2018	166 (55.3)	88 (49.2)	78 (64.5)	
Race				0.76
White	233 (77.7)	139 (77.7)	94 (77.7)	
Black	36 (12.0)	20 (11.2)	16 (13.2)	
Asian/Pacific	31 (10.3)	20 (11.2)	11 (9.1)	

Table 1 (*continued*)

Table 1 (*continued*)

Characteristic	Overall (N=300)	Adult (N=179)	Pediatric (N=121)	P
Marital status				<0.001
Married	108 (36.0)	108 (60.3)	0 (0)	
Divorced	14 (4.7)	14 (7.8)	0 (0)	
Single	167 (55.7)	46 (25.7)	121 (100.0)	
Widowed	6 (2.0)	6 (3.4)	0 (0)	
Unknown	5 (1.7)	5 (2.8)	0 (0)	
Size (mm)				0.16
≤15	21 (7.0)	15 (8.4)	6 (5.0)	
16–40	212 (70.7)	130 (72.6)	82 (67.8)	
>40	67 (22.3)	34 (19.0)	33 (27.3)	
Histology				0.049
GBM	189 (63.0)	122 (68.2)	67 (55.4)	
AO	4 (1.3)	3 (1.7)	1 (0.8)	
AA	107 (35.7)	54 (30.2)	53 (43.8)	
Surgery				0.19
GTR	21 (7.0)	13 (7.3)	8 (6.6)	
STR	67 (22.3)	33 (18.4)	34 (28.1)	
Biopsy	59 (19.7)	40 (22.3)	19 (15.7)	
NOS	153 (51.0)	93 (52.0)	60 (49.6)	
Radiation				0.03
No/unknown	52 (17.3)	38 (21.2)	14 (11.6)	
Yes	248 (82.7)	141 (78.8)	107 (88.4)	
Chemotherapy				0.33
No/unknown	109 (36.3)	69 (38.5)	40 (33.1)	
Yes	191 (63.7)	110 (61.5)	81 (66.9)	
Metastasis				0.35
No	295 (98.3)	175 (97.8)	120 (99.2)	
Yes	5 (1.7)	4 (2.2)	1 (0.8)	
Specific death				0.12
Alive	55 (18.3)	38 (21.2)	17 (14.0)	
Dead	245 (81.7)	141 (79.8)	104 (86.0)	
Vital status				0.60
Alive	41 (13.7)	26 (14.5)	15 (12.4)	
Dead	259 (86.3)	153 (85.5)	106 (87.6)	

Data are presented as n (%) unless otherwise specified. AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; GBM, glioblastoma; GTR, gross total resection; NOS, not otherwise specified (a surgical procedure was done, but no information on the type of surgical procedure was provided); STR, subtotal or partial resection.

0.3–0.72; P=0.001), 0–19 years old (HR, 0.57; 95% CI: 0.4–0.82; P=0.002), female (HR, 0.77; 95% CI: 0.59–0.99; P=0.004), Asian/Pacific group (HR, 0.57; 95% CI: 0.35–0.93; P=0.02), AA (HR, 0.63; 95% CI: 0.48–0.82; P=0.001), radiation(HR, 0.54; 95% CI: 0.38–0.75; P<0.001), and chemotherapy (HR, 0.55; 95% CI: 0.43-0.72; P<0.001) were factors that significantly increased CSS. However, widow (HR, 2.57; 95% CI: 1.03–6.73; P=0.042) was a factor that significantly reduced CSS. Multivariate Cox regression analysis showed that 20–39 years old (HR, 052; 95% CI: 0.31–0.81; P=0.01), 0–19 years old (HR, 0.45; 95% CI: 0.25–0.81; P=0.008), female (HR, 0.75; 95% CI: 0.57–0.97; P=0.03), Asian/Pacific group (HR, 0.54; 95% CI: 0.33–0.90; P=0.02), AA (HR, 0.66; 95% CI: 0.50–0.89; P=0.006), and chemotherapy (HR, 0.57; 95% CI: 0.42–0.77; P=0.001) were factors that significantly increased patient CSS. In contrast, being single (HR, 1.70; 95% CI: 1.08–2.66; P=0.02) was a factor that significantly reduced patient CSS. Results for other factors are shown in *Table 2*.

Kaplan-Meier curves were used to compare the effects of different factors on CSS in patients with HGBSG (*Figure 2*). There were significant differences in age groups (P=0.002), chemotherapy group (P<0.001), pathology group (P=0.001), race group (P=0.02), RT group (P<0.001) and gender group (P=0.04). To understand the survival benefit based on the extent of surgical resection, adjuvant RT, and chemotherapy for CSS in patients for the different age groups, we additionally grouped and plotted Kaplan-Meier curves (*Figure 3*). Our results showed that only the adult group had a significant difference for adjuvant RT and chemotherapy (P<0.001).

Prognostic nomogram for CSS

Assessing multiple factors could improve the accuracy of patient prognosis (13). We used race, pathology, gender, adjuvant chemotherapy, age, and marital status to construct a nomo program based on the results of multivariate Cox regression analyses. This was done to predict patient CSS at 0.5, 1, and 2 years (*Figure 4*). The calibration curve for the probability of postoperative CSS (*Figure 4*) at 0.5-, 1-, and 2-year showed that there was good consistency between the predicted survival probability and the actual survival probability. We plotted the ROC curve, resulting in a high area under the ROC curve (*Figure 4*). The area under the curve (AUC) of the 0.5-, 1- and 2-year CSS were 0.75, 0.724, 0.727, respectively.

Discussion

Based on a large number of cases, we investigated the impact of demographic characteristics, tumor characteristics, and

Table 2 Univariate and multivariate Cox proportional hazard regression analyses to determine prognostic factors of cancer-specific survival for patients with high-grade brainstem glioma

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age (years)				
≥60	1 (reference)		1 (reference)	
40–59	0.53 (0.36–0.79)	0.002	0.65 (0.42–1.01)	0.06
20–39	0.47 (0.3–0.0.72)	0.001	0.52 (0.31–0.87)	0.01
0–19	0.57 (0.4–0.82)	0.002	0.45 (0.25–0.81)	0.008
Sex				
Male	1 (reference)		1 (reference)	
Female	0.77 (0.59–0.99)	0.004	0.75 (0.57–0.97)	0.03
Year of diagnosis				
2000–2009	1 (reference)		1 (reference)	
2009–2013	1.00 (0.78–1.29)	>0.99	–	–

Table 2 (*continued*)

Table 2 (*continued*)

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Race				
White	1 (reference)		1 (reference)	
Black	1.29 (0.88–1.9)	0.20	1.22 (0.81–1.83)	0.34
Asian/Pacific	0.57 (0.35–0.93)	0.02	0.54 (0.33–0.90)	0.02
Marital status				
Married	1 (reference)		1 (reference)	
Divorced/separated	1.27 (0.71–2.28)	0.42	1.49 (0.81–2.73)	0.20
Single	1.05 (0.8–1.38)	0.71	1.70 (1.08–2.66)	0.02
Widow	2.57 (1.03–6.37)	0.042	1.98 (0.76–5.17)	0.16
Unknown	0.99 (0.36–2.7)	0.98	0.63 (0.22–1.83)	0.40
Histology				
GBM	1 (reference)		1 (reference)	
AO	0.45 (0.17–1.22)	0.12	0.51 (0.19–1.40)	0.19
AA	0.63 (0.48–0.82)	0.001	0.66 (0.50–0.89)	0.006
Surgery				
GTR	1 (reference)		1 (reference)	
STR	0.98 (0.57–1.7)	0.96	–	–
Biopsy	1.28 (0.74–2.23)	0.38	–	–
NOS	1.25 (0.75–2.08)	0.38	–	–
Radiation				
No/unknown	1 (reference)		1 (reference)	
Yes	0.54 (0.38–0.75)	<0.001	0.79 (0.54–1.17)	0.24
Chemotherapy				
No/unknown	1 (reference)		1 (reference)	
Yes	0.55 (0.43–0.72)	<0.001	0.57 (0.42–0.77)	<0.001
Size (mm)				
≤15	1 (reference)		1 (reference)	
16–40	1.04 (0.16–1.76)	0.89	–	–
>40	1.05 (0.59–1.87)	0.86	–	–
Metastasis				
No	1 (reference)		1 (reference)	
Yes	1.03 (0.42–2.5)	0.95	–	–

AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; CI, confidence interval; GBM, glioblastoma; GTR, gross total resection; HR, hazard ratio; NOS, not otherwise specified (a surgical procedure was done, but no information on the type of surgical procedure was provided); STR, subtotal or partial resection.

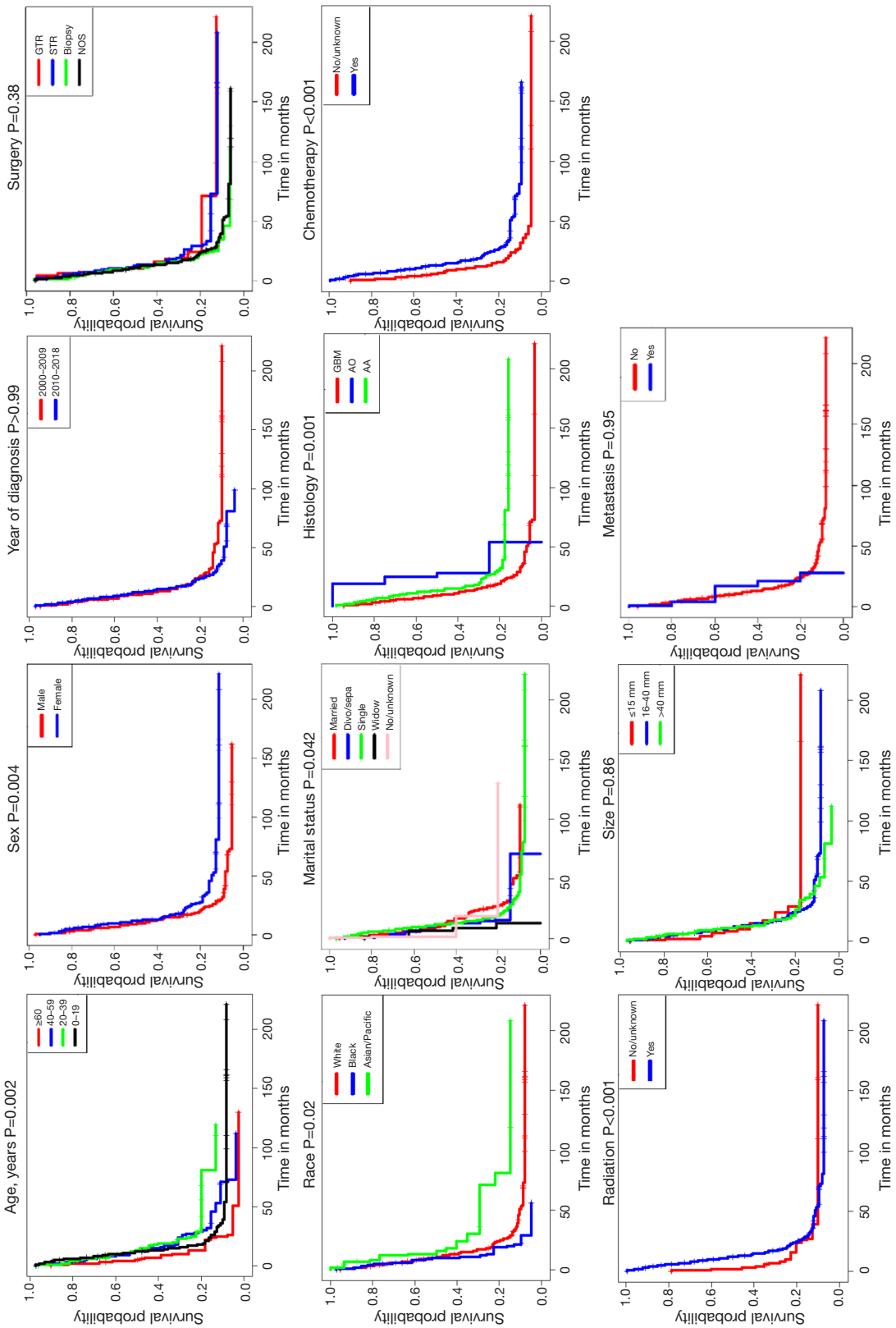

Figure 2 Kaplan-Meier curves for patients with HGBSG by different variates. AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; Divo/sepa, divorced/separated; GBM, glioblastoma; GTR, gross total resection; HGBSG, high-grade brainstem glioma; NOS, not otherwise specified (a surgical procedure was done, but no information on the type of surgical procedure was provided); STR, subtotal or partial resection.

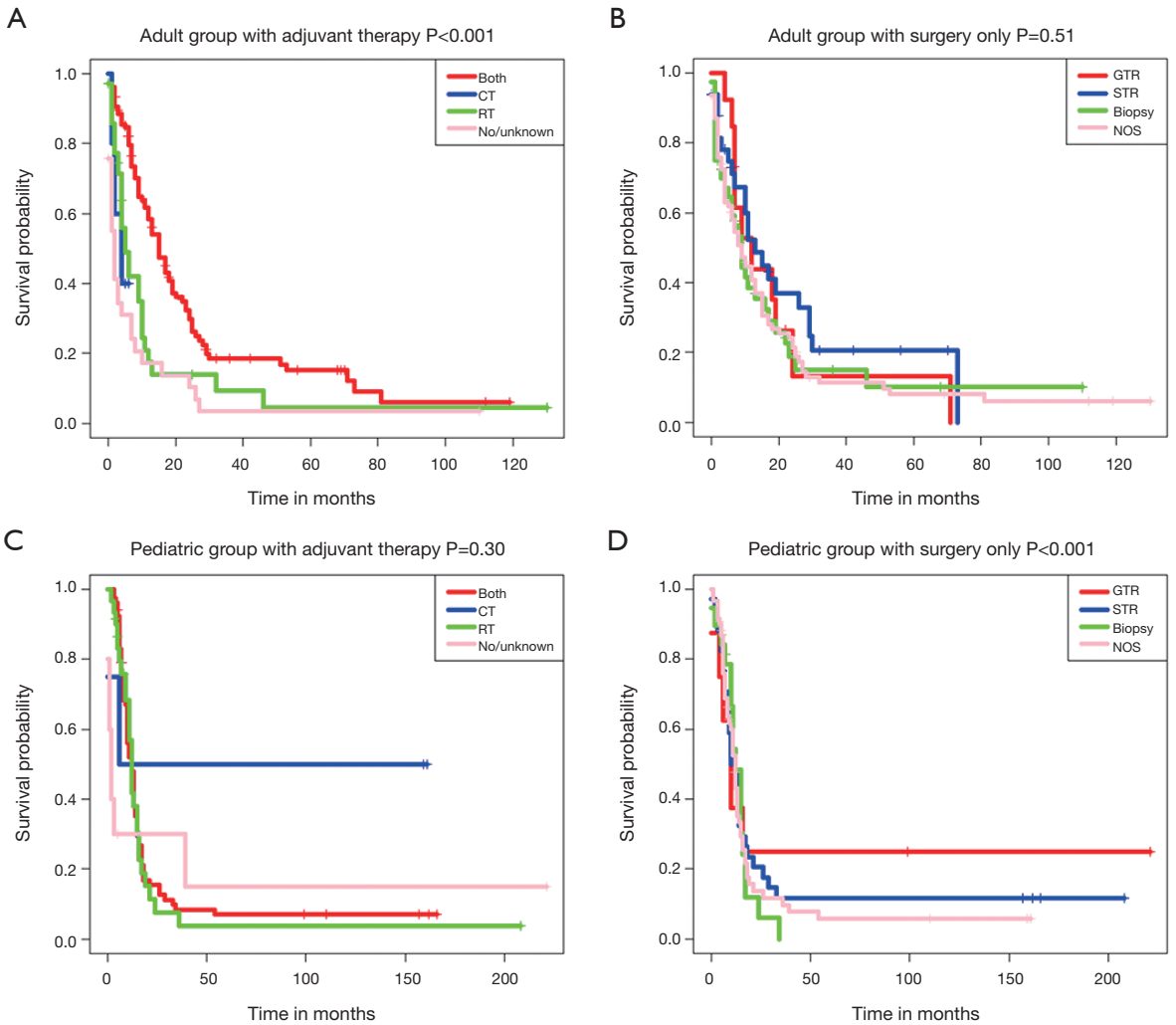

Figure 3 Kaplan-Meier curves for HGBSG patients stratified by age group and treatment type. Kaplan-Meier curve for patients with HGBSG in adult group (A) and pediatric group (C) treated with different adjuvant therapies. Kaplan-Meier curve for adult patients (B) and pediatric group (D) with surgery only. CT, chemotherapy; GTR, gross total resection; HGBSG, high-grade brainstem glioma; NOS, not otherwise specified (a surgical procedure was done, but no information on the type of surgical procedure was provided); RT, radiotherapy; STR, subtotal or partial resection.

treatment methods on the survival of patients with HGBSGs for all age groups. Due to the rarity of brainstem tumors, previous studies were comprised of a heterogeneous, small group of patients from a single institution. This population-based study is one of the largest to date and consists of a homogenous cohort of 300 patients with known tumor histology, enhancing generalizability and filling gaps in comprehensive age-related insights. Based on the results of multivariate Cox regression, the nomogram was built on 6 independent prognostic factors. Calibration curves demonstrate good consistency between predicted and actual survival, and ROC curves yield AUCs of 0.75, 0.724, 0.727 for 6-month, 1-year, 2-year CSS—statistically robust. Clinically, it enables individualized prognosis across all age groups, a feature lacking in most existing models tailored to single age groups, offering meaningful improvement.

Our study found that the survival time in children with HGBSG was significantly longer compared to adults (P=0.04). The median survival time of children and adults was the same as that of previous studies, with the median survival time for children being 10 months (14), while the median survival time for adult patients was 7 months (15).

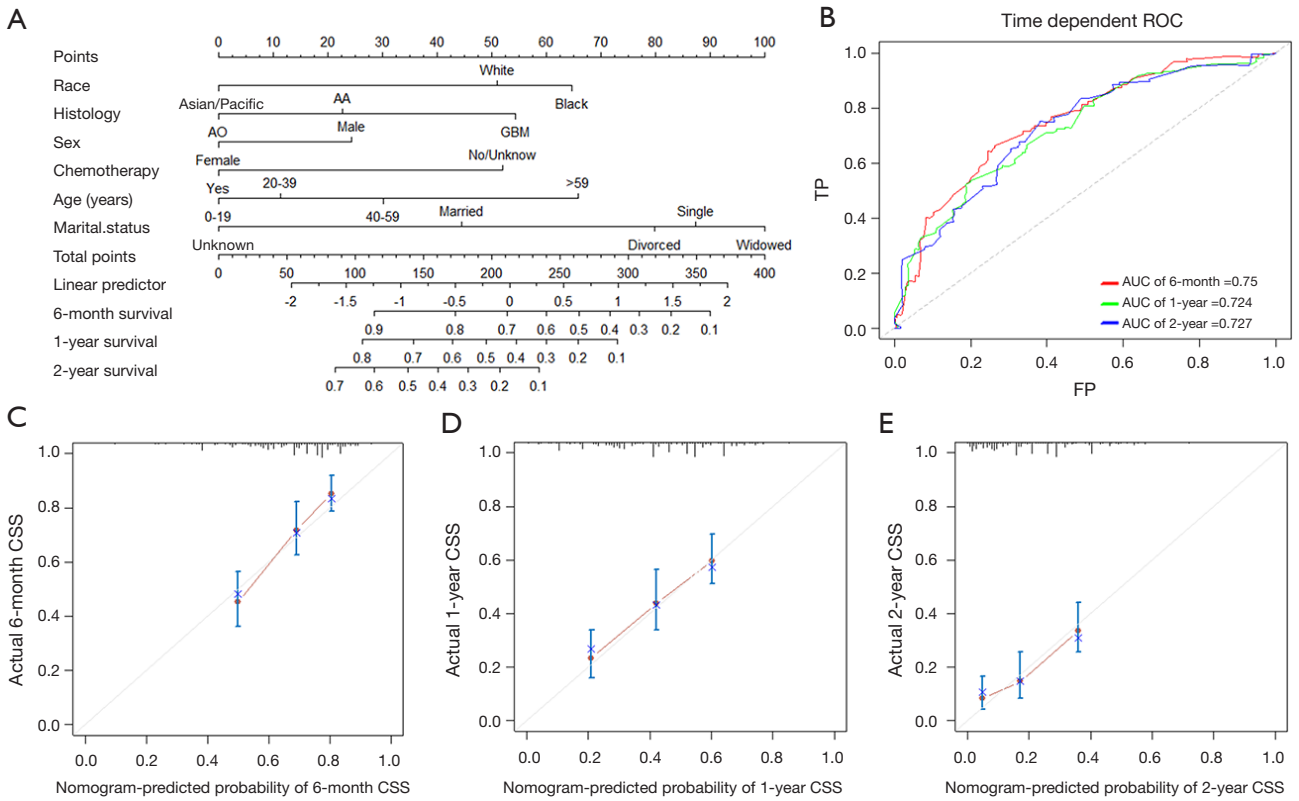

Figure 4 Nomogram and ROC curve and internal calibration for cancer-specific survival rate. (A) Nomogram to predict 6-month, 1- and 2-year CSS rates of high-grade brainstem glioma patients. (B) Time-dependent ROC curve and areas under ROC curve at different time points. (C) The calibration curve to predict 6-month CSS rate. (D) The internal calibration curve to predict 1-year CSS rate. (E) The calibration curve to predict 2-year CSS rate. AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; AUC, area under the curve; CSS, cancer-specific survival; FP, false positive; ROC, receiver operating characteristic; TP, true positive.

Multivariate Cox regression analysis and Kaplan-Meier curves showed that advanced age (≥60 years) was an independent factor leading to a shorter survival time. Possible reasons include: (I) with the increase of age, the repair ability of cells to damage decreases (16); (II) aging compromises the immune system resulting in decreased anti-tumor activity (17); (III) Karnofsky Performance Status (KPS) score decreases with age and was associated with poor prognosis (18).

In this study, the incidence of GBM in the adult group (68.2%) was significantly higher compared to the pediatric group (55.4%). This may be the reason why prognosis of adult patients was worse compared to pediatric patients. Based on the WHO classification, AA and GBM are grade 3 and grade 4 respectively. Several studies have shown that the survival time of patients with AA is significantly longer compared to GBM (19-21). This is consistent with our conclusions. In 2021, WHO has proposed new molecular classifications for gliomas. The 2021 schema integrates molecular markers such as IDH mutation status, 1p/19q codeletion, H3K27M alteration, TERT promoter mutation and CDKN2A/B homozygous deletion to redefine tumor entities. Such refinement may shift the distribution of WHO grades 3–4 lesions, re-classify a subset of tumors as diffuse midline glioma-H3K27-altered, and ultimately influence both prognostic modeling and therapeutic stratification. Future analyses must therefore incorporate both histological and molecular criteria (22). In our study, marriage was a factor that could significantly improve the prognosis of patients. Deng *et al.* studied the relationship between marital status and prognosis of glioma patients. The authors found that marriage was an independent influencing factor that improved patient prognosis. The hypothesis proposed by the authors points to spousal

support. Married patients were more likely to receive surgery and adjuvant chemo- or RT (23).

The current standard of care for HGBSG includes an initial, maximally safe surgical resection, followed by conformal RT with concurrent oral temozolomide chemotherapy, followed by adjuvant temozolomide therapy (24). Adams *et al.* found that GTR could significantly extend the survival time of patients with HGBSG (25). Liu *et al.* showed that total resection did not benefit HGBSG patient survival. However, their study included only 86 cases which were not sufficient to make a conclusive statement (26). The number of cases in our study was 300 cases. Our results showed that different resection ranges had an impact on the survival of HGBSG patients but were not statistically significant. The possible reasons may include: (I) GTR refers to complete tumor removal as confirmed by imaging; however, HGBSG exhibit high malignancy, and tumor cells often infiltrate regions beyond the macroscopically visible tumor boundaries. Consequently, GTR fails to achieve a radical cure, resulting in no significant impact on patient survival. (II) HGBSG was located in the core area of the human brain, and its growth pattern was highly aggressive. It is difficult to distinguish non-enhanced areas around high-grade tumors as peritumoral oedema or infiltration of tumor cells on magnetic resonance images (27). Optimization of surgical resection has led to supramarginal resection or removal beyond the contrast-enhancing region on magnetic resonance imaging (MRI) (28). However, this may damage nerve fiber bundles or nerve nucleus in the brainstem resulting in the loss of important nerve functions and reducing patient survival time. Thus, complete resection of brainstem high-grade gliomas requires further tumor characterization. It is necessary to further understand whether the tumor is focal or diffuse. This information will affect the choice of the optimal surgical method (29,30). Total resection of tumors located in the midbrain or pons is also very different (7,31). This information was lacking in the SEER database, hence additional studies are required.

Kerezoudis *et al.* concluded that HGBSG patients treated with combined RT and chemotherapy have a longer survival time compared to patients treated with RT alone, but only for Grade 4 tumors (32). In our study, Kaplan-Meier analysis revealed improved CSS for adults who received both CT and RT compared to patients who received only CT, RT, or unknown/no therapy. In multivariate Cox regression analysis, chemotherapy was an independent influencing factor that could prolong survival time in HGBSG.

In our study, the acceptance of RT in the pediatric group was higher compared to the adult group (88.4% *vs.* 78.8%, P=0.03). Results of the Kaplan-Meier curve and univariate Cox regression analysis showed that RT was a protective factor for HGBSG patients, however, multivariate analysis showed that RT was not an independent factor affecting patient prognosis. We hypothesize this discrepancy may stem from key factors: (I) pediatric patients were more likely to receive RT, and age (an independent protective factor) may have driven the univariate benefit (6); (II) larger tumors, which correlate with poorer prognosis and higher RT utilization may have inflated univariate associations (33); (III) RT is often combined with chemotherapy, and we consider adjusting for chemotherapy in multivariate analysis a likely contributor to the attenuated apparent effect of RT. A previous report suggested better prognostic value for brainstem glioma patients who underwent intense radio and chemotherapy compared with radiation therapy alone (32). We think the possible reasons include: (I) large RT treatment volumes with the prolonged need for dexamethasone after the completion of RT could lead to poorer overall survival (33). Unlike other parts of the brain, slight edema in the brainstem could result in fatal consequences; (II) irradiated cancer cells often acquire resistance mechanisms that permit survival or stimulate regrowth after treatment (34).

Limitation

There are several limitations in this study. First, SEER lacks data on anatomic subregion (midbrain, pons, medulla), focality, and key molecular markers such as H3K27M. These factors are well-established independent predictors of survival in HGBSGs; their absence from our model likely attenuated its discriminative accuracy and may partly explain the modest AUC. Future studies incorporating tumor location, growth pattern, and molecular profiling are needed to refine the model. Second, the marital status and race information of some patients were missing. Third, the SEER registry lacks operative notes and post-operative imaging, so the extent of resection (GTR/STR/biopsy) is derived solely from textual fields that are prone to misclassification and may underestimate the true prognostic benefit of GTR. Compounding this issue, the specific surgical approach is missing for a substantial proportion of patients, further restricting accurate assessment of how surgical technique influences post-operative outcomes.

Conclusions

Based on the results of this population-based study of 121 pediatric and 179 adult HGBSG patients, the overall patient survival rate was very low, and the survival time of pediatric patients was significantly longer compared to adult patients. For HGBSG patients, the extent of resection may not have a significant effect on the prognosis. Chemotherapy could significantly improve patient prognosis. The effect of RT on patient prognosis requires additional studies.

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Footnote

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

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