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Exploration of the prognostic value of the resection of adult brainstem high-grade glioma based on competing risk model, propensity score matching, and conditional survival rate

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Abstract

Background Adult brainstem high-grade glioma (HGG) is a refractory disease, and the treatment strategy of resection is still controversial.

Objective To investigate the prognostic value of brainstem HGG resection in adults.

Methods We collected 126,386 samples from the Surveillance, Epidemiology, and End Results (SEER) database between 1998 and 2016, and screened 973 patients diagnosed with adult brainstem HGG, who were in turn, grouped into 899 cases of non-resections and 74 cases of resections. Competing risk models were used to screen independent prognostic factors. Propensity score matching (PSM) was performed to reduce the influence of confounding factors. Conditional survival (CS) rate was considered to evaluate the changes in overall survival (OS) and disease-specific survival (DSS) of patients with HGG over time.

Results Based on the competing risk model and PSM, univariate analysis showed that age $\geq$ 45 years and male gender were poor prognostic factors for adult brainstem HGG. No previous history of glioma was a beneficial factor. Multivariate analysis revealed only the absence of a history of glioma to be a favorable prognostic factor. Considering the CS rate of the resection group, after the patient had survived for 3 years, the OS and DSS remained unchanged at 100% during the fourth and fifth years, whereas in the non-resection group, the OS and DSS of the patients were 82% and 74%, respectively.

Conclusion Adult brainstem HGG resection has a poor prognosis in the early stage; however, patients have a potentially significant survival benefit after 3 years of survival.

Keywords Resection · High-grade glioma · Brainstem · Competing risk model

Introduction

Brainstem high-grade glioma (HGG), a rare and aggressive tumor, occurs mostly in children [1, 2] and rarely in adults, accounting for 1–2% of all adult cases of central nervous system tumors [3–5]. There are crucial nerve centers in the brainstem, such as the cardiovascular movement, respiratory, and swallowing centers. Due to its special anatomical location, surgical resection of brainstem HGG is difficult, making the treatment of brainstem HGG challenging [6, 7]. Studies have reported that the median survival rate of patients that underwent surgical intervention was only 11 months, and the overall survival (OS) rate was very low [8]. Moreover, the patient's age, gender, radiotherapy, chemotherapy, tumor size, and scope of surgical resection have been reported to be related to HGG prognosis [9–12]. However, OS in adult patients with HGG and related survival factors are still controversial.

Competing events of non-cancer death, such as heart disease, cerebrovascular disease, and influenza, do exist in patients with cancer [9]. Therefore, compared with the Cox survival analysis, the use of a competing risk model would facilitate accurate assessment of the association of predictor

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variables with outcome events. Moreover, confounding factors are often ubiquitous in observational research. The current study aimed to achieve "randomization" through propensity score matching (PSM) to control the influence of confounding factors on research conclusions. Additionally, we found the conditional survival rate (CS) of patients to change over time. CS can quantify the degree of improvement in the prognosis of patients over time, facilitating the adjustment of long-term follow-up strategies.

Exploration of the prognostic value of expanded resection of adult brainstem HGG based on a single medical center often leads to a small sample size and low statistical power [13–15]. The patient selection bias based on hospital-centered data is often greater than that based on the Surveillance, Epidemiology, and End Results (SEER) data. With the above considerations, the current study aimed to include adult patients with brainstem HGG through the SEER database, based on the competitive risk model, PSM, and CS, to study the prognostic value of resection of adult brainstem HGG.

Methods

Baseline data

We collected 126,386 samples from the SEER database. The criteria for inclusion and exclusion were as follows: the histological code of the International Classification of Diseases for Oncology Third Edition (ICD-O-3) was 9380/9401/9440/9441/9442/9451, the age was ≥18 years old, the tumor occurred in the brainstem, and 973 people finally met the criteria. The main variables in this study are non-resection (including no operation/biopsy) and resection (including subtotal resection/total resection). The included covariates were age, gender, race, marital status, diagnosis time, radiotherapy/chemotherapy, tumor size, etc. (Table 1). The SEER database is the authoritative and public source of information about cancer incidence, mortality, and survival rates in the USA. We used SEER-Stat software (version 8.3.5) to download patients' clinical data. The data are publicly available and do not involve privacy of patients; therefore, so no ethical review was required.

Competing risk model

In this study, we chose death from brainstem HGG as the end event while deaths caused by other factors were regarded as competing risk events. Cumulative incidence function (CIF) was used to estimate the cumulative occurrence probability of an outcome event, which was then used to process the survival data from multiple endpoints and competing risk events. The CIF for death due to brainstem HGG and other competing risk events was calculated and was grouped by age, race, chemotherapy, etc. Using cmprsk's R package, we drew a CIF curve for each variable, and performed Gray's test to identify the difference between brainstem HGG and non-brain stem HGG deaths in CIF. Subsequently, for multivariate competing risk survival analysis, we constructed the Fine-Gray proportional sub-distribution hazards model, and used cmprsk and risk regression to predict the potential risk factors of death from brainstem HGG and death from non-brain stem HGG events.

Propensity score matching

This study used PSM to balance the clinical data between the resection group and the non-resection group in the SEER cohort, including the following baseline characteristics: age, gender, race, marital status, time of diagnosis, chemotherapy, tumor size, and past history, to achieve the effect of retrospective randomization. First, we used the multiple logistic regression model to calculate the propensity score (PS) of each patient according to surgery type (resection and non-resection). Second, we used the MatchIt package in R software to analyze the data, set the caliper value to 0.02, and evaluated the effect according to the standardized mean difference (SMD) and P value.

Conditional survival rate

Conditional survival rate was estimated from clinical data according to the Berkson-Gage method, and its variance and confidence interval were derived according to the binomial distribution theory. This study mainly analyzed the binary variables of resection and non-resection, the overall survival rate (OS), and disease-specific survival rate (DSS) after 0, 1, 2, 3, 4, and 5 years following surgery. The probability that a patient who has survived x years after the initial treatment will survive for another n years was expressed as CS(OS/DSS)$(n) = [(OS/DSS)(x + n)]/[(OS/DSS)(x)]$.

Results

Patient baseline information

In this study, 973 eligible patients were divided into non-resection ($n = 899$) and resection ($n = 74$) groups (Table 1). Including 448 males (46%) and 525 females (54%), the median survival time of non-resection group was 17 months and that of resection group was 12 months; 629 people died (64.6%) and 344 people survived (35.4%) during the follow-up; 570 people (63.4%) died and 329 people (36.6%) survived the non-resection; 59 people (79.7%) died and 15 people survived (20.3%) the resection. However, of the 899

Table 1 Sample baseline data

Variables	Total (n = 973)	Non-resection (n = 899)	Resection (n = 74)	P
Survival, months median (Q1, Q3)	16 (6, 52)	17 (6, 54)	12 (7, 25.5)	0.15
Outcome, n (%)				0.007
Death	629 (64.6)	570 (63.4)	59 (79.7)	
Live	344 (35.4)	329 (36.6)	15 (20.3)	
Outcome 3, n (%)				0.01
Death from glioma	500 (51.4)	450 (50.1)	50 (67.6)	
Death from others	129 (13.3)	120 (13.3)	9 (12.2)	
Live	344 (35.4)	329 (36.6)	15 (20.3)	
Age, median (Q1, Q3)	45 (32, 58)	45 (32, 58)	43 (30.25, 56.75)	0.375
Sex, n (%)				0.703
Female	448 (46)	416 (46.3)	32 (43.2)	
Male	525 (54)	483 (53.7)	42 (56.8)	
Race, n (%)				0.439
Black	104 (10.7)	94 (10.5)	10 (13.5)	
Others	102 (10.5)	92 (10.2)	10 (13.5)	
White	767 (78.8)	713 (79.3)	54 (73)	
Marital, n (%)				0.262
Divorced/separated	89 (9.1)	84 (9.3)	5 (6.8)	
Married	505 (51.9)	460 (51.2)	45 (60.8)	
Single/unmarried	291 (29.9)	270 (30)	21 (28.4)	
Widowed/others	88 (9)	85 (9.5)	3 (4.1)	
Diagnosis, n (%)				0.95
1998–2004	231 (23.7)	213 (23.7)	18 (24.3)	
2005–2009	255 (26.2)	234 (26)	21 (28.4)	
2010–2012	184 (18.9)	170 (18.9)	14 (18.9)	
2013–2016	303 (31.1)	282 (31.4)	21 (28.4)	
Past history type, n (%)				<0.001
GBM	180 (18.5)	142 (15.8)	38 (51.4)	
Others	793 (81.5)	757 (84.2)	36 (48.6)	
Radiotherapy, n (%)				<0.001
No	864 (88.8)	845 (94)	19 (25.7)	
Yes	109 (11.2)	54 (6)	55 (74.3)	
Chemotherapy, n (%)				<0.001
No	614 (63.1)	583 (64.8)	31 (41.9)	
Yes	359 (36.9)	316 (35.2)	43 (58.1)	
Tumor size, n (%)				0.014
Size < 20 mm	151 (15.5)	147 (16.4)	4 (5.4)	
Size ≥ 20 mm	310 (31.9)	278 (30.9)	32 (43.2)	
Unknown	512 (52.6)	474 (52.7)	38 (51.4)	
Age, n (%)				0.696
Age < 45	485 (49.8)	446 (49.6)	39 (52.7)	
Age ≥ 45	488 (50.2)	453 (50.4)	35 (47.3)	
Surgery 2, n (%)				<0.001
Biopsy	63 (6.5)	63 (7)	0 (0)	
Gross total	22 (2.3)	0 (0)	22 (29.7)	
None	836 (85.9)	836 (93)	0 (0)	
Subtotal	52 (5.3)	0 (0)	52 (70.3)	

Outcome: binary variables (0: live; 1: death); outcome 3: three categorical variables (0: live; 1: death from glioma; 2: death from others); surgery 2: four categorical variables (0: none; 1: biopsy; 2: subtotal resection; 3: gross total resection)

people who underwent non-resection, 450 (50.1%) died due to glioma, whereas 120 (13.3%) did not die from glioma; similarly, 74 underwent resection, 50 (67.6%) died due to glioma, and 9 (12.2%) died from other events.

KM curve of patient OS and DSS

From the KM survival curve of OS (Fig. 1), according to the median survival time, the prognosis of age < 45 years (48 months) is better than that of age ≥ 45 years (12 months) ($P = 0.00$); no chemotherapy (35 months) was better than chemotherapy patients (16 months) ($P = 0.00$). Surgically, non-resection (23 months) was significantly better than

resection (13 months) ($P = 0.00$). Similarly, the KM curve of DSS is shown in Fig. A.1.

Cumulative risk curve for each variable

Among the 973 cases, 500 (51.4%) died of glioma and 129 (13.3%) died of other events. The cumulative risk of death from other events was statistically significant between age < 45 and ≥45 years ($P = 0.00$). There was no statistically significant difference across gender ($P = 0.21$), chemotherapy ($P = 0.32$), tumor size ($P = 0.1$), and resection ($P = 0.72$). However, the cumulative risk of death due to glioma was statistically significant across age ($P = 0.00$), gender ($P = 0.02$), chemotherapy ($P = 0.00$), tumor size (P
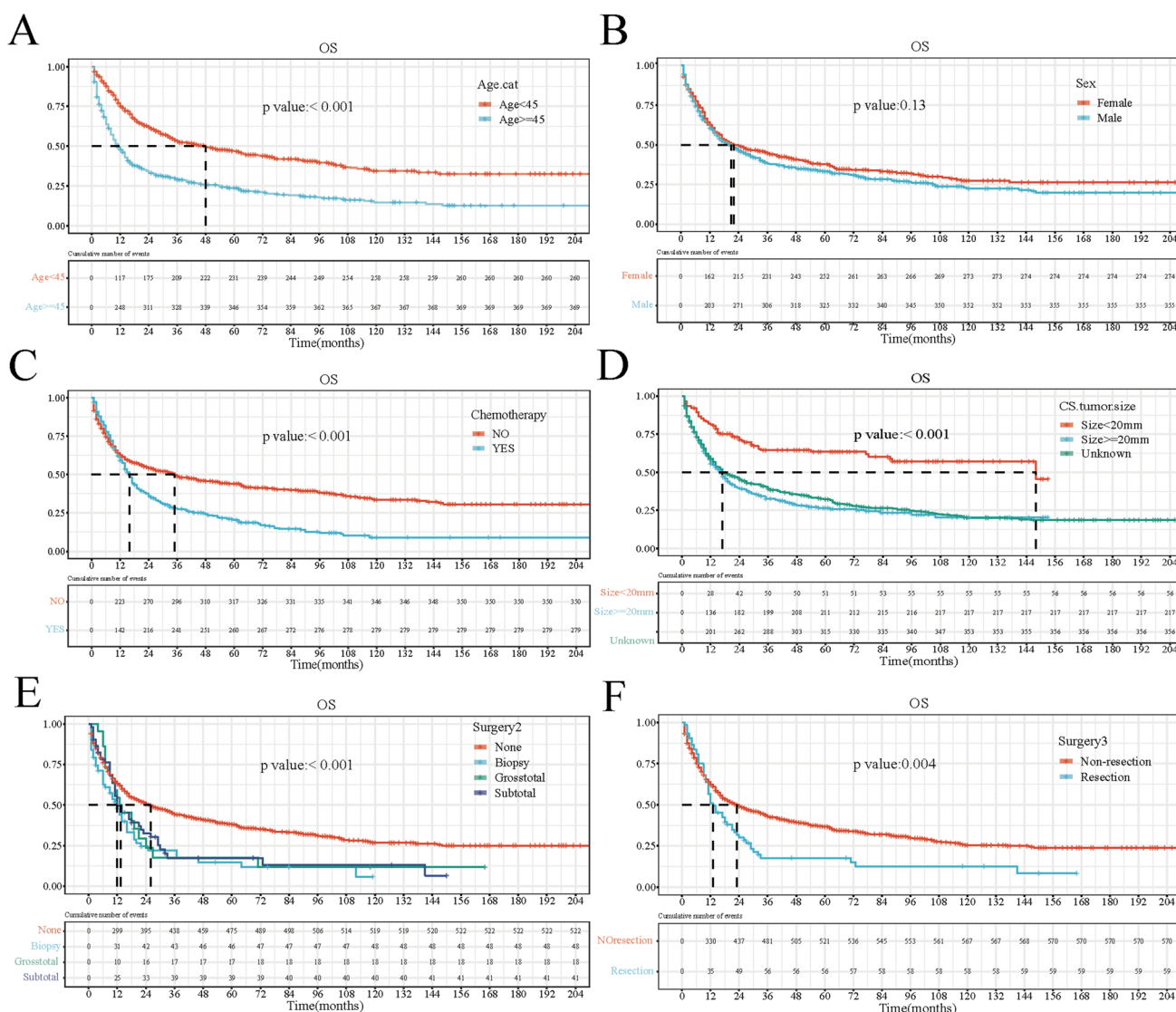

Fig. 1 Kaplan-Meier curves for overall survival (OS). **A** Age (<45 years or ≥45 years); **B** gender (male or female); **C** chemotherapy or not; **D** tumor size < 20 mm, ≥20 mm, or unknown; **E** surgery (no operation, biopsy, subtotal resection, or total resection); **F** surgical method (resection or non-resection)

= 0.00), surgical methods (*P* = 0.00), and resection (*P* = 0.00) (Fig. 2).

Screening factors affecting prognosis based on competitive risk model

Due to the impact of non-glioma deaths events, the Cox survival analysis (Table A.1.) would overestimate the incidence of events, so we introduced a competing risk model; multivariate analysis found age ≥ 45 years (HR = 1.57, 95% CI [1.31–1.90], *P* = 0.00), chemotherapeutic (HR = 1.48, 95% CI [1.2–1.83], *P* = 0.00), and tumor size ≥ 20 mm (HR = 1.81, 95% CI [1.29–2.53], *P* = 0.00) to still be unfavorable factors. Absence of a previous history of glioma (HR = 0.48, 95% CI [0.37–0.61], *P* = 0.00) was a favorable prognostic factor in adult brainstem HGG (Table 2).

Based on the competitive risk model, the factors that affect the prognosis after PSM

After PSM, 155 people were included in the analysis, of which 89 underwent non-resection and 66 underwent resection. Match results are unbiased (Table A.2, Fig. A.2). Based on the competing risk model, results showed that absence of a previous history of glioma (HR = 0.35, 95% CI [0.22–0.56], *P* = 0.00) was the only favorable factor for

brainstem HGG in adults. For others, such as age (HR = 1.51, 95% CI [0.99–2.34], *P* = 0.07), radiotherapy (HR = 1.05, 95% CI [0.59–1.86], *P* = 0.87), and tumor size (HR = 1.13, 95% CI [0.53–2.37], *P* = 0.75), the prognosis of adult brainstem HGG was not statistically different. It would be worth noting that resection (HR = 0.79, 95% CI [0.53–1.19], *P* = 0.26) was a favorable factor (HR < 1.0), although the results are still not statistically different (Table 3).

CS of resection after PSM

Based on conditional survival, after resection of adult brainstem HGG, patient survival rate remained stable during 3–5 years (Fig. 3A, C). In terms of OS, after 1 year of resection, the survival rate for 3–5 years was 39%; after 2 years of survival, the survival rate for 3–5 years was 72%. After 3 years of survival, the survival rate was 100% at 4–5 years (Fig. 3A). Also in terms of DSS, after 1 year of resection, the survival rate during the 3–5 years was 46%; after 2 years of survival, the survival rate during the 3–5 years was 78%. After 3 years of survival, the survival rate at 4–5 years was 100% (Fig. 3C). However, after non-resection, the survival rate decreased year by year (Fig. 3B, D). In particular, after 3 years of survival, the DSS in the fourth and fifth years were 82% and 74%, respectively (Fig. 3D); both were lower than
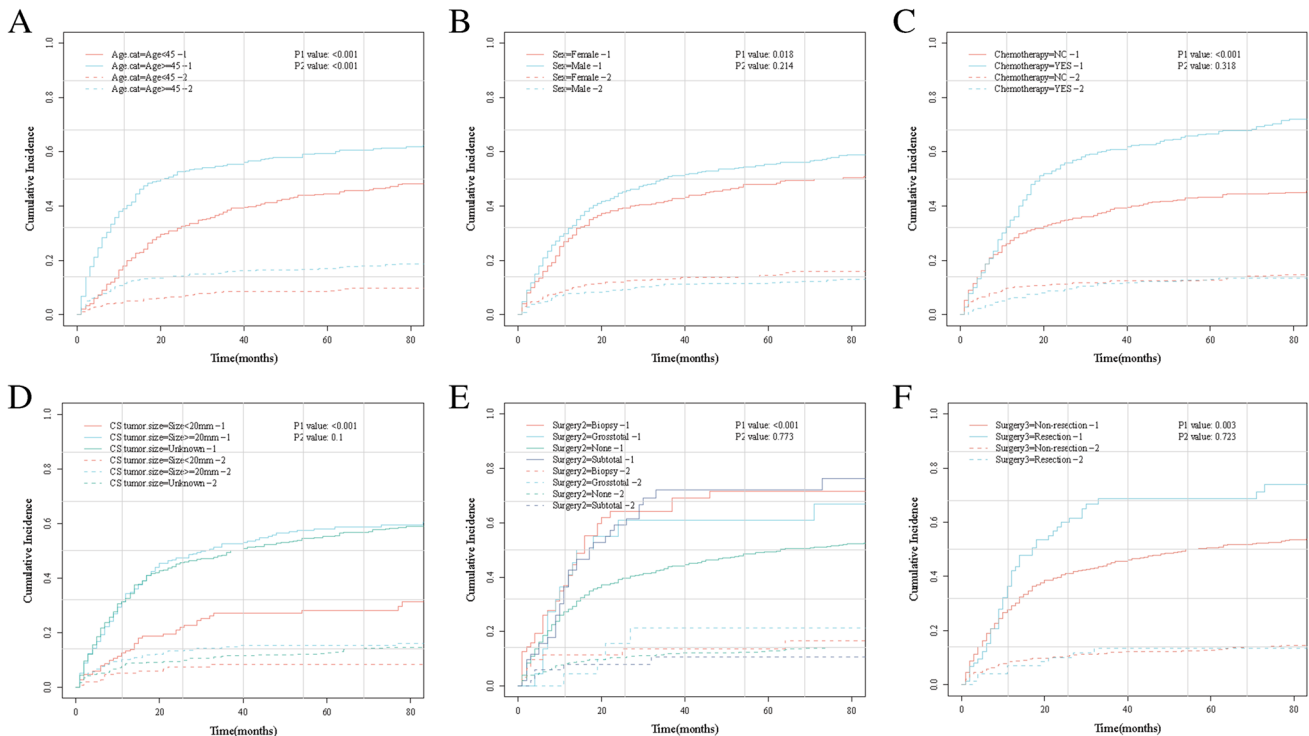

Fig. 2 Cumulative risk curve of each variable. **A** Age (<45 years or ≥45 years); **B** gender (male or female); **C** chemotherapy or not; **D** tumor size < 20 mm, ≥20 mm, or unknown; **E** surgical methods (no operation, biopsy, subtotal resection, and total resection); **F** surgical methods (resection or non-resection)

Table 2 Single-factor and multi-factor analyses based on competing risk model

Characteristics	n (%)	Univariate analysis		Multivariate analysis	
		SHR (95% CI)	P value	SHR (95% CI)	P value
Age (ref = age < 45)					
Age ≥ 45	488 (50.2)	1.647 (1.386–1.958)	<0.001	1.573 (1.305–1.895)	<0.001
Sex (ref = female)					
Male	525 (54)	1.238 (1.039–1.475)	0.017	1.157 (0.964–1.388)	0.12
Race (ref = White)					
Black	104 (10.7)	0.88 (0.66–1.175)	0.39	0.967 (0.709–1.319)	0.83
Others	102 (10.5)	0.815 (0.606–1.096)	0.18	0.778 (0.573–1.056)	0.11
Marital (ref = married)					
Divorced/separated	89 (9.1)	0.962 (0.696–1.329)	0.81	1.073 (0.767–1.502)	0.68
Single/unmarried	291 (29.9)	0.815 (0.669–0.993)	0.043	1.126 (0.909–1.395)	0.28
Widowed/others	88 (9)	0.905 (0.645–1.27)	0.56	1.075 (0.756–1.529)	0.69
Diagnosis (ref = 1998~2004)					
2005~2009	255 (26.2)	0.954 (0.767–1.188)	0.68	0.996 (0.771–1.288)	0.98
2010~2012	184 (18.9)	0.833 (0.646–1.074)	0.16	0.845 (0.621–1.149)	0.28
2013~2016	303 (31.1)	0.631 (0.49–0.812)	<0.001	0.675 (0.498–0.916)	0.011
Past history type (ref = GBM)					
Others	793 (81.5)	0.369 (0.302–0.451)	<0.001	0.476 (0.372–0.609)	<0.001
Radiotherapy (ref = no)					
Yes	109 (11.2)	1.864 (1.498–2.32)	<0.001	1.145 (0.712–1.843)	0.58
Chemotherapy (ref = no)					
Yes	359 (36.9)	1.793 (1.51–2.13)	<0.001	1.484 (1.2–1.834)	<0.001
Tumor size (ref = size < 20 mm)					
Size ≥ 20 mm	310 (31.9)	2.389 (1.725–3.308)	<0.001	1.806 (1.291–2.526)	<0.001
Unknown	512 (52.6)	2.362 (1.729–3.226)	<0.001	1.96 (1.4–2.742)	<0.001
Surgery 2 (ref = none)					
Biopsy	63 (6.5)	1.685 (1.221–2.325)	0.002	1.012 (0.602–1.7)	0.96
Gross total	22 (2.3)	1.413 (0.843–2.37)	0.19	0.698 (0.367–1.328)	0.27
Subtotal	52 (5.3)	1.701 (1.257–2.302)	0.001	1.029 (0.617–1.716)	0.91

SHR, subdistribution hazard ratio

the DSS in the same period after resection (100%, 100%) (Fig. 3C).

Discussion

Background on the treatment of adult brainstem HGG

Adult brainstem HGG are highly malignant and associated with a low survival rate; they have always been regarded as the most difficult to treat [16]. They mostly manifest as dizziness, nausea, and vomiting, along with symptoms such as limb numbness, facial paralysis, and dysphagia [17–19]. With the development of neuronavigation [20, 21], electrophysiological monitoring and diffusion-weighted magnetic resonance imaging technology [22], convection-enhanced separation and application of gamma knife and cyberknife [23–25], histological diagnosis [26], continuous upgradation

of radiotherapy, and that of anti-angiogenesis, monoclonal antibodies, and other chemotherapeutic drugs [27, 28], the treatment of adult brainstem HGG has become more feasible. However, the overall survival of patients with adult brainstem HGG and related survival factors are still unclear. Our current study revealed the following: first, age, tumor size, and previous history of glioma are closely related to adult brainstem HGG. Second, in terms of treatment measures, there is no significant statistical difference in improving the overall survival rate of patients with radiotherapy and chemotherapy. Third, and most importantly, for adults with brainstem HGG resection, patients have a significant survival benefit after 3 years of survival.

The impact of competing events on traditional survival analysis

If there are more than 10% competing events, such as heart disease and car accidents in cancer patients, the use of Cox

Table 3 Based on the competing risk model, after propensity score matching, results of single-factor and multi-factor analyses regarding resection

Characteristics	n (%)	Univariate analysis		Multivariate analysis	
		SHR (95% CI)	P value	SHR (95% CI)	P value
Age (ref = age < 45)					
Age ≥ 45	74 (47.7)	1.892 (1.283–2.791)	0.001	1.505 (0.968–2.341)	0.069
Sex (ref = female)					
Male	84 (54.2)	1.535 (1.013–2.326)	0.043	1.11 (0.628–1.963)	0.72
Race (ref = Black)					
Others	18 (11.6)	0.857 (0.364–2.021)	0.72	0.718 (0.235–2.193)	0.56
White	121 (78.1)	1.17 (0.588–2.329)	0.65	0.97 (0.439–2.143)	0.94
Marital (ref = married)					
Divorced/separated	9 (5.8)	0.854 (0.396–1.842)	0.69	0.984 (0.392–2.468)	0.97
Single/unmarried	38 (24.5)	0.785 (0.497–1.239)	0.3	1.125 (0.668–1.895)	0.66
Widowed/others	6 (3.9)	0.938 (0.262–3.36)	0.92	0.879 (0.244–3.161)	0.84
Diagnosis (ref = 1998~2004)					
2005~2009	39 (25.2)	0.8 (0.491–1.303)	0.37	0.873 (0.469–1.625)	0.67
2010~2012	28 (18.1)	0.861 (0.506–1.464)	0.58	1.031 (0.466–2.281)	0.94
2013~2016	46 (29.7)	0.609 (0.338–1.098)	0.099	0.686 (0.292–1.607)	0.39
Past history type (ref = GBM)					
Others	81 (52.3)	0.336 (0.228–0.497)	<0.001	0.347 (0.215–0.561)	<0.001
Radiotherapy (ref = no)					
Yes	98 (63.2)	1.407 (0.891–2.223)	0.14	1.049 (0.592–1.861)	0.87
Chemotherapy (ref = no)					
Yes	72 (46.5)	1.235 (0.831–1.836)	0.3	0.877 (0.475–1.618)	0.67
Tumor size (ref = size < 20 mm)					
Size ≥ 20 mm	63 (40.6)	1.474 (0.773–2.812)	0.24	1.126 (0.534–2.372)	0.75
Unknown	84 (54.2)	1.375 (0.734–2.577)	0.32	1.115 (0.516–2.411)	0.78
Surgery 3 (ref = non-resection)					
Resection	66 (42.6)	0.966 (0.657–1.419)	0.86	0.791 (0.527–1.188)	0.26

SHR, subdistribution hazard ratio

survival analysis may lead to an incorrect estimation. In this data, we found 20.51% (129/629) of the deaths to be due to non-HGG causes. Therefore, use of a competing risk model would facilitate the accurate assessment of the association between the surgical approach and the prognosis of HGG; multivariate analysis found age ≥ 45 years, chemotherapy, and tumor diameter ≥ 20 mm to be poor prognostic factors. This was basically consistent with the results of Dey et al. [29]. At the same time, compared with low-grade glioma, the more aggressive the tumor, the worse the prognosis of patients with brainstem glioma [30, 31]. Furthermore, factors associated with improved 5-year overall survival included female gender, higher income, and fewer comorbidities [32].

### Effects of radiotherapy on adult brainstem HGG

Radiotherapy is one of the main treatment methods for tumors. However, studies have reported that radiotherapy is significantly related to an increased risk of secondary malignant tumors [33]. For sub-ependymal tumors, radiotherapy

had no statistically significant impact on overall survival [34]. Nevertheless, a study by Reithmeier et al. [35] suggested that postoperative radiotherapy is the cornerstone of treatment and can reduce the risk of death by 0.4 times. Compared with radiotherapy alone, postoperative radiotherapy combined with chemotherapy has a significant survival benefit for HGG patients with WHO grade IV (HR: 0.46, 95% CI [0.28–0.76], $P = 0.00$) [36]. For HGG of the pons, radiotherapy remains the standard treatment, although it only provides a survival advantage of 3 to 4 months [37]. But, our study showed that radiotherapy (HR = 1.05, 95% CI [0.59–1.86], $P = 0.87$) had no statistically significant effect on the prognosis of adult brainstem HGG. Research by Hu et al. [38] also confirmed the same.

Effect of resection on adult brainstem HGG

Whether an adult brainstem HGG would need surgery and the scope of surgical resection have remained controversial. Our study found that resection of adult brainstem HGG has a higher risk of early death, although a stable period is reached

Fig. 3 The CS of resection and non-resection after PSM. **A** Overall conditional survival rate after resection; **B** overall conditional survival rate after non-resection; **C** disease-specific conditional survival rate after resection; **D** disease-specific conditional survival rate after non-resection. PSM, propensity score matching; CS, conditional survival
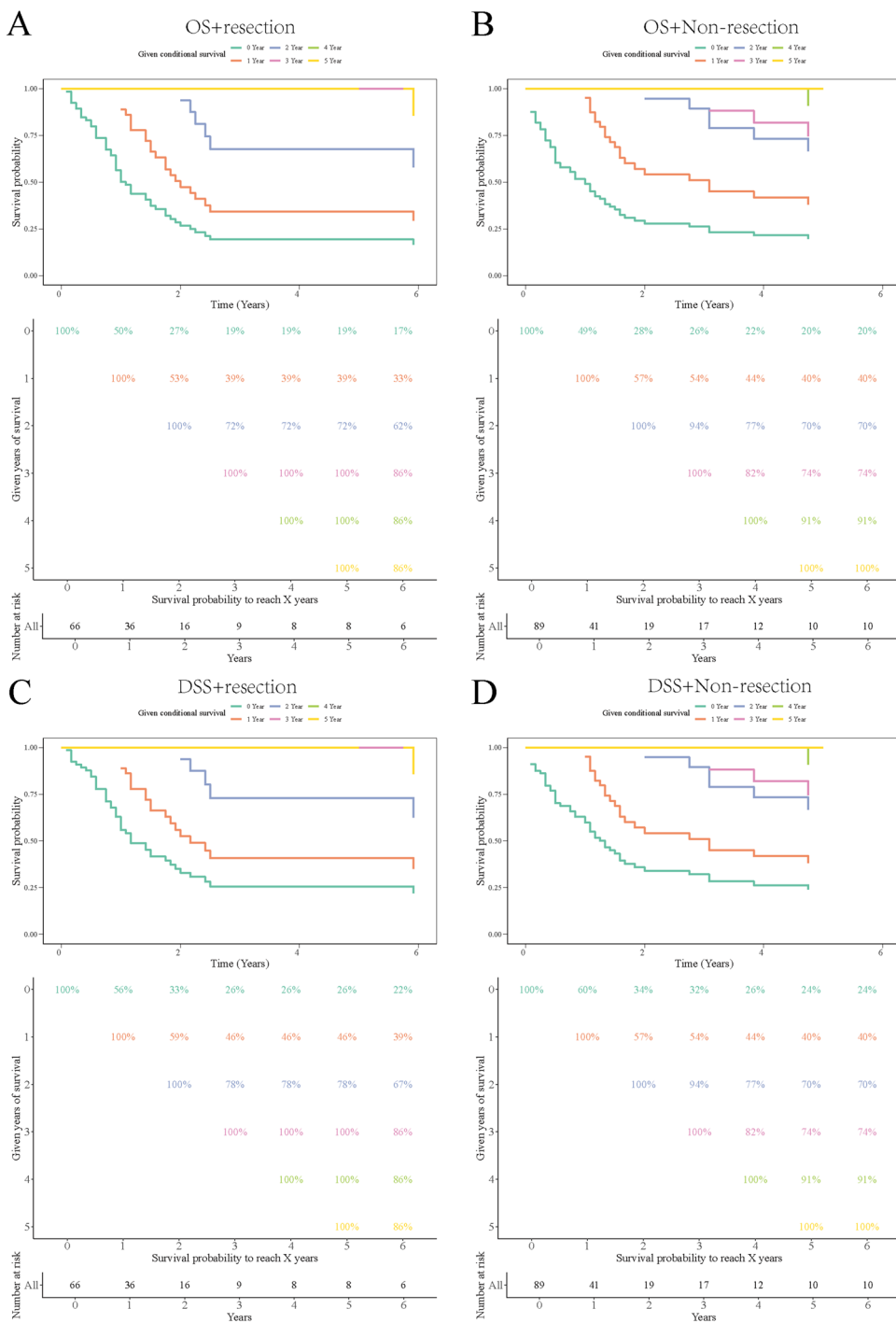
after 3 years of survival. In a regression analysis conducted by Majchrzak et al. [39] on 47 adult patients who had undergone surgery for brainstem glioma, the average progression-free survival time for malignant brainstem glioma was 14 months. While the average survival time was 20 months, partial resection of diffuse brainstem glioma did not extend the average survival time by more than 5 years. Rigamonti et al. [40] believed that tumor grade is the only factor that has a statistically significant impact on survival time ($P =$

0.00), whereas younger age, better physical status, and resection surgery showed prolonged survival. However, owing to the special brainstem site, surgery itself is highly risky, and the incidence of complications, such as postoperative bleeding, infection, edema, cerebral hernia, and respiratory insufficiency, is high (36.4%) [35, 41]. If there is a clear boundary between the tumor, normal cerebellum, and tentorium in imaging results, the tumor can be biopsied, and its exogenous part, the brainstem surface, and the accessible

part can be roughly/completely removed. Total resection is not possible, since high-grade tumors have strong invasiveness [42].

Limitations and strengths

First, it is a retrospective study with inherent limitations. With modern medical technology development, the survival rate of patients with adult brainstem HGG will also change. Secondly, the SEER database lacked detailed information about the patient's physical condition, such as family history and specific parts of tumor (midbrain, pons, or medulla oblongata), especially performance status (PS), is often positively correlated with the prognosis of patients. Thirdly, the database still lacks data of early postoperative mortality, which is of great significance in evaluating the safety of resection. Nevertheless, considering the huge sample size provided by the SEER database, the statistical results would still be very meaningful. In addition, the CS could be incorporated as a factor of survival time, which could assess the prognosis in survivors with HGG more accurately over time.

Conclusion

The purpose of this study was to investigate the prognostic value of brainstem HGG resection in adults using competing risk models, PSM, and CS based on the SEER database. The data show that the DSS of adult brainstem HGG is 82% and 74% in 1–2 years after non-resection survival for 3 years, but there is a stable survival rate (100%) in 1–2 years after 3 years of resection survival, which will be more effective in helping young patients cope with future uncertainty. Therefore, these data support neurosurgeons to perform maximal safe resection of adult brainstem HGG when available.

Declarations

Ethical approval This study was approved by the Ethics Committee of the First Affiliated Hospital of Xinxiang Medical College. The clinical study registration number is: EC-021-159.

Conflict of interest The authors declare no competing interests.

References

1. Lesniak MS, Klem JM, Weingart J, Carson BS Sr (2003) Surgical outcome following resection of contrast-enhanced pediatric brainstem gliomas. Pediatr Neurosurg 39(6):314–322
2. Yang T, Temkin N, Barber J et al (2013) Gross total resection correlates with long-term survival in pediatric patients with glioblastoma. World Neurosurg 79:537–544
3. Ostrom QT, Bauchet L, Davis FG et al (2014) The epidemiology of glioma in adults: a "state of the science" review. Neuro-oncology 16(7):896–913
4. Guillamo J, Doz F, Delattre J (2001) Brain stem gliomas. Curr Opin Neurol 14(6):711–715
5. Selvapandian S, Rajshekhar V, Chandy M (1999) Brainstem glioma: comparative study of clinico-radiological presentation, pathology and outcome in children and adults. Acta Neurochir 141(7):721–726 discussion 726-727
6. Eisele SC, Reardon DA (2016) Adult brainstem gliomas. Cancer. 122(18):2799–2809
7. Grimm S, Chamberlain M (2013) Brainstem glioma: a review. Curr Neurol Neurosci Rep 13(5):346
8. Doyle J, Khalafallah AM. Association between extent of resection on survival in adult brainstem high-grade glioma patients. 2019;145(3):479-486.
9. Best B, Nguyen HS, Doan NB et al (2019) Causes of death in glioblastoma: insights from the SEER database. J Neurosurg Sci 63(2):121–126
10. Kesari S, Kim RS, Markos V, Drappatz J, Wen PY, Pruitt AA (2008) Prognostic factors in adult brainstem gliomas: a multicenter, retrospective analysis of 101 cases. J Neuro-Oncol 88(2):175–183
11. Devaux BC, O'Fallon JR, Kelly PJ (1993) Resection, biopsy, and survival in malignant glial neoplasms. A retrospective study of clinical parameters, therapy, and outcome. J Neurosurg 78(5):767–775
12. Nishio S, Fukui M, Tateishi J (1988) Brain stem gliomas: a clinicopathological analysis of 23 histologically proven cases. J Neuro-Oncol 6(3):245–250
13. Theeler BJ, Ellezam B, Melguizo-Gavilanes I et al (2015) Adult brainstem gliomas: correlation of clinical and molecular features. J Neurol Sci 353(1-2):92–97
14. Guillamo JS, Monjour A, Taillandier L et al (2001) Brainstem gliomas in adults: prognostic factors and classification. Brain J Neurol 124(Pt 12):2528–2539
15. Salmaggi A, Fariselli L, Milanesi I et al (2008) Natural history and management of brainstem gliomas in adults. A retrospective Italian study. J Neurol 255(2):171–177
16. Tasic G, Repac N, Nikolic I et al (2017) Adult brainstem gliomas: retrospective analysis of 51 patients. Turkish Neurosurg 27(4):558–562
17. Shuangshoti S, Shuangshoti S (1996) Primary diffuse leptomeningeal glioblastoma multiforme of brainstem and spinal cord clinically mimicking meningitis: case report and review of literature. Journal of the Medical Association of Thailand =. Chotmaihet thangphaet 79(6):403–408

18. Turki S, Mardassi A, Nefzaoui S, Hachicha A, Rhouma S (2016) Brain stem glioma: a rare cause of central vertigo in adults. Pan Afr Med J 25:135

19. Packer R, Allen J, Nielsen S, Petito C, Deck M, Jereb B (1983) Brainstem glioma: clinical manifestations of meningeal gliomatosis. Ann Neurol 14(2):177–182

20. Sang S, Wanggou S, Wang Z et al (2018) Clinical long-term follow-up evaluation of functional neuronavigation in adult cerebral gliomas. World Neurosurg 119:e262–e271

21. Khalid M, Allen J, King N et al (2017) Characterization of pyramidal tract shift in high-grade glioma resection. World Neurosurg 107:612–622

22. Carceller F, Jerome NP, Fowkes LA et al (2019) Post-radiotherapy apparent diffusion coefficient (ADC) in children and young adults with high-grade gliomas and diffuse intrinsic pontine gliomas. Pediatr Hematol Oncol 36(2):103–112

23. Turek G, Pasterski T, Bankiewicz K, Dzierzęcki S, Ząbek M (2020) Current strategies for the treatment of malignant gliomas - experience of the Department of Neurosurgery, Brodno Masovian Hospital in Warsaw. Polski przeglad chirurgiczny 92(5):1–5

24. Gamma Knife surgery for focal brainstem gliomas (2007) J Neurosurg 106(1):6–7

25. Zhang J, Liu Q, Yuan Z, Zhao L, Wang X, Wang P (2019) Clinical efficacy of CyberKnife radiosurgery for adult brainstem glioma: 10 years experience at Tianjin CyberKnife Center and review of the literature. Front Oncol 9:257

26. Dellaretti M, Câmara B, Ferreira P, da Silva JJ, Arantes R (2020) Impact of histological diagnosis on the treatment of atypical brainstem lesions. Sci Rep 10(1):11065

27. Moriya S, Ohba S, Adachi K et al (2018) A retrospective study of bevacizumab for treatment of brainstem glioma with malignant features. J Clin Neurosci 47:228–233

28. Ahir BK, Engelhard HH, Lakka SS (2020) Tumor development and angiogenesis in adult brain tumor. Glioblastoma 57(5):2461–2478

29. Dey M, Lin Y, Melkonian S, Lam S (2014) Prognostic factors and survival in primary adult high grade brainstem astrocytoma: a population based study from 1973-2008. J Clin Neurosci 21(8):1298–1303

30. Ueoka D, Nogueira J, Campos J, Maranhão Filho P, Ferman S, Lima M (2009) Brainstem gliomas—retrospective analysis of 86 patients. J Neurol Sci 281:20–23

31. Anami S, Fukai J, Hama M et al (2021) Brainstem infiltration predicts survival in patients with high-grade gliomas treated with chemoradiotherapy. Anticancer Res 41(5):2583–2589

32. Cantrell J, Waddle M, Rotman M et al (2019) Progress toward long-term survivors of glioblastoma. Mayo Clin Proc 94(7):1278–1286

33. Li X, Li Y, Cao Y, et al. (2017) Risk of subsequent cancer among pediatric, adult and elderly patients following a primary diagnosis of glioblastoma multiforme: a population-based study of the SEER database 127(11):1005-1011.

34. Nguyen HS, Doan N, Gelsomino M, Shabani S (2017) Intracranial subependymoma: a SEER analysis 2004-2013. World Neurosurg 101:599–605

35. Reithmeier T, Kuzeawu A, Hentschel B, Loeffler M, Trippel M, Nikkhah G (2014) Retrospective analysis of 104 histologically proven adult brainstem gliomas: clinical symptoms, therapeutic approaches and prognostic factors. BMC Cancer 14:115

36. Kerezoudis P, Goyal A, Lu VM et al (2020) The role of radiation and chemotherapy in adult patients with high-grade brainstem gliomas: results from the National Cancer Database. J Neuro-Oncol 146(2):303–310

37. Hoffman L, Veldhuijzen van Zanten S, Colditz N et al (2018) Clinical, radiologic, pathologic, and molecular characteristics of long-term survivors of diffuse intrinsic pontine glioma (DIPG): a collaborative report from the International and European Society for Pediatric Oncology DIPG Registries. J Clinl Oncol 36(19):1963–1972

38. Hu X, Fang Y, Hui X, Jv Y, You C. Radiotherapy for diffuse brainstem glioma in children and young adults. Cochrane Database Syst Rev 2016(6):Cd010439.

39. Majchrzak K, Bobek-Billewicz B, Hebda A, Majchrzak H, Ładziński P, Krawczyk L (2018) Surgical treatment and prognosis of adult patients with brainstem gliomas. Neurol Neurochir Pol 52(5):623–633

40. Rigamonti A, Simonetti G, Silvani A et al (2021) Adult brainstem glioma: a multicentre retrospective analysis of 47 Italian patients. Neurol Sci 42(5):1879–1886

41. Silbergeld D, Rostomily R, Alvord E (1991) The cause of death in patients with glioblastoma is multifactorial: clinical factors and autopsy findings in 117 cases of supratentorial glioblastoma in adults. J Neuro-Oncol 10(2):179–185

42. Drumm M, Dixit K, Grimm S et al (2020) Extensive brainstem infiltration, not mass effect, is a common feature of end-stage cerebral glioblastomas. Neuro-oncology. 22(4):470–479