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Adult Cerebellar Glioblastoma: Understanding Survival and Prognostic Factors Using a Population-Based Database from 1973 to 2009

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Abstract

OBJECTIVE—Glioblastoma (GB) is rarely found in the cerebellum. Because of its rarity, it is poorly understood if cerebellar GB (CGB) behaves similarly to supratentorial GB. Studies have been limited to case reports and small case series. A better understanding of CGB may help guide treatment strategies.

METHODS—Surveillance, Epidemiology and End Results database was analyzed from 1973 to 2009 for all adult patients with GB located in the cerebellum. Stepwise multivariate proportional hazards regression analyses were used to identify factors independently associated with survival.

RESULTS—Two hundred eight (0.9%) patients with CGB were identified from 23,329 GB patients with known locality. The mean age was 58 years. Median survival was 8 months, with 1-, 2- and 5-year survival rates of 21%, 13%, and 2%. When compared to supratentorial GB, CGB occurred in younger patients (58 ± 16 vs. 61 ± 13 years, $P = 0.001$), less commonly in Whites (85.6% vs. 91.3%, $P = 0.005$), and were smaller (3.7 ± 1.1 vs. 4.5 ± 1.7 cm, $P = 0.001$). A cerebellar location independently predicted poorer survival when compared to other GB locations ($P = 0.048$). In multivariate analysis for patients with CGB, younger age ($P < 0.001$), Asian or Pacific Islander race ($P = 0.046$), and radiation therapy ($P < 0.001$) were independently associated with prolonged survival.

CONCLUSION—CGBs are difficult to analyze using institutional series because of their rarity. This study shows they are clinically different from supratentorial GB. Among patients with CGB, radiation therapy may prolong survival. This may help guide treatment strategies aimed at prolonging survival for patients with these extremely rare lesions.

Keywords

Cerebellar; Cerebellum; Glioblastoma; Glioma; SEER; Survival

INTRODUCTION

Glioblastoma (GB) persists as the most common primary brain neoplasm in adults (6, 10). In addition, several reports have suggested an increasing trend in incidence rates (12, 23, 37). GB is currently recognized as one of the most aggressive types of brain tumor, and unfortunately remains an incurable disease (45). This malignancy rarely arises from the cerebellum, where reports are limited to case reports and small case series (3, 4, 11, 16, 18, 20, 22, 24–26, 33, 34, 36, 40, 44, 51). Although prognostic factors in supratentorial GBs (STGBs) have been well established (29–31), these variables are not well characterized for cerebellar GB (CGB) because of their rarity (3, 4, 11, 16, 18, 20, 22, 24–26, 33, 34, 36, 40, 44, 51). It remains unknown if these tumors behave clinically like their supratentorial counterparts, and if the factors associated with survival for STGBs are the same for CGBs. The goals of this study therefore are to identify and analyze factors associated with survival using data from the population-based Surveillance, Epidemiology, and End Results (SEER) database between 1973 and 2009.

MATERIALS AND METHODS

Study Population

The SEER program of the National Cancer Institute includes population-based cancer registries from 20 selected geographic areas in the United States, covering approximately 28% of the U.S. population. Data were obtained from the SEER Program for the years 1973 through 2009. Cases were identified using both the site and histologic codes of the International Classification of Disease for Oncology (ICD-O-3), third edition (19). Only adult cases (≥ 18 years) classified as GB (ICD-O-3: 9440/3) were included in the current study. Diagnoses of Gliosarcoma and Giant Cell Glioblastoma were excluded from the present study. Inclusion criteria required cases to have been actively followed up, not previously diagnosed with a primary cancer, and to have pathologic confirmation of the GB diagnosis. From the 32,531 GBs that met the criteria above, a total of 23,329 cases had a specified anatomic tumor location of which 208 (0.9%) were located primarily in the cerebellum (C716). To allow proper comparison of CGBs with their supratentorial counterparts, the STGBs were defined as tumors occurring in the frontal, temporal, parietal, and occipital lobe (C711, C712, C713, and C714). Baseline patient, tumor, and treatment characteristics, including age at diagnosis, sex, race, decade of diagnosis, tumor extension and size, extent of resection, and radiation were evaluated. Because this data set is publicly available, we received exempt review status from our institutional review board.

Surgical Procedure Data

An important use of the SEER program is to evaluate the use and outcome of surgical treatment. According to SEER guidelines, trained coders have classified surgical procedures using the best source documents available. These guidelines suggest coders to use the face sheet and/or operative notes to determine the appropriate classification code. Operative procedure codes for cases diagnosed in 1998 and later were updated and classified in the SEER Program Code Manual using the American College of Surgeons Commission on

Cancer's Facility Oncology Registry Data Standards surgery codes (1). In order to review all cases from the pre- and post-1998 revisions, surgical procedures of all years were merged into five categories: no surgery, biopsy, partial resection, gross total resection (GTR), surgery not otherwise specified, and surgery unknown.

Survival and Statistical Analysis

All analyses were conducted using IBM SPSS Statistics version 20.0.0 (IBM Corporation, Armonk, New York, USA). Summary data were presented as mean $\pm$ standard deviation for parametric data and as median (interquartile range) for nonparametric data. Percentages were compared via Fisher exact test for categorical variables and Student *t* test for continuous variables. Survival was plotted using the Kaplan-Meier method, and the log-rank test was used to compare survival differences. Stepwise multivariate proportional hazards regression analyses were used to identify factors independently associated with survival. Values with $P < 0.05$ were considered statistically significant.

RESULTS

Patient Characteristics

From the 23,329 patients diagnosed with GB, 208 cases (0.9%) were identified in the cerebellum (Table 1). Mean $\pm$ standard deviation age was 58 ± 16 years for patients with CGB, with a range from 19 to 88 years. There was a slight predominance of males (58.7%). CGB was mostly diagnosed among Whites (85.6%). Mean tumor size was 3.7 ± 1.1 cm. Furthermore, 81.7% of the patients were coded to have received a surgical intervention, where 28.8% underwent a GTR, 26.0% a partial resection, and 12.5% a biopsy only. Overall, 14.9% of the patients had no cancer-directed surgical intervention performed. Even though no surgical interventions were performed in this latter group, all cases were coded to be actively followed up during the course of disease, and pathologic confirmation of the diagnosis GB was established post mortem. In addition, the great majority of CGB patients received radiotherapy (72.1%). The median (interquartile range) overall survival among patients with CGB was 8 (6.2–9.8) months, with 1-, 2-, and 5-year survival rates of 21%, 13%, and 2%, respectively (Figure 1).

Survival Analysis of Cerebellar Glioblastoma

A median overall survival of 8 months was observed in our entire cohort of CGBs (Figure 1). These 208 cases demonstrated 1-, 2-, and 5-year survival rates of 21%, 13%, and 2%, respectively. In subgroup analyses of age, the median survival for patients in the <40, 40–49, 50–59, 60–69, and 70 groups was 17, 23, 10, 4, and 4 months, respectively. Only patients in the 40–49 age group was statistically indifferent from the <40 group (Figure 2). The cohort of male patients had a median survival of 6 months versus 9 months for female patients ($P = 0.179$). For race, the median survival for White, Black, and Asians or Pacific Islanders was 8, 11, and 16 months. In log-rank analyses, however, there were no significant differences between Asians or Pacific Islanders and Whites ($P = 0.44$) and Blacks ($P = 0.95$). In regards to extent of resection, cases in the no-surgery group had a 4-month median survival, whereas patients in the biopsy, partial resection, and GTR groups had 7, 6, and 16 months, respectively ($P = 0.771$, $P = 0.392$, and $P = 0.003$, on log-rank analysis compared

with the no-surgery group) (Figure 3). Furthermore, the data show markedly prolonged survival ($P < 0.001$) in patients undergoing radiation versus no radiation of 11 months versus 2 months, respectively (Figure 4).

Factors Independently Associated with Survival for Patients with Cerebellar Glioblastoma

For patients with CGB, age at diagnosis, sex, race, decade of diagnosis, extent of resection, and radiotherapy were considered as potential prognostic variables and were included in the initial univariate and multivariate models. Tumor size was not included in these analyses because of its rarity in recording. The results of the univariate analysis identified age at diagnosis ($P < 0.001$), extent of resection ($P = 0.019$), and radiotherapy ($P < 0.001$) as being associated with survival (Table 2). Decade of diagnosis, gender, and race were not significantly associated with survival. In the forward stepwise multivariate proportional hazard regression analysis, age at diagnosis ($P < 0.001$), Asian or Pacific Islander race ($P = 0.016$), and radiotherapy ($P < 0.001$) were identified as significant predictors of CGB survival (Table 3).

Cerebellar Versus Supratentorial Glioblastoma

When comparing patients with CGB versus STGB, patients with CGB were younger (58 ± 16 vs. 61 ± 13 years, $P < 0.001$), occurred less commonly in Whites (85.6% vs. 91.3%, $P = 0.030$), and had smaller tumor sizes (3.7 ± 1.1 vs. 4.5 ± 1.7 cm, $P < 0.001$). There were no differences between patients with CGB and STGB in regards to distribution of gender ($P = 0.87$), decade of diagnosis ($P = 0.76$), extent of resection ($P = 0.76$), and radiation ($P = 0.11$) (Table 1). The association between cerebellar location and survival was further assessed using multivariate proportional regression analysis to compare patients with both STGB and CGB, after controlling for (potential) factors associated with survival (age, sex, decades of diagnosis, extent of resection, and radiation). Cerebellar location was independently associated with improved survival (HR [95% CI]: 0.847 [0.718–0.999], $P = 0.048$). The median survival for patients with CGB was 8 months, whereas it was 9 months for patients with STGB ($P = 0.14$) (Figure 1). The 1-, 2-, and 5-year survival of STGB demonstrated rates of 12%, 7%, and 1%, versus 21%, 13%, and 2% in CGB. However, only after adjusting for the stratification variables, there was evidence of a survival difference between the two groups in favor of CGB ($P = 0.048$).

DISCUSSION

In this study, using a national database, there were 208 adult patients with CGB. This is the largest series of CGB to date. Patients with CGB were typically younger, had smaller average tumor sizes, and less typically occurred in Whites as compared to patients with supratentorial lesions. More important, a cerebellar location was independently associated with prolonged survival for patients with GB. For patients with CGB, the median survival was 8 months. Among patients with CGB, the factors that were independently associated with prolonged survival were younger age, radiotherapy, and Asian/Pacific Islander race.

It remains unknown if CGBs are genetically identical to their supratentorial counterparts, and thus have similar clinical outcomes. Stark et al. suggest that clinically silent STGB may

give rise to CGB via dissemination mediated by the flow of cerebrospinal fluid; however, others hypothesize that CGB develop de novo or evolve from lower-grade gliomas (27, 38). Some have even suggested that cerebellar astrocytes may have a lesser tendency to anaplasia, thus occurring in fewer numbers (17). Regardless of its origin, CGB remains relatively rare. Because of its rarity, the biologic behavior of CGB has not yet been fully characterized as compared to STGB (47, 50). Utsuki et al. performed a genetic evaluation of 4 patients with CGB, and all were immunopositive for p53, epidermal growth factor receptor, and isocitrate dehydrogenase 1, which may be different from supratentorial lesions (47). Despite these findings, the clinical behavior of CGB remains poorly understood. This lack of understanding has made many assume that CGBs are equivalent to STGBs. Patients with CGB are treated similarly to their supratentorial counterparts. This assumption may be erroneous. A better understanding of the clinical differences between CGB and STGB may help guide treatment strategies for patients with these rare lesions. Furthermore, it may highlight the need to understand the molecular and genetic composition of these rare tumors as they may represent separate lesions as compared to STGB.

Prior studies on CGB are few and limited given the rarity of these lesions (13, 14, 41, 46, 48) (Table 4). In this cohort of 23,329 GB patients with known locality, only 208 patients were classified as having CGB. Dohrman and Dunsmore performed a review of the literature in 1975 and found 33 reported CGB cases (14). Their patient population had a mixture of pediatric and adult patients, and had a median survival of approximately 1 year. No survival analyses or analyses to determine factors associated with survival were made (14). Djalilian and Hall in 1998 reviewed 78 adult and pediatric cases of malignant cerebellar gliomas, of which 37 patients had anaplastic astrocytomas (13). The median age was 29 years, and the median survival for patients with CGB was 11 months (13). In a univariate analysis of 41 patients with CGB, they found that surgery versus biopsy and radiation therapy was associated with prolonged survival (13). Lastly, Weber et al. evaluated the outcomes for 45 adult patients with CGB in a multi-institutional case series (48). This study included patients with gliosarcomas and giant cell GBs as well as brainstem GBs (48). The median survival was 9.9 months, and they found that in multivariate analyses, extent of surgery and brainstem involvement were associated with poorer survival (48). Therefore, large studies dedicated to evaluating outcomes and identifying factors associated with survival for adult patients with non-brainstem CGB remain few and limited. This lack of understanding has made many treat these lesions as identical to their supratentorial counterparts, whereas others have recommended avoidance of surgery and use of adjuvant therapies (14, 48).

CGB appears to be clinically distinct from STGB in this study. Patients with CGB were younger, less commonly involved Whites, and were smaller than patients with STGB. Prior studies on CGB have included pediatric patients, making it difficult to discern if adult patients with CGB were truly younger than patients with STGB (21, 32). Moreover, many of these prior studies included patients with secondary GB or those that arise from low-grade gliomas, as well as prior radiated medulloblastomas (21, 32). This study shows that among adult patients with primary GB, patients with CGB were younger. In addition to age, these tumors occurred less frequently in Whites. This is important because a recent study found that GBs were more common in Whites, where no distinction was made between supra- and

infratentorial lesions (15). In addition to age and race, cerebellar tumors were typically smaller. This may be due to the fact the posterior fossa is less accommodating to masses. Nevertheless, CGB appears to have important clinical differences with STGB. These differences may make it erroneous to include these rare lesions into the cohorts with more common STGB.

Younger patients with CGB had significantly improved survival as compared to older patients. The most significant age in this study was 40 years of age or younger. This is similar to patients with supratentorial tumors, but the general cutoff in survival is best seen at around 60 years of age (6, 7). Older age may confer a decreased ability to withstand neurological insults including those caused by the tumor itself, surgery, and/or adjuvant therapy (28, 30, 31). Older patients may also harbor tumors with different molecular profiles and resistance genes that create a more aggressive-behaving tumor (2, 39, 43). These features may be the reasons why older patients with GBM tend to have poorer outcomes for both STGB and CGB. CGBs, however, have an apparently lower cutoff in age where this survival difference is seen.

GTR was only independently associated with prolonged survival for patients with CGB in this study on univariate analysis. It makes intuitive sense that increased resection would be associated with decreased tumor burden, increased efficacy of adjuvant therapies, and thus improved survival. However, this remains a controversy for patients with supratentorial lesions (8, 29, 31, 35). Studies devoted to adult patients with CGB are few and limited. Djalilian and Hall reviewed 71 cases with cerebellar high-grade gliomas from a meta-analysis (13). Among patients with GB, they found that patients who underwent surgical resection had improved survival over patients who underwent biopsy; however, no assessment was made on extent of resection (13). Tsung et al. studied 21 patients with CGB from a single institution and found no association between extent of resection and overall and/or progression-free survival (46). Interestingly, Weber et al. studied 45 patients from 15 institutions with CGB (48). They found that extent of surgery was associated with poorer survival even though all cases of recurrence were local (48). The present study is the largest study to date, and shows a positive association between extent of resection and survival on univariate analysis; however, this finding could not be confirmed on multivariate analysis.

Unlike extent of resection, radiation therapy was associated with prolonged survival for patients with CGB in this study on both uni- and multivariate analyses. Radiation is part of the routine treatment algorithm for patients with STGB (42). Radiation may play a role in killing the remaining tumor cells, and establishing local control. Djalilian and Hall also found a positive correlation between radiation and survival for patients with CGB (13). As with this prior study, this study shows that patients with CGB may also benefit from radiation therapy similar to patients with STGB.

Although modest in absolute terms, Asian or Pacific Islanders race did have significantly prolonged survival as compared to Whites in multivariate proportional hazards but not log-rank analysis. Studies have suggested that differences in genetic susceptibility and/or environmental exposures could explain why populations of Eastern and Southeastern Asian people have substantially lower incidences of brain tumors than other populations (9). More

recently, among elderly patients primarily with STGB, patients of Asian or Pacific Islander ethnicity had improved survival as compared to White patients (5). Our study shows a similar finding, but the number of Asian or Pacific Islanders in this study was limited ($n = 15$). The impact on race therefore needs to be studied further in order to learn about racial and ethnic differences in incidence and survival in CGB patients.

Strengths and Limitations

Studies evaluating patient characteristics and identifying factors associated with survival for patients with CGB are few and limited. The overwhelming majority of studies on CGB group these lesions into cohorts primarily composed of supratentorial lesions, whereas others include pediatric patients, lower-grade lesions, radiation-induced pathology, and brainstem tumors. A population-based study provides invaluable data on rare pathologies and enables analyses of large series than would not be possible from single-institutional studies. Findings from a population-based study are also more likely to apply to the general U.S. population than data from a single institution. Unlike the literature reviews and single-institutional studies previously published, population-based analyses do not carry the selection bias that can be associated with one referral center's experience. A better understanding of primary CGB is important for several reasons. First, studies devoted to adult patients with nonbrainstem CGB are few and limited. Second, a better understanding of the clinical characteristics of patients with CGB may help identify important differences between patients with STGB and CGB. Third, an understanding of clinical differences may help emphasize a need to understand the molecular and genetic differences between patients with STGB and CGB. Finally, identifying factors associated with survival may help guide clinical decision making to improve survival for patients harboring these rare tumors. The factors associated with survival for patients with STGB may not be applicable for patients with CGB.

This study, however, has some limitations. The data available in SEER is observational, and assignment of treatments to subjects has been haphazard (49). Lacking randomization, SEER can provide biased estimation of treatment effects and cannot be used as evidence of any type of treatment efficacy. Second, a limitation of the SEER registry is the lack of information regarding the use of chemotherapy. Currently chemotherapy is considered standard care for patients with high-grade gliomas in the United States. Additionally, other important factors were not readily available in the SEER database, which includes preoperative neurologic function, radiation dose-fractionation, and presence of leptomeningeal disease. Lastly, complete radiographic data including tumor size was not available for the majority of patients. Despite these inherent limitations, we tried to create a uniform patient population by using strict inclusion criteria, and may therefore not apply to all patients with CGB. We included only adult patients who were classified as having primary CGB, and excluded GB variants including gliosarcoma, giant cell GB, and prior cancers. In addition, we used multivariate analyses to control for confounding variables. Given these statistical controls and a relatively precise outcome measure, we believe our findings offer useful insights into the management of patients with CGB. Prospective studies are still needed to provide better data to guide clinical decision making. This, however, may not be possible as these lesions are exceedingly rare.

CONCLUSION

Patients with CGB are rare. We found that the incidence of CGB among patients with GB was 0.9%. These lesions are smaller, occur in younger patients, and comprise different proportions of certain racial ethnicities. More important, patients with CGB have prolonged survival as compared to patients with STGB. The factors independently associated with prolonged survival for patients with CGB are younger age at presentation, radiation therapy, and Asian or Pacific Islander race. These findings may help guide treatment and prognosticate survival for patients with these exceedingly rare lesions.

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Abbreviations and Acronyms

CGB	Cerebellar glioblastoma
GB	Glioblastoma
GTR	Gross total resection
ICD-O	International Classification of Disease for Oncology
SEER	Surveillance, Epidemiology and End Results
STGB	Supratentorial glioblastoma

References

1. American College of Surgeons: FORDS: Facility Oncology Registry Data Standards. Commission on Cancer. Chicago, IL: American College of Surgeons; 2002.
2. Alonso M, Hamelin R, Kim M, Porwancher K, Sung T, Parhar P, Miller DC, Newcomb EW. Microsatellite instability occurs in distinct subtypes of pediatric but not adult central nervous system tumors. *Cancer Res.* 2001; 61:2124–2128. [PubMed: 11280776]
3. Auff E, Vass K. Cerebellar glioblastoma presenting clinically as Wallenberg's syndrome. *Arch Psychiatr Nervenkr.* 1981; 230:361–364. [PubMed: 7316732]
4. Aziz TZ, Stoddart M. Cerebellar glioblastoma multiforme; a report of two cases and review of the literature. *West Engl Med J.* 1990; 105:39–42. [PubMed: 2173942]
5. Barnholtz-Sloan JS, Maldonado JL, Williams VL, Curry WT, Rodkey EA, Barker FG 2nd, Sloan AE. Racial/ethnic differences in survival among elderly patients with a primary glioblastoma. *J Neurooncol.* 2007; 85:171–180. [PubMed: 17530174]
6. Chaichana K, Parker S, Olivi A, Quinones-Hinojosa A. A proposed classification system that projects outcomes based on preoperative variables for adult patients with glioblastoma multiforme. *J Neurosurg.* 2010; 112:997–1004. [PubMed: 19817542]
7. Chaichana KL, Chaichana KK, Olivi A, Weingart JD, Bennett R, Brem H, Quinones-Hinojosa A. Surgical outcomes for older patients with glioblastoma multiforme: preoperative factors associated with decreased survival. *Clinical article. J Neurosurg.* 2011; 114:587–594. [PubMed: 20887095]
8. Chaichana KL, Garzon-Muvdi T, Parker S, Weingart JD, Olivi A, Bennett R, Brem H, Quinones-Hinojosa A. Supratentorial glioblastoma multiforme: the role of surgical resection versus biopsy among older patients. *Ann Surg Oncol.* 2011; 18:239–245. [PubMed: 20697823]

9. Darefsky AS, Dubrow R. International variation in the incidence of adult primary malignant neoplasms of the brain and central nervous system. *Cancer Causes Control*. 2009; 20:1593–1604. [PubMed: 19633913]
10. DeAngelis LM. Brain tumors. *N Engl J Med*. 2001; 344:114–123. [PubMed: 11150363]
11. Demir MK, Hakan T, Akinci O, Berkman Z. Primary cerebellar glioblastoma multiforme. *Diagn Interv Radiol*. 2005; 11:83–86. [PubMed: 15957093]
12. Deorah S, Lynch CF, Sibenaller ZA, Ryken TC. Trends in brain cancer incidence and survival in the United States: Surveillance, Epidemiology, and End Results Program, 1973 to 2001. *Neurosurg Focus*. 2006; 20:E1. [PubMed: 16709014]
13. Djalilian HR, Hall WA. Malignant gliomas of the cerebellum: an analytic review. *J Neurooncol*. 1998; 36:247–257. [PubMed: 9524103]
14. Dohrmann GJ, Dunsmore RH. Glioblastoma multiforme of the cerebellum. *Surg Neurol*. 1975; 3:219–223. [PubMed: 167463]
15. Dubrow R, Darefsky AS. Demographic variation in incidence of adult glioma by subtype, United States, 1992–2007. *BMC Cancer*. 2011; 11:325. [PubMed: 21801393]
16. Endo H, Kumabe T, Kon H, Yoshimoto T, Nakasato Y. A case of primary cerebellar glioblastoma in childhood [in Japanese]. *No Shinkei Geka*. 2002; 30:1325–1329. [PubMed: 12491584]
17. Escalona-Zapata J, Salinero E, Lacruz C. Malignant cerebellar gliomas. Report of 4 cases with special reference to tissue culture study. *J Neurosurg Sci*. 1981; 25:95–104. [PubMed: 6278109]
18. Fresh CB, Takei Y, O'Brien MS. Cerebellar glioblastoma in childhood. Case report. *J Neurosurg*. 1976; 45:705–708. [PubMed: 185342]
19. Fritz, AG. International classification of diseases for oncology: ICD-O. 3. Geneva: World Health Organization; 2000.
20. Georges PM, Noterman J, Flament-Durand J. Glioblastoma of the cerebellum in children and adolescents. Case report and review of the literature. *J Neurooncol*. 1983; 1:275–278. [PubMed: 6088719]
21. Grahovac G, Tomac D, Lambasa S, Zoric A, Habek M. Cerebellar glioblastomas: pathophysiology, clinical presentation and management. *Acta Neurochir (Wien)*. 2009; 151:653–657. [PubMed: 19319469]
22. Gupta V, Goyal A, Sinha S, Singh AK, Tatke M, Kumar S, Singh D, Sachdeva PK. Glioblastoma of the cerebellum. A report of 3 cases. *J Neurosurg Sci*. 2003; 47:157–164. discussion 164–165. [PubMed: 14618129]
23. Hess KR, Broglio KR, Bondy ML. Adult glioma incidence trends in the United States, 1977–2000. *Cancer*. 2004; 101:2293–2299. [PubMed: 15476282]
24. Hur H, Jung S, Jung TY, Kim IY. Cerebellar glioblastoma multiforme in an adult. *J Korean Neurosurg Soc*. 2008; 43:194–197. [PubMed: 19096643]
25. Jacquet G, Godard J, Carbillet G, Steimle R. Glioblastoma of the cerebellum in a child. Apropos of a case. A review of the literature [in French]. *Neurochirurgie*. 1989; 35:64–69. [PubMed: 2541353]
26. Katz DS, Poe LB, Winfield JA, Corona RJ. A rare case of cerebellar glioblastoma multiforme in childhood: MR imaging. *Clin Imaging*. 1995; 19:162–164. [PubMed: 7553429]
27. Kleihues P, Ohgaki H. Primary and secondary glioblastomas: from concept to clinical diagnosis. *Neuro Oncol*. 1999; 1:44–51. [PubMed: 11550301]
28. Krex D, Klink B, Hartmann C, von Deimling A, Pietsch T, Simon M, Sabel M, Steinbach JP, Heese O, Reifenberger G, Weller M, Schackert G. Long-term survival with glioblastoma multiforme. *Brain*. 2007; 130(Pt 10):2596–2606. [PubMed: 17785346]
29. Lacroix M, Abi-Said D, Fourney DR, Gokaslan ZL, Shi W, DeMonte F, Lang FF, McCutcheon IE, Hassenbusch SJ, Holland E, Hess K, Michael C, Miller D, Sawaya R. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. *J Neurosurg*. 2001; 95:190–198. [PubMed: 11780887]
30. Lamborn KR, Chang SM, Prados MD. Prognostic factors for survival of patients with glioblastoma: recursive partitioning analysis. *Neuro Oncol*. 2004; 6:227–235. [PubMed: 15279715]

31. Laws ER, Parney IF, Huang W, Anderson F, Morris AM, Asher A, Lillehei KO, Bernstein M, Brem H, Sloan A, Berger MS, Chang S. Survival following surgery and prognostic factors for recently diagnosed malignant glioma: data from the Glioma Outcomes Project. *J Neurosurg.* 2003; 99:467–473. [PubMed: 12959431]
32. Levine SA, McKeever PE, Greenberg HS. Primary cerebellar glioblastoma multiforme. *J Neurooncol.* 1987; 5:231–236. [PubMed: 2824711]
33. Luccarelli G. Glioblastoma multiforme of the cerebellum: description of three cases. *Acta Neurochirurgica.* 1980; 53:107–116. [PubMed: 6254346]
34. Mattos JP, Marengo HA, Campos JM, Faria AV, Queiroz LS, Borges G, Oliveira E. Cerebellar glioblastoma multiforme in an adult. *Arq Neuropsiquiatr.* 2006; 64:132–135. [PubMed: 16622570]
35. McGirt MJ, Chaichana KL, Gathinji M, Attenello FJ, Than K, Olivi A, Weingart JD, Brem H, Quinones-Hinojosa AR. Independent association of extent of resection with survival in patients with malignant brain astrocytoma. *J Neurosurg.* 2009; 110:156–162. [PubMed: 18847342]
36. Miller EM, Mani RL, Townsend JJ. Cerebellar glioblastoma multiforme in an adult. *Surg Neurol.* 1976; 5:341–343. [PubMed: 180621]
37. Modan B, Wagener DK, Feldman JJ, Rosenberg HM, Feinleib M. Increased mortality from brain tumors: a combined outcome of diagnostic technology and change of attitude toward the elderly. *Am J Epidemiol.* 1992; 135:1349–1357. [PubMed: 1510081]
38. Ohgaki H, Dessen P, Jourde B, Horstmann S, Nishikawa T, Di Patre PL, Burkhard C, Schuler D, Probst-Hensch NM, Maiorka PC, Baeza N, Pisani P, Yonekawa Y, Yasargil MG, Lutolf UM, Kleihues P. Genetic pathways to glioblastoma: a population-based study. *Cancer Res.* 2004; 64:6892–6899. [PubMed: 15466178]
39. Rickert CH, Strater R, Kaatsch P, Wassmann H, Jurgens H, Dockhorn-Dworniczak B, Paulus W. Pediatric high-grade astrocytomas show chromosomal imbalances distinct from adult cases. *Am J Pathol.* 2001; 158:1525–1532. [PubMed: 11290570]
40. Rosenfeld J, Rossi ML, Briggs M. Glioblastoma multiforme of the cerebellum in an elderly man. A case report. *Tumori.* 1989; 75:626–629. [PubMed: 2559527]
41. Stark AM, Maslehaty H, Hugo HH, Mahvash M, Mehdorn HM. Glioblastoma of the cerebellum and brainstem. *J Clin Neurosci.* 2010; 17:1248–1251. [PubMed: 20619657]
42. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, Belanger K, Brandes AA, Marosi C, Bogdahn U, Curschmann J, Janzer RC, Ludwin SK, Gorlia T, Allgeier A, Lacombe D, Cairncross JG, Eisenhauer E, Mirimanoff RO. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med.* 2005; 352:987–996. [PubMed: 15758009]
43. Sung T, Miller DC, Hayes RL, Alonso M, Yee H, Newcomb EW. Preferential inactivation of the p53 tumor suppressor pathway and lack of EGFR amplification distinguish de novo high grade pediatric astrocytomas from de novo adult astrocytomas. *Brain Pathol.* 2000; 10:249–259. [PubMed: 10764044]
44. Tamaki T, Eguchi T, Sakamoto M, Teramoto A. Glioblastoma multiforme of the cerebellum in an elderly man. *J Chin Med Assoc.* 2004; 67:301–304. [PubMed: 15366408]
45. Tran B, Rosenthal MA. Survival comparison between glioblastoma multiforme and other incurable cancers. *J Clin Neurosci.* 2010; 17:417–421. [PubMed: 20167494]
46. Tsung AJ, Prabhu SS, Lei X, Chern JJ, Benjamin Bekele N, Shonka NA. Cerebellar glioblastoma: a retrospective review of 21 patients at a single institution. *J Neurooncol.* 2011; 105:555–562. [PubMed: 21643841]
47. Utsuki S, Oka H, Miyajima Y, Kijima C, Yasui Y, Fujii K. Adult cerebellar glioblastoma cases have different characteristics from supratentorial glioblastoma. *Brain Tumor Pathol.* 2012; 29:87–95. [PubMed: 22076316]
48. Weber DC, Miller RC, Villa S, Hanssens P, Baumert BG, Castadot P, Varlet P, Abacioglu U, Igdem S, Szutowicz E, Nishioka H, Hofer S, Rutz HP, Ozsahin M, Taghian A, Mirimanoff RO. Outcome and prognostic factors in cerebellar glioblastoma multiforme in adults: a retrospective study from the Rare Cancer Network. *Int J Radiat Oncol Biol Phys.* 2006; 66:179–186. [PubMed: 16814953]
49. Woodworth GF, Baird CJ, Garces-Ambrossi G, Tonascia J, Tamargo RJ. Inaccuracy of the administrative database: comparative analysis of two databases for the diagnosis and treatment of

- intracranial aneurysms [discussion 256–257]. *Neurosurgery*. 2009; 65:251–256. [PubMed: 19625902]
50. Yan H, Parsons DW, Jin G, McLendon R, Rasheed BA, Yuan W, Kos I, Batinic-Haberle I, Jones S, Riggins GJ, Friedman H, Friedman A, Reardon D, Herndon J, Kinzler KW, Velculescu VE, Vogelstein B, Bigner DD. IDH1 and IDH2 mutations in gliomas. *N Engl J Med*. 2009; 360:765–773. [PubMed: 19228619]
51. Yang SY, Wang KC, Cho BK, Kim YY, Lim SY, Park SH, Kim IH, Kim SK. Radiation-induced cerebellar glioblastoma at the site of a treated medulloblastoma: case report. *J Neurosurg*. 2005; 102(4 Suppl):417–422. [PubMed: 15926395]

Figure 1.

Kaplan-Meier plots of survival for the entire cohort of adult patients with cerebellar glioblastoma (CGB) and supratentorial glioblastoma (STGB). Median survival for CGB was 8 months, and 1-, 2-, 5-year survival rates were 21%, 13%, and 2%, respectively. STGB demonstrated median survival of 9 months, with 1-, 2-, and 5-year survival rates of 12%, 7%, and 1%, respectively. The survival difference observed in these 2 groups did not reach statistical significance ($P = 0.143$). However, only after adjusting for the stratification variables in a multivariate analysis, there was evidence of a survival difference between the two groups in favor of CGB ($P = 0.048$).

Figure 2.

Kaplan-Meier plots of survival for the entire cohort of adult patients with cerebellar glioblastoma (CGB) stratified by age groups at diagnosis. Median survival for the <40, 40–49, 50–59, 60–69, and ≥70 group was 17, 23, 10, 4, and 4 months, respectively.

Survival decreased among CGB patients as age advances. Patients in the 50–59, 60–69, and ≥70 group were statistically different from the <40 group ($P = 0.035$, $P = 0.004$, and $P < 0.001$).

Figure 3.

Kaplan-Meier plots of survival for the entire cohort of adult patients with cerebellar glioblastoma (CGB) stratified by extent of resection. Median survival for the no-surgery (NS), biopsy (Bx), partial resection (PR), and gross total resection (GTR) group was 4, 7, 6, and 16 months, respectively. When compared to the NS group, only the GTR group was statistically different ($P = 0.003$).

Figure 4.

Kaplan-Meier plots of survival for the entire cohort of adult patients with cerebellar glioblastoma (CGB) stratified by the use of radiotherapy. Median survival for the radiation group was 11 months, and 2 months for the no-radiation group ($P < 0.001$).

Table 1

Patient, Tumor, and Treatment Characteristics of 208 Adult Patients with Primary Cerebellar Glioblastoma (CGB)

Characteristics	Number (%) of Patients
Age, years *	58 ± 16
<40	33 (16%)
40–49	32 (15%)
50–59	42 (20%)
60–69	43 (21%)
70	58 (28%)
Male gender	122 (59%)
Race	
White	178 (86%)
Black	15 (7%)
Asian or Pacific Islander	15 (7%)
Decade of diagnosis	
1970s	14 (7%)
1980s	29 (14%)
1990s	41 (20%)
2000	124 (60%)
Tumor characteristics	
Size, cm *,†	3.7 ± 1.1
Extent of resection	
No surgery	31 (15%)
Biopsy	26 (13%)
Partial resection	54 (26%)
Gross total resection	60 (29%)
Surgery, not specified	30 (14%)
Unknown	7 (3%)
Radiation therapy	
Yes	150 (72%)
No	57 (27%)
Unknown	1 (1%)

Data were collected from the Surveillance, Epidemiology, and End Results from 1973 to 2009.

* Mean ± standard deviation.

† Data on tumor size were available for 56% of the cases.

Table 2

Univariate and Multivariate Analyses of Risk Factors for Overall Mortality in Patients with Primary Cerebellar Glioblastoma (CGB)

Variables	Hazard Ratio (95% CI)	P- value*
Age		<0.001 [†]
<40 [‡]	1.00	
40–49	0.87 (0.49–1.55)	
50–59	1.63 (0.99–2.66)	
60–69	2.33 (1.39–3.90)	
70	2.83 (1.75–4.58)	
Sex		0.196
Male [‡]	1.00	
Female	0.82 (0.61–1.11)	
Race		0.611
White [‡]	1.00	
Black	0.78 (0.44–1.44)	
Asian or Pacific Islander	0.82 (0.46–1.44)	
Decade of diagnosis		0.633
1970s [‡]	1.00	
1980s	1.38 (0.73–2.63)	
1990s	1.04 (0.57–1.93)	
2000	1.21 (0.69–2.14)	
Extent of resection		0.019 [†]
No surgery [‡]	1.00	
Biopsy	0.93 (0.53–1.63)	
Partial resection	0.81 (0.51–1.30)	
Gross total resection	0.52 (0.33–0.83)	
Radiation therapy		<0.001 [†]
Yes [‡]	1.00	
No	2.44 (1.75–3.40)	

Only age at diagnosis, extent of resection, and radio-therapy reached a level of significance.

* Univariate Cox proportional hazard model was used to calculate the impact of the variable on overall survival.

[†] Statistical significance.

[‡] Reference category.

Table 3

Forward Stepwise Multivariate Analysis of Risk Factors for Overall Mortality in Patients with Primary Cerebellar Glioblastoma (CGB)

Variables	Hazard Ratio (95% CI)	P- value*
Age		<0.001 [†]
<40 [‡]	1.00	
40–49	1.33 (0.66–2.69)	
50–59	2.32 (1.25–4.33)	
60–69	2.65 (1.41–4.99)	
70	3.79 (2.08–6.91)	
Race		0.046 [†]
White [‡]	1.00	
Black	0.65 (0.36–1.17)	
Asian or Pacific Islander	0.45 (0.22–0.94)	
Extent of Resection		0.063
No surgery [‡]	1.00	
Biopsy	0.89 (0.49–1.63)	
Partial	0.64 (0.38–1.06)	
resection		
Gross total resection	0.55 (0.34–0.89)	
Radiation therapy		<0.001 [†]
Yes [‡]	1.00	
No	2.9 (1.96–4.41)	

Note: Age at diagnosis, race, and radiotherapy were significantly associated with survival.

CI, confidence interval.

* Multivariate Cox proportional hazard model was used to calculate the impact of variables on overall survival, adjusting for age at diagnosis, pediatric and adult age groups, sex, race, period of diagnoses, extent of resection, and radiotherapy. A total of 169 cases with complete data on all analysis variables were used.

[†] Statistical significance.

[‡] Reference category.

Table 4

Summary of Studies with More Than Five Patients on Outcomes for Adult Patients with Cerebellar Glioblastoma (CGB)

Studies	Number of CGB Patients	Included Pediatric Patients	Evaluated Factors Associated with Survival	Factors Associated with Survival
Present study, 2012	208	No	Yes	Age, race, radiation
Tsung et al., 2011 (46)	21	No	Yes	Leptomeningeal spread, chemotherapy
Stark et al., 2010 (41)	7	No	No	N/A
Weber et al., 2006 (48) *	45	No	Yes	Extent of surgery, brainstem involvement
Djalilian and Hall, 1998 (13)	41	Yes	Yes	Surgery
Dohrman and Dunsmore, 1975 (14)	33	Yes	No	N/A

* Included patients with brainstem tumors.