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Prognostic Factors and Survival in Primary Malignant Astrocytomas of the Spinal Cord: A Population-Based Analysis from 1973 to 2007

Hadie Adams, M.D.¹, Javier Avendaño, M.D.^{1,2}, Shaan M. Raza, M.D.¹, Ziya L. Gokaslan, M.D.¹, George I. Jallo, M.D.¹, and Alfredo Quiñones-Hinojosa, M.D.¹

¹Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, MD, USA

²Department of Neurosurgery, the National Institute of Neurology and Neurosurgery, Mexico City, Mexico

Abstract

Study Design—Observational cross-sectional study

Objective—Using data from the population-based cancer registries of the SEER program, we analyzed demographic features, tumor and treatment characteristics, as well as survival rates in patients with PMASC.

Summary of Background Data—Primary malignant astrocytomas of the spinal cord (PMASC) are a rare neoplasm and considered to carry the same dismal outcome as their cerebral counterparts. Our current knowledge is incomplete, and understanding the epidemiology, diagnosis and optimal treatment is still posing challenges.

Methods—The SEER data from 1973–2007 was reviewed for pathologically confirmed primary Anaplastic Astrocytomas (AA) and Glioblastomas (GB) of the spinal cord (C72.0). We compared the clinical features and outcomes of the cohort in uni- and multivariate fashion. Survival was calculated and compared using Kaplan-Meier curves and log-rank analysis.

Results—Our search criteria retrieved 135 patients diagnosed with PMASC. The median survival for PMASC was 13 months with 1, 2 and 5-year survival rates of 51.8%, 32.2% and 18.7%. Patient diagnosed with AA had a median survival time of 17 months versus 10 month in patients diagnosed with GB. Adult patients observed markedly prolonged survival compared to the pediatric group, with a 16 versus 9 months median survival, respectively. Multivariate analysis revealed age at diagnosis, pediatric and adult age groups, sex, tumor histology, and extent of resection as significant predictors of survival. Interestingly, outcomes did not significantly change throughout the last decades or by receiving radiotherapy.

Conclusion—Outcome for patients diagnosed with PMASC remains poor and presents an ongoing challenge for professionals in the field of neuro-spinal medicine and surgery. In our analyses AA, adult patients, males and patients undergoing radical resections were associated with increased survival. However, incidence of these lesions is low, hence building strong collaborative, interdisciplinary and multi-institutional study groups is necessary to define the optimal treatment of PMASC.

Please send correspondence to: Alfredo Quiñones-Hinojosa, M.D., Brain Tumor Stem Cell Laboratory, Department of Neurosurgery and Oncology, 1550 Orleans Street, Cancer Research Building II Room 253, Baltimore, MD 21231, Phone: 410-502-2906/Fax: 410-502-5559, aquinon2@jhmi.edu.

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Keywords

Spinal Cord; Astrocytoma; Anaplastic; Glioblastoma; SEER; Survival; Prognostic Factors; Treatment

INTRODUCTION

Spinal cord tumors are rare neoplasms that account for 4 to 10 percent of central nervous system (CNS) tumors.^{1,2} Astrocytomas represents 6 to 8 percent of all spinal cord tumors³ and one-third of these astrocytic tumors correspond to high grade lesions.⁴ These primary malignant astrocytomas of the spinal cord (PMASC) are considered to carry the same dismal outcome as their cerebral counterparts.⁵ The estimated median survival for primary anaplastic astrocytomas (AA) of the spinal cord has been reported to be in the range of 6 to 72 months, while a 6 to 10 months range has been described for patients with glioblastomas (GB).^{6–10} It is increasingly evident that data regarding intracranial astrocytomas cannot be generalized to those tumors affecting the spinal cord.

Our current knowledge is incomplete, and understanding the epidemiology, diagnosis and optimal treatment is still posing challenges.¹¹ While predictive factors of survival in malignant astrocytomas of the cerebral hemispheres have been well described,^{12–14} these factors cannot be firmly established for PMASC from case reports^{15–24} or small retrospective studies.^{5,7–9,25} Other case series evaluating spinal cord astrocytomas pooled low and high grade lesions together limiting the interpretability of their results.^{4,26–36} Due to the relative infrequency of this pathology, there is a paucity of studies analyzing adequate numbers of patients in order to draw conclusions that could guide surgical management.

With this analysis of primary AA and GB of the spinal cord we aimed to delineate factors associated with survival, including demographic, tumor and treatment characteristics by using information from the Surveillance, Epidemiology and End Results (SEER) program from 1973 to 2007.

MATERIALS AND METHODS

Study Population

Data for this analysis were obtained from the SEER program (1973–2007) of the National Cancer Institute (NCI). This cancer registry includes data from 17 geographic areas in the United States, representing approximately 26% of the U.S. population. Site and histology codes of the International Classification of Disease for Oncology (ICD-O-3) third edition were used to identify the cases. Only subjects classified as having a histopathologically confirmed Anaplastic Astrocytoma (ICD-O-3: 9401) or Glioblastoma (ICD-O-3: 9440) located in the Spinal Cord (C72.0) were included in this study. Patients coded to have lesions in the Cauda Equina (C72.1) or Spinal Meninges (C70.1) were excluded. Patient, tumor and treatment characteristics such as age at diagnosis, sex, race, extent of resection and radiation were evaluated. Decades of diagnosis were stratified according to 5-year interval groups to facilitate comparisons in uni- and multivariate models. Several patient and treatment-related factors (chemotherapeutic regimens, radiotherapy techniques and/or fractionation/dose schedules, neurological/performance status, comorbid conditions) were unaccounted for in SEER and could therefore not be included in our analyses. SEER data is publicly available; therefore we received exempt review status from our institutional review board.

Surgical Procedure Data

In order to evaluate operative procedures performed on patients with PMASC, a detailed assessment of extent of resection variables was carried out using SEER Program Code Manuals. In the SEER database surgical procedures were coded by trained coders according to established guidelines using the best source documents available in order to determine the extent of resection (SEER suggest coders to use the face sheet and/or operative notes). The variable containing surgery codes for cases diagnosed in 1998 to 2007, named “RX Summ--Surg Prim Site (1998+)”, was based on the American College of Surgeons Commission on Cancer’s Facility Oncology Registry Data Standards (FORDS).³⁷ Field codes of cases diagnosed up through 1997, were included in the “Site specific surgery (1983–1997)” variable. Cases diagnosed prior to 1983 were coded using a nonspecific scheme (Surgery Yes/No/Unknown) and specific extent of resection variables are therefore not available, limiting the inclusion of these cases in subsequent uni- and multivariate analyses. In order to review all cases from the pre- and post-1998 revisions, we recoded the surgical procedures of all years into 6 categories; No Surgery (NS, pre-1998 codes 00, 01, 03, 04, 07; for 1998+, code 00); Biopsy (Bx, pre-1998 code 02; for 1998+, code 20); Partial Resection (PR, pre-1998 codes 20, 40; for 1998+, code 40); Gross Total Resection (GTR, pre-1998 codes 30, 50, 60; for 1998+, code 55); Surgery Not Otherwise Specified (SNOS, pre-1998 codes 10, 90; for 1998+, codes 10, 90) and Surgery Status Unknown (SSU, pre-1998 codes 05, 06, 09, 80; for 1998+, code 99).

Survival and Statistical Analysis

The Kaplan-Meier method was used to estimate overall survival, and comparisons were performed using the two-tailed log-rank test. The association of variables with overall survival was quantified using hazard ratios estimated in Cox proportional hazard models (CPHM). A univariate CPHM was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) in order to estimate the influence of each variable on the hazard function. In addition, a multivariate CPHM was performed using a forward stepwise selection; predictors were removed when their p-value in the likelihood ratio-test was greater than 0.10. Proportional hazards assumptions were checked graphically. A value of $P < 0.05$ was considered statistically significant. The statistical analyses were carried out using Predictive Analytics SoftWare (PASW) Statistics version 17.0.2 (SPSS Inc., Chicago, IL).

RESULTS

Patient Population

From all 3065 histologically confirmed primary spinal cord tumors captured by SEER a total of 135 cases met our inclusion criteria (4.4%). Mean age (SD) was 35 (22) years, ranging from <1 to 87 years with a higher incidence in males (57.8%) (Table 1). The vast majority of patients were ‘Whites’ (83.7%), which generally reflects the racial distribution within the SEER population of CNS cancers.³⁸ Surgical procedures were performed in 84% of the cases; 22.2% underwent a GTR, 31.1% a PR, 16.3% a Bx, and in 11.1% no cancer directed surgical procedure was performed. All cases in the latter group were coded to be actively followed-up during the course of disease and pathological confirmation of the diagnosis GB was established postmortem. In addition, the great majority of PAMSC patients received radiotherapy (80.7%).

Uni- and Multivariate Analyses

Univariate CPHM demonstrated the effect of pediatric and adult age groups ($p=0.035$), sex ($p=0.048$), tumor histology ($p=0.003$) and extent of resection ($p=0.041$) as factors associated

with survival (Table 2). Age, race, period of diagnosis and radiation did not reach this level of significance. The multivariate CPHM identified the following as predictors of survival: age at diagnosis ($p=0.013$), pediatric and adult age groups ($p=0.002$), sex ($p=0.020$), tumor histology ($p=0.001$), and extent of resection ($p=0.054$) (Table 3). Race, period of diagnosis and radiotherapy did not reach statistical significance in the multivariate model. Although extent of resection did not reach our threshold for statistical significance, the forward stepwise CPHM returned it as a variable with predictive value for survival. Within the extent of resection variable, both the GTR and PR group demonstrated significant improved survival compared to the NS group (HR 0.38, CI 0.18–0.82 and HR 0.43, CI 0.20–0.90). Additionally, the trend towards statistical significance on univariate analysis for both age at diagnosis and radiation only reached statistical significance after multivariate adjustment for age at diagnosis ($p=0.013$). Although radiation was preselected by the forward stepwise CPHM, it was dropped at p value of 0.161 (not shown).

Outcome and Survival

A median overall survival of 13 months with a mean of 69.7 months was observed in our entire cohort (Figure 1). These 135 cases demonstrated 1-year, 2-year, and 5-year survival rates of 51.8%, 32.2%, and 18.7%. Adult patients observed markedly prolonged survival in comparison to the pediatric group, with a 16 versus 9 months median survival, respectively ($p=0.030$). (Figure 2). The cohort of male patients indicated median survival of 15 months versus 10 months in females ($p=0.042$) (Figure 3). Median survival for cases diagnosed with AA and GB was observed to be 17 and 10 months, respectively ($p=0.002$) (Figure 4). Cases in the NS group had a 9 months median survival, while patients in the Bx, PR and GTR group had 10, 11 and 24 months, respectively ($p=0.491$, $p=0.116$ and $p=0.002$ on log-rank analysis compared to the NS group) (Figure 5). Furthermore, the data shows a trend ($p=0.068$) of survival benefit in patients undergoing radiation versus no radiation of 15 months versus 5 months, respectively (Figure 6a). This trend is especially remarkable in adult patients (20 months versus 3 months, $p=0.078$, Figure 6b) if plotted and analyzed separately from the pediatric subgroup (9 months versus 13 months, $p=0.924$, Figure 6c). The survival benefit of radiotherapeutical treatment could not be sustained statistically as a prognostic variable, possibly due to the relatively small number of patients in the no-radiation group.

DISCUSSION

Using the large population-based SEER database, we have described PMASC patients' demographics, nationwide treatment results and prognostic factors influencing survival. Due to their rarity, population-based studies can increase our understanding of factors associated with survival because of its large study cohort and long follow-up. One hundred thirty five patients met our inclusion criteria for PMASC and were evaluated in detail.

From all variables analyzed, only age at diagnosis, pediatric and adult age groups, sex, histological subtype, and extent of resection were associated with survival in the final multivariate model. Age at diagnosis only reached statistical significance in the multivariate model. Case series of strictly PMASC analyzing age as a prognostic factor have reported heterogeneous results.^{7,9} In the study conducted by McGirt et al., age did not reach statistical significance.⁷ Conversely, Santi et al. confirmed age as a significant prognostic factor after controlling for gender, grade, therapy, and procedure.⁹ However, in Santi et al. age was treated as a categorical variable in their multivariate model. Both these studies' findings^{7,9} should be interpreted with caution, given the studies' small sample size. Additionally, studies not restricting their cohort to malignant astrocytomas by pooling low and high grade variants together have limited the interpretability of their results possibly explaining the inconsistent results when examining age.^{4,26–36} Our analyses have further

demonstrated a strong correlation between the pediatric and adult age groups and survival. Adult patients' survival in relation to the pediatric cohort was significantly better with 16 versus 9 months median survival. One, two and five-year survival rates observed in adult were approximately double those seen in the pediatric subpopulation. While this difference was not specifically studied before, Minehan et al. had found that ages greater than 20 years at diagnosis were associated with increased survival.³³ Our current understanding of high grade lesions is dictated by the molecular and genetic properties of these malignant tumors in the cerebrum. Further molecular and genetic interrogation of PMASC is warranted to fully understand the etiology and pathogenesis of these rare tumors.

Gender was also noted as a significant predictive factor of survival, with females having a poorer prognosis. A median survival of 10 months was observed compared to 15 months in males. Other studies have not, however, described differential mortality by gender in PMASC. To our knowledge, only one study has reported an association between female gender and decreased survival in a pediatric series of 73 patients with low and high grade astrocytomas.²⁹

Histological subtype was significantly associated with survival in our current study. GBs were associated with decreased survival compared to AAs (10 versus 17 months, $p=0.002$). McGirt et al. also demonstrated that histological subtype was strongly associated with survival (72 for AA versus 9 months for GB).⁷ However, Santi et al., Merchant et al. and Raco et al. did not find the histological variance of malignant astrocytomas to be associated with survival.^{8,9,25} The literature has described survival rates for AA varying from 6 to 72 months and for GB from 6 to 10 months.^{5,7-9}

Data from the SEER database demonstrated that radiation treatment was frequently used in PMASC (80.4%). Although our multivariate analysis suggested that individuals who underwent radiotherapy did not benefit in survival, this difference showed a trend toward significance in unadjusted analyses by log rank analysis in the survival curves ($p=0.068$, not shown) and univariate analysis using the CPHM ($p=0.076$, Table 2). From all studies analyzing radiotherapy treatment in malignant astrocytomas of the spinal cord, only one has reported a survival benefit from radiotherapy.⁸ Santi et al. did not observe a beneficiary effect of radiotherapy in their cohort and reported a 2 months median survival difference between the irradiated and non-irradiated patients (12 versus 10 months).⁹

Surgical interventions in intramedullary spinal cord tumors can be used to identify the tumor pathology, allow for neurological decompression, possibly improve the efficacy of adjuvant therapies and/or improve quality of life. In our analyses the majority of the cases in our cohort underwent a cancer-directed surgical intervention (84%). Extent of surgical resection showed a significant association with survival in both uni- and multivariate analyses. A median survival of 24 months was observed for cases undergoing a GTR, while the PR, Bx and NS group showed 11, 10 and 9 months, respectively. From all case series analyzing surgical extent of resection in their (sub)population of PMASC,^{7,9,26,28,29,32,35,39,40} only one has identified radical resection to be associated with survival.⁷ McGirt et al. conducted their analysis to determine the relationship between extent of resection and survival in a series of 35 consecutive patients with PMASC. The authors reported that radical resection was associated with extended survival for patients with AA but not GB. They concluded that patients with AA who underwent radical resection had increased overall survival rates compared with those who underwent subtotal resection.⁷ In the Raco et al. series the authors described the total surgical removal of these lesions to be rarely feasible and reported a worsening of the neurological deficit associated with extensive resections.²⁵ Also, the pediatric case series of PMASC published by Merchant et al. did not find prognostic relevance of surgical extent of resection and stated that aggressive surgery may lead to a

poor clinical outcome.⁸ In general, achieving a total resection in these cases is technically challenging and some authors have attributed the lack of complete surgical removal to the poor cleavage plane during tumor dissections.^{5,9,41,42} Interestingly, the 5-year periods of diagnosis did not demonstrate an improving trend or prognostic relevance in both the uni- and multivariate analysis, suggesting treatment outcomes have not changed over time. Since the first attempt to resect an intramedullary tumor in 1890,^{43,44} the field of neuro-spinal surgery has been the arena for major advances.⁴⁵ Unfortunately, prognosis for PMASC seems not to have changed over the last decades and outcome for PMASC patients still remains dismal.

Using data from the population-based cancer registries of the SEER program, we analyzed demographic features, tumor and treatment characteristics, as well as survival rates in patients with PMASC. We found that age at diagnosis, pediatric and adult age groups, sex, histological subtype and extent of resection were independent factors associated with survival in PMASC patients. Findings from a population-based study are more likely to apply to the general US 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. However, SEER data is observational in nature and cannot be used as evidence of any type of treatment efficacy. Importantly, patients' functional/neurological status is not recorded in SEER and could therefore not be analyzed. After carefully reviewing SEER's surgical procedure codes, it appears that the differentiation between excisional biopsy and partial resection is not based on accurate volumetric measurements and effectively there is overlap. Also, there were cases dating from the pre-MRI era that were classified and perceived as a gross total resection, at the time this could sometimes be a challenge to subjectively assess. This may have resulted in misclassification of some gross total resection cases and therefore biasing the results. A known limitation of the SEER program is the lack of information regarding the use of chemotherapy that is currently considered as standard care in the United States for patients with high grade astrocytomas.^{46,47} The radiotherapy data from the SEER records was used, however the lack of data regarding radiotherapy techniques and/or fractionation/dose schedules has limited the interpretation of the radiotherapy results. In order to accurately define prognostic factors and obtain the optimal treatment for PMASC, prospective studies are required. However, the incidence of these lesions is low, hence building strong collaborative, inter-disciplinary and multi-institutional study groups is necessary.

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KEY POINTS

- In PMASC cases survival seemed to be affected by age at diagnosis, pediatric and adult age groups, sex, tumor histology, and extent of resection.
- Despite therapeutic advances, population-based outcomes for PMASC have not improved substantially over the past decades.
- Collaborative study groups should be formed to define the optimal treatment of PMASC.

Figure 1. Kaplan-Meier curve: entire cohort of PMASC patients

Kaplan-Meier plot of survival for the entire cohort of patients with PMASC (n=135). Median (mean) survival was 13 (69.7) months, 6 months and 1-, 2-, 5-, 10-year survival rates were 72.3%, 51.8%, 32.2%, 18.7%, and 13.8%, respectively.

Figure 2. Kaplan-Meier curve: stratified by age groups

Kaplan-Meier plots of survival for the entire cohort of patients with PMASC stratified by pediatric and adult age groups. Median survival for the adult and pediatric age groups was 9 and 16 months. Adult patients (n=93) observed markedly prolonged survival compared to the pediatric group (n=42) (p=0.030 on Log Rank analysis). For the adult group 6-months and 1-, 2-, 5-, 10-year survival rates were 74.2%, 61.1%, 38.9%, 21.9%, and 15.1%, respectively. The pediatric cohort demonstrated survival rates of 67.8%, 30.1%, 17.0%, 11.3%, and 11.3%.

Figure 3. Kaplan-Meier curve: stratified by sex

Kaplan-Meier plots of survival for the entire cohort of patients with PMASC stratified by sex. Median survival for males and females was 15 and 10 months. Males (n=78) observed prolonged survival compared to females (n=57) ($p=0.042$ on Log Rank analysis). For male patients 6-months and 1-, 2-, 5-, 10-year survival rates were 80.6%, 60.8%, 37.5%, 24.0%, and 16.5%, respectively. The female cohort demonstrated survival rates of 61.0%, 39.5%, 25.1%, 11.7%, and 9.7%.

Figure 4. Kaplan-Meier curve: stratified by tumor histology

Kaplan-Meier plots of survival for the entire cohort of patients with PMASC stratified by tumor histology. Median survival for AA and GB cases was 17 and 10 months. AA cases (n=76) observed prolonged survival compared to GB cases (n=59) ($p=0.002$ on Log Rank analysis). For patients with AA 6-months and 1-, 2-, 5-, 10-year survival rates were 82.7%, 60.0%, 42.4%, 24.3%, and 19.0%, respectively. The GB cohort demonstrated survival rates of 59.0%, 41.1%, 18.7%, 11.2%, and 7.0%.

Figure 5. Kaplan-Meier curve: stratified by EOR

Kaplan-Meier plots of survival stratified by EOR for the PMASC cohort with known surgical data (n=109). Median survival for the NS, Bx, PR and GTR groups were 9, 10, 11, and 24 months, respectively. For patients not undergoing surgery the 6-months and 1-, 2-year survival rates were 60.0%, 37.5% and 10.0%, respectively. Patients undergoing a biopsy procedure demonstrated 6-months and 1-, 2-, 5-, 10-year survival rates of 67.2%, 48.0%, 24.0%, 19.2%, and 9.6%. The PR group had survival rates of 71.4%, 45.2%, 35.2%, 13.7% and 10.3%. Finally, patients undergoing a GTR showed survival rates of 85.0%, 72.9%, 48.6%, 25.9% and 22.2%. When compared to the NS group by log-rank analysis only the GTR group seemed to be statistically different ($p=0.002$).

Figure 6.

(A) Kaplan-Meier curve: stratified by the use of radiotherapy. Kaplan-Meier (KM) plots of survival for the entire cohort of patients with PMASC stratified by the use of radiotherapy. Median survival for the radiation and no-radiation groups was 15 and 5 months. Patients undergoing radiotherapy (n=109) showed a trend of prolonged survival compared to the no-radiation group (n=24) (p=0.068 on Log Rank analysis). **(B) Kaplan-Meier curve: adult cohort stratified by the use of radiotherapy.** KM plots for the adult cohort of patients with PMASC stratified by the use of radiotherapy. Median survival for radiation and no-radiation groups was 20 and 3 months. Patients undergoing radiotherapy (n=74) showed a trend of prolonged survival compared to the no-radiation group (n=17) (p=0.078 on Log Rank analysis). **(C) Kaplan-Meier curve: pediatric cohort stratified by the use of radiotherapy.** KM plots for the pediatric cohort of patients with PMASC stratified by the use of radiotherapy. Median survival for radiation and no-radiation groups was 9 and 13 months. Patients undergoing radiotherapy (n=35) did show a survival benefit compared to the no-radiation group (n=7) (p=0.924 on Log Rank analysis).

Table 1

Patient, tumor and treatment characteristics of 135 patients with PMASC. Data was collected from the SEER program 1973–2007.

Variable	No. of Patients (%)
Overall Age at Diagnosis (years)^a	35 ± 22
Pediatric cases (0–18y)	42 (31.1)
Age (years) ^a	11 ± 4
Range: <1 – 17	
Adult cases (>18y)	93 (68.9)
Age (years) ^a	46 ± 17
Range: 22 – 87	
Sex	
Male	78 (57.8)
Female	57 (42.2)
Histology	
Anaplastic Astrocytoma	76 (56.3)
Glioblastoma	59 (43.7)
Race	
White	113 (83.7)
Black	11 (8.1)
American Indian/Alaska Native	1 (0.7)
Asian or Pacific Islander	9 (6.7)
Other unspecified/Unknown	1 (0.7)
Period of Diagnosis	
< 1988	23 (17.0)
1988 – 1992	20 (14.8)
1993 – 1997	28 (20.7)
1998 – 2002	28 (20.7)
2003 – 2007	36 (26.7)
Extent of Resection	
No Surgery	15 (11.1)
Biopsy	22 (16.3)
Partial Resection	42 (31.1)
Gross total resection	30 (22.2)
Surgery: Not Specified	20 (14.8)
Unknown	6 (4.4)
Radiation therapy	
No	24 (17.8)
Yes	109 (80.7)
Unknown	2 (1.5)

^aMean ± Standard Deviation

Table 2

Univariate analysis of risk factors for overall mortality in patients with PMASC. P-values <0.05 indicate variables that are significantly associated with the risk of death. Only the pediatric and adult age groups, sex, histology, and extent of resection reached a level of significance. Among the extent of resection group, only the GTR group was significantly different from the NS group.

Variable	Hazard Ratio (CI)	P value ^b
Age at Diagnosis (years)		0.080
Age Groups		0.035
Pediatric (0–18y) ^a	1	
Adult (>18y)	0.65 (0.43–0.97)	
Sex		0.048
Male ^a	1	
Female	1.46 (1.00–2.13)	
Race		0.585
White ^a	1	
Black	1.26 (0.65–2.42)	
American Indian/Alaska Native	2.00 (0.28–14.49)	
Asian or Pacific Islander	1.51 (0.73–3.16)	
Histology		0.003
Anaplastic Astrocytoma ^a	1	
Glioblastoma	1.77 (1.22–2.58)	
Period of Diagnosis		0.343
< 1988 ^a	1	
1988 – 1992	0.66 (0.34–1.31)	
1993 – 1997	0.90 (0.49–1.65)	
1998 – 2002	1.13 (0.62–2.07)	
2003 – 2007	1.26 (0.70–2.28)	
Extent of Resection		0.041
No Surgery ^a	1	
Biopsy	0.67 (0.32–1.40)	
Partial Resection	0.60 (0.31–1.16)	
Gross Total Resection	0.37 (0.18–0.75)	
Radiation Therapy		0.076
Yes ^a	1	
No	1.55 (0.96–2.53)	

^aReference category

^bUnivariate Cox proportional hazard model was used to calculate the impact of the variable on overall survival. Values in bold indicate statistical significance.

Table 3

Multivariate analysis of risk factors for overall mortality in patients with PMASC. P-values <0.05 indicate variables that are significantly associated with the risk of death. Age at diagnosis, pediatric and adult age groups, sex, histology and extent of resection reached a level of significance. Among the EOR group, only the GTR and PR groups were significantly different from the NS group. Covariates dropped by the forward stepwise CPHM analysis are not reported.

Variable	Hazard Ratio (CI)	P value ^b
Age at Diagnosis (years)	1.02 (1.00–1.04)	0.013
Age groups		0.002
Pediatric (0–18y) ^a	1	
Adult (>18y)	0.28 (0.13–0.62)	
Sex		0.020
Male ^a	1	
Female	1.68 (1.09–2.59)	
Histology		0.001
Anaplastic Astrocytoma ^a	1	
Glioblastoma	2.29 (1.42–3.67)	
Extent of Resection		0.054
No Surgery ^a	1	
Biopsy	0.61 (0.28–1.34)	
Partial Resection	0.43 (0.20–0.90)	
Gross Total Resection	0.38 (0.18–0.82)	

^aReference category

^bMultivariate 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, histology, period of diagnoses, extent of resection and radiotherapy. A total of 106 cases with complete data on all analysis variables were used. Values in bold indicate statistical significance.