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The Impact of Vision Loss Among Survivors of Childhood Central Nervous System Astroglial Tumors

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Abstract

Background—The impact of impaired vision on cognitive and psychosocial outcomes among long-term survivors of childhood low-grade gliomas has not been investigated previously, but could inform therapeutic decision-making.

Methods—Data from the Childhood Cancer Survivor Study was used to investigate psychological (measures of cognitive/emotional function) and socioeconomic (education, income, employment, marital status, independent living) outcomes among astroglial tumors survivors grouped by: (a) vision without impairment, (b) vision with impairment including unilateral blindness, visual field deficits or amblyopia, or (c) bilateral blindness. The effect of vision status on outcomes was examined using multivariable logistic regression, adjusting for age, gender, cranial radiation therapy and medical comorbidities.

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Conflict of Interest: None

Results—Among 1,233 survivors of childhood astroglial tumor ≥ 5 years post-diagnosis, 277 (22.5%) had visual impairment. In multivariable analysis, survivors with bilateral blindness were more likely to be unmarried (adjusted odds ratio [95% confidence interval]: 4.7 [1.5, 15.0]), live with a caregiver (3.1 [1.3, 7.5]), and be unemployed (2.2 [1.1, 4.5]) compared to those without visual impairment. Bilateral blindness had no measureable effect on cognitive or emotional outcomes, and vision with impairment was not significantly associated with any psychological or socio-economic outcomes.

Conclusions—Adult survivors of childhood astroglial tumors with bilateral blindness are more likely to live unmarried and dependently and be unemployed. Survivors with visual impairment but some remaining vision did not differ significantly with regard to psychological function and socioeconomic status from those without visual impairment.

Keywords

pediatric glioma; vision loss; late effects; childhood cancer survivors; optic pathway glioma

Introduction

Astroglial tumors are the most common brain tumor in children[5] and can result in rapid vision loss by involvement of the visual pathways (as optic pathway gliomas, OPGs) or compression of visual circuits. In contrast to high grade malignancies, low grade astroglial tumors are associated with prolonged patient survival,[6] even in cases where surgical resection is not practical.[7] Therefore, preserving vision remains a high priority for both caregivers and families of individuals with astroglial tumors that threaten vision.[8] Fortunately, only a portion of tumors that directly involve the optic pathway will progress and/or result in visual deficits.[9, 10] However, identifying early vision loss can be challenging in children.[11] Treatments such as chemotherapy and radiation therapy can expose children to risks of serious infection, life-threatening allergic reaction, as well as neurologic or endocrine dysfunction.[12-14] Deciding whether and when to start therapy for low-grade gliomas affecting vision is a common clinical dilemma. We hypothesize that vision loss during childhood may affect academic and social development, and impair adult outcomes such as quality of life, emotional health, independence and financial security. Compared to adult-onset vision loss, childhood vision loss due to CNS tumors may cause disproportionate deficits in psychological and socio-economic outcomes due to a greater number of “blind years” as well as neurologic comorbidities, secondary to neurofibromatosis type 1 and the effect of treatment on a developing brain.[15] Alternatively, early adaptation leading to neural reorganization and ready access to social supports may help ameliorate the impact of visual impairments.[16]

To better advise patients with progressive astroglial tumors that threaten their vision regarding the risks and benefits of therapy, we must first understand the long-term effects of vision loss in the pediatric population. The purpose of this study was to compare the psychological and socioeconomic late outcomes in long-term survivors of childhood astroglial tumors with and without vision loss.

Methods

The CCSS is a multi-institutional retrospective study of individuals who survived at least 5 years after diagnosis of cancer.[17-19] Participants in the CCSS cohort were younger than 21 years old when diagnosed between January 1, 1970 and December 31, 1986. No additional age limitations were placed for this analysis. The current analyses were limited to survivors of astroglial tumors. Cumulative incidence of vision loss was measured in all survivors (N= 1233), while analyses involving the impact of impaired vision on psychological or socioeconomic outcomes were limited to those who completed relevant questions from the Follow-up 2 (FU2; 2002-2005) and Follow-up 4 (FU4; 2007-2010) surveys (N= 587, Figure 1). Among 1233 astroglial survivors, 115 (9.3%) died prior to completing the baseline survey, and 128 (10.3%) died before the FU4 survey. Survivors who developed a second malignant neoplasm of the CNS were excluded from analyses (i.e., diagnosis of meningioma did not exclude a survivor). Institutional review board approval was obtained. Participants or legal guardians provided informed consent.

Cumulative vision loss in all survivors of astroglial tumors was derived from answers to the baseline survey. Vision loss was defined as any positive response when respondents were asked if they have ever been told by a doctor or other health care professional that they are “legally blind in one or both eyes,” “have problems with double vision,” “any other problems with seeing with one or both eyes even when wearing glasses,” or if they described amblyopia or visual field deficits when asked about “other eye problems.” Vision impairment for multivariate analysis was defined categorically from the FU4 survey as (a) vision without impairment, (b) vision with impairment (including amblyopia, visual field deficits or unilateral blindness) or (c) bilateral blindness, as reported by survivors or their proxies. Vision with impairment was defined similar to above as “legally blind in only one eye”, “lazy eye (amblyopia)” or “any other trouble seeing with one or both eyes even when wearing glasses” or if respondents described visual field deficits. Bilateral blindness was defined as a positive response to the question of whether respondents had been told they are “legally blind in both eyes.”

Primary outcome variables included psychological and socioeconomic outcomes. Psychological outcomes utilized information from the FU2 survey and were derived from components of the Medical Outcomes Survey Short Form-36 (SF-36), the Brief Symptom Inventory-18 (BSI-18), the Cantril Ladder of Life and the CCSS neurocognitive questionnaire (NCQ). The SF-36 measured patient reported health outcomes and health-related quality of life over the last 4 weeks, including both physical and mental components.[20] The BSI-18 was used to measure psychological distress and emotional health among survivors. This inventory includes a summary scale (global distress index) and three subscales (depression, anxiety, and somatization) and has been previously used in cancer survivor cohorts.[21, 22] The Cantril Ladder of Life was used to measure life satisfaction among cancer survivors. Respondents rated their current lives on a 10-point scale ranging from “best possible life” to “worst possible life.”[23] This global rating of life satisfaction has been used in previous studies of survivors of adult and childhood cancer.[24, 25] Neurocognitive outcomes were assessed using the CCSS-NCQ, including subscales that measure task efficiency, emotional regulation, organization and memory. This scale was

developed and validated in adult survivors of childhood cancer to assess neurocognitive impairment including executive dysfunction.[26] Psychological impairment was determined in reference to standard norms and defined independently on each scale as follows: SF-36 T < 40; BSI-18 percentile > 10^{th}; CCSS-NCQ percentile < 10^{th}. The Cantril Ladder of Life (present) was considered impaired if subjects rated their current life satisfaction as less than 7 on a 10-point scale.

Socioeconomic outcomes included marital status, living independently, employment, income and education. Subjects were dichotomized as never married or married (including living as married, widowed or divorced). Living independently was defined as living alone or with a spouse/partner. Employment was defined as working full or part-time, and income was dichotomized as greater than or less than $20,000 per year. Education was dichotomized as no college attendance or some college attendance with or without a college degree. Socioeconomic and psychological measures were categorized consistent with previous reports to place outcomes of vision loss in the context of other late effects found in survivors of childhood brain tumors.

Potential covariates investigated for their effect on primary outcomes included age at diagnosis, age at survey, gender, history of cranial radiation therapy (CRT; none, ≤30Gy CRT, >30Gy CRT), presence of a meningioma, chronic conditions (coded according to Common Toxicity Criteria for Adverse Events[27] and defined as any grade 3 or 4 medical condition, except vision impairment, occurring before 2004). Because proxy reporting may misclassify psychological and socioeconomic outcomes, a sensitivity analysis was performed to examine the effect of proxy reporting during the FU2 survey. Final models were reported without a variable for proxy reporting. Among survivors with vision loss, age at vision loss was dichotomized as <6 years and ≥6 years because this represented a meaningful division (age at school entry) and conveniently presented equal proportions of subjects in either group. In an additional analysis, age at interview was replaced by time from diagnosis. No significant changes were found in our multivariable model, and our final model includes age at interview.

Summary statistics were constructed using frequencies and proportions for categorical data elements and means and medians for continuous variables. Frequency distributions were examined to categorize relevant covariates according to reasonable groupings and consistent with previous CCSS manuscripts. Univariate logistic regression was used to evaluate associations between each outcome variable and visual function as well as for candidate covariates listed above. Covariates with a p-value of <0.20 for a univariate association were included in the multivariable models for the relevant outcome. Multivariable logistic regression analyses were used to examine associations between vision status and each outcome, controlling for covariates selected as indicated above. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). SAS version 9.3 (Cary, N.C.) was used for analysis.

Results

Among astroglial survivors, 277 (22.5%) had vision with impairment and 47 (3.8%) were bilaterally blind. The vast majority of vision impairment occurred within 5 years of diagnosis (Figure 2).

Of the 1,233 survivors of astroglial tumors in the CCSS cohort identified at baseline survey, 646 were excluded from further analysis of psychological and socioeconomic outcomes due either to second CNS malignancies or lack of follow-up data. Evaluable survivors included in the analyses were more likely to be female, and less likely to have been exposed to chemotherapy or radiation (Table 1). Survivors with impaired vision were diagnosed at a younger age, were less likely to have undergone surgery and more likely to have used proxy reporting compared to survivors without vision impairment (Table 2).

In univariate analysis, survivors with bilateral blindness were more likely to never marry, live dependently, and/or not attend college and to demonstrate impairment on the Task Efficiency subscale of the NCQ (Table 3) when compared to those without vision impairment. They also demonstrated a trend (p=0.06) toward impairment in the physical component of the SF-36 and employment status compared to those without vision impairment. Impaired vision was not associated with measures of psychological distress (BSI-18), mental health-related quality of life (SF-36, mental component) or life satisfaction (Cantril Ladder of Life).

Table 4 displays the associations between impaired vision and each psychological and socioeconomic outcome, adjusting for age, gender, prior CRT, and chronic health conditions. Survivors with bilateral blindness were more likely to be unmarried (OR 4.74 [1.49, 15.00]), live dependently (OR 3.12 [1.30, 7.48]) and be unemployed (OR 2.17 [1.06, 4.46]) compared to those without vision impairment. Survivors with bilateral blindness may be less likely to attend college (OR 2.05 [0.99, 4.23]), but this did not achieve statistical significance. The multivariable analysis was repeated to include proxy reporting as a potential covariate. This model demonstrated that bilateral blindness was associated with similar late effects as those shown above, including being unmarried (OR 3.94 [1.22, 12.74]) and living dependently (OR 2.98 [1.23, 7.21]) (full model not shown). Impaired vision other than bilateral blindness was not associated with any of the psychological or socioeconomic outcomes. In survivors with visual impairment, there was no effect of age at first onset of visual impairment on psychological or socioeconomic outcomes (data not shown).

Discussion

This analysis suggests that bilateral blindness may be an important determinant of marital status, independent living and employment among adult survivors of childhood astroglial tumors. Our results also suggest that survivors with some visual impairment were not significantly different from those without visual impairment. Given this treatment era, when few patients diagnosed with high-grade astroglial tumors (such as anaplastic astrocytoma and glioblastoma multiforme) survived five years from diagnosis, these findings are most

directly relevant to aging survivors of low grade gliomas such as optic pathway gliomas (OPGs).[28, 29]

OPGs are the most common astroglial tumors to threaten vision. These tumors have a very high overall survival rate,[29] but can cause some vision impairment in up to half of affected patients.[30] Up to 70% of OPGs are associated with NF1,[31] and NF1-associated tumors are often diagnosed at an early age and rarely cause new vision loss after the age of 10 years.[32] In our cohort, 72% of astroglial survivors with impaired vision or bilateral blindness were diagnosed before 10 years of age, compared to 54% of those with unimpaired vision. Only 10% of the cohort died before FU4 survey, compared to 18% of all CNS tumor survivors in the CCSS,[33] suggesting a low overall late mortality consistent with low grade tumors. In addition, the median age at first visual deficit was 6 years, and few late visual deficits occurred (Figure 2), suggesting that the cohort with impaired vision is likely enriched for NF1-associated optic pathway tumors.

Few studies have examined the impact of tumor-associated vision loss. In 36 children with OPG, vision loss was associated with decreased vision-specific quality of life, and bilateral vision impairment was associated with greater difficulty with social interactions and pleasurable activities by parent report.[1] A small series of children with visual impairment not associated with CNS tumor (N=24, mean age 10.13+/−2.89) reported diminished vision-specific quality of life and that extent of visual impairment correlated with decreased quality of life measures.[2] In British birth cohort studies, all-cause visual impairment among adults has been associated with higher rates of unemployment (OR [95% CI]: 4.6 [2.7 – 8.0]) and lower socioeconomic status (1.9 [1.3 – 2.7]).[3, 4] These results are consistent with our findings that demonstrate an association between marital status, independent living and employment with bilateral blindness but not with vision with some impairment.

Although our study demonstrates an association between bilateral blindness in adult survivors of childhood astroglial tumors and certain socio-economic outcomes, it is important to note that many outcomes were unaffected by childhood vision loss. Adult survivors with childhood blindness failed to show any significant psychological distress, neurocognitive impairment or income deficit. Survivors with some remaining vision showed no significant impairment in any measured outcome. This lack of effect is seen, despite our sample of those with impaired vision or bilateral blindness being likely enriched for subjects with neurofibromatosis type 1, who frequently have learning differences and attention disorders that may hinder educational and employment opportunities.[15, 34] It is impossible to directly compare vision-specific quality of life from other studies of children with tumor-related vision loss to measures in this study; however, adult survivors with childhood vision loss showed no mental or physical impairment on the SF-36 or decreased life satisfaction on the Cantril Ladder of Life compared to survivors of similar tumors without vision loss.

The modest long-term effects of vision loss seen in this study are consistent with recent evidence in retinoblastoma that shows few cognitive or social attainment deficits in adult survivors with vision loss.[35] Studies have suggested that neural reorganization after early vision loss can ameliorate sensory deficits and may be associated with superior cognitive outcomes in subjects with early vision loss (occurring before 1 year of age),[16, 35] although

age at first onset of impaired vision was not associated with any adult outcomes in our study (data not shown).

Determining an optimal time to treat gliomas (such as OPGs) that threaten vision can be challenging. Traditional endpoints used to determine the need for treatment, such as radiographic progression, have not been associated with the important functional endpoint of vision loss.[36-38] Recent expert opinion suggests that visual outcomes may be the most important endpoint for future clinical trials.[39] However, before exposing children to the risks associated with chemotherapy or radiation, it is important to understand the impact that childhood vision loss may have on adult life. Our data suggest that tumors threatening vision in a single eye, such as solitary optic nerve gliomas, may have limited impact on adult psychological and socioeconomic outcomes.

This study represents one of the largest samples of adult survivors of astroglial tumors in the literature, suggesting that the effect size of any unrecognized association is likely small. Taken as a whole, this suggests that adult survivors of astroglial tumors adapt well to early impairment of vision, although survivors with bilateral vision loss may experience worse socioeconomic outcomes. The challenges of limited vision (including limitations in driving and difficulties with activities of daily living) should not be minimized; however, this remains promising news for children with OPG who may have permanent vision loss despite our best current therapies.

This study is subject to certain important limitations. Ten percent of astroglial survivors died before the FU4 survey, excluding them from analysis of psychological or socioeconomic outcomes. Subjects included in analysis also differed significantly from those excluded in terms of gender and exposure to chemotherapy and radiation, which may have resulted in an underestimate of negative outcomes.[40, 41] Self-report may overestimate or underestimate the severity of vision loss, and initial visual symptoms may be present earlier than realized by the survivor. However, many of our findings are comparable to those reported with direct assessment.[35] A significant portion of respondents used proxies to complete their surveys (41% with bilateral vision loss, 22% with some vision loss and 20% with no vision loss). Proxy reporting was not included in the main multivariable model because its strong association with vision loss may reduce the ability to find a significant association between vision loss and late outcomes. Proxy reports of observed behaviors (such as the socio-economic outcomes in this study) are generally closely correlated with self-report. Proxy reporting would have been included as a potential covariate in affective outcomes (such as depression and anxiety), which were excluded in univariate analysis. A multivariable analysis including proxy reporting demonstrates no difference in the outcomes associated with vision loss.

While our analysis investigates late effects of vision in survivors of low-grade glioma in the largest population yet published, precise tumor location and glioma subtype may predict adverse outcomes but were not available for the current study. In addition, Vision-specific quality of life was not assessed in the CCSS questionnaires and should be assessed in future studies of long-term survivors with vision loss to determine whether vision-specific quality of life deficits found in other studies persist into adulthood.[1] This is especially true since

more general measures of health-related quality of life (SF-36) failed to show a significant difference between survivors with and without vision loss in multivariable analysis.

Conclusions

Understanding the impact of childhood vision loss in adult survivors of childhood astroglial tumors is important as it may help guide clinical decision-making about potential therapies for astroglial tumors that threaten vision. Our study demonstrates that adult survivors of childhood astroglial tumors who are blind in both eyes are more likely to be unmarried, live dependently and be unemployed compared to survivors with unimpaired vision. Trends toward significance were also found between bilateral blindness and a lower level of attained education. However, there was no difference in psychological measures between adult survivors who were blind and those that had unimpaired vision, and survivors with vision but some impairment were not significantly different from those with normal vision in either psychological or socio-economic outcomes.

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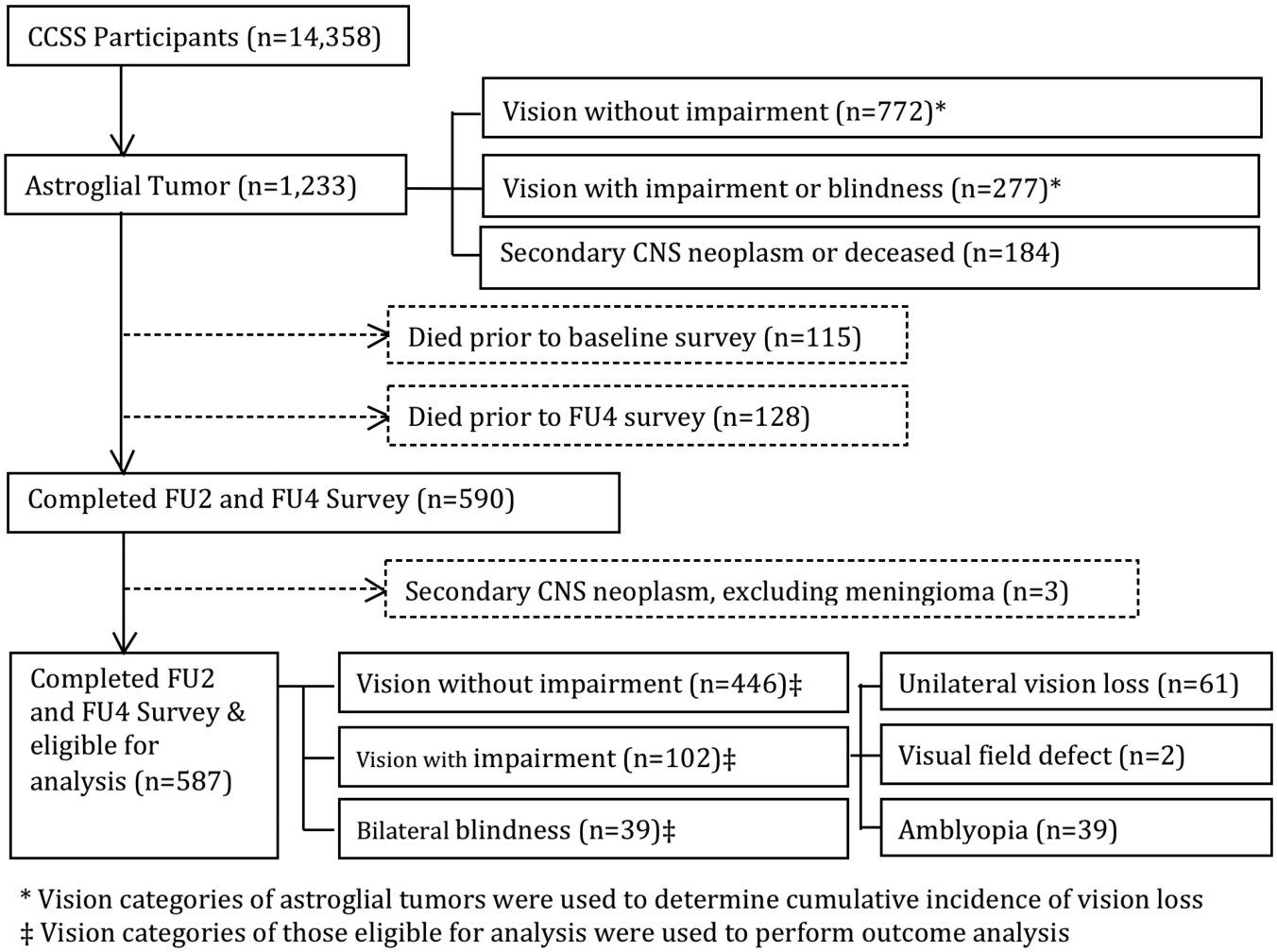
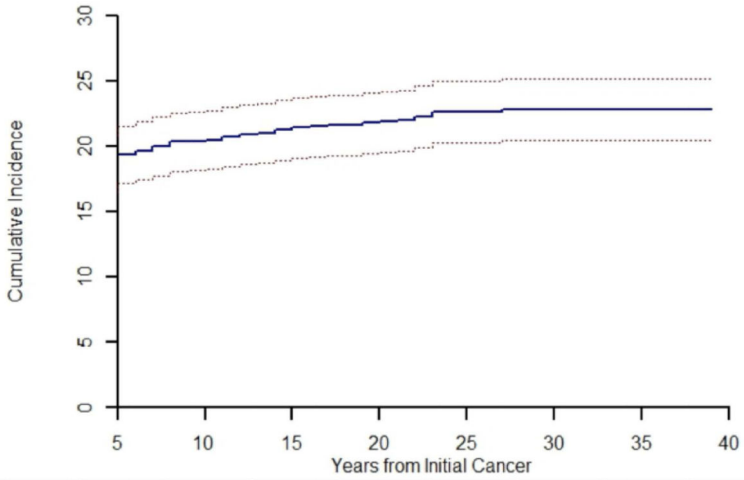


Figure 1.
Consort diagram of study participants with astroglial tumors.



Number at risk	1003	933	836	730	431	211	67	0
Number of events	22	10	6	8	1	0	0	0

Figure 2.

Cumulative incidence of first reported vision loss vs. years from initial diagnosis in survivors of childhood astroglial tumors. Number of survivors at risk and number of events shown for each five year period.

Table 1

Characteristics of survivors of childhood astroglial tumors who are and are not evaluable for study

Characteristic	Evaluable for late outcomes (n=587)	Not evaluable for late outcomes (n=646)	P value
Age at baseline, years (sd)	23.79 (7.30)	23.26 (7.52)	0.21
Sex [n (%)]			
Male	285 (48.6)	379 (58.7)	<0.001
Female	302 (51.4)	267 (41.3)	
Age at diagnosis [n (%)]			
≤4 years	210 (35.8)	226 (35.0)	0.34
5-9 years	134 (22.8)	129 (20.0)	
≥10 years	243 (41.4)	291 (45.0)	
Treatment*			
Surgery [n (%)]			
Yes	538 (98.0)	527 (96.9)	0.26
No	11 (2.0)	17 (3.1)	
Chemotherapy [n (%)]			
Yes	87 (15.8)	133 (24.4)	<0.001
No	463 (84.2)	412 (75.6)	
Radiation [n (%)]			
Yes	324 (58.9)	352 (64.8)	0.046
No	226 (41.1)	191 (35.2)	
Age at first vision problem [n (%)]			
</=6 years	73 (51.8)	75 (57.6)	0.39
>6 years	68 (48.2)	56 (42.4)	
Vision status at baseline			
Blind in one/both eye	91 (15.8)	126 (20.0)	0.09
No vision loss	486 (84.2)	503 (80.0)	

*38 evaluable survivors of astroglial tumors had missing treatment information (38 missing information on surgery, 37 missing information on radiation and chemotherapy), 103 inevaluable survivors had missing treatment information (102 missing information on surgery, 101 missing information on chemotherapy, 103 missing information on radiation).

Table 2

Characteristics of survivors of childhood astroglial tumors eligible for study by vision status

Characteristic	Vision without impairment (n=446)	Vision with impairment (n=102)	Bilateral blindness (n=39)	P-value
Age at Interview [n (%)]				
<30 years	186 (41.7)	58 (56.9)	20 (51.3)	0.08
30-39 years	205 (46.0)	34 (33.3)	16 (41.0)	
≥40 years	55 (12.3)	10 (9.8)	3 (7.7)	
Sex [n (%)]				
Male	224 (50.2)	43 (42.2)	18 (46.2)	0.32
Female	222 (49.8)	59 (57.8)	21 (53.8)	
Age at diagnosis [n (%)]				
≤4 years	138 (30.9)	54 (52.9)	18 (46.2)	<0.001
5-9 years	105 (23.5)	18 (17.6)	11 (28.2)	
≥10 years	203 (45.5)	30 (29.4)	10 (25.6)	
Treatment*				
Surgery [n (%)]				
Yes	413 (98.8)	91 (96.8)	34 (91.9)	0.03
No	5 (1.2)	3 (3.2)	3 (8.1)	
Chemotherapy [n (%)]				
Yes	63 (15.0)	14 (14.9)	10 (27.0)	0.17
No	356 (85.0)	80 (85.1)	27 (73.0)	
Radiation [n (%)]				
Yes	246 (58.7)	50 (53.2)	28 (75.7)	0.06
No	173 (41.3)	44 (46.8)	9 (24.3)	
Age at first vision problem				
≤6 years	NA	56 (54.9)	17 (43.6)	0.26
>6 years	NA	46 (45.1)	22 (56.4)	
Proxy reporting*				
Yes	88 (20.0)	22 (21.8)	16 (41.0)	0.01
No	351 (80.0)	79 (78.2)	23 (59.0)	

*38 survivors of astroglial tumors have no information on surgery (28 with no vision loss, 8 with some vision loss, 2 with bilateral vision loss). 37 survivors of astroglial tumors have no information on chemotherapy or radiation (27 with no vision loss, 8 with some vision loss, 2 with bilateral vision loss). 8 survivors of astroglial tumor did not answer the question for the proxy reporting (7 with no vision loss, 1 with some vision loss).

Table 3

Univariate comparison of psychological and socioeconomic outcomes among survivors of childhood astroglial tumors by vision status

Outcome			Vision Category			p value
			Vision without impairment	Vision with impairment	Bilateral blindness	
Psychological	Short Form-36					
	Physical	impaired	57	11	10	0.06
		not impaired	301	70	21	
		OR (95%CI)	reference	0.83(0.41,1.66)	2.52(1.13,5.62)	
	Mental	impaired	70	18	4	0.55
		not impaired	288	63	27	
		OR (95%CI)	reference	1.18(0.66,2.11)	0.61(0.21,1.80)	
	Brief Symptom Inventory-18					
	GDI	impaired	47	12	4	0.97
		not impaired	326	77	27	
		OR (95%CI)	reference	1.08(0.55,2.14)	1.03(0.34,3.07)	
	Depression	impaired	60	17	4	0.70
		not impaired	313	72	27	
		OR (95%CI)	reference	1.23(0.68,2.24)	0.77(0.26,2.29)	
	Anxiety	impaired	36	7	3	0.85
		not impaired	337	82	28	
		OR (95%CI)	reference	0.80(0.34,1.86)	1.00(0.29,3.46)	
	Somatization	impaired	48	14	6	0.43
		not impaired	325	75	25	
		OR (95%CI)	reference	1.26(0.66,2.41)	1.63(0.63,4.17)	
	Cantril Ladder of Life					
	Life Satisfaction (present)	impaired	129	25	8	0.46
		not impaired	225	55	22	
		OR (95%CI)	reference	0.79(0.47,1.33)	0.63(0.28,1.47)	
	NeuroCognitive Questionnaire					
	Task Efficiency	**impaired**	**133**	**40**	**16**	**0.049**
		not impaired	**209**	**40**	**12**	
		OR (95%CI)	**reference**	**1.57(0.96,2.56)**	**2.10(0.96,4.57)**	
	Emotional Regulation	impaired	48	12	6	0.56
		not impaired	307	68	24	
		OR (95%CI)	reference	1.13(0.57,2.24)	1.60(0.62,4.11)	
	Organization	impaired	71	17	7	0.86
		not impaired	283	65	23	
		OR (95%CI)	reference	1.04(0.58,1.89)	1.21(0.50,2.94)	
	Memory	impaired	91	21	10	0.67

Outcome			Vision Category			p value
			Vision without impairment	Vision with impairment	Bilateral blindness	
		not impaired	259	60	20	
		OR (95%CI)	reference	1.00(0.57,1.73)	1.42(0.64,3.15)	
Socioeconomic	**Marital Status**					
	Never Married		**275**	**70**	**34**	**<0.001**
	Married		**170**	**31**	**4**	
	OR (95% CI)		**reference**	**1.40(0.88,2.22)**	**5.26(1.83,15.07)**	
	Living Arrangement					
	Living Dependently		**212**	**57**	**31**	**<0.001**
	Living Independently		**234**	**45**	**8**	
	OR (95% CI)		**reference**	**1.40(0.91,2.16)**	**4.28(1.92,9.51)**	
	Employment Status					
	Unemployed		166	43	22	0.05
	Employed		280	59	17	
	OR (95% CI)		reference	1.23(0.79,1.90)	2.18(1.13,4.23)	
	Income					
	Income <=$20,000		269	68	27	0.11
	Income >$20,000		158	28	8	
	OR (95% CI)		reference	1.43(0.88,2.31)	1.98(0.88,4.47)	
	Education					
	Less than College		**149**	**35**	**22**	**0.02**
	College		**290**	**64**	**16**	
	OR (95% CI)		**reference**	**1.06(0.67,1.68)**	**2.68(1.36,5.25)**	

OR = odds ratio, 95%CI = 95% confidence interval, GDI = Global Disability Index. Bold text indicates statistical significance (p<0.05)

Table 4

Multivariate analysis reporting odds ratio (95%CI) for associations between psychological and socioeconomic outcomes and vision status among survivors of childhood astroglial tumor.

	Psychological Status		Socioeconomic Status				
	SF-36 Physical	**Task Efficiency**	**Not married**	**Live dependently**	**Not employed**	**Income ≤$20,000**	**Education < College**
Number of Analyzed Subjects (Total N=587)	**436**	**419**	**530**	**533**	**533**	**510**	**525**
Vision Status							
Vision without impairment	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Vision with impairment	0.81(0.38,1.74)	1.65(0.97,2.81)	1.19(0.68,2.10)	1.15(0.70,1.90)	1.29(0.79,2.09)	1.17(0.67,2.02)	0.93(0.56,1.55)
Bilateral Vision Loss	2.02(0.85,4.84)	1.71(0.74,3.93)	**4.74(1.49,15.00)**	**3.12(1.30,7.48)**	**2.17(1.06,4.46)**	1.58(0.61,4.08)	2.05(0.99,4.23)
Age at Diagnosis							
>/=10	*	*	*	Reference	*	Reference	Reference
5-9				1.23(0.75,2.03)		0.57(0.34,0.98)	1.41(0.86,2.30)
</=4				**1.97(1.19,3.27)**		1.32(0.75,2.29)	**2.01(1.29,3.12)**
Age at Interview, years							
>=40	*	*	Reference	Reference	*	Reference	*
30-39			**2.49(1.31,4.72)**	1.62(0.83,3.16)		1.81(0.96,3.42)	
<30			**21.49(10.43,44.26)**	**4.40(2.12,9.16)**		**5.10(2.45,10.63)**	
Sex							
Male	*	*	Reference	*	Reference	*	*
Female			0.47(0.30,0.72)		**1.68(1.16,2.44)**		
Cranial Radiation							
None	Reference	Reference	Reference	Reference	Reference	Reference	Reference
≤30Gy	**13.18(3.29,52.73)**	0.29(0.06,1.43)	0.90(0.27,3.04)	0.98(0.31,3.06)	2.41(0.78,7.46)	1.17(0.35,3.88)	0.53(0.14,1.98)
>30Gy	**1.89(1.01,3.55)**	**2.06(1.34,3.18)**	**2.19(1.39,3.45)**	**1.83(1.23,2.73)**	**1.74(1.17,2.59)**	**1.87(1.23,2.85)**	**2.05(1.37,3.06)**
Medical Comorbidity (Grade 3-5)							
No	Reference	Reference	Reference	Ref.	Ref.	Reference	Reference
Yes	**5.36(2.92,9.87)**	**2.50(1.63,3.85)**	**1.85(1.17,2.95)**	**1.83(1.22,2.73)**	**2.83(1.92,4.15)**	**2.67(1.71,4.17)**	**1.84(1.25,2.72)**

*Variable does not contribute to the overall multivariable model