

Chapter 25

Cancer of the Brain and Other Central Nervous System

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INTRODUCTION

This study provides survival analysis for 19,774 histologically confirmed first primary brain and other central nervous system (CNS) cancers diagnosed from 1988 through 2001 from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). The analysis performed in this study attempts to better understand the influence of morphologic and demographic factors on survival. Other CNS cancers include cancers of the central nervous system and malignant meningiomas of the brain. Benign and borderline tumors are not included in these analyses.

Brain and other CNS cancers are considered to be rare compared to prostate, lung, breast, or colon cancer. It is estimated there will be 18,820 new cases diagnosed of and 12,820 deaths from brain and other CNS cancer in the United States each year (1). The average annual age-adjusted incidence rate for brain and other CNS cancer in the United States is 7.6 per 100,000 for males and 5.4 per 100,000 for females (white males: 8.3 per 100,000; white females: 5.9 per 100,000; black males: 4.9 per 100,000; black females: 3.5 per 100,000) (2). The average annual age-adjusted mortality rate is approximately 4.5 per 100,000 for all races combined, with males having a higher mortality rate as compared to females (2).

Histologic type of tumor, age at diagnosis, race and treatment are all important predictors of survival, with a large variation in survival by histologic type of tumor (3, 4, 5, 6). The most common histologic subtypes of brain cancer are astrocytoma and glioblastoma multiforme (GBM), while the most common histologic subtypes of other CNS cancer are meningioma and ependymoma (3, 4, 7, 8, 9). Patients with GBM have the worst survival compared to any other histologic subtype (8).

No risk factor accounting for a large number of brain and other CNS cancers has been identified. There has been

some evidence for inherited factors, with approximately 16% of families studied having a family history of cancer (5, 10, 11). The only known risk factor for primary brain and other CNS cancers is exposure to therapeutic ionizing radiation. Other factors have been shown to cause increased risk, including exposure to synthetic rubber manufacturing, to vinyl chloride, to petroleum refining/production work, or to pesticides and consumption of cured foods, but the data are inconsistent (5). Exposure to filtered cigarettes, diagnostic ionizing radiation, residential electromagnetic fields, formaldehyde, cell phone use and active or passive maternal tobacco smoking are not proven risk factors (5). The most common presenting symptoms, progressive neurological deficit, motor weakness, headache and seizure, do not appear to be independent risk factors (5, 11).

MATERIALS AND METHODS

Exclusions

Between 1988 and 2001, 29,335 adult cases of malignant brain and other CNS cancer were diagnosed and reported to the NCI SEER Program. Children (aged less than 20) were excluded because brain and other CNS cancer are different in children compared to adults in terms of incidence and survival (8, 12). Patients were followed for vital status until 2001. The survival analysis was based on relative survival rates calculated by the life-table method (13). The relative rate was used to estimate the effect of cancer on the survival of the cohort. Relative survival, defined as observed survival divided by expected survival, adjusts for the expected mortality that the cohort would experience. Further descriptions of the NCI SEER program, data selection and relative survival analysis can be found in Chapter 1. Table 25.1 details the exclusions from this group of patients that resulted in a final group of 19,774 total patients, 18,669 brain cancer and 1,105 other CNS cancer.

Histologic Type of Tumor Classification

For brain and other CNS cancer, histologic type is one of three important clinical factors (the others are age at diagnosis and grade). In the SEER database, histologic classification for years of diagnosis 1988-2001 follows the ICD-O-2 and ICD-O-3 morphology codes. For the brain cancer cases, the histologic types were coded in the following manner: 9380, 9381, 9382 – glioma; 9390, 9443, 9473 – glioma, other; 9391, 9392, 9393 – ependymoma; 9400-9430 – astrocytoma; 9440-9442 – glioblastoma; 9450-9460 – oligodendroglioma; 9470-9472 – medulloblastoma; 9060-9085, 9490-9506, 8000-8002, 8680, 9364, 9370 – Other. For the other CNS cancer cases, the histologic types were coded in the following manner: 9391-9394 – ependymoma; 9400-9421 – astrocytoma; 9380-9382, 9473, 9440, 9450 – glioma; 9530-9539 – meningioma; 9490-9522, 8680-8693, 800-8001, 8990, 9064, 9364, 9370 – other.

Primary Site Classification

For brain cancers, primary site of tumor is classified as the following: C710 – Cerebrum, C711 - Frontal Lobe, C712 - Temporal Lobe, C713 - Parietal Lobe, C714 - Occipital Lobe, C715 – Ventricle, Not Otherwise Specified (NOS), C716 - Cerebellum, NOS, C717 - Brain Stem, C718 - Overlapping lesion of brain and C719 - Brain, NOS. For other CNS cancers, primary site of tumor is classified as the following: BRAIN: C700 - Cerebral meninges, C709 - Meninges, NOS, C710 – Cerebrum, C711 - Frontal Lobe, C712 - Temporal Lobe, C713 - Parietal Lobe, C714 - Occipital Lobe, C715 - Ventricle,

NOS, C716 - Cerebellum, NOS, C717 - Brain Stem, C718 - Overlapping lesion of brain and C719 - Brain, NOS; SPINE: C701 - Spinal meninges, C720 - Spinal Cord and C721 - Cauda equine and OTHER: C723 - Optic nerve, C724 - Acoustic nerve, C725 - Cranial nerve, NOS, C728 - Overlapping lesion of brain and CNS and C729 – Nervous system, NOS.

Stage Classification

Stage is not presented for brain cancer; however, stage is presented for other CNS cancer. In the SEER database, the categories for SEER stage are in situ, localized, regional, distant and unstaged. In situ cases are excluded from this study as seen in Table 25.1. Localized stage is defined as an invasive neoplasm confined entirely to the organ. Regional stage is defined as a neoplasm that has extended either beyond the organ or into regional lymph nodes. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Unstaged cancers lack sufficient information to assign stage. The American Joint Committee on Cancer (AJCC) TNM staging system, 5th Edition, (14) is also used.

RESULTS

In general, 24% and 69% of patients survived 5 years for brain cancer and other CNS cancer, respectively (Table 25.2). Figure 25.1 shows the 10-year relative survival curves for these two distinct types of cancer.

Table 25.1: Cancer of the Brain & Other Central Nervous System: Number of Cases and Exclusions, 12 SEER Areas, 1988-2001

Brain		Other CNS		Reason for Exclusion/selection
Number Selected/ Remaining	Number Excluded	Number Selected/ Remaining	Number Excluded	
27,479	0	1,856	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
25,159	2,320	1,680	176	Select first primary only
24,647	512	1,656	24	Exclude death certificate only or at autopsy
24,562	85	1,644	12	Exclude unknown race
24,502	60	1,639	5	Active follow-up and exclude alive with no survival time
20,937	3,565	1,306	333	Exclude children (000-019)
20,937	0	1,306	0	Exclude in situ cancers
18,740	2,197	1,196	110	Exclude no or unknown microscopic confirmation
18,674	66	1,118	78	Exclude sarcomas
18,669	5	1,105	13	Exclude Melanomas

For all analyses, brain cancer and other CNS cancer are analyzed separately because of the distinct differences between these two groups in clinical presentation, treatment patterns, response to treatment, and survival (12). In some of the tables, 1-, 2-, 3-, 5-, 8-, and 10-year relative survival rates are presented and in the figures, they are presented annually.

Brain Cancer

The prognostic factors of interest for the brain cancer analysis were: race, sex, age at diagnosis, histologic type, grade and primary site. The combinations of particular interest were: race and sex, histologic type and sex and histologic type and race. Size of tumor information was not analyzed because of the large amount of missing data (46.8%) (Table 25.3).

Race and Sex

For the analyses of relative survival, SEER classifies patients by race in three basic categories: white, black and

other. For all race specific analyses, only white and black patients are used because the other category is made up of a mix of racial groups. In general, whites will develop brain cancer more often than blacks and survival in blacks was similar to whites (5-year relative survival rate: 23%). Males generally had a slightly higher incidence of brain cancer as compared to females, and females had better survival than males (5-year relative survival rate: 25% versus 23%). 5-year relative survival rate was highest for black males. Tables 25.3 and 25.4 show the relative survival rates for brain cancer by race and gender.

Age at Diagnosis

The average age of onset for adult brain cancer is in the mid-fifties, although this does vary by histologic subtype of tumor. As with most other cancer sites, survival decreased as age at diagnosis increased. The 5-year relative survival rates (%) for brain cancer by age at diagnosis categories 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+ were 64%, 55%, 33%, 14%, 6%, 2% and 1%, respectively (Table 25.3). Figure 25.2 shows the 10-year relative survival curves by age at diagnosis.

Figure 25.1: Brain & Other Central Nervous System Cancer: Relative Survival by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

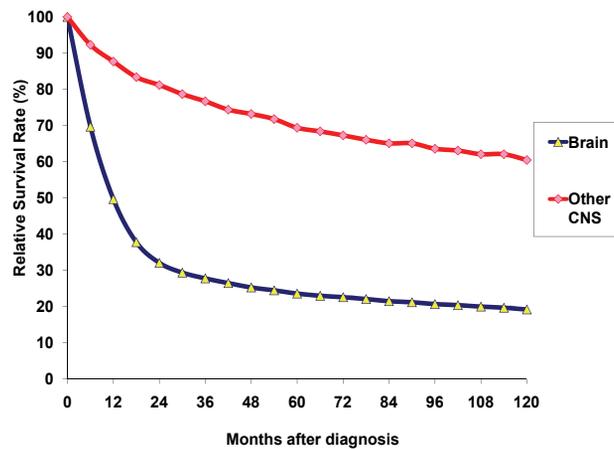


Table 25.2: Cancer of the Brain & Other CNS : 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Site, Ages 20+, 12 SEER Areas, 1988-2001

Site	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year %	2-Year %	3-Year %	5-Year %	8-Year %	10-Year %
Total	19,774	100.0	51.8	34.9	30.5	26.2	23.2	21.6
Brain	18,669	94.4	49.7	32.1	27.8	23.6	20.7	19.2
Other Central Nervous System	1,105	5.6	87.7	81.2	76.7	69.5	63.7	60.6

Table 25.3: Cancer of the Brain: Race, Sex, Age (20+), Grade and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	% of Cases	Relative Survival Rate 5-Year (%)
Total Brain	18,669	100.0	23.6
Race			
White	16,824	90.1	23.4
Black	924	4.9	22.8
Other	921	4.9	29.2
Sex			
Male	10,701	57.3	22.9
Female	7,968	42.7	24.6
Age			
20-29	1,504	8.1	64.4
30-39	2,469	13.2	55.2
40-49	3,011	16.1	32.8
50-59	3,521	18.9	13.6
60-69	3,854	20.6	5.8
70-79	3,388	18.1	1.9
80+	922	4.9	1.3
Grade (Differentiation)			
Well differentiated; Grade I	478	2.6	77.0
Moderately differentiated; Grade II	1,885	10.1	62.4
Poorly differentiated; Grade III	1,642	8.8	18.3
Undifferentiated; anaplastic; Grade IV	7,442	39.9	13.1
Unknown	7,222	38.7	21.1
Size of tumor			
<=2cm	1,110	5.9	31.5
2-5 cm	6,201	33.2	19.8
>5 cm	2,619	14.0	20.8
Unknown	8,739	46.8	26.1

Grade

Tumors are graded as Grades 1, 2, 3, 4, and unknown. Grade 1 tumors are well differentiated, grade 2 tumors are moderately differentiated, grade 3 tumors are poorly differentiated and grade 4 tumors are undifferentiated. A tumor that has an unknown grade means that there was insufficient information to grade the tumor. It is important to note that for brain cancer, grade is directly correlated with the histologic type of tumor classification.

Survival for patients with brain cancer decreased from grade 1 to grade 4. The 5-year relative survival rates (%) for grade 1, grade 2, grade 3, grade 4 and unknown were 77%, 62%, 18%, 13% and 21%. However, it is important to note that 39% of patients had unknown grade in this study sample. Figure 25.3 shows the 10-year relative survival curves by grade.

Table 25.4: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Sex/Race	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
			%	%	%	%	%	%
All	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Male	10,701	57.3	50.5	31.7	27.2	22.9	19.8	18.3
White	9,670	51.8	49.9	31.0	26.7	22.5	19.5	18.0
Black	491	2.6	54.1	34.4	29.7	24.8	20.8	20.8
Female	7,968	42.7	48.6	32.7	28.4	24.6	21.9	20.3
White	7,154	38.3	47.9	32.3	28.2	24.5	21.9	20.3
Black	433	2.3	49.3	31.3	25.4	20.7	19.1	16.6

Figure 25.2: Brain Cancer: Relative Survival Rates by Age Group, Ages 20+, 12 SEER Areas, 1988-2001

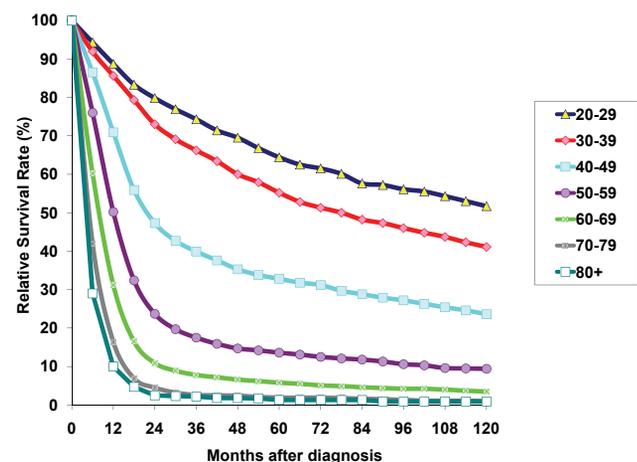
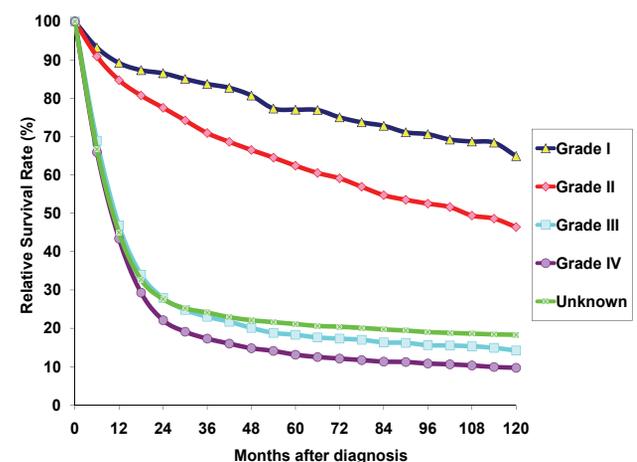


Figure 25.3: Brain Cancer: Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001



Histology

An individual's course of treatment, response to treatment and expected survival are all highly dependent on histologic type. Relative survival rates (%) varied greatly by histologic type (Table 25.5). The categories of histologic types of tumor used in this analysis (for brain cancer cases) were: glioma, glioma (other), ependymoma, astrocytoma, glioblastoma, oligodendroglioma, medulloblastoma, and other (germ cell neoplasms, neuroepitheliomatous neoplasms, other). Figure 25.4 shows the 10-year relative survival curves by histologic type.

Figure 25.4: Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

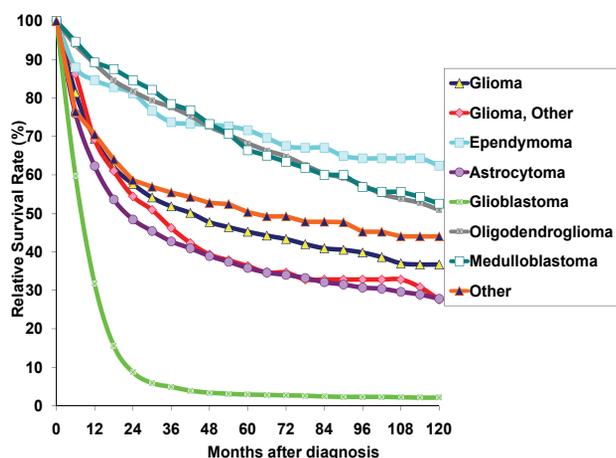
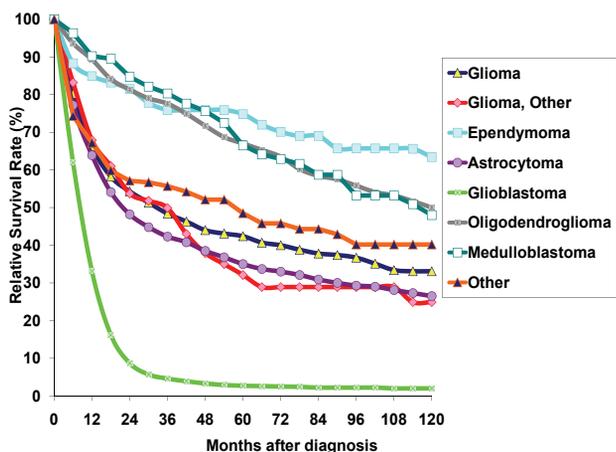


Figure 25.5: Male Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001



Histology and Sex

Males had similar proportions of astrocytomas (26-27%) and glioblastomas (53-54%) as compared to females. Survival rates by histologic type were similar or slightly higher for females compared to males except for ependymoma where males had a 5-year relative survival rate of 75% compared to 68% for females. Figures 25.5 and 25.6 show the 10-year relative survival rate (%) by histologic type and sex (males and females, respectively).

Histology and Race

Whites had a higher frequency of oligodendrogliomas and glioblastomas as compared to blacks (oligodendroglioma: 9.5% vs. 8.2% and glioblastoma: 54.3% vs. 49.6%, respectively) and a lower frequency of astrocytoma as compared to blacks (astrocytoma: 26.5% vs. 28.5%). Relative survival rates (%) did differ by race for each histologic type. Table 25.5 shows the relative survival rates for invasive brain cancer by histologic type and race.

Primary Site

Brain cancer occurring in the frontal lobes (25.8% of total), temporal lobe (20.1% of total), parietal lobe (14.6% of total) and overlapping lesions of the brain (19.8% of total) were the most common. Relative survival rates (%) did differ by primary site, with tumors in the cerebrum, parietal lobe, occipital lobe, brain NOS, and overlapping lesions of the brain having the poorest survival, less than 20% at 5 years.

Figure 25.6: Female Brain Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

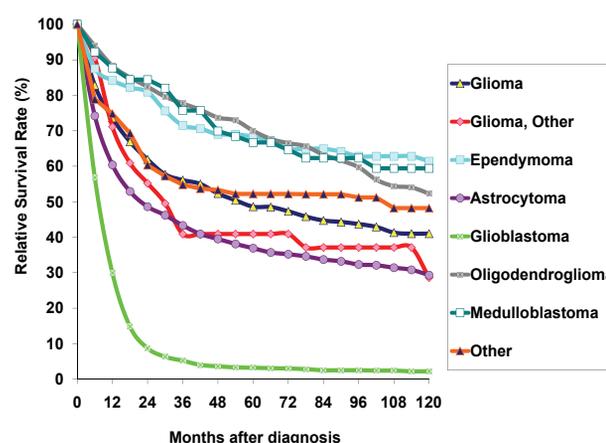


Table 25.5: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Histology, Ages 20+, 12 SEER Areas, 1988-2001

Race/ Histology	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All Races	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Glioma	1,076	5.8	69.4	57.6	51.8	45.2	39.8	36.7
Glioma, Other	100	0.5	69.2	54.4	46.2	36.3	32.8	27.6
Ependymoma	282	1.5	84.6	81.2	73.7	71.6	64.3	62.4
Astrocytoma	4,972	26.6	62.3	48.4	42.7	35.8	30.7	27.8
Glioblastoma	10,037	53.8	31.7	8.7	4.9	2.9	2.3	2.1
Oligodendroglioma	1,796	9.6	88.9	81.7	77.6	68.2	57.4	50.9
Medulloblastoma	216	1.2	89.2	84.6	78.4	66.4	56.8	52.5
Other	190	1.0	70.5	58.6	55.4	50.3	45.2	44.0
White	16,824	100.0	49.1	31.6	27.4	23.4	20.5	19.0
Glioma	966	5.7	68.5	57.3	51.2	44.9	39.4	36.3
Glioma, Other	85	0.5	69.9	55.2	47.3	37.5	35.6	29.5
Ependymoma	238	1.4	85.8	82.7	75.2	73.0	65.9	63.5
Astrocytoma	4,465	26.5	61.7	47.9	42.6	35.9	30.5	27.6
Glioblastoma	9,135	54.3	31.3	8.4	4.6	2.8	2.2	2.0
Oligodendroglioma	1,590	9.5	89.1	81.7	77.9	68.8	58.7	52.2
Medulloblastoma	195	1.2	89.6	85.5	79.2	65.5	57.2	52.2
Other	150	0.9	71.0	59.9	57.2	53.0	47.2	45.4
Black	924	100.0	51.8	32.9	27.7	22.8	20.0	19.4
Glioma	60	6.5	67.8	49.1	43.6	31.0	31.0	31.0
Glioma, Other	9	1.0	~	~	~	~	~	~
Ependymoma	22	2.4	~	~	~	~	~	~
Astrocytoma	263	28.5	64.4	48.1	40.6	33.3	29.5	27.5
Glioblastoma	458	49.6	33.9	10.1	7.1	5.3	3.0	3.0
Oligodendroglioma	76	8.2	79.6	71.9	63.1	50.2	37.6	28.5
Medulloblastoma	12	1.3	~	~	~	~	~	~
Other	24	2.6	~	~	~	~	~	~

~ Statistic not displayed due to less than 25 cases.

Other CNS Cancer

The prognostic factors of interest for the other CNS cancer analysis were: race, sex, age at diagnosis, histologic type, grade, SEER stage of disease and primary site. Size of tumor information was not analyzed because of the large amount of missing data (65.9%) (Table 25.7). The combinations of interest were: race and sex, SEER stage and sex, SEER stage and grade, histologic type, race and sex and histologic type and SEER stage.

Race and Sex

For all race specific analyses of the 1,105 patients, only white and black patients (91%) are used, because the other category is made up of a mix of racial groups. As with the brain cancer group, the proportion of whites with other CNS cancer was much higher than the proportion of blacks with the same disease. However, survival was worse in blacks than in whites with other CNS cancer (5-year relative survival rate: 59% vs. 72%). Males and females develop other CNS cancer in comparable proportions and the relative survival rate was the same (69.5%). 5-year relative survival rate was shortest for black males. Table 25.7 and 25.8 show the relative survival rates for other CNS cancer by race and sex.

Age at Diagnosis

Survival for patients diagnosed with other CNS cancer decreased as age at diagnosis increased except for ages 20-29 which had poorer survival than 30-39, 40-49 and 50-59 year olds and 80+ which had better survival than 70-79 years of age. The 5-year relative survival rate (%) for other CNS cancer by age at diagnosis categories 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+ were 70%, 81%, 77%, 72%, 66%, 41% and 58%, respectively (Table 25.7). Figure 25.7 shows the 10-year relative survival curves by age at diagnosis.

Grade

Survival for patients with other CNS cancer decreased from grade 1 to grade 4. The 5-year relative survival rate (%) for grade 1, grade 2, grade 3, grade 4 and unknown were 86%, 80%, 43%, 35% and 72%. However, it is important to note that 71.0% of patients had unknown grade in this study sample. Figure 25.8 shows the 10-year relative survival curves by grade.

Table 25.6: Cancer of the Brain: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Cases	% of Cases	Relative Survival Rate					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	18,669	100.0	49.7	32.1	27.8	23.6	20.7	19.2
Cerebrum	844	4.5	37.5	21.8	16.3	12.7	11.6	9.9
Frontal Lobe	4,812	25.8	58.9	42.9	37.9	32.4	27.8	25.6
Temporal Lobe	3,759	20.1	50.8	28.1	24.2	20.4	18.1	17.1
Parietal Lobe	2,735	14.6	43.5	23.9	19.8	16.1	13.8	12.8
Occipital Lobe	584	3.1	42.8	19.9	14.6	13.4	12.3	10.7
Ventricle, NOS	227	1.2	66.8	57.8	55.4	50.3	45.0	43.2
Cerebellum, NOS	545	2.9	82.4	74.6	68.4	62.9	58.0	55.4
Brain Stem	374	2.0	68.8	59.2	55.6	50.7	45.2	43.8
Overlapping lesion of brain	3,695	19.8	40.5	23.4	19.0	15.2	12.3	10.6
Brain, NOS	1,094	5.9	38.4	26.3	23.1	19.8	16.8	15.4

* NOS, Not Otherwise Specified

Table 25.7: Cancer of the Other Central Nervous System: Distributions and 5-Year Relative Survival Rates (%) by Race, Age(20+), Grade, and Tumor Size, 12 SEER Areas, 1988-2001

Characteristics	Cases	% of Cases	Relative Survival Rate 5-Year (%)
All Cases	1,105	100.0	69.5
Race			
White	886	80.2	71.5
Black	120	10.9	59.1
Other	99	9.0	62.9
Sex			
Male	565	51.1	69.5
Female	540	48.9	69.5
Age			
20-29	114	10.3	70.1
30-39	167	15.1	80.8
40-49	248	22.4	77.1
50-59	202	18.3	72.4
60-69	164	14.8	66.2
70-79	154	13.9	40.7
80+	56	5.1	57.5
Grade (Differentiation)			
Well differentiated; Grade I	73	6.6	85.5
Moderately differentiated; Grade II	113	10.2	79.7
Poorly differentiated; Grade III	40	3.6	43.3
Undifferentiated; anaplastic; Grade IV	95	8.6	35.4
Unknown	784	71.0	72.3
Size of tumor			
<=2cm	78	7.1	89.2
2-5 cm	198	17.9	71.2
>5 cm	101	9.1	58.3
Unknown	728	65.9	68.1

Figure 25.7: Other Central Nervous System Cancer: Relative Survival Rates by Age Group (20+), 12 SEER Areas, 1988-2001

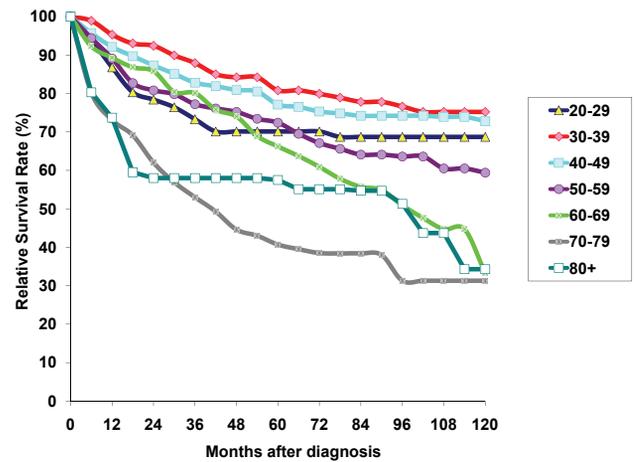


Figure 25.8: Other Central Nervous System Cancer: Relative Survival Rates by Grade, Ages 20+, 12 SEER Areas, 1988-2001

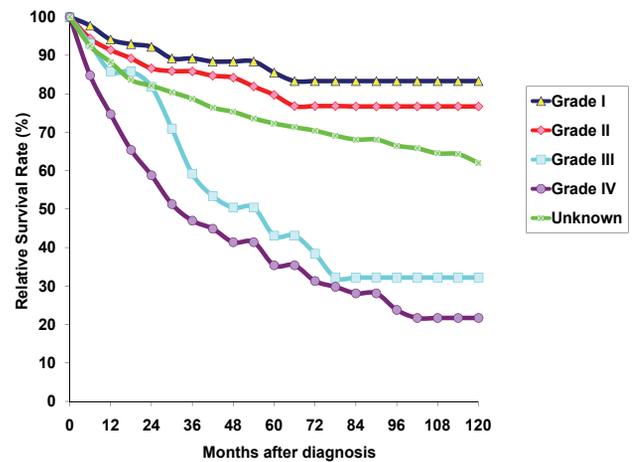


Table 25.8: Cancer of the Other Central Nervous System Cancer: 1-, 2-, 3-, 5-, 8- & 10-Year Relative Survival Rates (%) by Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Sex/Race	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
All	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Male	565	51.1	88.0	82.5	77.6	69.5	66.6	64.0
White	476	43.1	88.9	85.3	80.3	72.4	69.2	67.0
Black	49	4.4	87.1	65.4	63.9	57.9	57.2	49.5
Female	540	48.9	87.3	79.9	75.7	69.5	60.1	56.9
White	410	37.1	88.2	81.6	76.9	70.5	61.4	60.4
Black	71	6.4	83.2	68.1	67.3	59.7	53.9	47.5

Table 25.9: Cancer of the Other Central Nervous System Cancer: 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by SEER Historic Stage, Ages 20+, 12 SEER Areas, 1988-2001

Stage	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Localized	680	61.5	90.8	85.1	80.4	75.1	70.2	66.6
Regional	192	17.4	79.2	71.3	67.3	57.0	45.9	45.2
Distant	81	7.3	76.6	70.9	69.4	60.2	53.5	53.5
Unstaged	152	13.8	90.0	81.5	74.9	65.0	60.0	52.4

Table 25.10: Cancer of the Other Central Nervous System : Distribution of Cases by SEER Stage, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

SEER Stage	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	476	100.0	410	100.0	49	100.0	71	100.0
Localized	680	61.5	303	63.7	257	62.7	30	61.2	40	56.3
Regional	192	17.4	77	16.2	65	15.9	11	22.4	9	12.7
Distant	81	7.3	35	7.4	28	6.8	<5	-	7	9.9
Unstaged	152	13.8	61	12.8	60	14.6	<5	-	15	21.1

Table 25.11: Cancer of the Other Central Nervous System: Distribution of Cases by Histology, Race and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Histology	Total		Race/Sex							
			White				Black			
			Male		Female		Male		Female	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	476	100.0	410	100.0	49	100.0	71	100.0
Ependymoma	355	32.1	190	39.9	130	31.7	7	14.3	11	15.5
Astrocytoma	167	15.1	75	15.8	53	12.9	13	26.5	13	18.3
Glioma	65	5.9	28	5.9	21	5.1	<5	-	<8	-
Meningioma	456	41.3	152	31.9	182	44.4	23	46.9	38	53.5
Other	62	5.6	31	6.5	24	5.9	<5	-	<5	-

SEER Stage of Disease

SEER classifies invasive stage of disease into 4 categories: localized, regional, distant and unstaged. Survival decreased as the staging category progressed from localized to regional to distant. The 5-year relative survival rates (%) for other CNS cancer patients with localized, regional, distant and unknown stages of disease were 75%, 57%, 60% and 65%, respectively. It is also important to note that the majority of the other CNS patients were in the localized SEER stage category. Relative survival rates for other CNS cancer are shown by stage (Table 25.9) and stage by race/sex (Table 25.10).

Histology

As previously noted, relative survival varied greatly by histology. The categories of histology of tumor used in this analysis, for other CNS cancer patients only, were: glioma, ependymoma, astrocytoma, meningioma and other (other, neuroepitheliomatous neoplasms, paragangliomas, and glomus tumors). Figure 25.9 shows the 10-year relative survival curves by histologic type. Tables 25.11 and 25.12 show the distribution of patients by histology, race and sex and by histology and SEER stage of disease, respectively.

Primary Site

For patients with other CNS cancer, the spine was the most common primary site (53.9% of total), followed by the brain (41.3% of total) and other (4.8% of total). Other CNS cancers in the brain (malignant meningiomas) had worse survival compared to other CNS cancers in the spine (Table 25.13).

Figure 25.9: Other Central Nervous System Cancer: Relative Survival Rates by Histology, Ages 20+, 12 SEER Areas, 1988-2001

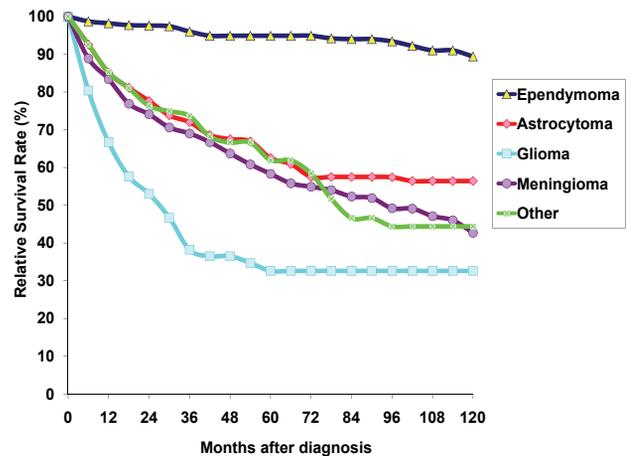


Table 25.12: Cancer of the Other Central Nervous System: Distribution of Cases by Histology and SEER Summary Stage, Ages 20+, 12 SEER Areas, 1988-2001

Histology	SEER Summary Stage									
	Total		Local		Regional		Distant		Unstaged	
	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent	Cases	Percent
Total	1,105	100.0	680	100.0	192	100.0	81	100.0	152	100.0
Ependymoma	355	32.1	287	42.2	25	13.0	14	17.3	29	19.1
Astrocytoma	167	15.1	127	18.7	10	5.2	8	9.9	22	14.5
Glioma	65	5.9	37	5.4	11	5.7	5	6.2	12	7.9
Meningioma	456	41.3	208	30.6	136	70.8	40	49.4	72	47.4
Other	62	5.6	21	3.1	10	5.2	14	17.3	17	11.2

Table 25.13: Cancer of the Other Central Nervous System: 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Primary Site, Ages 20+, 12 SEER Areas, 1988-2001

Primary Site	Cases	% of Cases	Relative Survival Rate (%)					
			1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	1,105	100.0	87.7	81.2	76.7	69.5	63.7	60.6
Brain	456	41.3	83.0	73.8	68.2	56.9	48.0	41.7
Spine	596	53.9	92.1	87.9	83.5	78.8	74.8	73.0
Other	53	4.8	77.9	68.8	68.8	65.1	57.9	57.9

DISCUSSION

Brain and other CNS cancer are rare, occurring at an incidence rate of approximately 6 cases per 100,000 per year. Malignant brain cancer cases excluding malignant meningiomas comprised 94% of the sample used for this analysis (18,669 patients out of 19,774 total combined patients). Five-year relative survival rate after diagnosis with brain cancer or other CNS cancer was 24% and 69%, respectively. Hence, individuals with brain cancer have a very poor prognosis as compared to individuals with other CNS cancer. These relative survival estimates show the distinct difference between the two types of cancer even though they both affect the central nervous system; therefore, brain cancer and other CNS cancer were analyzed separately.

For the brain cancer patients, survival varied only slightly by race and sex. Blacks had a similar 5-year relative survival rate as compared to whites and females had a slightly better 5-year relative survival rate as compared to males. Black males had a 5-year relative survival rate of 25%, which is higher than black females (21%) or white males (23%) and similar to white females (25%). Survival differed the most by age at diagnosis, grade, and histologic type. As age increased the 5-year relative survival rate decreased from 64% for ages 20-29 to 1% for ages 80+, with the highest proportion of patients diagnosed at age 60-69 (20.6% of total). Relative survival decreased as the grade of the tumor progressed from 1 to 4. Most of the patients had grade 4 or grade unknown tumors (39.9% and 38.7%).

For brain cancer patients, survival also differed by histologic type of tumor and race, although most differences were small. Glioblastomas had the worst 5-year relative survival rate of 3% and ependymomas had the best 5-year relative survival rate of 74%. Fifty-four percent had glioblastomas and 1.5% had ependymomas. The distribution of histologic type by race differed slightly for whites and blacks. Malignant brain tumors in the temporal, frontal, parietal lobes and overlapping lesions of the brain were the most common locations in the brain. Malignant tumors in cerebrum and tumors in the occipital lobe had the worst survival at 5 years.

For the other CNS cancer patients, survival varied more by race than by sex. Whites had a better 5-year relative survival rate as compared to blacks (72% vs. 59%), and males and females had the same 5-year relative survival rate (70%). Black males had a 5-year relative survival rate of 58%, which was lower than black females (60%), or white males (72%) or females (71%). Survival differed most by age at diagnosis, grade, histologic type and SEER stage. As age increased the 5-year relative survival rate

decreased from 81% for ages 30-39 to 41% for ages 70-79, with the highest proportion of patients being diagnosed at age 40-49 (22.4% of total). Relative survival decreased as the grade of the tumor progressed from 1 to 4. However, over 70% of the 1,103 total patients had unknown grade information. Five-year relative survival rate decreased as SEER stage of disease became more advanced (localized 75%; regional 57% and distant 60%). There was no difference in the distribution of SEER stage by race and sex. Patients in the glioma category had the worst 5-year relative survival rate of 33% and ependymoma patients had the best 5-year relative survival rate of 95%. Less than 6% had glioma tumors and 32.1% had ependymomas. Black males and females had a higher proportion of astrocytomas and meningiomas as compared to white males and females. Whites had a much higher proportion of ependymomas. Tumors of the spine were the most common site with other CNS cancers, although malignant meningiomas of the brain had worse survival than those with malignant tumors in the spine.

Hence, race, age at diagnosis, grade, histologic type and primary site for both brain and other CNS cancers, and SEER stage (for other CNS cancers only) are all important predictors of survival, concurring with previous literature studying survival in brain and other CNS cancer patients (3, 4, 5, 6, 15). These variables are all used to determine one's course of treatment and prognosis after diagnosis. The slight differences in survival by race and by race and histologic type of tumor for brain and other CNS cancers could be due to access to health care and/or socioeconomic status differences. However, recent studies suggest that these differences by race cannot be completely attributed to access to health care and/or diagnostic practices (6, 9) and may in fact be caused by biological differences. Older men and women would be more likely to have competing risks of death as compared to younger individuals with the same diagnosis, which would negatively affect their survival. Though competing risk information was unavailable for this analysis, performing relative survival analysis rather than absolute survival analysis allows for the adjustment of the expected mortality that the cohort would experience. Having a higher grade of tumor or a higher stage of cancer directly correlates with worse survival for almost every type of cancer (2). The patterns seen in this analysis for survival by histologic type for brain and other CNS cancers have been shown previously (3, 4, 6, 8), where brain cancer patients with GBM have the poorest survival, patients with oligodendroglioma have the best survival compared to any other histologic subtype, and other CNS cancer patients with ependymoma have the best survival compared to any other histologic subtype. Similar patterns by primary site of tumor have been seen previously also (8, 4, 15).

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta: American Cancer Society; 2006.
2. Ries LAG, Harkins D, Krapcho M, Mariotto A, Miller BA, Feuer EJ, Clegg L, Eisner MP, Horner MJ, Howlander N, Hayat M, Hankey BF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2003, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2003/, based on November 2005 SEER data submission, posted to the SEER web site, 2006.
3. Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: an analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. *J Neurosurg* 1998;88:1-10
4. Surawicz TS, Davis F, Freels S, Laws ER Jr, Menck HR. Brain tumor survival: results from the National Cancer Data Base. *J Neurooncol* 1998; 40:151-60.
5. Wrensch M, Minn Y, Chew T, Bondy M, Berger MS. Epidemiology of primary brain tumors: current concepts and review of the literature. *Neuro-oncol* 2002; 4:278-99.
6. Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Racial differences in survival after diagnosis with primary malignant brain tumor. *Cancer* 98:603-609, 2003a.
7. Polednak AP, Flannery BS. Brain, other central nervous system and eye cancer. *Cancer Suppl* 1995; 75:330-337.
8. Central Brain Tumor Registry of the United States (CBTRUS). Statistical Report: Primary Brain Tumors in the United States, 1992-1997, Central Brain Tumor Registry of the United States (CBTRUS), www.cbtrus.org, 2003.
9. Surawicz TS, McCarthy BJ, Kupelian V, Jukich PJ, Bruner JM, Davis FG. Descriptive epidemiology of primary brain and CNS tumors: results from the Central Brain Tumor Registry of the United States, 1990-1994. *Neuro-oncol.* 1999; 1:14-25.
10. Mahaley MS Jr, Mettlin C, Natarajan N, Laws ER Jr, Peace BB. National survey of patterns of care for brain-tumor patients. *J Neurosurg* 1989; 71:826-36
11. Mahaley MS Jr, Mettlin C, Natarajan N, Laws ER Jr, Peace BB. Analysis of patterns of care of brain tumor patients in the United States: a study of the Brain Tumor Section of the AANS and the CNS and the Commission on Cancer of the ACS. *Clin Neurosurg* 1990;36:347-52.
12. Gurney JG, Smith MA, Bunin GR. Chapter III: CNS and Miscellaneous Intracranial and Intraspinal Neoplasms. In: Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). *Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995*, National Cancer Institute, SEER Program. NIH Pub. No. 99-4649. Bethesda, MD, 1999.
13. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958; 53:457-481.
14. Fleming ID, Cooper JS, Henson DE, Hutter RVP, Kennedy BJ, Murphy GP, O'Sullivan B, Sobin LH, Yarbrow JW (Eds.) *AJCC Cancer Staging Manual*, 5th edition. American Joint Committee on Cancer. Philadelphia: Lippincott-Raven, 1997.
15. Barnholtz-Sloan JS, Sloan AE, Schwartz AG. Relative survival and patterns of diagnosis by time period for individuals with primary malignant brain tumor 1973-1997. *Journal of Neurosurgery* 99:458-466, 2003b.

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