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Outcomes of Malignant CNS Ependymomas: An Examination of 2408 Cases Through the Surveillance, Epidemiology, and End Results (SEER) Database (1973–2005)

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Abstract

Background—Determine the role of surgery and radiation therapy for patients with malignant CNS ependymomas.

Methods—The Surveillance, Epidemiology, and End Results (SEER) database (1973–2005) was queried.

Results—Overall, a total of 2408 cases of malignant ependymomas were identified. Of these, 2132 cases (88.5%) were identified as WHO grade II ependymomas and 276 cases (11.5%) as WHO grade III (anaplastic) ependymomas. The annual incidence of ependymomas was approximately 1.97 cases per million in 2005. Overall median survival for all patients was 230 mo, with a significant difference between women and men (262 mo *versus* 196 mo, respectively) ($P = 0.004$). Median age at diagnosis was 37 y among females and 34 y in males. Patients who successfully underwent surgical resection had a considerably longer median survival (237 mo *versus* 215 mo, $P < 0.001$) as well as a significantly improved five-year survival (72.4% *versus* 52.6%, $P < 0.001$). Univariate analysis demonstrated that age, gender, ethnicity, primary tumor site, WHO grade and surgical resection were significant predictors of improved survival for ependymoma patients. Multivariate analysis identified that a WHO grade III tumor, male gender, patient age, intracranial tumor locations and failure to undergo surgical resection were independent predictors of poorer outcomes. Multivariate analysis of partially resection cases revealed that lack of radiation was a sign of poor prognosis (HR 1.748, $P = 0.024$).

Conclusion—Surgical extirpation of ependymomas is associated with significantly improved patient survival. For partially resected tumors, radiation therapy provides significant survival benefit.

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Keywords

malignancy; cancer; survival; surgery; ependymoma; radiation; outcomes; SEER

INTRODUCTION

Ependymomas are an uncommon group of CNS neoplasms of neuroectodermal origin that arise from the ependymal cells of the cerebral ventricles, choroid plexus, the central canal of the medulla and spinal cord, and the filum terminale [1–7]. In addition, ependymomas can be found in the brain parenchyma, arising from rests of fetal ependymal cells during development [7, 8]. Ependymomas constitute 2% to 8% of all primary central nervous system tumors, and up to 12% of pediatric brain tumors [9–14].

Due to the low incidence of this tumor, outcome studies on prognostic factors in ependymomas are limited and have generally focused on these tumors in children. The current literature is generally composed of single cases reports, small case series, or single-institution experiences with relatively few patients [10–12, 15–19]. While a number of reports describe the prognosis in children, prognostic factors and outcomes for adults diagnosed with ependymomas remain less well-defined [20]. We sought, therefore, to provide an overview of ependymomas with the goal of elucidating incident trends, prognostic indicators, and changes in the role of surgery and radiotherapy for both children and adults. In order to examine a larger patient cohort than previously examined, we utilized a national tumor registry, the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI), a population-based, prospectively collected United States cancer registry.

MATERIAL AND METHODS**The Surveillance, Epidemiology, and End Results (SEER) Program**

The SEER Program of the National Cancer Institute (NCI) is the largest registry source of information on cancer incidence and survival in the United States. SEER currently collects and publishes cancer incidence and survival data from 17 population-based cancer registries encompassing approximately 26% of the U.S. population. With just over 6,100,000 incident cancer cases, SEER represents the largest cancer database in the country. The SEER program is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and patient survival data [21]. The scope and magnitude of SEER data makes it an excellent resource to study rare malignancies [22–29]. The data collected provides insight into tumor behavior, and allow us to examine outcomes from current treatment strategies

Ependymoma Case Definition

The Surveillance, Epidemiology, and End Results (SEER) April 2008 release was used to identify all incident cases of malignant ependymoma diagnosed from 1973 to 2005, using the International Classification of Diseases for Oncology-Morphology codes 9331–9332 [30]. Only the percentages based on available data for each individual variable are given.

Patients with missing data were excluded from each respective univariate and multivariate analysis. According to the World Health Organization (WHO), ependymal neoplasms are classified as WHO grade I: myxopapillary ependymomas, and subependymomas (both having a very favorable prognosis), WHO grade II ependymomas, and WHO grade III anaplastic ependymomas [31]. Currently, ependymoblastomas are classified under embryonal primitive neuroectodermal tumor, and are no longer considered ependymomas.

Incidence

The SEER*Stat software (vers. 6.1.4, NCI, Bethesda, MD) was used to analyze incidence rates and trends from 1973 to 2005. All incidence data were age-adjusted and normalized to the 2000 U.S Standard Population; incidence rates are expressed as new cases per 100,000 population. Annual percentage change (APC) was calculated using the weighted least squares method. A P value < 0.05 was considered significant.

Treatment

The SEER database contains information regarding treatment offered to ependymoma patients during the first 4 mo following diagnosis. Treatment was defined as any anticancer therapy received within 4 mo of diagnosis. We used these data to assess patterns of first treatment for ependymomas. Patients were regarded as having received radiation alone if they received radiation and had no surgery. Treatment status was classified as unknown if all details of either surgery or radiotherapy were not known. For this analysis, if a particular therapy was recommended but not given or not known to be given, the patient was considered to have not received the treatment.

Survival Calculations and Statistical Analysis

Primary tumor sites were grouped according to ICDO-3 classification into six different categories: spinal cord, brain parenchyma, ventricle, brain stem, cerebellum, and other. Age and year of diagnosis were divided into four equal groups (quartiles). A distinction was made between tumors residing in the supratentorial and infratentorial regions of the brain. Statistical analysis was performed with SPSS Statistical Package ver. 15.0 (SPSS Inc., Chicago, IL). Correlations between categorical variables were made using the χ^2 test. A P value < 0.05 was considered significant. A further distinction was drawn at 0.01 and 0.001 to identify highly significant differences. All statistical tests were two-sided. Median, 5-, 10-, 15-, and 20-y overall and disease-specific survivals were calculated by the Kaplan-Meier method. This method is most suitable for small data sets with precisely measured event times. Survival was calculated from the time of the initial diagnosis to the date of last contact (or the date of death, if the patient was deceased).

The effects of demographic, clinical, pathologic, and treatment variables on survival were tested by utilizing the Log rank test for categorical values. A multivariate analysis using the Cox proportional hazards model was used to further test prognostic factors found to be significant in the univariate analysis. Specifically, age, gender, race, ethnicity, WHO tumor grade, primary tumor site, surgical resection, and radiation were included in the multivariate analysis.

RESULTS

Patient Demographics and Clinical Data

From 1973 to 2005, a total of 2408 cases of malignant ependymomas were identified in the SEER database. A majority of the cases were identified as WHO grade II ependymomas (88.5%), while 11.5% were WHO grade III anaplastic ependymomas. Demographic, tumor, and treatment characteristics of the study population are summarized in Table 1. The overall median age at diagnosis was 35 y (range 0–91 y). Over two-thirds of the patients were above the age of 20. Women comprised a smaller proportion of the cohort than men (45.6% *versus* 54.4%). Median age at diagnosis was 37 y among women and 34 y among men. Of the 2393 cases of known race, 2048 (85.6%) were white, 192 (8.0%) were black, and 153 (6.4%) were of other races. Furthermore, 13.7% of the patients were of Hispanic decent. The largest proportion of the tumors were located in the spinal cord ($n = 958$, 39.8%), followed by brain parenchyma ($n = 628$, 26.1%) (Fig. 1). Supratentorial tumors comprised a larger proportion of the study population than infratentorial neoplasms (37.8% *versus* 22.0%). In the majority of cases, surgical extirpation was undertaken ($n = 2132$, 91.4%). Radiation was given to approximately half of the patients ($n = 1104$, 45.8%).

Tumors occurring in the cerebellum and brain parenchyma were diagnosed at an earlier age (median age at diagnosis of 14 and 16 y, respectively) compared with those neoplasms occurring in the spinal cord (median age of diagnosis 45 y). WHO grade III anaplastic ependymomas occurred at a much earlier age compared with WHO grade II ependymomas, with a median age at diagnosis of 12.5 and 37 y, respectively. It was also observed that those patients receiving surgical or radiotherapy treatment were diagnosed at a much earlier age than those who did not receive either treatment (Table 1).

Incidence of Ependymomas

The overall incidence of ependymomas was approximately 1.97 cases per million in 2005. A significant trend toward increasing incidence for all ependymomas was observed throughout the study period ($APC = 1.83$, $P < 0.05$) (Fig. 2A). There was a significant difference in the incidence of ependymomas according to age group. Ependymomas more often affected patients in the first decade of life with an incidence of 9.98 per million. In addition, a second peak in incidence was observed at 50–59 y (Fig. 2B). Adjusted incidence rates to the 2000 U.S. standard population demonstrated that females have a higher incidence of the disease (2.44 per million) compared with males (2.24 per million) ($P < 0.05$). Although an increase in the incidence of ependymomas was observed in both men and women throughout the study period, women showed a greater annual percent change ($APC = 2.16$, $P < 0.05$) than men ($APC = 1.49$, $P < 0.05$) (data not shown). Ependymoma was uncommon in African-Americans with an incidence rate of 1.41 per million compared with whites, who had an incidence rate of 2.11 per million. While the incidence rate varied between white men and women (2.45 per million among white males and 1.80 per million among white females), the incidence rate did not vary significantly between black men and women (1.41 and 1.42 per million, respectively). Black patients were observed to present with ependymomas earlier in life (0–9) y (Fig. 3).

Characteristics of Disease

As summarized in Table 2, 39.8% cases of ependymomas presented in the spinal cord, 37.8% cases were supratentorial, and 22.0% cases were infratentorial. We observed a higher propensity toward supratentorial sites in patients under 10 y of age. In patients older than 20 y, however, spinal cord ependymomas were observed to increase in frequency. In patients younger than 30 y, more than half of the tumors presented intracranial. The median age at diagnosis of supratentorial and infratentorial tumors was 20 and 24 y, respectively. This was observed to be two decades earlier than the median age at diagnosis of tumors located in the spinal cord (45 y). Data regarding initial treatment were available for 94.2% cases (Table 3). A majority of the cases (96.3%) received treatment, usually surgery alone (48.9%) or in combination with radiotherapy (45.9%). A very small subset of the entire cohort (1.3%) received only radiotherapy. No patients under the age of 3 y received radiation alone as therapy. Patients older than 80 y of age were more likely than younger patients not to receive any treatment (40.0%). Those who were treated were more likely to be treated with surgery alone, and were less likely to have surgery in combination with radiotherapy (4.0%). Spinal cord lesions were more likely to be treated with surgery alone (69.1%), and less likely to be treated with the combination of surgery and radiotherapy (25.8%). Conversely, supratentorial and infratentorial lesions were more likely to be treated with the combination of surgery and radiotherapy (59.1% and 61.0%, respectively) than with surgery alone (34.7% and 35.2%, respectively). Supratentorial lesions were less likely to receive treatment (4.6%), with ventricle lesions receiving the least treatment. When treatment modality was analyzed as a function of year of diagnosis, use of surgery increased and established itself as the mainstay of treatment, while use of dual modality therapy decreased with time.

Survival and Clinicopathologic Variables

Median, 5-, and 10-y survival for ependymomas are summarized in Table 4. Median overall survival was 230 mo, with a significant difference between women and men (262 mo *versus* 196 mo, respectively) ($P = 0.004$). Ependymomas in children of ages 0 to 2 y, and in those older than 80 y, were observed to have a particularly aggressive behavior with a median survival of 37 mo and 19 mo, respectively. Median survival in patients diagnosed between the ages of 20 and 29 y has not yet been reached. No significant difference in overall survival was observed between races. Hispanics had a lower median survival compared with non-Hispanics (197 mo *versus* 249 mo, $P = 0.05$). Patients with spinal cord tumors were observed to have the longest median survival time (303 mo), while infratentorial lesions had better outcome than supratentorial lesions (137 mo *versus* 93 mo, $P < 0.001$). WHO grade III anaplastic ependymomas had a worse outcome than WHO grade II ependymomas (249 mo *versus* 53 mo) ($P < 0.001$).

Treatment and Survival

The median overall survival of patients who received surgical extirpation was 237 mo, compared with 215 mo for nonoperative cases ($P < 0.001$) (Table 5). Both males and females derived benefits from surgery, with females having a better outcome overall (267 *versus* 215 mo median survival, respectively). Furthermore, surgery improved survival in patients with ependymomas in the spinal cord ($P < 0.001$), the brain parenchyma ($P < 0.001$), ventricles (P

< 0.001), and brain stem ($P < 0.001$). No significant improvement in survival was observed for surgical extirpation of tumors located in the cerebellum or other sites.

By univariate analysis, significant survival benefit was observed with surgical resection for both WHO grades II and III tumors. Those undergoing total surgical resection were observed to have a better 10-y progression-free survival compared with those undergoing partial resection (75% *versus* 60%, $P < 0.05$). Kaplan-Meier survival curves illustrating these results are shown in Fig. 4. Although radiation therapy was not found to affect survival for the overall cohort ($P = 0.718$), further univariate analysis revealed that radiation significantly improved survival when used for tumors of the ventricle (238 mo *versus* 126 mo, $P = 0.001$) and brain stem (162 mo *versus* 102 mo, $P < 0.001$). Radiation was also associated with a significantly improved 10-y progression-free survival rate for patients undergoing partial tumor resection (65% *versus* 56%) ($P < 0.05$). No difference in median survival was observed with the use of radiotherapy in young children (0–2 y) (35 mo *versus* 39 mo, $P < 0.999$).

When comparing gross total resection without radiation to subtotal resection with radiation, we found 5 and 10-y survival statistically equivalent for lesions in the brain (5 y 65% *versus* 49%; 10 y 65% *versus* 37%, $P = 0.820$) brain stem (5 y 69% *versus* 85%; 10 y 69% *versus* 74% $P = 0.43$), ventricle (5 y 76% *versus* 52%; 10 y 76% *versus* 44% $P = 0.169$), and cerebellum (5 year 87% *vs* 74%; 10 year 87% *versus* 74% $P = 0.373$). For the spinal cord, gross total resection was found to be superior to partial resection with radiation (5 y 97% *versus* 85%; 10 y 90% *versus* 85, $P = 0.001$).

Independent Risk Factors

Using variables identified as significant by univariate analysis (gender, age, ethnicity, primary tumor site, WHO grade and surgical resection), a stepwise multivariate analysis was undertaken using the Cox regression model. Among preoperative variables, increasing age after 50 y and gender were identified as independent predictors of survival (Table 6). Lack of surgical resection (HR = 1.820, $P < 0.001$), WHO grade III (HR = 1.745, $P < 0.001$) and intracranial tumor locations were independent predictors of poorer outcomes. In a subset analysis of patients undergoing partial surgical resection, we observed that not receiving radiotherapy was indicative of a poor prognosis (HR = 1.748).

DISCUSSION

Utilizing the SEER cancer registry, we identified 2408 cases of malignant ependymomas between 1973 and 2005. This is the largest series of ependymoma cases reported in the literature. In addition, this is also the largest collection of adult cases, with over two-thirds of the patients in the cohort over the age of 20 y. To our knowledge, the largest series in the literature prior to this study contained only 258 cases [32].

Incidence Trends

We note that ependymomas have a bimodal age distribution with the first peak incidence occurring between 0 and 9 y of age, and the second peak occurring between 50 and 59 y of age (Fig. 2B). Mork *et al.* in a series of 101 cases reported a similar bimodal distribution

however with an earlier peak of 40 to 50 y of age [15]. We have also confirmed that the anatomic distribution of ependymomas appears to vary by age [33, 34]. We note that intracranial ependymomas mainly occurred in young patients, with a median age of diagnosis of supratentorial and infratentorial tumors being 20 and 24 y, respectively. Spinal ependymomas, on the other hand, occurred more frequently in older patients, with a median age of diagnosis of 45 y.

The overall incidence rate of ependymomas was found to be increasing at an annual percent change of 1.83%. It remains unclear, however, if this increased incidence represents a true increase in prevalence or increased diagnosis due to increased utilization of CT and MRI imaging. Our incidence data indicate that ependymomas are overall less common in African American patients compared with Caucasians, but that a higher proportion of ependymomas occurred earlier in life in African American patients (34.9% *versus* 20.1% in the first decade of life) and with a greater predilection for supratentorial locations.

Treatment Strategies

Surgery was associated with a significantly improved median survival for ependymomas, (237 mo *versus* 215 mo, $P < 0.001$) suggesting that surgery plays a vital role in therapeutic management. These results are consistent with smaller series that have previously shown that surgical resection, whether partial or total, significantly prolongs the median survival of patients [10,12, 14, 35–37]. Similarly, extent of resection of other CNS tumors is also known to significantly affect outcome [38,39]. Examination of the data where surgical margin information was available ($n = 977$) demonstrated that gross total resection (GTR) was the most common surgical outcome reported, comprising two-thirds of cases. Furthermore, those patients who underwent GTR were found to have better outcomes than those with subtotal resection (STR) (10 y survival 75% *versus* 60%, respectively, $P < 0.05$). Other investigators have also reported a better prognosis in patients with total GTR [2, 12, 13, 17, 34, 40, 41]. Interestingly, surgery was found to improve median survival for all known tumor locations except the cerebellum. This may be partially due to the finding that cerebellar tumors are found in the oldest and youngest age groups who have overall worse prognosis.

Upon analysis of the entire cohort, radiation therapy was not found to affect overall survival ($P = 0.718$), and radiotherapy combined with total resection was not found to be beneficial. In fact, patients with tumors of the brain stem and brain parenchyma had a significantly decreased survival when gross total resection was combined with radiation, (data not shown). However, univariate analysis revealed that radiation was associated with improved survival for patients undergoing partial resections as well as in regions where true negative resections would be difficult, such as the brain stem and ventricles. The benefit of radiation on survival was statistically significant for partially resected lesions in both the cortex and brainstem (data not shown). To further examine the role of radiation in the treatment of partially resected tumors, we performed a multivariate Cox regression analysis only on those cases with partial resection. The analysis showed that lack of radiation was a sign of poor prognosis with a hazard ratio of 1.748 ($P = 0.024$) (Table 6). Comparing GTR (without radiation) to STR with radiation, we found no difference in 5- and 10-y survival for tumors in the brain, ventricle, cerebellum, and brainstem. Since STR with radiation provides a

similar outcome as total resection, this suggests that surgical treatment should be attempted even if achieving a GTR is not expected.

The use of surgery as a sole treatment has increased over the study period, while the combination of surgery and radiation has decreased. This is likely secondary to improved neurosurgical techniques, such as neuromonitoring for spinal cord tumors, and intraoperative awake/motor mapping and neuronavigation for cranial tumors [42–46]. These improved techniques may yield higher numbers of GTRs and obviate the need for radiation. Our data would support this rationale, since radiation is not associated with improved outcomes for totally resected ependymoma.

Prognostic Factors

Previous studies have found that the grade of the tumor had a significant prognostic value for the survival of the patient [2, 13, 33, 41, 47, 48]. Among the histologic features evaluated in our study, tumor grade was associated with statistically significant survival differences in the univariate analysis. In the multivariate Cox regression model analysis, grade was further identified as an independent predictor of overall survival. WHO grade III tumor differentiation was particularly associated with lower median survival time of 53 mo, with a hazard ratio of 1.745 ($P < 0.001$).

According to the literature the distribution of ependymomas in female and male patients varies between 40%-53% and 45%-60%, respectively [16, 49–54]. In our study, females comprised 45.6% of the cohort and males 54.4%, both falling within the parameters that have been reported in the literature. Many investigators have concluded that the gender of the patient is probably not a significant prognostic factor [2, 18, 40, 55], while others have suggested that survival for female patients is worse [34, 56]. Contrary to these previous studies, we observe that female patients do significantly better than male patients with a difference in median survival of 262 mo *versus* 196 mo, respectively ($P = 0.004$). This is similar to the report of Vanuytsel *et al.* [41] who reported a 15-y survival of 19% for males in — 38) and 40% ($n = 55$) for female patients with intracranial ependymoma.

Regarding prognosis by race, Goldwein *et al.* [11] previously reported that Caucasian children did significantly better than non-Caucasian (5-y survival 43% versus 14%, respectively). In our series, however, we observed that non-Caucasian patients had a longer median survival, although the observed differences were not statistically significant ($P = 0.096$). Furthermore, by multivariate analysis correcting for anatomic site, we do not observe differences by race in outcomes for ependymomas. Black patients presented with less spinal tumors and more supratentorial tumors than white patients; the reasons for these racial disparities are not clear.

In addition to these racial differences, we have also found Hispanic patients to have a significantly lower median survival compared with non-Hispanics (197 mo *versus* 249 mo, $P = 0.05$). Previous studies have generally not found a survival difference among ethnic groups. One review found Hispanics with CNS tumors to have lower incidence and mortality rates and higher 5-y survival compared with non-Hispanics [57]. Another study focused on pediatric patients with CNS tumors found that although there were no survival disparities

among ethnic groups, Hispanics, African Americans, and Asians diagnosed with astrocytoma had trends towards an increased risk of death compared with non-Hispanics [58].

Compared with adults, we found that children (0–19 y) had a significantly worse prognosis than adults (156 mo *versus* 237 mo, $P < 0.001$). While children under 9 y of age at diagnosis had the best response to radiation, overall they carried a particularly poor prognosis. Patients diagnosed with ependymoma under the age of 4 y demonstrated a 5-y survival rate of 52%. Those diagnosed between 5 to 9 y of age carried a 5-y survival rate of 66% ($P = 0.04$ under 4 y *versus* 5–9 y). Similar observations have been made in other smaller series [12,17,56, 59]. It has been suggested that the reason for aggressive tumor behavior may be due to the more immature neural tissue of children and the unfavorable immunohistochemical findings of pediatric ependymoma [7, 60]. Furthermore, both supratentorial and infratentorial ependymomas (more common in children) have been found to arise from different populations of neural progenitor cells from each other and from spinal tumors (more common in adults). WHO grade III tumors, known to be particularly aggressive, occurred in a younger age than WHO grade II. However, it is possible that aggressive tumor behavior is largely a function of genetic profiles rather than histology [61]. We found that radiation did not improve survival in patients younger than 3 y of age. Current protocols consist of postoperative chemotherapy with delayed radiation in children less than three y of age [62–64].

The SEER database, although an excellent resource for comparative outcomes analysis, has its limitations. Although the database relies on active follow-up for its registered cases, incomplete data reporting remains a problem. In some instances, demographic or disease data, such as race and tumor grade, were not specified. This may reflect a reporting omission or the absence of the data in the patient's medical record. The status of surgical resection margins was missing in many cases from the database, and those cases could not be included in the partial *versus* total resection analysis. Furthermore, centralized confirmation of pathologic specimens is not undertaken. Clinical information is limited since SEER does not include information on Karnofsky Performance Status, clinical symptoms, duration of symptoms, postsurgical outcomes and deficits, and whether or not surgery was to obtain a biopsy or for treatment purposes. Information on whether the patient received palliative radiation *versus* adjuvant or neoadjuvant treatment, including the specific regimen and dosage, were also unavailable. Furthermore, there may have been selection bias in the subset of patients treated with surgery. Some bias towards a positive outcome may have been introduced by treating those patients who did not have advanced tumor burden. Although data on radiotherapy was examined, data on chemotherapy is lacking in the SEER registry. Since chemotherapy has generally not been found to be beneficial for patients with ependymoma [65–67], the utility of this information is uncertain.

In conclusion, examination of a large, populationbased, nationwide cancer registry study revealed that age, gender, tumor grade, and tumor location were independently predictive of prognosis in malignant ependymomas. Surgery proved to significantly prolong median survival for these patients, while radiation conferred a significant overall survival benefit only for partially resected tumors. This analysis of a large national tumor registry confirmed

the conclusions of some smaller studies concerning prognostic value of age, tumor grade, and tumor location, and challenges the effects of race and gender previously reported in the literature. In addition, we were able to identify changes in incidence and treatment strategies over a 32 y study period. For rare tumors in which prospective randomized trials are scarce, such as in the case of this uncommon CNS neoplasm, examination of large cancer databases is an excellent method to understand the prognostic factors, incidence trends, and the affects of various treatments. Further prospective analysis of ependymomas will be necessary in the future to further delineate optimal medical, surgical, and radiation treatment strategies.

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FIG. 1.
Distribution by primary site of all malignant ependymomas reported in the SEER database (1973–2005).

FIG. 2.

(A) Age adjusted incidence rate to 2000 U.S. standard population by decade of life. (B) Overall incidence of malignant CNS ependymoma from y 1973 to 2004. Solid line represents rate per 100,000 per year. Broken line represents best fit straight line.

FIG. 3.
Primary ependymoma incidence rates by age at diagnosis and race. SEER 1973–2005.

FIG. 4.

Kaplan-Meier curve for (A) overall survival of entire cohort, (B) overall survival of cohorts having surgery *versus* not having surgery, (C) overall survival of cohorts according to grade, and (D) overall survival by gender. *P* value shown for log rank test between variables.

TABLE 1

Demographics and Clinical Characteristics of Study Population

	Overall		Median age of diagnosis (y)	Gender		Race		
	n	(% of Total)		Female n = 1097 (% of total)	Male n = 1311 (% of total)	White n = 2048 (% of total)	Black n = 192 (% of total)	Other n = 153 (% of total)
Cohort	2408	100.0	35	45.6	54.4	85.6	8	6.4
Gender								
Female	1097	45.6	28	ND	ND	44.6	50.5	53.6
Male	1311	54.4	37	ND	ND	55.4	49.5	46.4
Age (y)								
0–2	252	10.5	1	8.9	11.7	10.3	14.6	9.2
3–9	269	11.2	5	11.1	11.2	9.7	20.3	18.3
10–19	234	9.7	14	8.8	10.5	9.6	11.5	9.2
20–29	264	11.0	25	11.2	10.8	10.5	10.4	15.7
30–39	335	13.9	35	15.2	12.8	14.2	11.5	12.4
40–49	377	15.7	45	16.0	15.3	16.2	12.5	12.4
50–59	340	14.1	55	14.8	13.6	14.5	12.5	12.4
60–69	196	8.1	65	7.8	8.4	8.7	4.2	5.9
70–79	114	4.7	74	4.9	4.6	5.1	2.1	3.9
80+	27	1.1	83	1.1	1.1			
Race								
White	2048	85.0	35	83.6	87.2	ND	ND	ND
Black	192	8.0	33	8.9	7.3	ND	ND	ND
Other	153	6.4	23	7.5	5.5	ND	ND	ND
Unknown	15	0.6						
Ethnicity								
Hispanic	331	13.7	29	14.1	13.6	15.7	2.1	2
Non-Hispanic	2063	85.7	38	85.9	86.4	84.3	97.9	98
Unknown	14	0.6						
Site								
Spinal cord	958	39.8	45	40.5	39.2	41.3	28.6	32
Supratentorial	910	37.8	20	37.8	37.8	35.8	50.5	49

	Overall		Gender		Race			
	n	(% of Total)	Median age of diagnosis (y)	Female n = 1097 (% of total)	Male n = 1311 (% of total)	White n = 2048 (% of total)	Black n = 192 (% of total)	Other n = 153 (% of total)
Cortex	628	26.1	16	27	25.3	24.3	40.1	32.7
Ventricle	282	11.7	27	10.8	12.5	11.5	10.4	16.3
Infratentorial	530	22	24	21.3	22.6	22.6	20.8	17.6
Brain stem	384	15.9	27.5	16.6	15.4	16.3	15.6	12.4
Cerebellum	146	6.1	14	4.7	7.2	6.3	5.2	5.2
Other	10	0.4	36.5	0.5	0.4	0.4	0	1.3
WHO grade								
Grade II ependymomas	2132	88.5	37	89.5	87.7	89.3	88	80.4
Grade III anaplastic ependymomas	276	11.5	12.5	10.5	12.3	10.7	12	19.6
Surgery								
Yes	2202	91.4	32	5.6	4.8	5.2	4.4	3.3
No	120	5.0	47	94.4	95.2	94.8	95.6	96.7
Unknown	86	3.6						
Radiation								
Yes	1104	45.8	28.5	44.3	47.1	47	45.7	54.3
No	1235	51.3	38	53.3	49.6	53	54.3	45.7
Unknown	69	2.9						

TABLE 2

Distribution of Anatomic Sites and Presentation by Age

All ages			Age (y)											
n	%		0-2	3-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80+		
			%	%	%	%	%	%	%	%	%	%		
Extra-cranial	Spinal cord	958	39.8	1.2	4.8	21.4	43.6	54.0	63.9	55.0	48.0	51.9		
Intracranial	Supratentorial	910	37.8	56.7	64.7	54.7	36.7	27.5	21.8	27.9	28.1	44.4		
	Cortex	628	26.1	40.5	50.6	41.5	21.2	17.6	14.6	17.4	18.4	33.3		
	Ventricle	282	11.7	16.3	14.1	13.2	15.5	9.9	7.2	10.6	9.7	11.1		
	Infratentorial	530	22	42.1	29.7	23.9	18.9	18.2	13.8	16.5	23.5	3.7		
	Brain stem	384	15.9	26.6	20.4	16.2	15.9	15.5	9.8	12.6	18.9	0.0		
	Cerebellum	146	6.1	15.5	9.3	7.7	3.0	2.7	4.0	3.8	4.6	3.7		
Other		10	0.4	0.0	0.7	0.0	0.8	0.3	0.5	0.6	0.5	0.0		
	Total	2408	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0		

TABLE 3
Treatment Modalities Employed Following Ependymoma Diagnosis According to Age and Diagnosis Year

	n	Treatment unknown		Treatment known		No treatment		Surgery alone		Surgery and radiation		Radiation alone	
		%		%		%		%		%		%	
Age (y)													
0–2	252	6.0	94.0	3.0	59.1	38.0	0.0						
3–9	269	3.3	96.7	1.2	21.5	76.2	1.2						
10–19	234	9.0	91.0	2.8	31.0	65.3	0.9						
20–29	264	9.5	90.5	4.2	47.3	47.7	0.8						
30–39	335	3.6	96.4	2.5	52.6	44.3	0.6						
40–49	377	4.5	95.5	3.6	60.0	35.3	1.1						
50–59	340	4.1	95.9	4.3	55.5	37.7	2.5						
60–69	196	7.7	92.3	4.4	55.8	38.1	1.7						
70–79	114	7.9	92.1	10.5	49.5	35.2	4.8						
80+	27	7.4	92.6	40.0	56.0	4.0	0.0						
Presenting Site													
Spinal cord	958	4.1	95.9	3.9	69.1	25.8	1.2						
Supratentorial	910	8.5	91.5	4.6	34.7	59.1	1.7						
Cortex	628	8.0	92.0	4.3	32.7	61.2	1.7						
Ventricle	282	9.6	90.4	5.1	39.2	54.1	1.6						
Infratentorial	530	4.2	95.8	3.1	35.2	61.0	0.6						
Brain Stem	384	3.6	96.4	3.8	33.2	62.2	0.8						
Cerebellum	146	5.5	94.5	1.4	40.6	58.0	0.0						
Other	10	10.0	90.0	0.0	66.7	22.2	11.1						
Total	2408	5.8	94.2	4.0	48.9	45.9	1.3						
Year of diagnosis quartile													
1973–1980	240	20.0	80.0	3.1	24.5	72.4	0.0						
1981–1988	296	11.1	88.9	2.3	33.1	64.6	0.0						
1989–1996	532	3.6	96.4	1.8	54.8	42.7	0.8						
1997–2005	1340	2.9	97.1	5.3	53.3	39.4	1.9						

TABLE 4

Median, 5-, and 10-y Survival

		<i>n</i>	%	Median survival (mo)	5 y	10 y	<i>P</i> value
Overall		2408	100.0	230	70.0	61.0	
Gender							
	Female	1097	45.6	262	73.0	65.6	0.004
	Male	1311	54.4	196	68.0	57.6	
Age (y)							
	0–2	252	10.5	37	42.5	35.2	<0.001
	3–9	269	11.2	288	63.5	57.3	
	10–19	234	9.7	348	78.0	66.7	
	20–29	264	11.0	ND	80.2	74.1	
	30–39	335	13.9	267	88.3	80.0	
	40–49	377	15.7	288	81.2	76.7	
	50–59	340	14.1	185	71.5	59.3	
	60–69	196	8.1	88	61.0	41.0	
	70–79	114	4.7	62	48.7	25.4	
	80+	27	1.1	19	26.1	26.1	
Race							
	White	2048	85.6	228	71.0	61.4	0.096
	Black/African American	192	8.0	253	60.9	56.3	
	Other	153	6.4	315	71.8	60.8	
Ethnicity							
	Hispanic	331	13.7	197	80.2	70.6	0.05
	Non-Hispanic	2063	85.7	249	72.2	62.5	
Site							
	Spinal cord	958	39.8	303	89.9	81.4	<0.001
	Supratentorial	910	37.8	93	55.6	47.2	
	Brain	628	26.1	87	54.0	46.5	
	Ventricle	282	11.7	126	59.0	49.0	
	Infratentorial	530	22	137	63.7	51.5	

		<i>n</i>	%	Median survival (mo)	5 y	10 y	<i>P</i> value
	Brain stem	384	15.9	137	66.4	52.2	
	Cerebellum	146	6.1	102	56.4	50.2	
	Other	10	0.4	107	73.3	73.3	
WHO grade							
	Grade II ependymomas	2132	88.5	249	73.1	63.4	<0.001
	Grade III anaplastic ependymomas	276	11.5	53	49.0	42.1	
Surgery							
	Yes	2202	94.8	237	72.4	62.7	<0.001
	No	120	5.2	215	52.6	48.6	
Radiation							
	Yes	1104	47.2	176	69.0	57.2	0.718
	No	1235	100.0	344	73.0	66.3	

TABLE 5

Effect of Surgery on Overall Survival

		<u>Median survival (mo)</u>		<i>P</i> value
		Surgery	No surgery	
Overall		237	215	<0.001
Gender				
	Male	215	166	<0.001
	Female	267	211	0.002
Age (y)				
	0–2	39	1	<0.001
	3–9	288	101	0.896
	10–19	348	64	0.428
	20–29	379	115	0.735
	30–39	267	162	0.043
	40–49	288	215	0.464
	50–59	164	77	0.192
	60–69	97	15	0.006
	70–79	79	9	<0.001
	80+	37	4	0.017
Race				
	White	237	215	<0.001
	Black	253	15	0.003
	Other	315	72	0.349
Ethnicity				
	Hispanic	196	83	0.026
	Non-Hispanic	237	215	<0.001
Site				
	Spinal cord	300	166	<0.001
	Supratentorial	117	31	<0.001
	Brain	93	34	0.012
	Ventricle	136	3	0.001
	Infratentorial	145	16	0.002
	Brain stem	145	15	0.003
	Cerebellum	102	75	0.365
	Other	107	2	0.779
WHO grade				
	Grade II ependymomas	254	215	<0.001
	Grade III anaplastic ependymomas	54	11	0.003
Radiation				
	Yes	180	72	0.298
	No	280	215	<0.001

TABLE 6

Cox Proportional Hazard Model for Ependymomas

		Hazard ratio	95% CI	P value
Gender	Female	Reference group		
	Male	1.17	1.034 to 1.379	0.043
Age (y)	0–2	Reference group		
	3–9	0.439	0.332 to 0.582	<0.001
	10–19	0.317	0.226 to 0.445	<0.001
	20–29	0.384	0.276 to 0.534	0.001
	30–39	0.357	0.259 to 0.493	<0.001
	40–49	0.479	0.352 to 0.652	<0.001
	50–59	0.839	0.636 to 1.108	0.216
	60–69	1.384	1.029 to 1.861	0.031
	70–79	1.992	1.435 to 2.765	<0.001
	80+	2.949	1.724 to 5.042	<0.001
Site				
Spinal cord		Reference group		
Supratentorial		3.575	2.881 to 4.435	<0.001
	Cortex	3.517	2.795 to 4.425	<0.001
	Ventricle	3.24	2.507 to 4.188	<0.001
Infratentorial		3.143	2.490 to 3.967	<0.001
	Brain stem	3.081	2.410 to 3.938	<0.001
	Cerebellum	3.214	2.335 to 4.423	<0.001
Other		2.911	0.717 to 11.829	0.135
WHO grade				
Grade II ependymomas		Reference group		
Grade III anaplastic ependymomas		1.639	1.325 to 2.028	<0.001
Surgery				
	Yes	Reference group		
	No	1.992	1.441 to 2.754	<0.001

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	Hazard ratio	95% CI	P value
*Radiation	Reference group		
	Yes No	1.748 1.078 to 2.834	0.024

* Subset of patients (*n* = 316) who had partial resection.