DOI: https://doi.org/10.11144/Javeriana.umed61-3.sobr

Survival of Primary Brain Tumors in Colombia

Sobrevida de los tumores cerebrales primarios en Colombia

Received: 27 November 2019 | Accepted: 06 March 2020

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How to cite: Gómez Vega JC, Ocampo Navia MI, De Vries E, Feo Lee OH. Survival of primary brain tumors in Colombia. Univ. Med. 2020; 61(3). https://doi.org/10-11144/Javeriana.umed61-3.sobr

RESUMEN

Introducción: En 2018, los tumores del sistema nervioso representaron aproximadamente el 1,4 % de los nuevos diagnósticos de cáncer, que causaron el 2,6 % de las muertes por esta enfermedad. En Colombia hay pocos informes sobre la epidemiología de los tumores cerebrales, y los que existen son a partir de bases de datos locales que no tienen representatividad poblacional.

Objetivo: Determinar la sobrevida de los tumores cerebrales en Colombia.

Materiales y métodos: Estudio observacional descriptivo y retrospectivo, mediante las bases de datos de registros de cáncer de base poblacional de Colombia para el periodo 2003-2012, sin restricción por grupo etario. Se calcularon las tasas de sobrevida por el método de Kaplan-Meier y se usó el *software* estadístico Stata 14.0.

Resultados: En el periodo 2003-2012 se reportaron 775 pacientes adultos y 123 pediátricos con un nuevo diagnóstico de un tumor del sistema nervioso. Los más frecuentes en la edad pediátrica fueron los tumores neuroepiteliales, los embrionarios y los ependimarios; mientras que para los adultos fueron los tumores neuroepiteliales, los meningiomas y los hematolinfoides. La sobrevida global a seis meses, un año, dos años y tres años, en la población pediátrica fue de 49,9 %, 35,2 %, 21,4 % y 15,3 %, respectivamente; para los adultos fue del 70,2 %, 58,9 %, 43,3 % y 35,4 %.

Conclusiones: Este estudio constituye el trabajo más reciente sobre la epidemiología de los tumores cerebrales en Colombia. Se evidenció un claro subregistro general y estadísticas inferiores a las comparadas con la literatura. Se pretende ampliar la cobertura y recolección de datos en los registros de cáncer de base poblacional.

Palabras clave
tumores cerebrales; sobrevida global; incidencia; mortalidad; epidemiología.

ABSTRACT

Introduction: In 2018, central nervous system tumors represented approximately 1.4% of new cancer diagnoses, causing 2.6% of deaths by cancer. In Colombia, there are few reports on the epidemiology of brain tumors, and those that exist are from local databases that don´t have a rigorous and massive registry.

Aim: To determine the survival rates of brain tumors in Colombia.

Methods: A retrospective descriptive observational study was conducted, using databases of population-based cancer registries in Colombia. We extracted information from 2003-2012 of patients with tumors without age group restriction. The survival rates were calculated, using the Kaplan-Meier method and the statistical software Stata 14.0.

Results: From 2003-2012, 775 adult patients and 123 pediatric patients were reported with a new central nervous system tumor diagnosis in the four cities. The most frequent tumors in the pediatric age group were neuroepithelial tumors, embryonal tumors and ependymal tumors; whereas for adults, the most frequent were neuroepithelial tumors, meningiomas and hematolymphoid tumors. The global survival rate at six months, 1 year, 2 years and 3 years, were approximately 49.9%, 35.2%, 21.4% and 15.3% in the pediatric population, and 70.2%, 58.9%, 43.3% and 35.4% in the adult population.

Conclusions: The present work constitutes the most recent and multicenter study on the epidemiology of brain tumors in Colombia. There was a clear underreport of this type of tumor and inferior rates compared to the literature. Despite this, these results will help to widen data recollection and coverage in population-based cancer registries.

Keywords

brain tumors; global survival rates; incidence; mortality; epidemiology.

Introduction

Nervous system tumors accounted for approximately 1.4% of new cancer diagnoses in the United States in 2018. Their prevalence decreases with age, although between 0 and 14 years of age it is the leading cause of malignancy, since they represent approximately 30% of cancer deaths in this population (1-9). The most common central nervous system (CNS) tumors in children are pilocytic astrocytoma, embryonal tumors and malignant gliomas, while in adults the most common are meningiomas, pituitary tumors and malignant gliomas (1-3,10-14).

Our team has focused attention on the importance of collecting data on the pathology of brain tumors, and recently published a paper on the general epidemiology of these tumors. The paper was based mainly on population-based registries from North America and Europe, since in Colombia there are few reports on the epidemiology and disease burden of brain tumors, and the existing reports show the reality of specific cities, and do not show them globally (9,15-17).

We consider it necessary to know the epidemiology and survival of brain tumors in our country, in order to be able to propose health policies, carry out diagnostic screening and manage strategies to plan preventive activities to improve the quality of medical care and the provision of health services (18-21). This article reports on the survival rates of brain tumors in Colombia at six months, 1, 2, and 3 years, from population-based cancer registries from different cities, collected over a period of 10 years. Furthermore, it is one of three articles in which the epidemiological information on brain tumors in our country is compiled, in order to generate knowledge and provide data to the actors involved in the social security system and the health regulatory bodies.

Materials and methods

A descriptive retrospective observational study was carried out using the databases of Colombian population-based cancer registries, collected by the Colombian Cancer Information System (SICC-Infocancer), which collects general information on mortality and incidence from the cities of Bucaramanga, Pasto, Manizales and Barranquilla (22,23). Attached to this was the individual population register for Cali (Valle del Cauca, Colombia) (24) and information from international bodies (network of national cancer institutes and institutions, Ministry of Health, International Agency for Research on Cancer [IARC]/Globocan) (3,4).

Anonymized data from 2003 to 2012 of patients with brain tumors (malignant or

benign) were extracted. The information, without age group restriction, was grouped as follows: pediatric patients (under 18 years old) and adult patients (18 years old or older). The general population characteristics and the characterization of brain tumors were analyzed. General mortality was calculated for each department in Colombia, presented in SICC-Infocancer, but extracted from data of the National Administrative Department of Statistics (DANE). Standardized mortality rates were also averaged, grouped by five-year periods (2003-2007 and 2008-2012), for convenience in carrying out the analyses, without affecting the reliability of the results, since the variation was minimal over the course of the 10 years. On the other hand, since the registry covers from 2003 to 2012, the classification prior to the last update proposed by the World Health Organization in 2016 was used for the histological reference of the tumor subtypes.

Statistical analysis

First, a database was created with the data and raw information collected. Descriptive statistical analysis was also performed for all the variables considered in the analysis and for the selected subgroups. The Shapiro-Wilk test was applied to determine the normality of the data; those that followed a normal distribution are presented as mean and standard deviation (SD), while categorical variables are presented as proportions or percentages. Incidences and mortalities are presented as relative frequencies, crude rates and age-adjusted rates (under 18 years and over 18 years), expressed per 100,000 person-years.

The standard population used was the world population, according to Mitsou Segi (SEGI), as is convention when comparing standardized rates using data from population-based cancer registries (23). Global survivals by age group, gender, city and histology were calculated using Kaplan-Meier's method. For survival analysis and sub-analysis, the first three years in the Kaplan-Meier curves were taken, since the number of cases reported was not representative after this period. Stata version 14.0 was used for the statistical analysis.

Results

Central nervous system tumors in pediatric patients

General demographic characteristics. In the pediatric population, a total of 123 cases of brain tumors were reported in SICC-Infocancer in the 2003-2012 period, mostly in men (53.7%), with an average age at diagnosis of 8.4 years (SD ± 5.43 years). With regard to their behavior, 95.1% were malignant, 3.3% uncertain and 1.6% benign. The incidence rate was 1.55 per 100,000 person-years and the mortality rate was 0.063 per 100,000 person-years (Table 1).

Table 1
Sociodemographic characterization of the pediatric and adult population

	Pediatric		Adult	
Variable	**n = 123**	**%**	**n = 775**	**%**
Age	8.39 ± 5.43		52.7 ± 17.1	
Tumor sequence				
Single Tumor	123	100	760	98.06
First of more	0	0	7	0.90
Second of more	0	0	8	1.03
Gender				
Male	66	53.66	386	49.81
Female	57	46.34	389	50.19
Behavior				
Malignant	117	95.12	714	92.1
Benign	2	1.63	54	6.97
Uncertain*	4	3.25	7	0.9
Basis for diagnosis				
DCO**	7	5.69	88	11,35
Clinical	25	20.33	115	14,84
Microscopic verification	91	73.98	572	73,81
Vital status				
Alive	36	29.27	192	24.77
Dead	61	49.59	453	58.45
No data	26	21.14	130	16,77
Incidence+	1.55		3.19	
Mortality+	0.063		1.86	

*Whether it is benign or malignant.
**Death certificate only.
+Rates expressed per 100,000 person-years, standard SEGI population.

Characterization of brain tumors. The most common tumors were malignant supratentorial, which represented 63.4%. According to the histological subgroup, the most common in ascending order were glial lesions, embryonal tumors and ependymal tumors, of which the predominant histological subtypes were astrocytoma, medulloblastoma and ependymoma.

Survival. Overall survival at six months, 1, 2, and 3 years was 49%, 35%, 21% and 15%, respectively. Survival by gender and by city was better in men and in Bucaramanga, respectively. Survival for the most common histological subtypes was longer for glial lesions, being at six months, 1 year, 2 years and 3 years of 54%, 42%, 33% and 25%, respectively (Table 2, Figure 1).

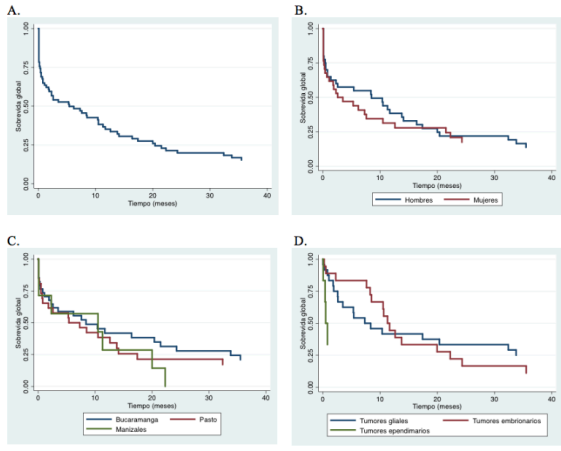
Table 2

Pediatric survival: overall, by city, by gender and by histology (in percentages)

Survival	6 months	1 year	2 years	3 years
Overall	49.85	35.17	21.41	15.29
Gender				
Men	54.89	38.42	21.95	13.72
Women	43.92	31.37	20.92	17.43
City				
Bucaramanga	58.82	41.83	31.37	20.92
Pasto	50	38.46	21.37	17.09
Manizales	57.14	28.57	0	0
Most common histologies				
Glial	54.17	41.67	33.33	25
Embryonal	83	44.44	22.22	11.11
Ependymal	33.33	33.33	33.33	33.33

Figure 1

Kaplan-Meier curves for pediatric survival of up to 3 years. A) Overall survival. B) Survival by gender. C) Survival by city. D) Survival by most common histologies



Central nervous system tumors in adults

General demographic characteristics. A total of 775 cases of adult brain tumors were reported to SICC-Infocancer. The average age was 52.7 years (SD 17.1 years), with an equitable distribution by gender. 92.1% of the tumors showed a malignant behavior, 7% had a benign behavior and 0.9% an uncertain behavior. The main basis for diagnosis was histological, represented in 73.8% of cases. The incidence rate was 3.19 per 100,000 person-years and the mortality rate was 1.86 per 100,000 person-years.

Characterization of brain tumors. 92% of the tumors were supratentorial, and within these glial lesions, meningiomas and haematolymphoid tumors were the most common histological types, in 82.4%, 8.9% and 2.3%, respectively.

Survival. The overall survival at six months, 1, 2, and 3 years was 70%, 59%, 43% and 35%, respectively. Survival by gender and by city was better in men and in Manizales. Survival for the most common histological subtypes was longer for meningiomas, being at six months, 1, 2, and 3 years of 84%, 82%, 71% and 39%, respectively. Within the subanalysis of neuroepithelial tumors, oligodendrogliomas are the tumors with best survival rates. On the other hand, within the histological subtypes of low and high-grade glial lesions, the fibrillar pattern obtained better survival rates (Table 3, Figures 2 and 3).

Table 3
Adult survival: overall, by city, by gender, histology, glial tumor, astrocytoma subtypes (in percentages)

Survival	6 months	1 year	2 years	3 years
Overall	70.17	58.87	43.33	35.59
Gender				
Men	74.03	61.14	44.02	35.49
Women	66.18	56.53	42.75	35.94
City				
Bucaramanga	72.88	59.59	36.24	27.27
Pasto	65.18	53.33	36.54	27.84
Manizales	75.17	64.76	54.21	47
Most common histologies				
Glial tumors	73.39	60.55	36.24	27.06
Meningiomas	84.21	81.58	71.05	39.47
Hematolymphoid	44.44	11.11	11.11	11.11
Glial tumor subtypes				
Glioblastomas	66.67	54.17	18.75	12.50
Oligodendrogliomas	89.47	89.47	73.68	68.42
Astrocytomas	76.47	60.78	45.10	32.35
Astrocytoma subtypes				
Anaplastic	61.90	38.10	23.81	19.50
Gemistocytic	85.71	71.43	71.43	57.14
Fibrillar	100.00	84.62	69.23	61.54

Figure 2
Kaplan-Meier curves for adult survival up to 3 years. A) Overall survival. B) Survival by gender. C) Survival by city

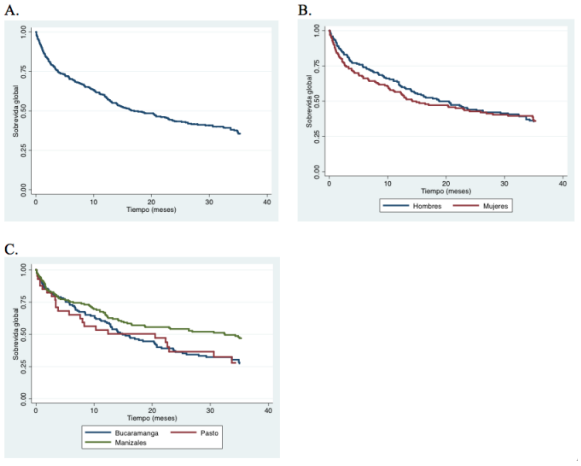
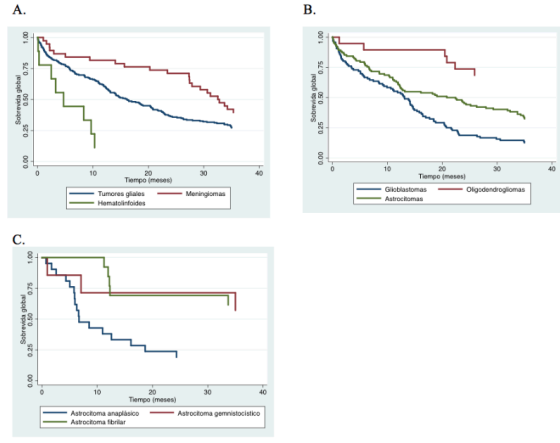


Figure 3
Kaplan-Meier curves for adult survival by histology up to 3 years. A) Survival by most common histologies. B) Survival by glial tumor subtypes C) Survival by astrocytoma subtypes



Discussion

According to the latest data from the U.S. Central Registry of Brain Tumors, in 2015 the incidence rate of primary malignant brain tumors in the United States was 6.95, and that of non-malignant tumors was 15.64 (25,26). Compared to data from high-income countries, the incidence rates range between 10.57 and 25.5 in countries such as Japan, France and Italy (27-30). When compared to Latin America, they tend to be similar to our report; Brazil, Mexico and Ecuador found incidence rates of 5.5, 2.4 and 3.7 per 100,000 inhabitants, respectively (8). Mortality figures show a similar behavior: by 2018, the United States reported a mortality rate of 4.3 per 100,000 inhabitants (26), while the rate in Australia was 5.3 per 100,000 inhabitants (31). As with incidence, Latin American countries tend to have lower rates compared to higher income countries (Brazil with 3.6, Mexico with 1.9 and Ecuador with 1.9 per 100,000 inhabitants); this may be related to the few population databases available (8).

The overall survival rates behaved similarly in the adult and pediatric populations, with low percentages from the initial follow-up, which

may correlate with the general underreporting of the databases. In addition, most neoplastic CNS lesions in the pediatric population are diagnosed after the child's death, so there is no clarity about the extent of the lesion (malignant and benign) prior to death. A local study published by Páez-Rodríguez et al. (15) showed similar results, where the overall survival was 3.4 years, and in 45% of the patients it was not possible to define the survival time, due to the difficulty in obtaining updated personal data from the clinical history.

The most common pediatric tumors reported in the literature are low and high-grade glial lesions and embryonal tumors, which correlates with what was found in the present study (9). For low-grade glial lesions, a good long-term survival has been demonstrated, up to 87% accumulated over 20 years, by Bandopadhay et al. (32). According to the National Cancer Institute (22), WHO I gliomas have a first-, second- and fifth-year survival rate of 95%, 93% and 91%, respectively; and the survival rate for WHO II gliomas in the same periods is 82%, 66% and 52%, respectively.

When evaluating survival in cases of pilocytic astrocytoma, similarities are found in the overall survival rates of the different publications. Survival at 5 and 10 years is between 80 and 100%, and between 81 and 95.8%, respectively (33-35). In this population, the survival scenario is less favorable with high-grade glial lesions, since for WHO III and IV lesions survival at 5 years was 29% and 18%, respectively (36,37). With regard to embryonal tumors, an overall survival at 1, 2 and 5 years of 80.6%, 71% and 62.6%, respectively, has been described (26).

According to the histological subtypes, the German study by Tulla et al. (38) showed a survival rate for medulloblastoma of 69% at 5 years and of 61% at 10 years, and for peripheral primitive neuroectodermal tumors a survival rate of 38% at 5 years and 34% at 10 years. Similar data was found in the work of Indelicato et al (39). In the present study, survival rates could not be compared with those previously described, given the small number of patients included.

The adult primary tumors most commonly reported in the literature are meningiomas, pituitary adenomas, and glioblastomas. This differs from what we found in our study, in which, as in the literature, we found that meningioma and glioblastoma were among the three most common subtypes. However, we found that the third in frequency were not pituitary adenomas, but hematolymphoid tumors (9). This may be due to bias in the database registry, since patients whose cause of death is related to a brain tumor are entered, making it unlikely that a pituitary adenoma per se is the causal link of death. On the other hand, many patients may have incidentally had a pituitary adenoma, without being diagnosed previously or at autopsy.

Overall survival of meningiomas tends to be good; for benign meningiomas, survival at 1, 2 and 5 years is reported to be 92.6%, 90.7% and 86.7%, respectively. However, for malignant meningiomas a survival at 1, 2 and 5 years of 82.1%, 74.9% and 63.8%, respectively, is reported (40-42). A similar behavior was observed for pituitary adenomas during survival; they usually have a benign behavior, with an overall one-year survival rate between 96 and 98% (40).

In the Iranian study by Anvari et al. (43) differences were found based on whether they were functioning or nonfunctioning. For functioning adenomas, the survival rate at 1 and 3 years was 84.6% and 23% respectively, and in the same period, the survival rate for nonfunctioning adenomas was 90.9% and 22.7% respectively. For this last subgroup of nonfunctioning pituitary tumors, the European study by Ntali et al. (11) found a difference in the survival rate according to whether the diagnosis had been made before the age of 50 or after, obtaining a survival rate of 98.5% at 10 years for diagnoses made before the age of 50, and a survival rate of 80.9% at 10 years for diagnoses made above that age.

Finally, for glioblastoma multiforme, which is the most common primary malignant tumor, survival is known to be low, despite medical-surgical management. Different survival rates were found in the studies. However, the

overall survival rate at 1, 2 and 5 years ranges between 20 and 38%, 17 and 27% and 10%, respectively (40,41,44-47). Currently, in the molecular age of brain tumors, Lin et al. (48) correlated the molecular subtypes of glioblastoma (classic, mesenchymal, proneural and neural) and demonstrated that there is no clear relationship with overall survival. However, they were able to establish that the proneural subtype had a good prognosis, the neural and mesenchymal subtypes, an intermediate prognosis, and the classical subtype, the worst prognosis.

Conclusions

The present study is the most recent work on the epidemiology and, more precisely, the survival for brain tumors in Colombia, whose statistics are low in relation to those reported in the literature. This article does not reflect the total epidemiology of brain tumors in Colombia, given that these results represent some cities in the country and are associated with an underreporting found in the databases. However, further studies are required to make a comparison with other countries. We believe that for future population-based studies it is essential to expand coverage and data collection in population-based cancer registries, which are necessary to implement health policies and strategies.

Limitations and future directions

There are few reports on the epidemiology of brain tumors in Colombia (15,18,20), and those that do exist are local records that are neither rigorous nor massive. Few Colombian cities (five of the country's 118 cities) have a formal population-based cancer registry, and general data are collected from these (49-51). These results have helped us to visualize the current situation of registration in databases in Colombia, which not only applies to nervous system tumors; it could also be extrapolated to other types of malignancies (breast, lung, digestive tract), which is a call to the authorities to improv and create population-based registries. Thesee registries will help us to create health policy decision-making strategies to plan preventive activities and clinical trials to optimize the quality of medical care (19,52).

Acknowledgments

To SICC-Infocancer and the population-based cancer registries in Colombia, for their great collaboration in sending the anonymized databases. Without their help, this article could not have been written.

Conflicts of interest: All authors certify that they are aware of the Journal's conflict of interest policy and that they have no conflict of interest in relation to the publication of this manuscript.

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