

Incidence, Mortality, and Survival Trends of Primary CNS Tumors in Cali, Colombia, From 1962 to 2019

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PURPOSE Global studies have shown varying trends of CNS tumors within geographic regions. In Colombia, the epidemiologic characteristics of CNS neoplasms are not well elucidated. We aimed to provide a summary of the descriptive epidemiology of primary CNS tumors among the urban population of Cali, Colombia.

METHODS We conducted a time-trend study from 1962 to 2019 using the Population-Based Cali Cancer Registry. The age-standardized rates per 100,000 person-years were obtained by direct method using the world standard population. Results were stratified by sex, age group at diagnosis, and histologic subtype. We used Joinpoint regression analysis to detect trends and obtain annual percentage change (APC) with 95% CIs. We estimated 5-year net survival using the Pohar-Perme method.

RESULTS During 1962 to 2016, 4,732 new cases of CNS tumors were reported. From 1985 to 2019, a total of 2,475 deaths from malignant CNS tumors were registered. A statistically significant increase in the trends of incidence (APC, 2.8; 95% CI, 2.1 to 3.5) and mortality (APC, 1.5; 95% CI, 1.1 to 2.0) rates was observed during the study. The most common malignant CNS tumor was glioblastoma (17.8% of all tumors), and the most frequent benign tumor was meningioma (17.2%). Malignancy was more common in males than in females. Unspecified malignant neoplasms represented 32% of all cases. The highest 5-year net survival was 31.4% during 2012 to 2016.

CONCLUSION Our findings demonstrate an increasing burden of primary CNS tumors for the last 60 years, with a steady rate from the early 2010s. There was an improvement of 5-year net survival for the last decade. Males had higher mortality than did females. Additional efforts are needed to fully explore the geographic, environmental, and genetic contributors of CNS malignancies within the region.

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INTRODUCTION

Primary CNS tumors represent a heterogeneous group of benign and malignant tumors arising mainly from the brain and less frequently from the spinal cord, cranial nerves, and meninges.¹ Histologically, brain tumors encompass a wide collection of neoplasms.² Compared with other malignancies, brain and CNS tumors are rare in adults, yet they are a significant burden of morbidity and mortality.³ According to GLOBOCAN 2018, brain and CNS malignancies were the 14th cause of cancer morbidity and 10th cause of cancer mortality, representing 2.1% (29,539) of new cases and 3.3% (22,312) of deaths from all primary malignancies in Latin America and the Caribbean.⁴

Incidence rates of CNS tumor, despite its rarity, showed an increasing trend from the 1970s to the early 1990s in high-income countries. This variation was partly attributable to the advent of high-throughput

diagnostic markers and tools—for example, introduction of computed tomography scan in the 1970s and magnetic resonance imaging in the mid-1980s, and the development of specialized medical care.^{5,6} Nevertheless, whereas some cancer registries continue to report an increase in incidence rates since the end of the 1990s, others have shown a downtrend.^{6,7}

The etiology of intracranial neoplasms is poorly understood. Trends of incidence and mortality have been helpful to characterize CNS tumor morphology and clinical behavior related to age.^{8,9} Moreover, the distribution of histologic types also varies according to sex.⁹ Thus, increasing the epidemiologic characterization of CNS cancers might elucidate disease patterns within a geographic region.

The Population-Based Cali Cancer Registry (PCCR) started in 1962 as a research program of the Department of Pathology of the Universidad del Valle

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CONTEXT

Key Objective

What are the incidence, mortality, and survival trends of primary CNS tumors from 1962 to 2019 in Cali, Colombia?

Knowledge Generated

There is an important burden of primary CNS tumors in the last 60 years in Cali, Colombia, with a steady trend since the last decade (2010). For patients who were diagnosed during 2012 to 2016, 5-year survival was 31.4%, which is the highest rate reported historically for Cali, Colombia.

Relevance

This is the largest epidemiologic description of primary CNS tumors in a city from Colombia. The findings of this study provide a better understanding of the geographic variations in morbidity, mortality, and survival over time. More research is required to identify novel risk factors associated with CNS malignancies.

School of Medicine in Cali, Colombia. Currently, PCCR is recognized by the International Agency for Research on Cancer (IARC), an entity of WHO. PCCR uses quality assurance procedures based on IARC guidelines to validate the quality of cancer registration. It is estimated that the reporting is at least 95% complete. The registry has been an advisor to the Colombian government, contributing significantly to different aspects of cancer control in Colombia.^{10,11}

In this study, we used data registered from 1962 to 2019 in the PCCR to provide a population-based description of trends in incidence, mortality, and survival rates of primary CNS tumors in Cali, Colombia, presented by age at diagnosis, sex, and histologic type. We aimed to provide a more complete understanding of these malignancy variations within the region.

METHODS

Patient Population

We conducted a population-based study to describe the incidence, mortality, and survival rates of primary brain and other CNS tumors reported to the PCCR in Cali, Colombia, from 1962 to 2019. In this study, we retrieved incidences of cases collected by PCCR from 1962 to 2016, and mortality data between 1985 and 2019. Tumors of benign behavior were included since 1992. Cancer registries record cancer cases, not patients; therefore, case reports were obtained continuously through an active search by visiting all sources of information, including hospitals, clinics, pathology departments, and oncology facilities—approximately 165—located in the urban area of Cali. Retrieval of new death registries was performed periodically from death certificates shared by the Cali Municipal Office of Vital Statistics. The information was integrated into the PCCR database using international standards of good practice.^{10,12}

Cali is the third-largest city in Colombia and the most densely inhabited city in the Colombian Southwest. According to the 2018 census of the National Administrative

Department of Statistics of Colombia, the population of Cali was 2,227,642: 52.8% were female and 47.2% male, and 26.2% self-identified as Black.¹³ Overall life expectancy at birth was 74.4 years.¹⁴ In this study, the total population of Cali was obtained from the official census data provided by the National Administrative Department of Statistics of Colombia during 1964, 1973, 1983, 1993, and 2005.

CNS Tumor Definition

Primary malignant CNS tumors were coded using the International Classification of Diseases (ICD) for Oncology, 3rd edition, by IARC/WHO.¹⁵ Three ICD versions were used throughout the registration period: 8th (1962 to 1978), 9th (1979 to 1998), and 10th revision (1998 to present). The IARCTools program was used in 1998 to convert codes between ICD versions.

Histologic types were clustered by their tissue of origin using the ICD for Oncology, 3rd edition, morphology codes and were classified according to major WHO categories for brain and CNS tumors as follows: tumors of neuroepithelial tissue, tumors of the meninges, tumors of the paraspinal nerves, tumors of the sellar region, germ cell tumors, lymphomas, and malignant tumors not otherwise specified (NOS). On the basis of their biologic behavior, CNS neoplasms fall into two categories: nonmalignant (previously called benign [0] and borderline [1]) and malignant (/3). There is no /2 code—neoplasia in situ—in the CNS morphology classification.¹⁶ The study population was stratified by sex and age at diagnosis into broad groups: children (0 to 14 years), teenagers (15 to 19 years), adults (20 to 64 years), and older adults (65 years or older).

Statistical Analysis

The crude and age-standardized incidence and mortality rates were reported as the number of cases per 100,000 person-years at risk using the urban standard population of Cali, Colombia, for each year. For every 5-year study period, an age-standardized rate (ASR) per 100,000 person-years was assessed by the direct method using the standard world population. Joinpoint regression

analysis was used to detect changes in rate trends and obtain the annual percentage change (APC) in incidence and mortality rates with 95% CIs. APC was considered statistically significant if the 95% CI did not include 0. For this analysis, we used SEER*Stat software (National Cancer Institute).

We estimated the 5-year net survival for adults (age 15 to 99 years) who were diagnosed with malignant brain tumors using the Pohar-Perme method. This estimator allows for an unbiased estimate of net survival—for example, the probability for patients to survive their cancer up to a given time since diagnosis—after controlling for other causes of death.¹⁷ Exclusion, failure, and survival time criteria were previously described.¹² Estimation of 15-year survival analysis was obtained by combining the cohort analyses for the intervals 2000 to 2004 and 2005 to 2009 as well as the period analysis for the interval 2012 to 2016. Survival possibilities were estimated by applying the extended life

table method.¹⁸ Life tables of all-cause mortality in the general population of Cali were constructed from the number of deaths and the population by single year of age, sex, and calendar year.¹⁹ Age standardization used International Cancer Survival Standard-2 weights.²⁰

RESULTS

Incidence

A total of 4,732 new cases of malignant and nonmalignant primary brain and other CNS tumors were reported in Cali, Colombia, from 1962 to 2016. During the last period, 2012 to 2016, CNS tumors represented 3.6% of all primary cancers in males and 3.2% in females. For the first period in the study (1962 to 1966), the annual age-adjusted incidence rate of all malignant and benign CNS tumors was 3.6 per 100,000 person-years, whereas for the last period of the study, 2012 to 2016, the rate increased to 7.8 per 100,000 person-years. The major increase in the

TABLE 1. Trends in Incidence (1962-2016) and Mortality (1985-2019) Rates for All Primary Brain and Other CNS Tumors Grouped by Age of Diagnosis and Sex

Period	Age-Specific Rate				Sex								
	Age at Diagnosis, Years				Male			Female			Both		
	0-14	15-19	20-64	≥ 65	No.	CR	ASR	No.	CR	ASR	No.	CR	ASR
Incidence													
1962-1966	2.1	0.6	4.3	8.9	52	3.6	5.0	29	1.8	2.5	81	2.7	3.6
1967-1971	1.9	1.1	3.4	2.9	56	3.2	3.7	29	1.4	1.7	85	2.3	2.7
1972-1976	1.3	0.7	3.4	5.9	49	2.3	2.8	49	2.0	2.6	98	2.1	2.7
1977-1981	2.2	0.9	3.0	10.9	80	3.2	4.1	59	2.1	2.4	139	2.6	3.1
1982-1986	2.0	1.1	3.3	11.2	87	2.9	3.6	83	2.5	3.0	170	2.7	3.3
1987-1991	1.4	0.7	4.8	14.0	124	3.6	4.5	112	2.9	3.6	236	3.2	4.0
1992-1996	2.1	1.6	7.7	30.2	233	6.0	7.3	249	5.7	6.7	482	5.8	7.0
1998-2001	3.1	2.4	9.1	33.0	295	6.9	7.9	386	8.1	8.6	681	7.5	8.3
2002-2006	2.7	1.9	9.1	33.9	338	7.1	7.8	455	8.6	8.6	793	7.9	8.2
2007-2011	3.0	2.1	9.2	35.5	419	7.9	8.3	540	9.4	8.6	959	8.7	8.5
2012-2016	3.1	2.3	8.2	33.0	439	7.8	7.7	569	9.3	7.9	1,008	8.6	7.8
APC (95% CI)					2.4 ^a (1.9 to 2.9)			1.8 ^a (1.3 to 2.3)			2.8 ^a (2.1 to 3.5)		
Mortality													
1985-1989	0.7	0.7	2.7	12.7	63	1.9	2.6	71	1.9	2.6	134	1.9	2.6
1990-1994	0.8	0.3	3.0	14.3	88	2.4	3.2	85	2.0	2.5	173	2.2	2.9
1995-1999	0.9	0.6	3.7	16.0	143	3.5	4.4	102	2.2	2.6	245	2.8	3.4
2000-2004	1.0	0.7	3.9	17.3	152	3.4	3.9	168	3.3	3.4	320	3.4	3.6
2005-2009	1.2	0.8	4.5	22.2	222	4.3	4.8	242	4.3	4.0	464	4.3	4.4
2010-2014	1.7	0.5	3.7	25.4	269	4.9	4.9	272	4.5	3.9	541	4.7	4.3
2015-2019	1.3	1.1	3.8	23.5	294	5.1	4.8	304	4.8	3.8	598	4.9	4.2
APC (95% CI)					1.5 ^a (0.9 to 2.0)			1.6 ^a (1.0 to 2.2)			1.5 ^a (1.1 to 2.0)		

NOTE. Data from the Population-Based Cali Cancer Registry, Cali, Colombia.

Abbreviations: APC, annual percent change; ASR, age-standardized rate per 100,000 person-years (world population); CR, crude rate.

^aAPC statistically different from zero ($P < .05$).

TABLE 2. Age-Standardized Incidence Rate (per 100,000 person-years) for All Primary CNS Tumors Categorized by Behavior (benign, borderline, malignant) and Sex, 1962-2016

Period	ASR								
	Benign			Borderline			Malignant		
	Both	Male	Female	Both	Male	Female	Both	Male	Female
1962-1966	0.5	0.4	0.5	0.0	0.1	0.0	3.2	4.5	2.1
1967-1971	0.1	0.2	0.0	0.0	0.0	0.0	2.6	3.5	1.7
1972-1976	0.0	0.0	0.1	0.1	0.1	0.1	2.6	2.7	2.5
1977-1981	0.0	0.0	0.0	0.0	0.0	0.0	3.1	4.0	2.4
1982-1986	0.0	0.0	0.0	0.0	0.0	0.0	3.3	3.6	2.9
1987-1991	0.0	0.0	0.0	0.0	0.0	0.0	4.0	4.5	3.6
1992-1996	2.0	1.6	2.3	0.7	0.6	0.8	4.3	5.1	3.6
1997-2001	2.2	1.1	3.1	1.1	0.8	1.3	5.0	6.0	4.2
2002-2006	2.1	1.1	2.9	1.0	1.0	1.1	5.1	5.8	4.6
2007-2011	2.1	1.2	2.9	1.2	1.3	1.1	5.1	5.7	4.6
2012-2016	1.9	1.2	2.5	0.9	0.9	0.9	5.1	5.7	4.5

NOTE. Data from the Population-Based Cali Cancer Registry, Cali, Colombia. Abbreviation: ASR, age-standardized rate per 100,000 person-years (world population).

age-adjusted incidence rate for the study was demonstrated between the intervals 1987 to 1991 and 1992 to 1996 (4.0 v 7.0 per 100,000 person-years, respectively).

Overall, 45.9% of all brain and other CNS tumors diagnosed between 1962 and 2016 occurred in males ($n = 2,172$) and 54.1% in females ($n = 2,560$); however, when reported by periods, incidence rates in females were lower compared with those of males until 1996. From 1997 to 2016, female incidence rates started to exceed those observed in males: For the last period of study, ASR was 7.9 versus 7.2 per 100,000 person-years, respectively (Table 1).

Regarding biologic behavior, whereas the average annual age-adjusted incidence rate of benign CNS tumors was persistently higher in females compared with males, the opposite occurred for malignant CNS tumors. For example, during the period 2012 to 2016, the ASR of benign tumors in females was 2.5 versus 1.2 per 100,000 person-years in males (Table 2), whereas the ASR of malignant CNS tumors in males was 5.7 versus 4.5 per 100,000 person-years in females during the last period (Table 2).

Approximately 11.8% ($n = 559$) of reported brain and CNS tumors during 1962 to 2016 occurred in children (age 0 to 14 years) and 82.2% ($n = 4,173$) in the population age 15 years or older (Table 3). Incidence rates in children and teenagers were persistently lower compared with adults from 1962 to 2016 (Table 1).

Trends in the incidence rates of all primary brain and other CNS tumors showed a statistically significant increase in morbidity from 1962 to 2016 (APC, 2.8; 95% CI, 2.1 to 3.5; Table 1), yet the analysis by behavior revealed a difference

in trends. Malignant CNS tumors showed a statistically significant increased incidence trend in both sexes (females: APC, 1.6; 95% CI, 1.1 to 2.1; and males: APC, 1.1; 95% CI, 0.7 to 1.6; Fig 1) from 1962 to 2016. On the contrary, primary benign CNS neoplasm showed a decreased incidence trend (females: APC, -0.2 ; 95% CI, -2.0 to 1.6; and males: APC, -0.9 ; 95% CI, -3.1 to 1.4; Fig 1) from 1992 to 2016.

Mortality

Altogether, a total of 2,475 deaths from primary malignant brain and other CNS tumors were registered from 1985 to 2019. The annual mortality rate was 2.6 per 100,000 person-years during 1985 to 1989 compared with 4.2 per 100,000 person-years during 2015 to 2019 (Table 1). Males had greater mortality rates than did females throughout the study time—for example, ASR was 4.8 versus 3.8 per 100,000 person-years, respectively, during the 2015 to 2019 period (the mortality male:female ratio was 1.3:1; Fig 2). Trends analysis revealed a statistically significant increase in mortality between 1985 and 2019 (APC, 1.5; 95% CI, 1.1 to 2.0).

Histologic Types

The distribution of all brain and other CNS tumors by histology and age at diagnosis is presented in Table 3. The most common of all malignant CNS tumors was glioblastoma (17.8% of all tumors; $n = 840$). This malignancy was most frequent in the population age 15 years or older and less common in children. Meningioma was the second most frequently reported CNS histology (17.2%; $n = 812$) and the most common benign tumor overall (Table 3). For children (age 0 to 14 years), the largest group of CNS tumors was diffuse astrocytoma followed by medulloblastoma (16.6% and 14.5%, respectively). Other frequent CNS tumors in children were pilocytic astrocytoma (9.7%), glioblastoma (8.6%), and ependymoma (8.2%; Table 3), yet 27.7% represented unclassified tumors in this age group.

Among major histology groupings, tumors of neuroepithelial tissue (43.4%) and tumors of the meninges (17.6%) were more common, followed far behind by tumors of paraspinal nerves (1.8%), lymphomas (0.9%), germ cell tumors (0.2%), and tumors of the sellar region (0.04%). Nonetheless, the proportion of unspecified neoplasms was 36.0% of all cases (Table 3). The overlapping lesion of brain and the CNS represented only 2% ($n = 100$ cases).

The most prevalent glioma subtype was that of astrocytic origin—diffuse astrocytoma, anaplastic astrocytoma, glioblastoma, oligodendroglioma, anaplastic oligodendroglioma, oligoastrocytoma—accounting for 36.1% of all tumors. The most recurrent benign nerve sheath tumor was schwannoma (Table 3).

TABLE 3. Histologic Types of Brain and Other CNS Tumors Ordered By Age at Diagnosis, 1962-2016

Histology	ICD-0-3 Histology and Behavior Code	Age at Diagnosis, Years, No.		Total	%
		0-14	≥ 15		
Tumors of neuroepithelial tissue		389	1,665	2,054	43.4
Diffuse astrocytic and oligodendroglial tumors		227	1,483	1,710	
Diffuse astrocytoma	9400/3	93	294	387	
Anaplastic astrocytoma	9401/3	14	153	167	
Glioblastoma ^a	9440/3; 9441/3; 9442/3	48	792	840	
Oligodendroglioma	9450/3	12	113	125	
Anaplastic oligodendroglioma	9451/3; 9460/3	3	21	24	
Oligoastrocytoma	9382/3	3	31	34	
Other astrocytic tumors ^b	9421/1; 9425/3; 9384/1; 9424/3; 9411/3; 9420/3	54	79	133	
Ependymal tumors		46	92	138	
Ependymoma	9391/3	32	76	108	
Other tumors ^c	9392/3; 9383/1; 9394/1; 9393/3	14	16	30	
Choroid plexus tumors ^d	9390/1; 9390/3	3	2	5	
Other neuroepithelial tumors ^e	9444/1; 9431/1; 9430/3	0	1	1	
Neuronal and mixed neuronal-glial tumors		4	10	14	
Ganglioglioma	9505/1	0	1	1	
Others tumors ^f	9505/3; 9509/1; 9506/1; 9505/1	4	9	13	
Tumor of the pineal region ^g	9361/1; 9362/3; 9395/3	0	0	0	
Embryonal tumors		109	77	186	
Medulloblastoma	9471/3; 9470/3; 9472/3; 9474/3	81	54	135	
Other tumors ^h	9478/3; 9501/3; 9500/3; 9490/3; 9473/3; 9508/3	28	23	51	
Tumors of the paraspinal nerves		1	83	84	1.8
Schwannoma	9560/0	1	82	83	
Neurofibroma	9540/0	0	1	1	
Tumors of the meninges		7	828	835	17.6
Meningioma	9530/0-9534/0; 9537/0-9539/0	6	806	812	
Mesenchymal, nonmeningothelial tumors ⁱ	8815/0; 9161/1; 9120/3; 9140/3; 9364/3; 8850/3; 8810/3; 8890/3; 8900/3; 9220/3; 9220/0; 9180/0; 9210/0; 9180/3	1	21	22	
Melanocytic tumors	8728/0; 8728/1; 8720/3; 8728/3	0	1	1	
Tumor of the sellar region		1	1	2	0.04
Craniopharyngioma and other tumors ^j	9350/1; 9351/1; 9352/1; 9582/0; 9432/1; 8290/0				
Germ cell tumors		6	5	11	0.2
Germinoma	9064/3	4	4	8	
Other tumors ^k	9070/3; 9100/3; 9071/3; 9080/3; 9080/1; 9084/3; 9085/3	2	1	3	

(Continued on following page)

TABLE 3. Histologic Types of Brain and Other CNS Tumors Ordered By Age at Diagnosis, 1962-2016 (Continued)

Histology	ICD-O-3 Histology and Behavior Code	Age at Diagnosis, Years, No.		Total	%
		0-14	≥ 15		
Lymphomas		0	42	42	0.9
Diffuse large B-cell lymphoma of the CNS	9680/3	0	38	38	
Other lymphomas ^l	9766/1; 9712/3; 9714/3; 9702/3; 9699/3	0	4	4	
Unclassified tumors, NOS		155	1,549	1,704	36.0
Total		559	4,173	4,732	100.0

NOTE. Data from the Population-Based Cali Cancer Registry, Cali, Colombia. Behavior codes are as follows: /0 benign; /1 borderline; /3 malignant. Abbreviations: ICD-O-3: International Classification of Diseases for Oncology, 3rd Edition; NOS, not otherwise specified.

^aIncludes giant cell glioblastoma, gliosarcoma, and epithelioid gliosarcoma.

^bIncludes pilocytic astrocytoma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma, gemistocytic astrocytoma, and fibrillary astrocytoma.

^cIncludes subependymoma, mixopapillary ependymoma, anaplastic ependymoma, and papillary ependymoma.

^dIncludes choroid plexus papilloma, atypical choroid plexus papilloma, and choroid plexus carcinoma.

^eIncludes astroblastoma, glioma of the 3rd ventricle, and angiocentric glioma.

^fIncludes anaplastic ganglioma, desmoplastic infantile astrocytoma and ganglioglioma, papillary glioneuronal tumor, cerebellar liponeurocytoma, and Rosette-forming glioneuronal tumor of 4th ventricle.

^gIncludes pineocytoma, pineal parenchymal tumor, pineoblastoma, and papillary tumor.

^hIncludes CNS neuroblastoma, medulloepithelioma, atypical teratoid, and CNS ganglioneuroblastoma.

ⁱIncludes hemangioblastoma, angiosarcoma, Kaposi sarcoma, Ewing sarcoma, liposarcoma, leiomyoma, leiomyosarcoma, rhabdomyosarcoma, osteoma, osteochondroma, and osteosarcoma.

^jIncludes granular cell tumor of neurohypophysis, spindle cell oncocytoma of adenohypophysis, and pituicytoma.

^kIncludes embryonal carcinoma, Yolk sac tumor, choriocarcinoma, teratoma, teratoma with malignant transformation, and mixed germ cell tumor.

^lIncludes immunodeficiency-associated CNS lymphoma, intravascular large B-cell lymphoma, T-cell and NK-cell lymphoma, anaplastic large cell lymphoma, and MALT lymphoma.

With respect to diagnostic methods, 74.4% (n = 3,519) of all brain and CNS tumors had microscopic confirmation during the study period (1962 to 2016), whereas 20.0% (n = 947) were radiographically confirmed, and 5.6% (n = 266) were obtained from death certificates (n = 28). All histologic behaviors were included.

Survival

The highest 5-year net survival after the diagnosis of malignant brain tumors among adults (age 15 to 99 years) was 31.4%, occurring during the 2012 to 2016 period. There was variation in survival estimates upon the calendar period of diagnosis: Five-year net survival was lower for the period 2000 to 2004 (23.4%) and increased during 2005 to 2009 (28.2%; Fig 3).

DISCUSSION

Overall, new cases of brain and other CNS tumors increased steadily between 1962 and 2016 in both males and females across all ages. The highest burden of new diagnoses was observed predominantly since the early 1990s. Upward trends may reflect the development of enhanced diagnostic practices and more readily available access to health care services in Colombia, rather than a true change in the natural history of CNS cancers.²¹⁻²⁴ It is also reasonable that, given the lack of diagnostic imaging

during the first decades, there was an underdiagnosis of CNS tumors.²¹

However, an alternative interpretation is that exposures to harmful environmental agents might contribute to

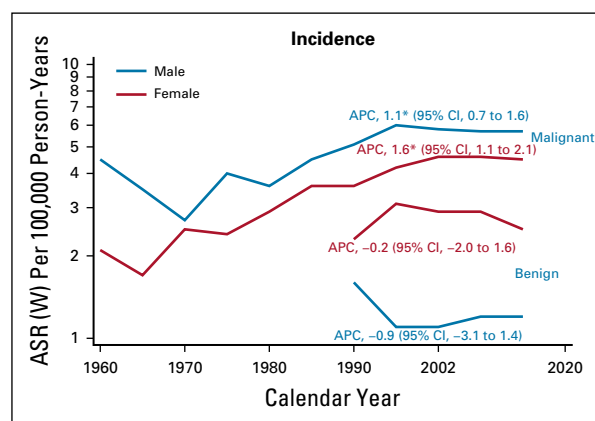


FIG 1. Trends in incidence rates of primary brain and other CNS tumors presented by sex and behavior, 1962-2016. Data are from the Population-Based Cali Cancer Registry, Cali, Colombia. APC, annual percentage change; ASR, age-standardized rate per 100,000 person-years (world population [W]). The 10% of tumors with borderline behavior was excluded. (*) APC statistically different from zero ($P < .05$).

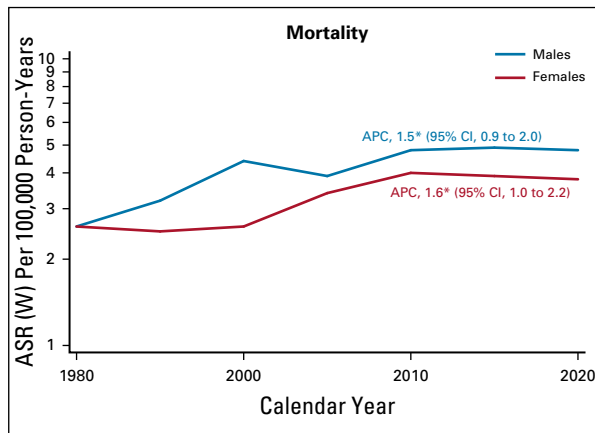


FIG 2. Trends in mortality rates of primary brain and other CNS tumors presented by sex, 1985–2019. Data are from the Population-Based Cali Cancer Registry, Cali, Colombia. APC, annual percentage change; ASR, age-standardized rate per 100,000 person-years (world population [W]). (*) APC statistically different from zero ($P < .05$).

a measurable change in incidence rates on the timescale of decades.²⁴ Known risk factors, such as ionizing radiation, are uncommon and explain only a small percentage of incidences of intracranial malignancies.²³ It is difficult to disentangle the specific environmental causes that could lead to the increased incidence observed in this study; however, during the time the data were collected, no dramatic changes were observed in Cali that suggest a single factor is causally associated with the rates described above.^{21,24} One intriguing possibility is that pesticide exposure during agriculture activities might be related to an increase in CNS malignancies.²⁵ The agricultural sector has traditionally been of key importance to the Colombian economy and pesticides are intensively used within the country.²⁶ Although our description involved only the urban population, additional research is necessary to explore the effects of occupational exposure with regard to CNS cancers recorded in rural areas.

Furthermore, other factors can affect incidence rates over time, such as demographic shifts, changes in pathology classification (histologic interpretation of specific CNS lesion, development of molecular markers, etc), and coding completeness of cancer registries, that are not related to real changes in the incidence of CNS cancers.²⁷ For instance, tumors of benign behavior were recorded in the PCCR until the early 1990s, which explains the burden of CNS tumors noted for females from this particular period.

Although mortality across all malignant brain and other CNS tumors had a statistically significant increase over the study period, it showed a steady improvement for the last decade. In a Colombian nationwide study, a statistically significant increasing trend in CNS mortality was also observed (APC, 3.0; 95% CI, 2.7 to 3.4 in males; and APC, 3.4; 95% CI, 3.0 to 3.8 in females) during 1984 to 2008.²⁸ This pattern is

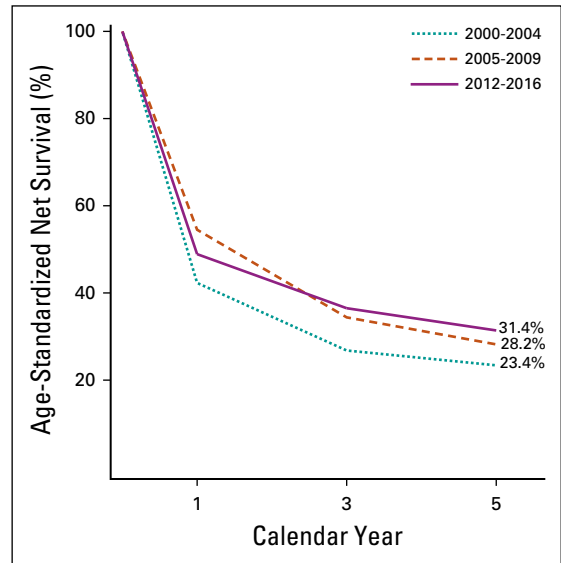


FIG 3. Age-standardized 5-year net survival in adults (age 15 to 99 years) diagnosed with malignant brain tumors during 2000 to 2016, by calendar period of diagnosis. Data are from the Population-Based Cali Cancer Registry, Cali, Colombia.

similar to the one observed in our study during the same period of time.

For patients who were diagnosed during 2012 to 2016, 5-year survival was 31.4%, which is the highest rate reported historically for Cali, Colombia. Countries with survival rates ranging between 30% and 40% during 2010 to 2014 were the United States, Canada, Nordic countries, and Germany, according to the CONCORD-3 study.¹⁹ This finding was also consistent with the Central Brain Tumor Registry of the United States, which informed a 5-year survival of 35.8% between 2012 and 2016.²⁹ Of note, survival increased by 8% from 2000 to 2016 in Cali, Colombia. Improvement in socioeconomic development has been associated with decreasing mortality ratios.³⁰

Our findings also reveal gender disparities. The mortality rate of malignant CNS tumors was higher among males. Conversely, incidence of benign tumors was more frequently reported in females. Our local trends are consistent with worldwide tendencies.^{7,31} Differences in genetic features and hormonal profiles have been suggested as causative factors. Moreover, a higher occupational exposure to environmental factors—for example, pesticides—has been reported for males.³² Nevertheless, on the basis of the nature of our data, we cannot make any assumptions.

In terms of tumor morphology, a similar distribution of histologic subtypes was also consistent with previous studies, with astrocytic tumors being the most common.²¹ The unclassified neoplasms-NOS comprised a substantial proportion of all CNS tumors (approximately 30%), despite the fact that approximately 75% of all NOS tumors had a microscopic confirmation. The high percentage of

unspecified malignancies likely reflects the difficulty in making an accurate diagnosis in certain subtypes of brain tumors, a limitation that has been widely recognized in the neuropathology arena.^{7,33} Optimal diagnosis of CNS tumors entails surgery, with the exception of some unresectable cancers with distinctive radiographic findings and poor clinical outcomes independent of the grade, where biopsies are not recommended—for example, brainstem tumors and infiltrative astrocytomas.³⁴

Our study is not without limitations. First, some benign tumors were included in the PCCR from 1992; therefore, the difference in descriptive trends warrants a cautious interpretation. Second, our data do not provide demographic information, such as race/ethnicity, which is an important factor in the incidence of some cancers. One third of the Cali population self-identify as Black. Thus, we are not able to determine the role of environmental factors and their interplay with genetic makeup. Another limitation is the lack of diagnosis harmonization with the latest WHO classification (2016) guidance, which incorporates molecular markers. In addition, PCCR has information about the cause of death through death certificates, but in some cases it can be difficult to determine whether cancer is the basic cause of death. Nonetheless, our findings contribute to the understanding of geographic variations in morbidity, mortality, and survival over time.

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Provision of study materials or patients: Paola Collazos

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This epidemiologic description of primary brain and other CNS tumors, despite their rarity, provides an overview of their incidence and mortality burden in Cali, Colombia, over the last 60 years. Our findings demonstrate an increasing mortality trend for malignant CNS tumors, although with steady rates from the early 2010s and improvement of 5-year net survival for the last decade. Overall characteristics of primary CNS cancers described in our study were consistent with those of other studies worldwide.^{6,35,36} Nonetheless, comparison of data should be cautiously interpreted, considering differences in data collection methods and the quality of different cancer registries. Moreover, there is a mandatory reporting system established since 2014 by the Colombian government; however, this registry is in the consolidation process and correlations can bias the results.³⁷ Comparisons of the rates observed in this study with other registries in Colombia—Bucaramanga, Medellin, and Pasto—and other Latin American countries are limited by the lack of information published over a comparable period. We encourage improving unified diagnosis and report among pathologists from Colombia and the region. As a result, this study will provide a baseline for future comparison analysis with other cancer registries in the region for a better understanding of CNS cancers. Additional epidemiologic investigations are needed, particularly in light of the exposures and factors associated with increased risk of CNS cancers in the region.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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