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Descriptive epidemiology of craniopharyngiomas in the United States

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Abstract

Purpose Craniopharyngiomas are rare benign brain tumors originating from errors in differentiation during embryogenesis. Given current interest in treatments that target genetic and molecular signatures of specific craniopharyngioma subtypes, updated and comprehensive epidemiologic data of these subtypes are necessary to inform and direct resources.

Methods We utilized data from the Central Brain Tumor Registry of the United States (CBTRUS), which represents 100% of the US population. Incidence by demographics was calculated only for histologically-confirmed cases. Age-adjusted annual incidence was calculated and is reported per 100,000 persons. Annual percent change (APC) in incidence rates from 2004 to 2016 was calculated to assess trends.

Results From 2004 to 2016, 7441 craniopharyngiomas were diagnosed in the United States, representing approximately 620 new cases each year. The incidence for histologically-confirmed cases was 0.16 per 100,000 persons. The age distribution was bimodal, with one peak in 5- to 9-year-olds and another in 55- to 69-year-olds. Compared with adamantinomatous tumors, papillary craniopharyngiomas only represented 5.5% of the histologically diagnosed craniopharyngiomas in 0- to 29-year-olds, 30.6% in 30- to 59-year-olds, and 30.4% in 60 + year-olds. Incidence was highest amongst Blacks (0.22), followed by Whites (0.15), Asians or Pacific Islanders (0.14), and American Indians/Alaska Natives (0.10). No significant difference was discovered in incidence rates between males and females or Hispanic and non-Hispanic ethnicities.

Conclusions Craniopharyngiomas are rare tumors with a bimodal age distribution and an equal male-to-female incidence. Black patients had the highest incidence, and adamantinomatous craniopharyngiomas were significantly more common than papillary tumors in adolescent, adult, and elderly populations.

Keywords Craniopharyngiomas · Epidemiology · Adamantinomatous · Papillary · CBTRUS

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Introduction

Craniopharyngiomas are rare benign brain tumors that arise from remnants of the craniopharyngeal duct epithelium (i.e., Rathke's pouch) or odontogenic tissue and account for approximately 1.1% of all non-malignant primary brain tumors [1, 2]. They are histologically benign but can be locally aggressive within the sellar/suprasellar region, with a 5-year relative survival rate of 86.1% [2]. Management of these tumors is challenging and can be controversial; however, a recent systematic review has formulated evidence-based recommendations and addressed the more controversial points of the management that exist in current neurosurgical practice [3].

Of the two prior epidemiologic studies of craniopharyngiomas in the United States (US), one includes data prior to the enactment of the Benign Brain Tumor Cancer Registries Amendment Act in 2004 and the other includes data on only 26% of the US population [4, 5]. In 1992, the Cancer Registries Amendment Act mandated the collection of central cancer registry data and was expanded with the Benign Brain Tumor Cancer Registries Amendment Act in 2004, mandating the registration of all non-malignant brain tumors in the US. More recently, histologic subtype has become increasingly important for molecular targeting as there are ongoing studies on the use of BRAF-inhibitors in papillary craniopharyngiomas [6–8]. An updated and more comprehensive study measuring the incidence of the entire US population and detailed epidemiologic data on histologic subtypes is needed to provide precise epidemiological information on craniopharyngiomas and inform resource allocation.

The Central Brain Tumor Registry of the United States (CBTRUS) – which includes incidence data from 51 central cancer registries (47 Centers for Disease Control and Prevention's National Program of Cancer Registries [NPCR] and 4 National Cancer Institute's Surveillance Epidemiology and End Results Program [SEER]) – is the largest primary brain tumor registry in the US, encompassing 100% of the US population. In this study, we used the CBTRUS to present the most comprehensive epidemiologic study of craniopharyngioma in the current literature.

Methods

Data collection

In this study, we queried the CBTRUS for all craniopharyngiomas diagnosed between 2004 and 2016. The following International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) histology codes were used: craniopharyngioma, not otherwise specified (NOS) (9350/0, 9350/1); craniopharyngioma, adamantinomatous subtype (9351/0, 9351/1); and craniopharyngioma, papillary subtype (9352/0, 9352/1). There was no age at diagnosis exclusion in this study. Histologically-confirmed cases and radiographically-confirmed cases were analyzed separately. Examination of incidence by demographics was only conducted on histologically-confirmed cases. Patients with stated race of other, unspecified, or unknown were excluded from race-specific statistics. Counts and rates are not presented per CBTRUS policy when fewer than 16 cases were reported for the specific category, or where the inclusion of the count and rate would allow for back-calculation of suppressed values.

Statistical analysis

All incidences are reported per 100,000 persons per year. Age-adjusted incidence rates, adjusted to the 2000 US standard population, were calculated using Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.3.8. Annual percent change (APC) in incidence rates between 2004 and 2016 was calculated using Joinpoint Regression Program 4.8.0.1 (National Cancer Institute, Bethesda, MD, USA). All figures were generated using RStudio software (RStudio Team, Boston, MA). A 95% confidence interval (CI) is provided with each statistic.

Results

Overall incidence

Between 2004 and 2016, a total of 7441 craniopharyngiomas were diagnosed in the US, of which 6430 (86.4%) were histologically-confirmed and 1011 (13.6%) were radiographically diagnosed. Overall incidence rate of combined histologically and radiographically diagnosed craniopharyngiomas was 0.18 (95% CI: 0.180–0.188) per 100,000.

The age-adjusted incidence rate of histologically-confirmed craniopharyngiomas was 0.16 (95% CI: 0.15–0.16). The incidence decreased from 0.16 (95% CI: 0.15–0.18) in 2004 to 0.14 (95% CI: 0.13–0.15) in 2016, representing a non-significant APC of -0.73% (95% CI: -1.53% to 0.07%) during the study period (Fig. 1).

Compared to the histologically diagnosed cases, radiographically diagnosed cases only represented 8.8% of the total cases in 0- to 19-year-olds, 12.7% in 20- to 39-year-olds, 12.7% in 40- to 59-year-olds, 18.5% in 60- to 79-year-olds, and 50.9% in 80 + year-olds (Fig. 2).

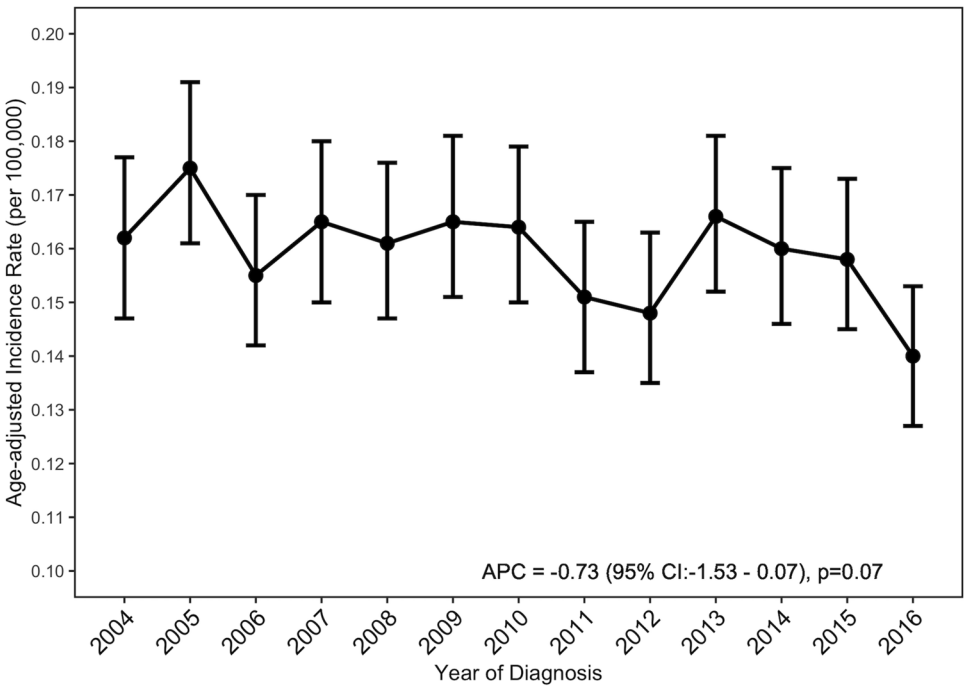

Fig. 1 Age-adjusted incidence of microscopically-confirmed craniopharyngiomas over the study period. *APC* annual percent change (expressed as percent with 95% confidence interval), CBTRUS 2004–2016

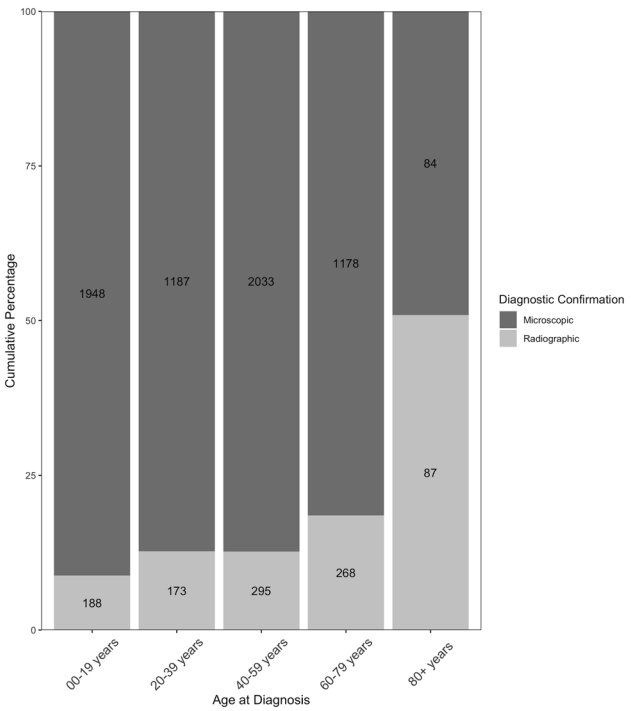

Fig. 2 Percentage of microscopically diagnosed cases vs radiographically diagnosed cases of craniopharyngiomas by age, CBTRUS 2004–2016

Incidence by demographics for histologically-confirmed cases

Table 1 shows demographic and histological characteristics of all histologically-confirmed craniopharyngiomas diagnosed between 2004 and 2016. For craniopharyngiomas, a bimodal age distribution was observed, with a peak incidence first seen in children at 5 to 9 years (0.27; 95% CI: 0.25–0.29) and second in adults at 55 to 69 years (0.21; 95% CI: 0.19–0.23). Incidence reached a nadir at 80 years and older (0.06; 95% CI: 0.05–0.07) (Fig. 3a). There were 2,901 cases in which the subtype of craniopharyngiomas was specified, 605 were papillary and 2,296 were adamantinomatous craniopharyngiomas. Compared with adamantinomatous tumors, papillary craniopharyngiomas only represented 5.5% of the histologically diagnosed craniopharyngiomas in 0–29-year-olds, 30.6% in 30–59-year-olds, and 30.4% in 60 + year-olds.

Overall, there was no significant difference in incidence between male and females (male-to-female incidence rate ratio [IRR]: 0.96; 95% CI: 0.91–1.01) even when stratifying by age (Fig. 3b). The incidence rate was highest in Blacks (0.22; 95% CI: 0.21–0.23), followed by Whites (0.15; 95% CI: 0.14–0.15), Asian or Pacific Islanders (0.14; 95% CI: 0.12–0.16), and American Indian/Alaska Natives (0.1; 95% CI: 0.07–0.14). Incidence was not significantly different between Spanish-Hispanic-Latino and Non-Spanish-Hispanic-Latino ethnicity (0.15 vs 0.16; p = 0.16) (Fig. 4).

Table 1 Age-adjusted incidence rate (per 100,000 population) of craniopharyngiomas by demographic and histological variables, CBTRUS 2004–2016

	Count (%)	Rate (95% CI)[a]
Total	6430	0.16 (0.15—0.16)
Age at Diagnosis, Years		
0–9	1038 (16.1%)	0.20 (0.19–0.21)
10–19	910 (14.2%)	0.17 (0.16–0.18)
20–29	548 (8.5%)	0.10 (0.09–0.11)
30–39	639 (9.9%)	0.12 (0.11–0.13)
40–49	952 (14.8%)	0.17 (0.16–0.18)
50–59	1081 (16.8%)	0.20 (0.19–0.21)
60–69	787 (12.3%)	0.21 (0.19–0.22)
70–79	391 (6.1%)	0.17 (0.16–0.19)
80 +	84 (1.3%)	0.06 (0.05–0.07)
Sex		
Male	3234 (50.3%)	0.16 (0.16–0.17)
Female	3196 (49.7%)	0.16 (0.15–0.16)
Ethnicity		
Non-Spanish-Hispanic-Latino	5441 (84.6%)	0.16 (0.16–0.16)
Spanish-Hispanic-Latino	989 (15.4%)	0.15 (0.14–0.16)
Race[b]		
White	4795 (74.6%)	0.15 (0.14–0.15)
Black	1184 (18.4%)	0.22 (0.21–0.23)
American Indian/Alaska Native	48 (0.7%)	0.10 (0.07–0.14)
Asian or Pacific Islander	309 (4.8%)	0.14 (0.12–0.16)

[a]Incidence rates are age-adjusted to the 2000 US standard population

[b]Patients with a stated race of other, unspecified, or unknown were excluded from race-specific analyses

Discussion

In this study, we report the overall incidence and incidence by demographics for craniopharyngiomas diagnosed in the entire US population. We found that the overall age-adjusted incidence rate in the US between 2004 and 2016 was 0.16 cases per 100,000 person-years. Our results are consistent with a study by Zacharia et al., which reported an overall incidence rate of 0.17 cases per 100,000 person-years, but show a slightly higher rate than was reported by Bunin et al. – 0.13 cases per 100,000 person-years [4, 5]. Discrepancies in incidence rates between studies are likely due to differences in study period and data derived from less than the entire US population. Bunin et al. included patients before the Benign Brain Tumor Cancer Registries Amendment Act in 2004, likely underestimating the true incidence of craniopharyngiomas because collection of data on non-malignant brain tumors was not yet mandatory [4]. Zacharia et al. used data from SEER, representing approximately 26% of the US population [5].

Consistent with prior studies, we observed a bimodal age distribution in the incidence of craniopharyngiomas and a stable incidence rate was seen over the 12-year study period [4, 5]. Incidence was highest in children 5 to 9 years of age and in adults 55 to 69 years of age. Adamantinomatous tumors were significantly more common than papillary tumors in adolescent, adult, and elderly populations. Our study demonstrates robustly that even in patients over 60 years old, adamantinomatous tumors are still significantly more common than papillary subtypes. There was no significant difference in the incidence of craniopharyngiomas between males and females, which has been similarly

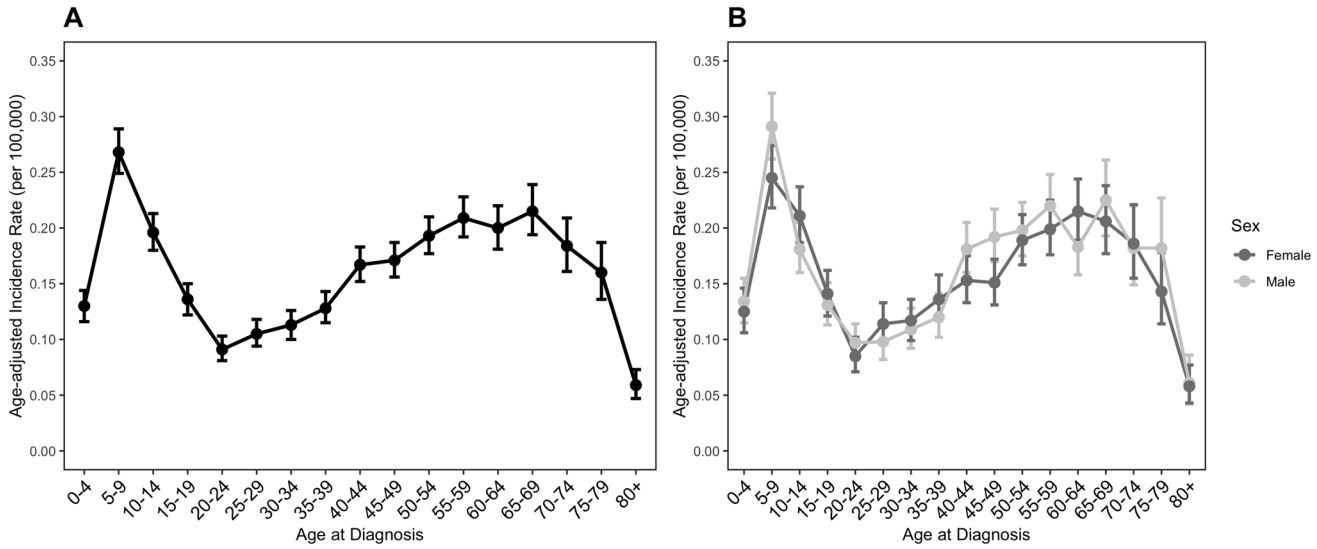

Fig. 3 Overall age-adjusted incidence of microscopically-confirmed craniopharyngiomas (**a**), and age-adjusted incidence stratified by age at diagnosis and sex (**b**), CBTRUS 2004–2016

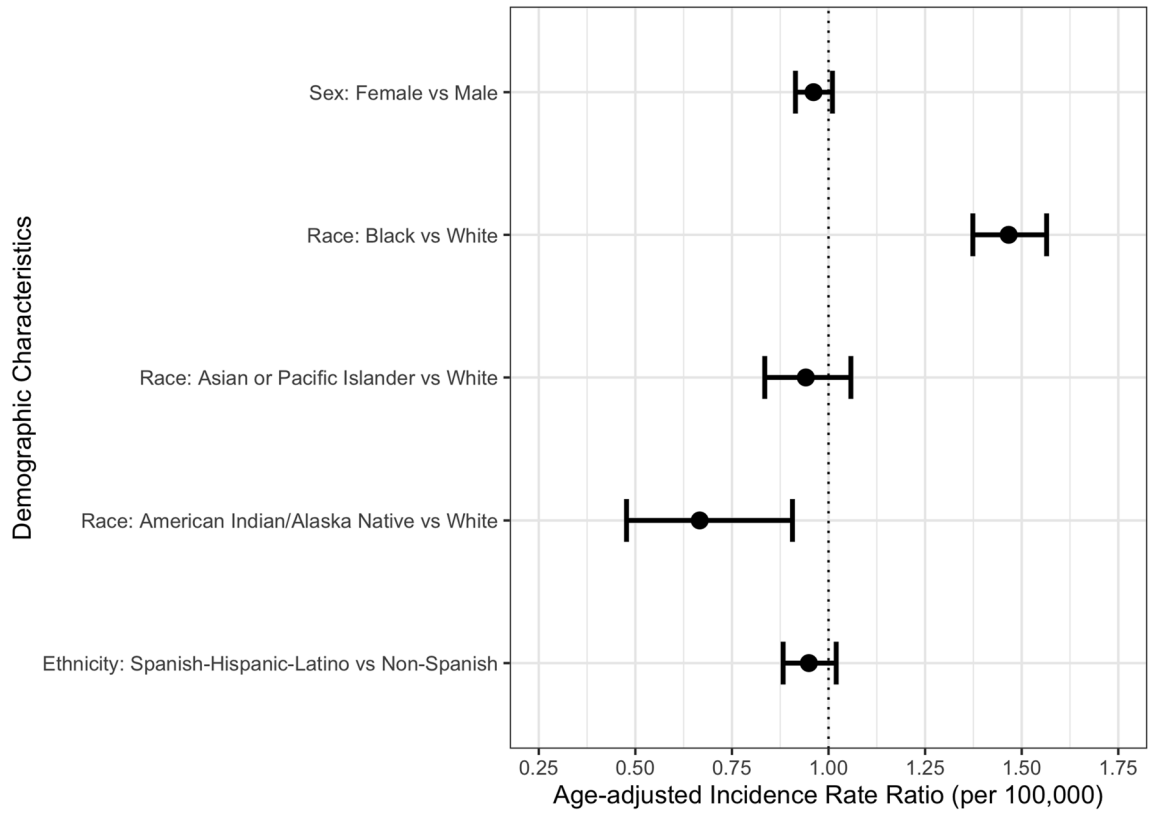

Fig. 4 Incidence rate ratios of craniopharyngiomas by sex, race, and ethnicity, CBTRUS 2004–2016

reported in previous population-based studies [4, 5, 9]. In this study, we found a higher incidence of craniopharyngiomas in Blacks compared with Whites. Bunin et al. found no significant difference in the overall incidence of craniopharyngiomas between Black and White individuals, but this was likely due to the small number of Black patients in their population-based study. In children, however, Bunin et al., did report a higher incidence of craniopharyngiomas in Black children compared with White children [4]. Zacharia et al. reported a similarly higher incidence of craniopharyngiomas in Black individuals compared with White individuals [5]. Our study is the first to report the incidence of craniopharyngiomas in Asian or Pacific Islanders, which is similar to that in Whites, and American Indian/Alaska Natives, which is significantly lower compared with Whites. Our study also showed no significant difference in incidence of craniopharyngiomas between Spanish-Hispanic-Latino and Non-Spanish-Hispanic-Latino ethnicity, which has not been previously reported.

The primary analyses in this study excluded radiographically diagnosed cases and only included cases with histological confirmation, in order to strengthen the reliability of recorded histology in this study and limit errors in cases diagnosed radiographically. Interestingly, when examining radiographically diagnosed cases, the greatest proportion were seen in the elderly population; which may suggest indolent tumor growth in this age group and a greater tendency to manage with observation.

Craniopharyngiomas are rare tumors, with single-center descriptive studies typically reporting fewer than 100 cases [10, 11]. In contrast, the data from this study represents the most accurate and complete estimate of the incidence of craniopharyngiomas in the US to date. Given the predilection for adamantimomatous subtype in all age groups, even in elderly patients, further efforts at molecular targeting of this specific subtype are necessary.

Limitations

Although this study represents the largest population-based study examining the incidence of craniopharyngiomas in the US to date, the results of this study should be interpreted in the context of its limitations. First, aggregating and analyzing data from multiple sites offers a large sample size and increases the study's generalizability; however, inaccuracies in data collection and lack of central pathology or imaging review of cases presents limitations associated with US cancer registry studies. Second, CBTRUS does not offer clinical information about treatment parameters or tumor recurrence. Therefore, inferential statistics on survival outcomes

cannot be performed, and only descriptive measures can be reported. Third, due to differences in genetic and environmental factors in other countries, these results may not be generalizable to countries outside the US. Lastly, race and ethnicity data provided to the CBTRUS database is reported from patients' medical records. If Hispanic ethnicity is not explicitly indicated in the medical record, then it is assessed using the North American Association of Central Cancer Registries (NAACCR) Hispanic/Latino identification algorithm. The algorithm uses a patient's name and place of birth to assess ethnicity. Therefore, inaccuracies in assigning race and ethnicity is a potential limitation in this study.

Conclusion

From 2004 to 2016, the age-adjusted incidence of histologically-confirmed craniopharyngiomas was 0.16 cases per 100,000 populations. Incidence was highest in children 5–9 years of age and in adults 55–69 years of age. Relative to papillary craniopharyngiomas, adamantinomatous craniopharyngiomas are significantly more common in all age groups. Black individuals had the highest overall incidence of craniopharyngiomas, followed by White, Asian or Pacific Islander, and American Indian/Alaska Native individuals. This study represents the most comprehensive population-based study of the incidence of craniopharyngiomas in the US.

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Compliance with ethical standards

Conflict of interest Pablo F. Recinos (consultant, Stryker); Varun R. Kshettry (consultant, Stryker, Integra).

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