The epidemiology of spinal schwannoma in the United States between 2006 and 2014

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OBJECTIVE Spinal schwannoma remains the third most common intradural spinal tumor following spinal meningioma and ependymoma. The available literature is generally limited to single-institution reports rather than epidemiological investigations. As of 1/1/2004, registration of all benign central nervous system tumors in the United States became mandatory after the Benign Brain Tumor Cancer Registries Amendment Act took action, which provided massive resources for United States population-based epidemiological studies. This article describes the epidemiology of spinal schwannoma in the United States from January 1, 2006, through December 31, 2014.

METHODS In this study, the authors utilized the Central Brain Tumor Registry of the United States, which corresponds to 100% of the American population. The Centers for Disease Control and Prevention's National Program of Cancer Registries and the National Cancer Institute's Surveillance Epidemiology and End Results program provide the resource for this data registry. The authors included diagnosis years 2006 to 2014. They used the codes per the *International Coding of Diseases for Oncology, 3rd Edition*: histology code 9560/0 and site codes C72.0 (spinal cord), C70.1 (spinal meninges), and C72.1 (cauda equina). Rates are per 100,000 persons and are age-adjusted to the 2000 United States standard population. The age-adjusted incidence rates and 95% confidence intervals are calculated by age, sex, race, and ethnicity.

RESULTS There were 6989 spinal schwannoma cases between the years 2006 and 2014. The yearly incidence eminently increased between 2010 and 2014. Total incidence rate was 0.24 (95% CI 0.23–0.24) per 100,000 persons. The peak adjusted incidence rate was seen in patients who ranged in age from 65 to 74 years. Spinal schwannomas were less common in females than they were in males (incidence rate ratio = 0.85; $p < 0.001$), and they were less common in blacks than they were in whites (IRR = 0.52; $p < 0.001$) and American Indians/Alaska Natives (IRR = 0.50; $p < 0.001$) compared to whites. There was no statistically significant difference in incidence rate between whites and Asian or Pacific Islanders (IRR = 0.92; $p = 0.16$).

CONCLUSIONS The authors' study results demonstrated a steady increase in the incidence of spinal schwannomas between 2010 and 2014. Male sex and the age range 65–74 years were associated with higher incidence rates of spinal schwannomas, whereas black and American Indian/Alaska Native races were associated with lower incidence rates. The present study represents the most thorough assessment of spinal schwannoma epidemiology in the American population.

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KEYWORDS spinal schwannoma; incidence; spinal tumor; NPCR; SEER; CBTRUS; oncology

ABBREVIATIONS APC = annual percentage change; CBTRUS = Central Brain Tumor Registry of the United States; CDC = Centers for Disease Control and Prevention; ICD-O-3 = *International Coding of Diseases for Oncology, 3rd Edition*; IR = incidence rate; IRR = IR ratio; NCI = National Cancer Institute; NPCR = National Program of Cancer Registries; SEER = Surveillance Epidemiology and End Results.

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P RIMARY spinal tumors are rare in nature. The most common intradural spinal tumor is spinal meningioma, followed by ependymoma and spinal schwannoma. Spinal schwannoma remains the second most common intradural extramedullary tumor following spinal meningioma.² There is a paucity of studies in the literature evaluating the population-based incidence of this tumor. A better understanding of the true incidence of spinal schwannomas, along with risk factors for an increased incidence, is needed to further our understanding of this disease process and to direct future research efforts.

Registration of all benign central nervous system tumors in the United States became mandatory in 2004 after the Benign Brain Tumor Cancer Registries Amendment Act took action. This act provided massive resources for United States population-based epidemiological studies. We utilized data from the Central Brain Tumor Registry of the United States (CBTRUS), which represents 100% of the American population. CBTRUS carries data from the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries (NPCR) and the National Cancer Institute's (NCI's) Surveillance Epidemiology and End Results (SEER).¹⁰ This article describes the epidemiology of spinal schwannoma in the United States from January 1, 2006, through December 31, 2014.

Methods

Data Source and Data Collection

The CBTRUS data are provided by the CDC/NPCR and NCI/SEER programs, which correspond to 100% of the American population.¹⁰ The University Hospitals Cleveland Medical Center's Institutional Review Board approved this study as an exempt study under the ongoing CBTRUS protocol. The CBTRUS database was queried for diagnosis years 2006 to 2014, *International Coding of Diseases for Oncology, 3rd Edition* (ICD-O-3),¹¹ histology code (9560/0) for nonmalignant spinal schwannoma, and for ICD-O-3 site codes C72.0 (spinal cord), C70.1 (spinal meninges), and C72.1 (cauda equina). Other location codes were not used in the query process due to the small case count. We included microscopically confirmed cases and cases that were radiologically confirmed but lacked histological confirmation. We excluded cases with positive exfoliative cytology and clinically diagnosed cases.

Data Analysis

The CBTRUS data analysis methods were demonstrated in our previous CBTRUS-sourced reports: "SEER*Stat Software 8.3.4 (National Cancer Institute) was used to calculate age-adjusted incidence rates. Rates are per 100,000 persons and are age-adjusted to the 2000 U.S. standard population (19 age groups – Census P25–1130). Age-adjusted incidence rates and confidence intervals were calculated by age, gender, race and ethnicity."^{7,12,13} SEER*Stat used methods described by Fay to calculate incidence rate ratios (IRRs) and p values.^{3,6}

As previously explained in the CBTRUS 2017 annual report, "Joinpoint 4.2.0.2 was used to estimate incidence time trends, and generate annual percentage change

(APC) and 95% confidence intervals. The models allowed for a maximum of 2 joinpoints (1 for non-malignant tumors), a minimum of 3 observations from a joinpoint to either end of the data, and a minimum of 3 observations between joinpoints. Annual percent change (APC) is the average percent change in incidence per year over the time period included in the trend segment."¹⁰ It is a linear regression model that was used to give a demonstration of the yearly incidence change over time and to generate the APC. The "joinpoint" is where the connected lines change directions, mirroring the change in incidence trend over the study years⁶ (Fig. 1).

Results

The complete count of spinal schwannoma cases in the United States was 6989 cases between 2006 and 2014. Of these cases, 93.3% were microscopically confirmed and 6.7% were radiologically confirmed without histological confirmation. The number of diagnosed cases per year ranged from 629 to 1090. We noted a statistically significant difference in the yearly incidence rising in 2010 (0.19% [95% CI 0.18%–0.21]) through 2014 (0.32 [95% CI 0.30%–0.34%]), with the APC being 13.01 ($p < 0.05$) (Fig. 1).

The overall annual incidence of spinal schwannoma was 0.24 (95% CI 0.23–0.24). The incidence rate (IR) was the highest among the 65- to 75-year age group (0.57 [95% CI 0.53–0.60]) and lowest in the 0- to 19-year age group (0.03 [95% CI 0.02–0.03]) (Table 1).

The IR was marginally lower in females compared to males (0.22 [95% CI 0.21–0.23] and 0.26 [95% CI 0.25–0.27], respectively) (Table 2). When comparing females to males, the IRR was 0.85 ($p < 0.001$) (Fig. 2A). When examining age distribution by sex, the peak adjusted IR was seen in females and males in the 65- to 75-year age group; (0.52 [95% CI 0.48–0.56] and 0.62 [0.57–0.67], respectively) (Fig. 3).

When comparing females to males across races, in white individuals the IRR was slightly lower in females than it was in males (0.86 [95% CI 0.81–0.90]; $p < 0.001$). There was no statistically significant difference between females and males across black, American Indian/Alaska Native, and Asian or Pacific Islander individuals (Table 3).

The incidence rate was lower in black (0.13 [95% CI 0.12–0.14]) and American Indian/Alaska Native (0.13 [95% CI 0.09–0.17]) individuals and higher in white (0.25 [95% CI 0.24–0.26]) and Asians or Pacific Islander (0.23 [95% CI 0.21–0.26]) individuals (Table 2). Compared to whites, the IRR was 0.92 ($p = 0.16$) for Asian/Pacific Islanders, 0.52 ($p < 0.001$) for blacks, and 0.50 ($p < 0.001$) for American Indians/Alaska Natives (Fig. 2B).

Discussion

Spinal schwannoma is a benign WHO grade I nerve sheath neoplasm that arises from Schwann cells. It comprises 29% of spinal nerve root tumors.⁵ It is usually sporadic and solitary, affecting all ages, but it can also occur in a more diffuse manner as a part of neurofibromatosis type 2 or schwannomatosis. Microscopically, it shows alternating patterns of compact elongated cells with palisad-

FIG. 1. Graph showing IRs per year for spinal schwannomas and the APC. Asterisk indicates that the APC is significantly different from zero at the alpha level of 0.05. Figure is available in color online only.

ing (Antoni A) and smaller loosely arranged round cells (Antoni B). Immunostaining is usually positive for S100 and type IV collagen.⁵ It can be asymptomatic due to the slow growth. Symptoms usually arise when the tumor grows enough to cause signs and symptoms of compression from myelopathy or radiculopathy. The decision to resect is usually made on seeing clinical and radiological findings, including any evidence of compressive symptoms and/or radiographic tumor progression.¹

The literature available on spinal schwannoma is very

sparse and restricted by the small number of cases and is generally limited to single-institutional studies.^{4,8,9} The largest existing epidemiological study on spinal malignant and nonmalignant pathologies was published in 2012 by Duong et al., who reported the distribution of various spinal cord tumors in the United States between 2004 and 2007 from the SEER database without focusing on spinal schwannoma.²

Spinal meningioma is more common than spinal schwannoma in the intradural extramedullary compartment and has an age-adjusted reported incidence of 0.33

TABLE 1. Age-adjusted IRs for spinal schwannoma per age group

Age Group, yrs	IR (95% CI)	Case Count*
0–19	0.03 (0.02–0.03)	190
20–34	0.15 (0.14–0.16)	834
35–44	0.29 (0.27–0.31)	1072
45–54	0.41 (0.39–0.43)	1618
55–64	0.48 (0.45–0.50)	1562
65–74	0.57 (0.53–0.60)	1142
75–84	0.42 (0.38–0.46)	491
≥85	0.16 (0.13–0.20)	80

* The total case count from 2006 through 2014.

TABLE 2. IRs and case counts for spinal schwannoma by sex and race

Demographic	IR (95% CI)	Case Count
Sex		
Female	0.22 (0.21–0.23)	3358
Male	0.26 (0.25–0.27)	3631
Race		
White	0.25 (0.24–0.26)	5994
Asian	0.23 (0.21–0.26)	351
Black	0.13 (0.12–0.14)	466
American Indian/Alaskan Native	0.13 (0.09–0.17)	41

FIG. 2. Graphs showing IRRs for sex and race. **A:** IRR for sex (female/male). *Single asterisk* indicates statistical significance ($p < 0.05$). *Double asterisk* indicates that values are relative to males. **B:** IRR for Asian or Pacific Islanders, American Indians/Alaska Natives, and blacks compared to whites. *Single asterisk* indicates statistical significance ($p < 0.05$). *Double asterisk* indicates that values are relative to whites. Figure is available in color online only.

(95% CI 0.32–0.3]) and higher female prevalence.⁷ Our study showed an age-adjusted IR of 0.24 (95% CI 0.23–0.24) for spinal schwannoma and a peak adjusted incidence rate in the 65- to 74-year age range. We noted a persistent increase in the annual incidence in 2010 through 2014 which could be partially attributed to enhanced reporting and the augmented integration of image-based diagnostics in the disease workup process over time. White race and specifically male sex in whites were associated with a higher incidence. Further work needs to be done to better understand this association and to determine if any genetic or environmental factors might increase susceptibility to this tumor.

Limitations

When dealing with national databases, several limitations might arise, including inaccurate coding and a small number of patients with lesions in some anatomical lo-

cations, which restricts the researchers ability to analyze such data.

We included both histologically and radiologically confirmed spinal schwannomas given the typical appearance of spinal schwannoma. Differentiating spinal schwannoma from other tumors (including meningioma) can be challenging due to some overlap in radiological features and clinical course. However, spinal schwannomas tend to affect the posterior and lateral aspects of the thoracic and lumbar spine segments and grow along a given nerve root, as opposed to spinal meningiomas, which tend to be distributed in the anterolateral aspects of the thoracic spine and show a diffuse enhancement with a dural tail.¹⁴ We excluded cases with positive exfoliative cytology and cases that were diagnosed clinically. We do not believe that this would affect the overall incidence given the very small number of these cases over the entire study period (19 cases and 16 cases, respectively). Since we also ex-

FIG. 3. Age-adjusted incidence distribution per 100,000 population for both male and female patients with spinal schwannomas. Figure is available in color online only.

cluded other means of diagnosis like death certificate only, the actual incidence may be slightly underestimated. The higher incidence in certain races could be attributed to true variation in incidence or could reflect differences in access to healthcare.

Conclusions

Spinal schwannoma is an understudied primary central nervous system histology and has a favorable prognosis. It is less common in females than males and has a higher incidence in the 65- to 74-year age group in both sexes. The incidence is lower in blacks and American Indians/Alaska Natives compared to whites. This represents the

most thorough assessment of the epidemiology of spinal schwannoma in the American population.

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TABLE 3. IRs and IRRs by sex for each race

Race	IR for Females (95% CI)	IR for Males (95% CI)	IRR (95% CI)
White	0.23 (0.22–0.24)	0.27 (0.26–0.28)	0.86 (0.81–0.90)*
Black	0.13 (0.11–0.14)	0.14 (0.12–0.16)	0.93 (0.77–1.13)
American Indian/Alaska Native	0.13 (0.08–0.20)	0.12 (0.07–0.20)	1.00 (0.52–2.13)
Asian or Pacific Islander	0.21 (0.18–0.25)	0.26 (0.22–0.30)	0.82 (0.66–1.03)

* Statistically significant ($p < 0.05$).

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Disclosures

Dr. Kshetty reports being a consultant for Integra.

Author Contributions

Conception and design: Kshetty, Tish. Acquisition of data: Tish, Habboub, Lang. Analysis and interpretation of data: Tish, Habboub, Lang. Drafting the article: Tish. Critically revising the article: Kshetty, Tish, Recinos. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kshetty. Statistical analysis: Tish. Administrative/technical/material support: Kshetty, Ostrom, Kruchko, Barnholtz-Sloan. Study supervision: Kshetty, Recinos.

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