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Prevalence of sporadic vestibular schwannoma: reconciling temporal bone, radiologic, and population-based studies

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Abstract

Objective: Reported epidemiologic data surrounding vestibular schwannoma (VS) are controversial. Temporal bone studies have suggested that VS affects up to 2.4% of the population, whereas magnetic resonance imaging (MRI) studies have reported VS to affect 0.017%. Moreover, existing population-based data seem to underestimate the prevalence of VS. For these reasons, the current study was conceived to determine the prevalence of VS in Olmsted County, Minnesota in an attempt to reconcile temporal bone, radiologic, and population-based reports regarding VS.

Patients: All persons living in Olmsted County, Minnesota on 1 Jan 2017 with a confirmed diagnosis of sporadic VS identified using the Rochester Epidemiology Project (REP) medical records-linkage system.

Main Outcome Measures: Prevalence of all VS and asymptomatic, incidentally diagnosed VS.

Results: Sixty-seven patients from a population of nearly 160,000 were living with VS on 1 Jan 2017, resulting in a point prevalence of 42.0 per 100,000 persons. The prevalence increased with age, reaching 212.4 per 100,000 in those ≥ 70 years. The prevalence of asymptomatic, incidentally diagnosed VS was 7.5 per 100,000 persons and 10.3 when restricted to those aged 20 years and older.

Conclusions: Using the unique infrastructure of the REP, the current study suggests that sporadic VS affects about 1 in every 500 persons aged 70 years and older, with the prevalence of incidentally diagnosed tumors closely paralleling past MRI studies. Though once considered an extremely rare tumor, it is evident that many more people develop VS than previous population-based studies estimated. This evolving patient demographic necessitates a change in perspective on VS, as now many people bearing a diagnosis of VS would have previously succumbed without the knowledge of their disease ever rising to the foreground. Indeed, these observations typify an

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emerging transition from an era of microsurgery and radiosurgery to the beginnings of an era of chronic disease management.

Keywords

vestibular schwannoma; acoustic neuroma; sporadic; incidence; prevalence; incidental; asymptomatic; epidemiology; Rochester Epidemiology Project

INTRODUCTION

Since the first temporal bone study published in 1936, research surrounding the epidemiology of vestibular schwannoma (VS) has generated controversy.¹ For instance, historical review of radiologic reports from 46,414 magnetic resonance imaging (MRI) scans detected 8 incidental cases of VS – a prevalence of 0.017% (17 cases per 100,000 persons).² However, temporal bone studies performed at autopsy have reported disease prevalence as high as 2.4% (2,400 cases per 100,000 persons).¹ In contrast to both of these study designs, population-based research has estimated the incidence of VS to be much lower. For instance, using the Surveillance, Epidemiology, and End Results (SEER) database, the incidence of VS from 2004 to 2010 in the United States was reported to be 1.09 per 100,000 person-years.³ Even when using Denmark's robust national database, the incidence of VS was 2.3 per 100,000 person-years in 2004 and 1.8 by 2008.^{4,5} Despite including all cases of VS and not exclusively a subset of incidentally diagnosed cases, these population-based incidence rates are an order of magnitude less than MRI data that include only incidentally diagnosed cases.

Germane to reconciling these various reports regarding VS epidemiology, it is first critical to understand the distinction between disease *incidence* and *prevalence* within the confines of epidemiologic research (Table 1). The incidence rate of a disease is defined as the rate of new, previously undiagnosed cases in a population (i.e., the *conversion rate* from a non-disease state to a disease state over a defined time period). By contrast, prevalence is the percentage of a population on a specific date who has ever been diagnosed with VS (i.e., currently living with VS in a *snapshot* of a fixed point in time). Temporal bone and MRI studies typically employ a methodology that is consistent with determining prevalence of VS. In the case of MRI studies, a collection of historical imaging reports are searched and prevalence is calculated as the number of persons with incidentally diagnosed VS divided by the number of total scans reviewed (the prevalence date is the date of the MRI, and varies from person to person). For temporal bone studies, specimens from autopsies are reviewed and prevalence is calculated as the number of specimens (persons) demonstrating VS divided by the number of persons reviewed (the prevalence date is the date of death, and varies from person to person).

In a disease such as VS, it is expected that disease prevalence would exceed the incidence rate. Particularly characteristic of the modern era, the natural history of VS results in many patients who never receive curative treatment of their tumor – for instance, nearly 60% of persons diagnosed with VS between 2006 and 2016 in Olmsted County, Minnesota were treated exclusively with observation and serial imaging for their tumor.⁶ Since most patients

die of other causes and many are never “cured” of their disease, incident cases accumulate over time resulting in increased disease prevalence and a trend towards increased prevalence at older ages.

Recently, using the unique resources provided by the Rochester Epidemiology Project (REP),⁷ the incidence of VS over the past decade in Olmsted County was found to be 4.2 per 100,000 person-years, with individuals aged 70 years and older exhibiting the highest incidence rate at 18.3.⁶ Almost a quarter of incident cases were diagnosed incidentally with asymptomatic VS in the last decade. Since these findings marked a notable divergence from previous population-based incidence estimates, we sought to investigate the modern prevalence of all sporadic VS and specifically asymptomatic, incidentally diagnosed sporadic VS using the REP in order to provide a complementing and more intuitive comparison between these population-based data and previous prevalence reports.

METHODS

Patient Data

The REP represents a collaboration between all healthcare providers in Olmsted County and the Mayo Clinic.⁷ All medical records from each healthcare visit for every resident within Olmsted County are available through the REP, and the available data are not confined to a single institutional database. Using the medical records-linkage infrastructure provided by the REP, a historical review was performed of the medical records of all residents of Olmsted County, Minnesota on 1 Jan 2017. Prevalent persons living with VS were identified using the methodology outlined in the incidence study by Marinelli, et al.⁶ Incident cases from the previous study were included in the prevalence estimates if the person still lived in Olmsted County on 1 Jan 2017. In addition, VS cases excluded from the incidence study (i.e., persons who moved into Olmsted County during the previous incidence period with a known diagnosis of VS) were now included. Patients who underwent a gross total resection before 1 Jan 2017 were considered to be “cured” of their disease and were not included in the numerator for prevalence calculations. Lastly, patients were considered to have asymptomatic, incidentally diagnosed tumors if they met the following criteria: (1) they underwent MRI for an indication(s) other than audiovestibular symptoms or suspicion of VS, and (2) review of all medical records available through the REP, both prior to and following the diagnostic MRI, disclosed no existing symptomatology that was attributable to their tumor.

Statistical Methods

Prevalence per 100,000 persons was calculated using prevalent cases of VS as the numerator and age- and sex-specific counts of the population of Olmsted County, Minnesota on 1 Jan 2017 as the denominator. The denominators were obtained from a complete enumeration of the Olmsted County population provided as part of the REP.⁸ Prevalence was reported separately in age- and sex-strata as non-standardized prevalence, and also after direct standardization by age and sex to the total US population from the 2000 US Census.

RESULTS

The total population of Olmsted County, Minnesota on the prevalence date 1 Jan 2017 was 159,689 persons (52.2% women). Among these persons, we identified 67 cases of sporadic VS resulting in a non-standardized prevalence of 42.0 per 100,000 persons and an age- and sex-standardized prevalence of 35.7 (Table 2). The prevalence of VS was higher in older persons, reaching 212.4 cases per 100,000 persons in those aged 70 years and older (Figure 1). Twelve of the 67 cases were asymptomatic and incidentally diagnosed resulting in a non-standardized prevalence of 7.5 per 100,000 persons and an age- and sex-standardized prevalence of 7.4. All 12 incidentally diagnosed cases were diagnosed on gadolinium-enhanced MRI scans for unrelated indications. The prevalence of asymptomatic and incidentally diagnosed cases of VS was distinctly higher among older persons, with those aged 70 years and older exhibiting the highest prevalence at 31.2 cases per 100,000 persons. Among adults aged 20 years and older, the prevalence of asymptomatic and incidentally diagnosed VS was 10.3 per 100,000 persons.

DISCUSSION

Given the varying reports among previous temporal bone, radiologic, and population-based studies, the current study was conceived with the chief objective of determining the modern prevalence of all sporadic VS and specifically asymptomatic, incidentally diagnosed sporadic VS using the unique resources of the REP medical records-linkage system. The prevalence of asymptomatic, incidentally diagnosed VS in the current study was only slightly lower than past MRI reports (0.0075% vs. 0.0108%, or 8 vs. 11 cases per 100,000 persons; Table 3).^{1,2,9-12} However, this difference should be expected for several reasons. First, by definition, MRI studies include persons who have all undergone head imaging. Although the percentage of the Olmsted County population who has undergone head imaging is unknown, it undoubtedly represents a subset of the population. In this way, it is reasonable to suspect that the prevalence in the current study would be less than that reported in MRI studies because MRI constitutes the primary diagnostic mechanism for VS. Similarly, since people are more likely to undergo head imaging as they age, the selected population comprising MRI studies are biased towards an older patient group who are known to more commonly present with incidental VS.⁶ In the current population-based study, the denominator for prevalence calculations includes persons of all ages, despite the fact that the sporadic development of VS before age 20 is exceedingly rare.⁶ Indeed, although Lin, et al. did not report the age range for the 46,414 patients comprising the denominator of their prevalence calculations, the average age of the 8 patients identified with VS was 58 years with the first case of VS identified in a person aged 20 years.² Considering this characteristic of their study, we reported prevalence calculations for asymptomatic, incidentally diagnosed VS in persons aged 20 years and older in Olmsted County, and the resulting prevalence closely approximated the study by Lin, et al. (0.0103% vs. 0.0108%, or 10 vs. 11 cases per 100,000 persons).

Another similarly interesting MRI study was performed by Anderson and colleagues.¹¹ They searched 24,246 dictated radiology reports from 1 Jan 1993 to 31 Dec 1997 and found 17 cases of unsuspected VS in MRIs performed for indications other than “to rule out VS,”

SNHL, tinnitus, or vertigo, resulting in a prevalence of 0.07% (70 cases per 100,000 persons).¹¹ However, when interpreting the current study in the context of their findings, it is critical to note that the current study reports *asymptomatic* incidentally diagnosed VS. In contrast, Anderson, et al. did not collect symptomatology data, and as highlighted in the study by Lin, et al., it is likely that their cases of unsuspected VS include symptomatic patients. Interestingly, Lin and colleagues found that the difference between their study and the study by Anderson, et al. could not be adequately attributed to just random variability (Fisher exact test $P=.002$).² They subsequently noted that Anderson, et al. did not specifically exclude MRIs of the internal auditory canals (IACs), highlighting that MRIs of the IACs are almost invariably obtained for audiovestibular symptomatology or suspicion of a VS. Because Lin, et al. excluded MRIs of the IACs, other authors have concluded that their study represents the best estimate of incidental VS to date,¹³ and their observations emphasize the limitations surrounding the methodology of retrospectively searching radiologic reports.

Yet, of all reports describing the prevalence of VS, temporal bone studies often report distinctly higher estimates of disease prevalence than past MRI investigations and the current population-based study. Shortly after Harvey Cushing described an “acoustic tumor” that histologically resembled the tumors found in von Recklinghausen’s disease (neurofibromatosis), Hardy and Crowe presented the findings of 250 serially sectioned temporal bones in 1936.¹ Using the first audiometers capable of producing pure tones developed by Western Electric in the 1920s,¹⁵ they described 6 cases of what they believed to represent asymptomatic VS with normal audiometric findings (prevalence of 2.4%, or 2,400 per 100,000 persons). They also reported that 5 of the 6 patients had advanced comorbidities immediately prior to death that complicated inpatient audiologic testing (e.g., syphilitic aortitis, tuberculosis, nosocomial pneumonia following resection of bilateral adrenal “neuroblastomas”). In addition, the authors noted that 2 of the 6 tumors appeared to develop from either the meninges or glial tissue. Notwithstanding, considering the limitations of light microscopy and postmortem tissue preservation at the time,¹⁶ Hardy and Crowe’s study marked a pivotal inflection point in the understanding of disease prevalence in VS.

Thirty-four years later, Leonard and Talbot reviewed 883 serially sectioned temporal bones from 490 different cadavers in The Johns Hopkins Hospital temporal bone collection.⁹ Included in their 490 cases were Hardy and Crowe’s original 250 temporal bones, and the authors noted that the temporal bones were largely an unselected hospital population, although they also remarked that many patients were from the neurosurgical service.⁹ Nevertheless, they found that only 3 of the original 6 cases reported by Hardy and Crowe represented true VS, and they presented the case of 1 additional patient, resulting in a prevalence estimation of 0.82% (820 cases per 100,000 persons). All 4 patients underwent otologic evaluation immediately prior to death as inpatients during or before 1932, and in 2 of the 4 instances, the authors noted that the clinical history was impaired by their medical condition. Despite this, even if both patients happened to disclose a significant audiovestibular history, the resulting prevalence would still exceed MRI estimations and even the oldest age group within the current population-based study by over one order of magnitude (0.41% vs. 0.031%, or 410 vs. 31 cases per 100,000 persons). In part, because

slice thicknesses can be performed on the order of micrometers (10^{-6} m vs. MRI slice thickness in millimeters, 10^{-3} m), it is likely that temporal bone studies uniquely capture the smallest of VSs, which was evidenced by 1 case described by Leonard and Talbot of a VS with a largest diameter of less than 1 mm.

Still, the most appropriate interpretation of the temporal bone data is difficult to ascertain. For instance, later autopsy studies with perhaps the most transparent method of temporal bone selection showed 0 VSs in 298 unselected temporal bones.¹² Moreover, the inherent bias of autopsies towards older patients with significant comorbidities combined with the vastly changed cultural practices, medical technology, and understanding of VS over the last 80 years, have led many authors to conclude that temporal bone studies greatly overestimate the true prevalence of asymptomatic, incidentally diagnosed VS.^{5,13}

Therefore, taking the current population-based study, past MRI reports, and previous temporal bone studies together, it is likely that the true prevalence of asymptomatic, incidentally diagnosed VS in the general population falls between the estimates of the current study / previous MRI reports and temporal bone data. Nonetheless, it is likely that the clinical prevalence of incidental tumors is between 5 to 20 cases per 100,000 persons, and the current study data obtained through the REP closely parallel the findings of the MRI study by Lin, et al. Further, among persons aged 70 and older, the prevalence of asymptomatic incidental VS exceeds 30 per 100,000 persons.

Unique to the capabilities of the current study, the prevalence of all sporadic VS, not only asymptomatic tumors, could be estimated. The prevalence of sporadic VS in the general population of Olmsted County was 42 per 100,000 persons, with a notable increase in those aged 70 years and older at 212 per 100,000 persons – or, over 1 per 500 persons. Similarly, among adults aged 20 years and older, a prevalence of 57 per 100,000 persons, or over 1 per 2,000 persons, was observed. To contextualize these results, these prevalence rates render sporadic VS on par with other diseases that have historically garnered far more national attention in the lay press. For instance, these data suggest that sporadic VS is slightly more common than multiple sclerosis and slightly less common than type 1 diabetes.^{17,18} Lastly, the notable correlation between the current findings surrounding asymptomatic VS and the study by Lin, et al. help substantiate the recently reported incidence rates of VS in Olmsted County, suggesting that VS affects over 4 new people per 100,000 person-years.⁶

In addition to the limitations mentioned above, several pertinent limitations to the methodology behind the current report have already been elucidated in the study by Marinelli, et al.⁶ Notwithstanding, it should additionally be noted that the prevalence of VS in Olmsted County may be elevated compared to national disease prevalence as a result of the increased life expectancy within Olmsted County. Specifically, Olmsted County's life expectancy exceeds national life expectancy by approximately 4 years. Recognizing that the highest incidence rate and prevalence of VS over the past decade in Olmsted County was in persons aged 70 years and older, this characteristic of Olmsted County warrants mention.

CONCLUSIONS

Using the unique infrastructure provided by the REP, the current population-based study shows that sporadic VS affects over 42 people per 100,000 with modern diagnostic imaging and screening protocols for asymmetrical sensorineural hearing loss. One in every 500 persons aged 70 years or older was living with VS on 1 Jan 2017 in Olmsted County, Minnesota. Asymptomatic, incidentally diagnosed VS were found to affect about 7 people per 100,000 – a prevalence that closely compares to past radiologic studies of MRI data. Though once considered an extremely rare tumor that presented with multiple cranial neuropathies and hydrocephalus, it is evident that many more people develop VS than previous population-based studies estimated, and this change in patient demographic is largely comprised by older individuals with small, often incidentally diagnosed tumors. This evolving patient demographic necessitates a change in perspective on VS, as now many people bearing a diagnosis of VS would have previously succumbed without the knowledge of their disease ever rising to the foreground. Indeed, these observations underscore an emerging transition from an era of microsurgery and radiosurgery to the beginnings of an era of chronic disease management.

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The currently submitted manuscript represents original research that has not been previously submitted and is not under consideration for publication elsewhere. The corresponding abstract was submitted for presentation at the 2019 North American Skull Base Society Meeting in Orlando, Florida. We performed this research with approval from the Mayo Clinic and Olmsted County Medical Center Institutional Review Boards (IRB 15-006036 and 050-OMC-15, respectively).

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Figure 1.
Prevalence of vestibular schwannoma (VS) in Olmsted County, Minnesota on January 1, 2017.

Key epidemiological definitions for interpreting disease incidence and prevalence in vestibular schwannoma (VS).

Table 1.

Incidence	<p>The incidence rate of a disease is defined as the rate of new, previously undiagnosed cases in a population</p> <p><i>Examples within the VS literature:</i></p> <ul style="list-style-type: none">● Incidence of VS using Denmark's national database, with reported rates of 1.8 per 100,000 person-years in 2008⁴● Incidence of VS using the SEER database from 2004-2010, with a reported rate of 1.1 per 100,000 person-years³● Incidence of VS in Olmsted County, MN using the REP, with a reported incidence rate over the most recent decade of 4.2 per 100,000 person-years⁶
Prevalence	<p>Prevalence is the percentage of a population on a specific date who has ever been diagnosed with VS</p> <p><i>Examples within the VS literature:</i></p> <ul style="list-style-type: none">● Temporal bone studies, which report prevalence of incidental VSs as high as 2,400 per 100,000 persons^{1,9,10,12}● Magnetic resonance imaging studies, which report prevalence of incidental VS to be 17 per 100,000 persons^{2,11}

Table 2:

Prevalence of vestibular schwannoma (VS) in Olmsted County, Minnesota on 1 Jan 2017

Age, years	Women			Men			Women and men		
	VS, N	Population	Prevalence [*]	VS, N	Population	Prevalence [*]	VS, N	Population	Prevalence [*]
All VS									
0-19	0	20,971	0	0	21,910	0	0	42,881	0
20-29	0	11,572	0	0	9,977	0	0	21,549	0
30-39	1	12,420	8.1	0	11,173	0	1	23,593	4.2
40-49	4	8,709	45.9	0	8,045	0	4	16,754	23.9
50-59	5	11,885	42.1	5	10,529	47.5	10	22,414	44.6
60-69	9	8,832	101.9	9	7,662	117.5	18	16,494	109.1
70	14	9,037	154.9	20	6,967	287.1	34	16,004	212.4
All ages	33	83,426	39.6 (34.2) [‡]	34	76,263	44.6 (39.7) [‡]	67	159,689	42.0 (35.7) [‡]
Ages 20 [§]	33	62,455	52.8 (48.0) [‡]	34	54,353	62.6 (55.6) [‡]	67	116,808	57.4 (50.0) [‡]
Asymptomatic, incidental VS									
0-19	0	20,971	0	0	21,910	0	0	42,881	0
20-29	0	11,572	0	0	9,977	0	0	21,549	0
30-39	0	12,420	0	0	11,173	0	0	23,593	0
40-49	3	8,709	34.4	0	8,045	0	3	16,754	17.9
50-59	0	11,885	0	1	10,529	9.5	1	22,414	4.5
60-69	2	8,832	22.6	1	7,662	13.1	3	16,494	18.2
70	4	9,037	44.3	1	6,967	14.4	5	16,004	31.2
All ages	9	83,426	10.8 (10.8) [‡]	3	76,263	3.9 (3.3) [‡]	12	159,689	7.5 (7.4) [‡]
Ages 20 [§]	9	62,455	14.4 (15.2) [‡]	3	54,353	5.5 (4.6) [‡]	12	116,808	10.3 (10.4) [‡]

^{*} Prevalence per 100,000 persons.[‡] Prevalence per 100,000 persons directly standardized by age to the 2000 US Census total population.[‡] Prevalence per 100,000 persons directly standardized by age and sex to the 2000 US Census total population.[§] Prevalence per 100,000 persons restricted to the population ages 20 years old for comparison with Lin, et al.²

Prevalence of incidentally diagnosed vestibular schwannoma among temporal bone, radiologic, and population-based studies

Table 3:

Study publication	Type of study	Persons		Incidental VS		Asymptomatic, incidental VS	
		Included, N	No. cases	No. cases	Prevalence (%)	No. cases	Prevalence (%)
Hardy & Crowe, 1936 ¹	Temporal bone	250	6	2.4	n/a [*]	n/a [*]	n/a [*]
Leonard & Talbot, 1970 ⁹	Temporal bone	490	4	0.82	n/a [*]	n/a [*]	n/a [*]
Stewart, et al., 1975 ¹⁰	Temporal bone	517	5	0.97	1	0.19	0.19
Karjalainen, et al., 1984 ¹²	Temporal bone	168	0	0	0	0	0
Anderson, et al., 2000 ^{11,†}	MRI	24,246	17	0.07	n/a [*]	n/a [*]	n/a [*]
Lin, et al., 2005 ^{2,‡}	MRI	46,414	8	0.017	5	0.0108	0.0108
Current study ^{*,§}	Population-based	159,689	12	0.0075	12	0.0075	0.0075

Abbreviations: MRI = magnetic resonance imaging; n/a = not applicable; N = population at-risk; No. = number; VS = vestibular schwannoma

*These studies either had incomplete data surrounding the presence of absence of attributable symptoms in reported cases of incidental VS (Hardy & Crowe and Leonard & Talbot) or did not collect patient symptomatology data during the study (Anderson, et al.).

[†]In Anderson, et al., the youngest patient with incidental VS was diagnosed at an age of 26 years, and in Lin, et al., the youngest patient was 20 years.

[‡]When restricted to those age 20 years, similar to MRI studies, the prevalence of asymptomatic, incidental VS is 0.0103%.

**When using the subset of the Olmsted County population who have undergone head MRI, the prevalence amongst adults age 20 years is 69.9 per 100,000 (or 0.0699%), therefore closely approximating the MRI study by Anderson, et al.