Neuroepidemiology

Vestibular Schwannoma, Tinnitus and Cellular Telephones

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Abstract
Cases with tinnitus after using analogue cellular telephones are presented. An increased odds ratio of 3.45, 95% confidence interval (CI) 1.77–6.76, was found for vestibular schwannoma (VS) associated with the use of analogue cell phones. During the time period 1960–1998, the age-standardized incidence of VS in Sweden significantly increased yearly by +2.53% (CI 1.71–3.35). A significant increase in the incidence of VS was only found for the latter of the two time periods 1960–1979 and 1980–1998. For all other brain tumors taken together, the incidence significantly increased yearly by +0.80% (CI 0.59–1.02) for the time period 1960–1998, although the increase was only significant for benign tumors other than VS during 1960–1979.

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Vestibular schwannoma (VS), or acoustic neurinoma, accounts for 8–10% of intracranial tumors [1, 2]. They constitute 90% of all tumors found in the cerebellopontine angle [3]. It is a benign tumor with the histopathology of neurinoma or neurilemmoma (C24 code = 541,

Snomed code = 95600) of the nerve sheet of the eighth cranial nerve. The vast majority of these histopathology types constitute VS and only a few with intracerebral localization have been reported [1]. The reported incidence of this tumor varies between 1 in 50,000 adults per year [4] and 1 in 81,000 adults per year [5].

The natural history of VS is one of slow growth, although a potential for growth spurts has been reported [6, 7]. The tumor manifests itself in imbalance and progressive hearing loss with tinnitus in the affected ear. The development of these symptoms tends to be slow. In a series from Cambridge, progressive hearing loss was the most common initial symptom reported by 59% of the patients [8]. Tinnitus was the principal presenting symptom in 11%, but was reported by 73% during the clinical course. Similar results were reported in a case series from Finland [9].

VS may present clinically in one of two forms: sporadic unilateral or hereditary bilateral [10]. An increasing incidence was reported from Denmark for the time period 1977–1995 [11]. This is at least partly explained by the introduction of computed tomography (CT) and magnetic resonance imaging (MRI).

We report here findings of both tinnitus and VS among cell phone users as well as the incidence of VS and other brain tumors during 1960–1998 based on the Swedish Cancer Registry.

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Materials and Methods

Details of these studies are presented elsewhere and only briefly in the following.

Symptoms Experienced in Connection with Cell Phone Use

A cross-sectional epidemiological study of symptoms among users of cell phones was performed in Norway and Sweden. The study included 12,000 cell phone users in Sweden and 5,000 in Norway. Symptoms were assessed by a questionnaire. More details of the study have been published elsewhere [12, 13]. In addition to the structured questionnaire, other symptoms were spontaneously reported, i.e., tinnitus in the Swedish part of the study. We also present some case reports outside the study.

Case-Control Study on Cell Phones and Brain Tumors

Our study encompassed 1,617 cases with brain tumor diagnosed during January 1, 1997 and June 30, 2000, who were reported to the Swedish Cancer Registry, living in the medical administrative areas of Stockholm, Uppsala/Örebro, Linköping and Gothenburg, Sweden. One control was extracted from the Swedish Population Registry for each case and was matched for sex, age and geographical area. Exposure was assessed by self-administered questionnaires, as described elsewhere [14]. For all cases, histopathology as well as anatomical tumor localization was assessed using CT and MRI scans. This paper only concerns vestibular neurinoma.

For the calculation of odds ratios (ORs) and 95% confidence intervals (CIs), conditional logistic regression analysis for matched studies was used (SAS Institute, Cary, N.C., USA). Only complete pairs (1:1) were used.

Incidence of VS

In Sweden, it is compulsory to report all brain tumors (both benign and malignant) to the Swedish Cancer Registry, which started in 1958 and is regarded to be reliable from 1960. VS is identified by using anatomical site (brain, ICD-7 code 193.0) and histopathology (neurinoma, neurilemmoma, C24 code 451, Snomed code 95600). The age-standardized incidence rates were calculated for each year from 1960 to 1998, expressed per 100,000 person-years. The background population was obtained from Statistical Yearbooks 1960–1967 and from Statistics Sweden 1968–1998. The incidence rates were standardized to the world population in 1970 [15]. Trends were analyzed using the exponential regression model to obtain the annual percent change in incidence.

Results

Symptoms Experienced in Connection with Cell Phone Use

Of 7,803 answering Swedish subjects, 76 (1%) reported spontaneously some kind of ear symptoms, such as hearing problems (n = 14), sensations of pricking, swelling or pressure around the ear (n = 27), pulsation (n = 3), tinnitus (n = 18), and pain in the ear (n = 14). These symptoms were not reported in more detail, since this was not the aim of the study.

Outside this study, we had been contacted by 3 men with tinnitus in the same ear as used during cell phone calls.

Case 1. A man born in 1941 who had used an analogue phone (450 MHz) during 1982–1992 and a digital phone since then. He estimated daily use up to 45 min on average for each phone types. He had always used his left ear. In the fall of 2000, he felt increasing tinnitus and pulsation in his left ear. Both clinical investigation and MRI failed to reveal anything abnormal. He experienced no impairment of his hearing.

Case 2. A man born in 1954 who had used an analogue phone (450 MHz) during 1986–1989, an analogue phone (900 MHz) during 1989–1998 and a digital phone since 1998 always with his left ear. The average daily use was 45 min for each phone type. During 1986–1989, he used his analogue phone in a car connected to an external antenna. In the year 2000, he experienced a swollen sensation around his left ear with pricking and first appearance of tinnitus. The tinnitus has increased since then and the symptoms also occur during daytime. Clinical examination has revealed no explanation, no tumor and no hearing loss.

Case 3. A man born in 1956 who had used an analogue cell phone since 1994 (450 MHz) for 45 min per day on average with his left ear. Tinnitus appeared in 1996 in his left ear and in 1997 also in his right ear. In 1999, sensations of his pulse 'in the head' appeared. The clinical examination did not show any anatomical defects that could explain his symptoms.

Additionally, we had also been contacted by 2 further persons with appearance of tinnitus in the ear used during cell phone calls.

Case-Control Study on Cell Phones and Brain Tumors

Of the 1,429 cases with brain tumor who answered the questionnaire, 159 (11.1%) had VS, a slight excess compared with other case series [1, 2]. Of all 1,617 cases with brain tumor fulfilling the inclusion criteria [14], 177 had VS, and 18 (10%) of these did not answer the questionnaire. The use of an analogue phone yielded an OR of 3.45 (CI 1.77–6.76), digital phone an OR of 1.21 (CI 0.66–2.22), and cordless phone an OR of 1.03 (CI 0.62–1.72) with a latency (tumor induction) period of >1 year (table 1). Using a latency period of >5 years, the risk further increased.

The median latency (presumed tumor induction) time among the cases for the use of an analogue phone was 8 years (range 2–17), for a digital phone 3 years (range 2–7) and for a cordless phone 4 years (range 2–11).
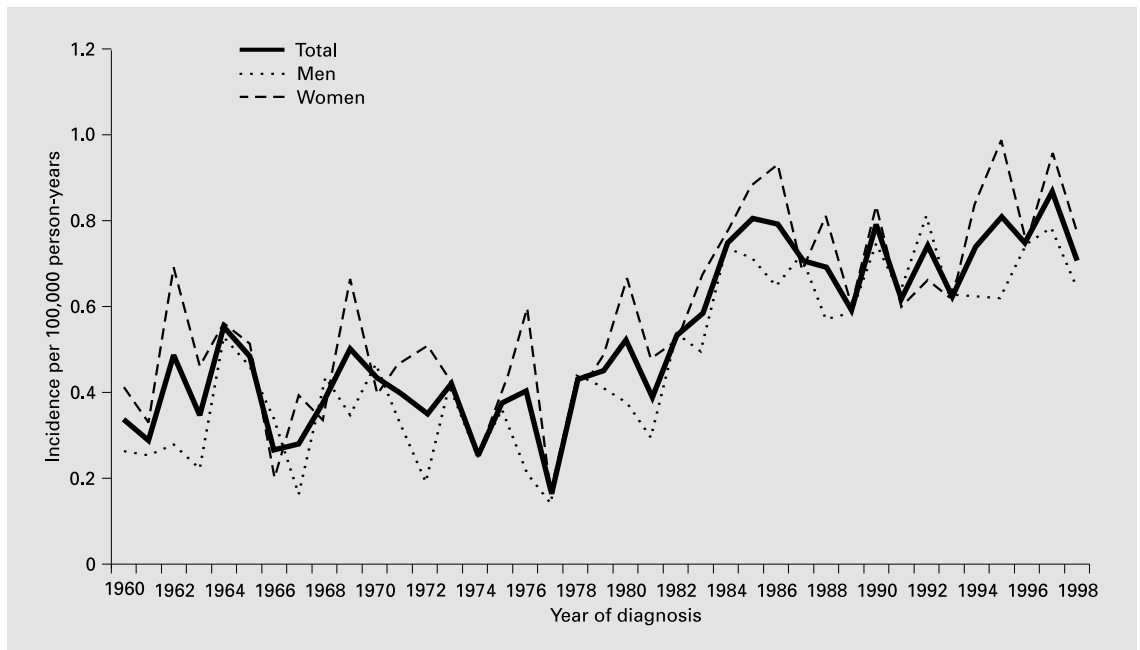
Fig. 1. Incidence of VS during 1960–1998 (total, men, women). Age adjusted to the world standard population.

Table 1. ORs and 95% CIs for VS and the use of analogue, digital or cordless phones

Latency period	Analogue		Digital		Cordless	
	Ca/Co	OR	Ca/Co	OR	Ca/Co	OR
>1 year	38/11	3.45 (1.77–6.76)	23/19	1.21 (0.66–2.22)	30/29	1.03 (0.62–1.72)
>5 years	26/7	3.71 (1.61–8.56)	2/1	2.00 (0.18–22.1)	11/6	1.83 (0.68–4.96)
>10 years	7/2	3.50 (0.73–16.8)	0/0	–	2/1	2.00 (0.18–22.1)

Ca = Cases; Co = control. Figures in parentheses are 95% CIs.

Incidence of VS

During the time period 1960–1998, there was a significant increase by +2.53% (CI 1.71–3.35) in the age-standardized yearly incidence of VS (table 2, fig. 1). The increase was highest among men and for both sexes, it was highest in the age group 50–59 years (fig. 2). The time period was divided into two groups (1960–1979 and 1980–1998), since there was a steep increase in incidence during the first part of the 1980s (fig. 1). For the time period 1960–1979 (n = 791), the age-standardized incidence changed yearly by –0.64% (CI –3.02 to 1.80), and for the time period 1980–1998 (n = 1441), it significantly increased yearly by +2.16% (CI 0.72–3.62; table 3).

For all other brain tumors excluding VS, the age-standardized incidence significantly increased yearly by +0.80% (CI 0.59–1.02; table 4, fig. 3). The increase was somewhat higher in women and highest in the age group 10–19 years. For the time period 1960–1979, malignant brain tumors increased yearly by +0.44% (CI –0.31 to 1.20) and for other benign brain tumors than VS by +2.38% (CI 1.80–2.97). For the period 1980–1998, the corresponding results for malignant tumors was –0.06 (CI –0.64 to 0.51) and for other benign tumors than VS –0.01 (CI –0.79 to 0.78; table 3).

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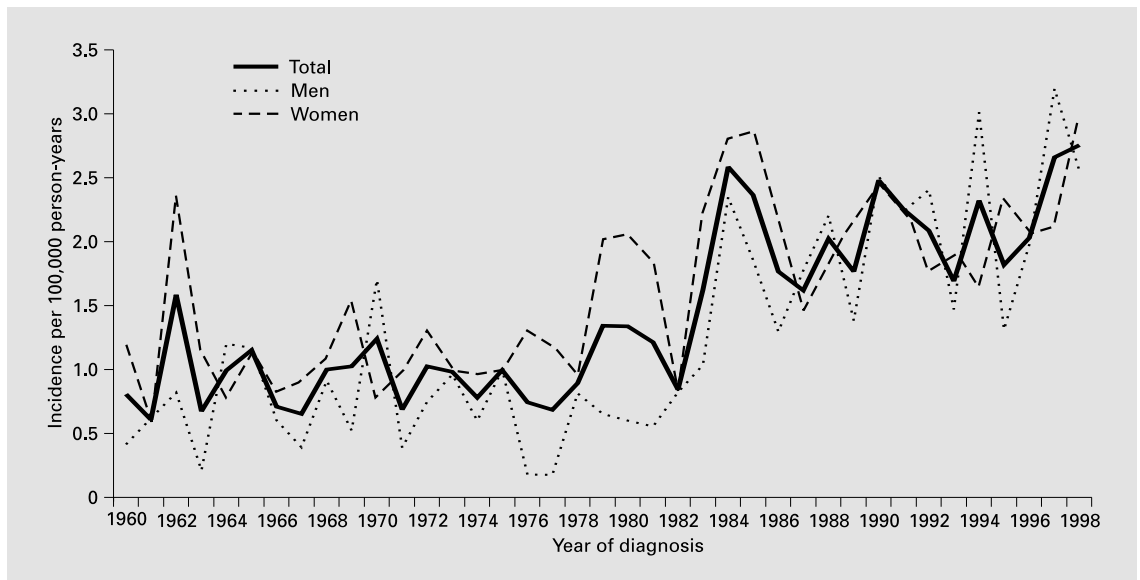Carlberg/Hallquist/Påhlson

Fig. 2. Incidence of VS during 1960–1998, in the age group 50–59 years (total, men, women). Age adjusted to the world standard population.

Table 2. Increase in the age-standardized yearly incidence of VS during the time period 1960–1998

Group	Increase, %	95% CI	Cases
All	+2.53	+1.71–3.35	2,232
Men	+3.05	+2.03–4.08	975
Women	+2.27	+1.33–3.21	1,257
0–9 years	*	*	8
10–19 years	*	*	30
20–29 years	*	*	133
30–39 years	*	*	250
40–49 years	+2.33	+1.09–3.59	407
50–59 years	+3.36	+2.51–4.20	552
60–69 years	+2.61	+1.53–3.70	545
70–79 years	+1.71	+0.35–3.08	259
80+ years	*	*	48

* = Not calculated due to low numbers.

Table 3. Changes of the age-standardized yearly incidence (%) with 95% CIs of VS, all other benign brain tumors and malignant brain tumors for different time periods

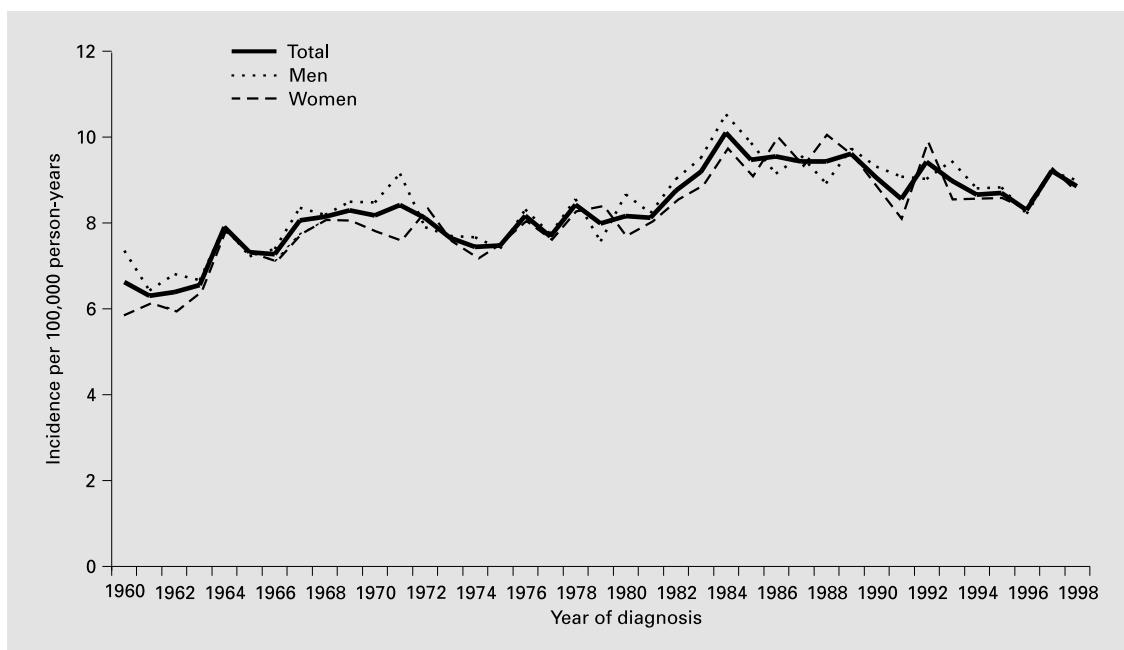|	1960–1998	1960–1979	1980–1998
Vestibular schwannoma	+2.53 (1.71–3.35)	−0.64 (−3.02 to 1.80)	+2.16 (0.72–3.62)
All other benign tumors	+1.60 (1.29–1.91)	+2.38 (1.80–2.97)	−0.01 (−0.79 to 0.78)
Malignant tumors	+0.41 (0.17–0.64)	+0.44 (−0.31 to 1.20)	−0.06 (−0.64 to 0.51)

Figures in parentheses are 95% CIs.

Fig. 3. Incidence of brain tumors excluding VS during 1960–1998 (total, men, women). Age adjusted to the world standard population.

Table 4. Increase in the age-standardized yearly incidence of all other brain tumors (excluding VS) during the time period 1960–1998

Group	Increase, %	95% CI	Cases
All	+0.80	+0.59–1.02	36,184
Men	+0.73	+0.50–0.96	17,418
Women	+0.90	+0.66–1.14	18,766
0–9 years	+1.43	+0.92–1.93	1,568
10–19 years	+1.72	+1.15–2.30	1,315
20–29 years	+1.32	+0.82–1.81	1,532
30–39 years	+0.52	+0.07–0.97	2,527
40–49 years	+0.40	+0.14–0.67	4,316
50–59 years	+0.24	–0.07 to 0.55	6,684
60–69 years	+1.01	+0.71–1.31	8,482
70–79 years	+1.46	+0.98–1.94	6,653
80+ years	–0.90	–1.98 to +0.19	3,107

Discussion

We report cases of unilateral tinnitus in some persons using a cell phone on the same (ipsilateral) side. Of course, a causal association cannot be established from a case report. However, of interest is that these persons were clinically examined including MRI without pathological findings of tumor, hearing loss (noise injury) or other diseases. In a series of 174 patients in whom unilateral tinnitus was investigated, only 0.6% (1 case) were due to VS [16]. If tinnitus is associated with cell phones, the mechanism is unclear. However, the inner part of the ear is located in an area with high exposure to microwaves. About 40–60% of radio frequency (RF) energy was calculated to be absorbed by the brain [17]. Auditory brain stem response to digital RF exposure was studied among healthy volunteers. A hearing deficiency was only found on the exposed side [18].

Furthermore, we report results on the risk for VS among cell phone users. A significantly increased risk was found for analogue phone users. However, in the calculations using different latency periods, digital and cordless phones also revealed an increased risk, although it was not significant and based on low numbers (table 1). It is noteworthy that the median latency period for the use of analogue phones was 8 years, but much shorter for digital and cordless phones.

An increasing incidence of brain tumors in the western world has previously been reported [19, 20]. The increase has been marked during the early 1980s, as also shown in our data. It has been much discussed if this increase represents a true increase or reflects better diagnostic tools such

as CT and MRI. The first CT was introduced in Sweden in 1974 and the first MRI in 1984. For that reason, we used the year 1980 as a cut-off time point when we studied the incidence during two time periods.

Our result showed a stable incidence of VS from 1960 until the early 1980s for both sexes. For the period 1980–1998, the age-standardized incidence increased yearly by 2.16%. As for other brain tumors, the increase was more marked during the first part of the 1980s, although the incidence also increased for the later time period. These data suggest that the increasing incidence is not only related to improved diagnosis, but does not exclude a true increase.

This increase may be compared with the results for all other brain tumors excluding VS. The results showed that the age-standardized incidence significantly increased yearly for the whole time period. However, for different periods, the incidence significantly increased only for benign brain tumors other than VS during the time period 1960–1979.

One explanation for the decreasing incidence of brain tumors during the recent years may be the decreasing frequency of autopsies in Sweden. The frequency of autopsy of patients with a diagnosis of brain tumor was 39.6% in the 1960s, 38.3% in the 1970s, 25.1% in the 1980s and 10.5% in the 1990s. Of the brain tumors, 13% were diagnosed during autopsy in 1984, 8% in 1994 and 5% in 1999 for men. The corresponding frequencies for females were 18, 7 and 4%, respectively [21]. Due to this large decline in autopsy diagnosis, it is doubtful whether a true decline in the incidence of brain tumors has occurred during the last two decades.

As to the association between VS and cellular and cordless phones, it is of interest to find that the highest increasing incidence was found for men and the age group 50–59 years. These results differ from the findings for other types of brain tumors. Since the highest prevalence of cell phone use is among younger men, the results regarding VS might be worth investigating in more detail. One important question is of course, how our results should be interpreted for a person using a cell phone with ipsilateral occurrence of tinnitus. Since tinnitus may be an early sign of VS, a full clinical examination of these patients is necessary including MRI. To be prudent, these persons should also reduce RF exposure from cellular telephones.

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