Acoustic Neuroma: Correlation Among Tumor Size, Symptoms, and Patient Age

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Due to improved diagnostic techniques, acoustic neuromas more frequently are detected at an early stage. Subsequent treatment depends on such factors as expected tumor growth rate, tumor size, and patient age. The natural history of acoustic neuromas is still uncertain:

This study was performed to examine possible correlations among tumor size, patient age, signs and symptoms, and duration of symptoms. The study included 164 patients with an acoustic neuroma who were treated at University Hospital Nijmegen, The Netherlands, over a period of 13 years. Comparisons were made between the findings of this study and the reports in the literature. No support was found for any of the correlations mentioned in other studies, and no relationships could be demonstrated between the parameters evaluated in this study. The authors therefore recommend that treatment policies be based only on well-established correlations.

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INTRODUCTION

Diagnostic procedures to detect an acoustic neuroma have become much more sensitive since the introduction of brainstem evoked response audiometry, computed tomographic (CT) scanning, and magnetic resonance imaging, (MRI) which has further improved sensitivity and specificity. These diagnostic procedures also are less difficult on patients than the previously used air cisternography. The newer diagnostic techniques have sometimes led to the unexpected diagnosis of an acoustic neuroma in patients with only slight symptoms. These visualization techniques have also made it possible for physicians to follow the growth of an acoustic neuroma before deciding whether surgical intervention is necessary. It has recently been established that fairly small differences in the size of an acoustic neuroma can influence the occurrence of surgical complications.[1]

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Since many acoustic neuromas now are followed using MRI, various questions have arisen about the natural history of these tumors. The most important questions concern the relationship between tumor growth rate, tumor size, and patient age. In addition, little is known about the distribution in individual growth rates. To answer these questions, it is necessary to perform descriptive studies that focus on possible correlations between tumor size, signs and symptoms, and patient age.

From 1980 through 1992, 164 patients underwent primary surgery for an acoustic neuroma at the University Hospital Nijmegen, The Netherlands. Using the diagnostic data recorded on these patients, the authors of this study examined correlations between tumor size, signs and symptoms, and patient age. Where possible, these findings were compared with those reported in a similar study that was performed in Copenhagen.[2]

MATERIALS AND METHODS

From 1980 through 1992, 258 operations for various types of space-occupying lesion in the cerebellopontine angle were conducted at the University Hospital Nijmegen. This study is based on the diagnostic data from the 164 patients who were operated on for an acoustic neuroma for the first time. In performing the surgeries, the suboccipital approach was used in 106 patients, the translabyrinthine, transotic, or combined approach was used in 56 patients, and the middle fossa approach was used in 2 patients. Excluded from the study were 36 patients who underwent a second surgery for an acoustic neuroma, 54 patients who were operated on for other histological diagnoses (N = 54), and 4 patients who were known to have central neurofibromatosis type I or II and a tumor in the cerebellopontine angle.

Tumor size was determined by a neuroradiologist. The maximum diameter of the total tumor was recorded, including the intrameatal part. There was a good agreement between these values and those found during surgery. Data on patient sex, patient age at surgery, signs and symptoms, and duration of symptoms were collected from the medical files. The results of pure-tone audiometry and speech audiometry were also collected. In this way, it was possible to examine various correlations using linear regression lines between tumor size, patient sex, patient age, separate symptoms, duration of symptoms, extent of hearing loss, and speech recog-

TABLE I.
Patient Age at the Time an Acoustic Neuroma was Diagnosed: Comparison Between the Copenhagen and Nijmegen Series.

Patient Age	Nijmegen	Copenhagen
<40 y	25%	24%
40–60 y	52%	45%
>60 y	23%	31%

nition. In the correlations, the number of patients (N), the correlation coefficient *(r)*, and the *P* value are reported.

Unexplained perceptive asymmetry in the pure-tone audiogram was the most frequent reason for further otoneurological investigation. The maximum differences in perception for the frequencies 0.5, 1.0, 2.0, and 4.0 kHz were determined for the patients with a unilateral acoustic neuroma in order to establish the extent of asymmetry for at least one frequency. This approach gave a practical indication of the degree of asymmetry in the hearing loss. Certain levels of asymmetry may give rise to the suspicion of an acoustic neuroma.

RESULTS

The study group included 88 women and 76 men, 17 to 79 years of age, with a mean age of 49.2 years. The majority of patients were between 40 and 60 years of age (Table I). In the literature, the mean age varied between 45 and 51 years, with a maximum range of 3 to 90 years.[2–4] The number of patients with an acoustic neuroma who were operated on for the first time at the University Hospital Nijmegen from 1980 through 1992 varied from 7 to 20 per year. The mean tumor size was 26.5 mm (SD ± 13.2 mm) with a range of 8 to 72 mm. As shown in Figure 1, the mean tumor size decreased gradually but significantly during the study period (N = 163, $r = .279$, $P = .00034$).

The relationship between tumor size and patient age at surgery is presented in a scatter diagram (Fig. 2). No significant correlation was found between tumor size and patient age (N = 164, $r = .0054$, $P = .49$), since large and small tumors occurred in both young and older patients. To compare the findings of this study with those of the Copenhagen study,[2] the tumors were classified into the same three groups according to size (*i.e.*, 1 to 25 mm, 26 to 40 mm, and greater than 40 mm). The number of patients in each group is shown in Table II. The majority of tumors were found to occur in patients between 40 and 60

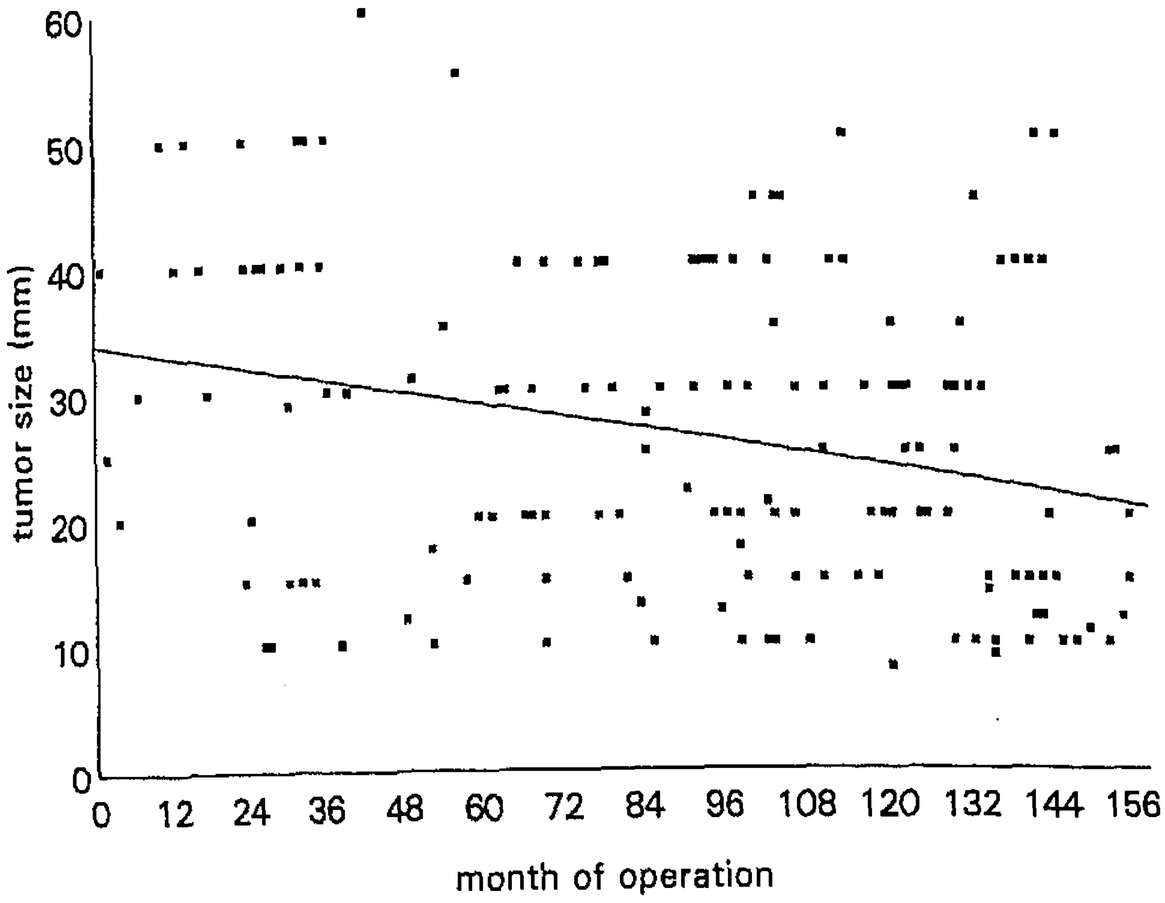

Fig. 1. Mean tumor size, in millimeters, of the acoustic neuromas operated on at University Hospital Nijmegen, The Netherlands, from January 1980 (month 1) through December 1992 (month 156). The study included 164 patients; one patient with a tumor measuring 72 mm is not shown in this figure. The regression line is $y = -0.084x + 34$.

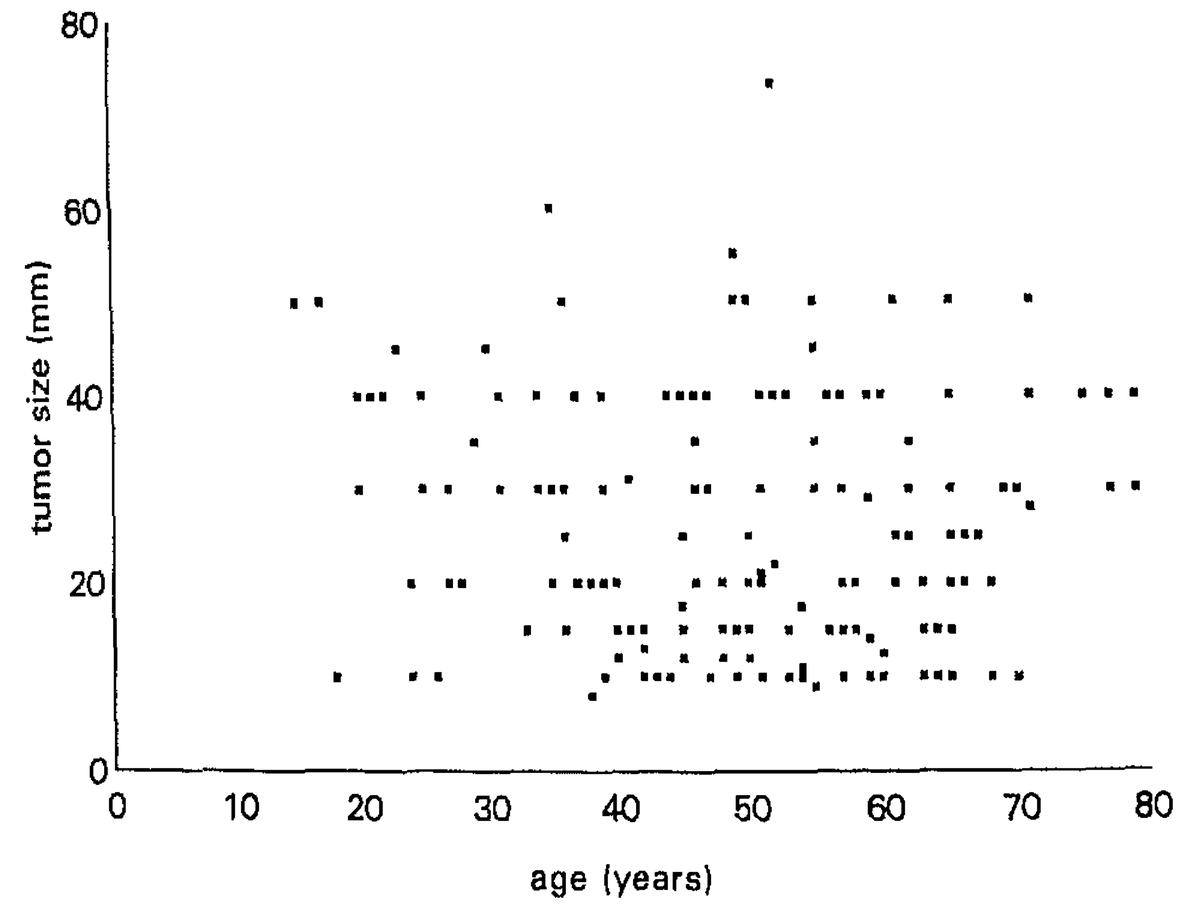

Fig. 2. Relationship between patient age at surgery and tumor size for the 164 patients in the Nijmegen series.

years of age. For each tumor size, the mean age and the male:female ratio were also determined (Table III). As tumor size increased, there was a nonsignificant decrease in mean age, from 50.1 to 45.5 years per year. A slightly higher proportion of women had a tu-

TABLE II.
Tumor Size and Patient Age: Comparison Between the Nijmegen and Copenhagen Series.

	Tumor Size							
	1–25 mm		26–40 mm		>40 mm		All Sizes	
Patient Age	Nijmegen (n = 87)	Copenhagen	Nijmegen (n = 60)	Copenhagen	Nijmegen (n= 17)	Copenhagen	Nijmegen (n = 164)	Copenhagen (n = 300)
<40 y	18.4% (16)	12%	33% (20)	26%	35.3% (6)	31%	25% (41)	24%
40–60y	57.5% (50)	49%	44% (26)	48%	47.1% (8)	38%	51.8% (85)	45%
>60 y	24.1% (21)	39%	23% (14)	26%	17.6% (3)	31%	14.0% (23)	31%

TABLE III.
Tumor Size, Patient Sex, and Patient Age in the Nijmegen Series (N = 164).

Tumor Size	Men (n = 76)	Women (n = 88)	Mean Patient Age*	SD†
1–25 mm	41	46	50.1 y	±11.8
26–40 mm	28	32	49.2 y	±16.3
>40 mm	7	10	45.5 y	±14.2

*Overall mean age for all patients was 49.2 years.
†Overall SD was ±14.2.

mor (male:female rate of 1:1.16).

Symptoms of an acoustic neuroma were divided into the presenting (main) symptom and all the symptoms in the history up to the time of surgery (Table IV). The results reported in several other studies were included for comparison.[2,5–7] The presenting symptom in the majority of cases was unilateral hearing loss. Less frequent presenting symptoms included tinnitus, vertigo, and facial paresthesia. Figure 3 shows an overview of the percentage of patients with various signs and symptoms per tumor size at the first otological consultation. Small tumors in particular were associated with hearing loss and tinnitus, while vertigo and otalgia were infrequent symptoms. Large tumors were associated with headaches, facial parasthesia, and ataxia, while eye symptoms and dysarthria were less frequent. These findings agreed with those reported in the literature.[11]

When all the signs and symptoms were analyzed together, their incidence changed and other symptoms gained more importance (Table V).[5,8–10] Various symptoms were not always mentioned, including otalgia, sudden deafness, epilepsy, ataxia, nausea and vomiting, and dysarthria. In some studies, vertigo was recorded as a symptom, while in others it was subclassified into, for example, true vertigo, unsteadiness, and dizziness. This made comparison of the incidence impossible. Tumor size and the duration of the first symptom up to the diagnosis are presented in a scatter diagram in Figure 4. The symptoms of small and large tumors were of both short and long duration. Therefore, there was no relationship at all between, for example, a long history of a symptom and

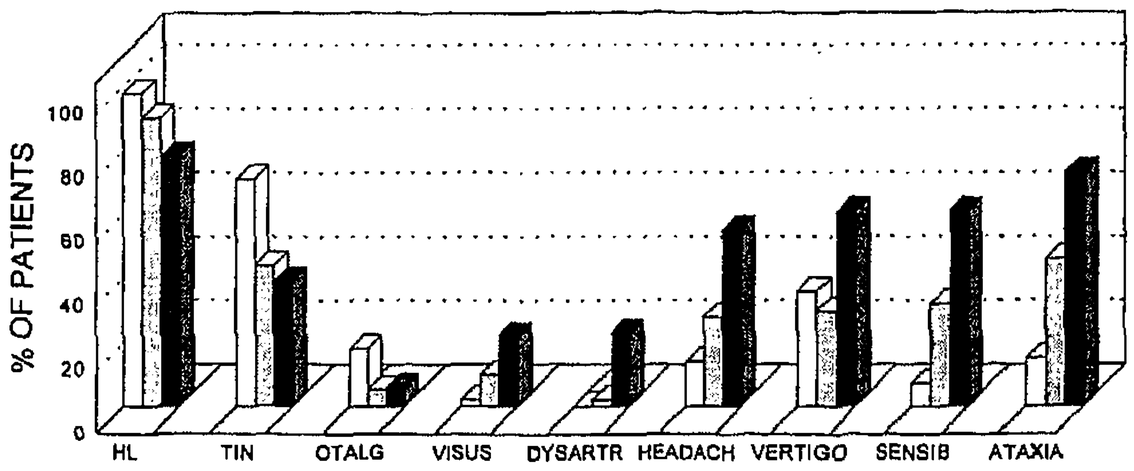

Fig. 3. Percentage of different symptoms of an acoustic neuroma related to tumor size in the 164 patients in the Nijmegen series. The three categories of tumor size are 1 to 25 mm (white bars), 26 to 40 mm (grey bars) and more than 40 mm (black bars). The abbreviations used are as follows: HL = hearing loss; TIN = tinnitus; VISUS = eye problems such as diplopia; DYSARTR = dysarthria; HEADACH = headaches; SENSIB = facial paresthesia.

a large tumor diameter.

Preoperative pure-tone audiometry results were available for 158 of the 164 patients. The remaining 6 patients had been considered neurosurgical emergencies. The mean hearing loss at the frequencies 0.5, 1.0, and 2.0 kHz (Fletcher index) is shown in Figure 5. There was no significant correlation between the level of hearing loss and the size of the tumor (N = 158, $r = .068$, $P = .40$). Small tumors could be associated with considerable hearing loss, and large tumors with slight hearing loss—all the combinations occurred frequently. When these data were analyzed per tumor size (Table VI), the majority of patients (51%) had a hearing loss of between 41 and 80 dB, irrespective of tumor size.

The difference in hearing thresholds between the affected ear and the normal ear was also assessed. The largest bone conducting difference was noted per frequency, between 0.5 and 4.0 kHz. As shown in Table VII, the mean asymmetry for one frequency was 57.7 dB (SD ± 23.1 dB). The patients in this study usually had asymmetrical hearing loss; in 95% of cases, there was at least a 20-dB difference for one of the frequencies between 0.5 and 4.0 kHz.

A speech audiogram was available for 122 of the 164 patients. Maximum speech recognition scores were determined (Table VIII). In Figure 6, speech

TABLE IV.
Main or Presenting Symptom of an Acoustic Neuroma in the Nijmegen Series and Other Studies.*

Main or Presenting Symptom	Nijmegen Series, 1994 (N = 164)	Selesnick, *et al.*,[5] 1993 (N = 126)	Thomsen and Tos,[2] 1990 (N = 300)	Ellis and Wright,[6] 1974 (N = 214)	Ojemann *et al.*,[7] 1972 (N = 46)
Hearing loss	73%	50%	75%	71%	73%
Tinnitus	13%	36%	7%	14%	2%
Vertigo/unsteadiness	7%	16%	8%	8%	11%
Facial paresthesia	1%	3%	3%	1%	2%
Headaches	0%	2%	—	12%	9%
Sudden deafness	3%	—	7%	—	—

*Certain symptoms were not mentioned in some studies.

TABLE V.
All Signs and Symptoms of an Acoustic Neuroma in the Nijmegen Series and Other Studies.*

Signs and Symptoms	Nijmegen Series, 1994 (N = 164)	Selesnick, *et al.*,[5] 1993 (N = 126)	Pfaltz, *et al.*,[8] 1991 (N = 93)	Wiegand and Fickel,[9] 1989 (N = 541)	Mathew, *et al.*,[10] 1978 (N = 206)
Hearing loss	93%	85%	83%	86%	97%
Tinnitus	57%	56%	70%	57%	66%
Vertigo/unsteadiness/ dizziness (combined)	29%	67%	50%	61%	69%
Otalgia/otic pressure sensation	12%	—	—	28%	—
Sudden deafness	3%	—	—	—	4%
Headaches	24%	19%	25%	36%	29%
Epilipsy	4%	—	—	—	—
Ataxia/tremor	33%	—	—	—	8%
Eye symptoms	7%	3%	—	22%	15%
Paresis of seventh cranial nerve	5%	10%	10%	—	22%
Facial paresthesia	22%	20%	20%	29%	33%
Nausea/vomiting	3%	—	—	—	11%
Dysarthria	3%	—	—	—	—

*Certain symptoms were not mentioned in some studies.

recognition values and tumor size are presented in a scatter diagram. In accordance with the pure-tone audiogram, tumor size did not significantly influence speech recognition (N = 122, $r = .134$, $P = .14$).

DISCUSSION

The fact that there was no clear relationship between tumor size, signs and symptoms, and the level of hearing loss means that even with optimal diagnostic facilities, it is difficult to ensure that all tumors are detected in an early, small stage. In reviewing the relationships between tumor size, level of hearing loss, and patient age, the authors of this study found it striking that the expected correlations did not exist. It would not have been surprising to find a relationship between tumor size and patient age or between tumor size and the level of hearing loss.

An acoustic neuroma can occur at almost any age, but most tumors are found in patients 40 to 60 years of age. In the present series, 75% of the patients were older than 40 years. In younger patients, the symptoms may be caused by central neurofibromatosis type II, which cannot always be recognized immediately. The average age of the patients at surgery was similar in all series.[2,5–10]

The size of the tumors operated on at the University Hospital Nijmegen decreased gradually over the time period of the study (Fig. 1). The significant gradual decrease in mean tumor size per year, from 34

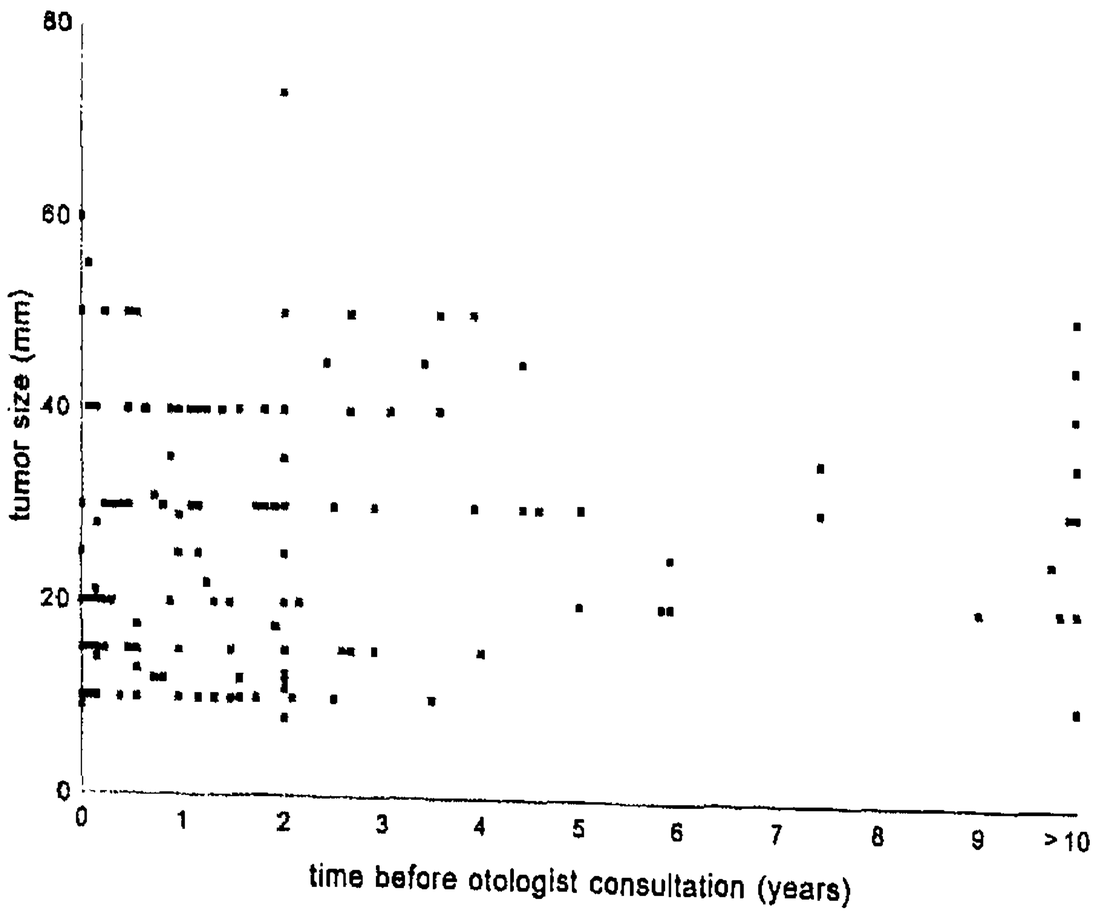

Fig. 4. Time interval between first symptoms and first consultation with otologist or neurosurgeon related to tumor size in the 164 patients in the Nijmegen series.

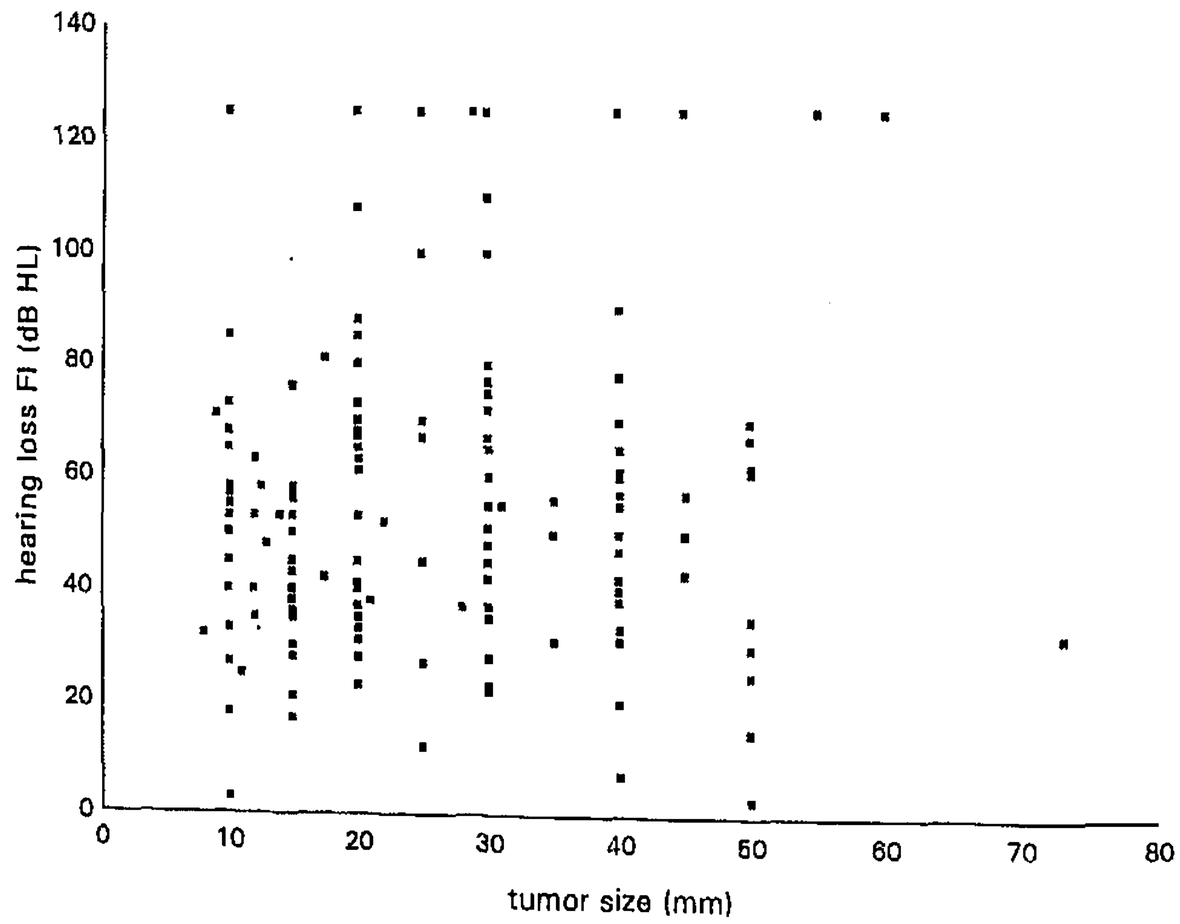

Fig. 5. Degree of sensorineural hearing loss (mean value at 0.5, 1.0, and 2.0 kHz) related to tumor size in 158 of the 164 patients in the Nijmegen series.

TABLE VI.
Tumor Size and Hearing Loss in the Pure-Tone Audiogram at 0.5, 1.0, and 2.0 Kilohertz (Fletcher Index): Comparison Between the Nijmegen and Copenhagen Series.

	Tumor Size							
	1–25 mm		26–40 mm		>40 mm		All Sizes	
Fletcher Index	Nijmegen (n = 87)	Copenhagen (n = 97)	Nijmegen (n = 60)*	Copenhagen (n = 85)	Nijmegen (n= 17)	Copenhagen (n = 118)	Nijmegen (n = 164)	Copenhagen (n = 300)
0–20 dB	7% (6)	5%	3% (2)	3%	18% (3)	1%	7% (11)	3%
21–40 dB	29% (25)	13%	22% (13)	21%	24% (4)	14%	26% (42)	16%
41–80 dB	53% (46)	59%	50% (30)	49%	40% (7)	43%	51% (83)	46%
>80 dB	11% (10)	23%	15% (9)	27%	18% (3)	51%	13% (22)	35%

*In the Nijmegen series, the results are unknown for 6 patients with a tumor size of 26 to 40 mm.

TABLE VII.
The Maximum Difference in Hearing Loss for at Least One of the Frequencies from 0.5 to 4.0 Kilohertz as Related to Tumor Size in the Nijmegen Series.

Tumor Size	Maximum Difference	SD
1–25 mm	57.7 dB	±22.5 dB
26–40 mm	57.1 dB	±20.9 dB
>40 mm	57.3 dB	±31.4 dB
Average	57.5 dB	±23.1 dB

TABLE VIII.
Phoneme Score Related to Tumor Size in the Nijmegen Series.

Maximum Speech Recognition	Tumor Size		
	<26 mm (n = 75)	26–40 mm (n = 31)	>40 mm (n = 7)
70–100%	37 (50%)	17 (55%)	9 (56%)
40–69%	25 (33%)	9 (29%)	5 (31%)
<40%	13 (17%)	5 (16%)	2 (13%)

mm to 22 mm, is probably due to earlier consultation with a physician, improved diagnostic techniques, and increased awareness of the doctors. In particular, MRI has facilitated the early detection of small tumors.

Other authors[4,5] also have noted gradually decreasing tumor size at presentation in recent years. However, the opposite was reported in the Copenhagen study,[2] which is representative of the whole of Denmark. The distribution of patients over the three age groups in the present study was very similar to that in the Copenhagen series. One striking difference was the number of patients with a tumor larger than 40 mm: 118 patients (33%) in the Copenhagen series versus 17 patients (10%) in the Nijmegen series. In view of the decrease in the number of large tumors found at various centers throughout the world, it may be appropriate to interpret the Copenhagen data cautiously, particularly with regard to the existence of correlations, because these correlations may be specific to the Danish patient population. External factors that influence the size of the tumors referred to a center may include, for example, the referral pattern in that particular region and the expertise of the surgeon.

An acoustic neuroma can occur at almost any age, and the tumor growth rate can vary greatly from individual to individual.[12] Little is known about the average growth rate and the distribution in the growth rates of acoustic tumors. Whether these tumors grow more slowly in older patients also is uncertain. If the growth rate remains fairly constant, larger tumors generally should be found in elderly patients. No large tumors were found in the elderly patients in the present study. Various growth rates appear to be possible

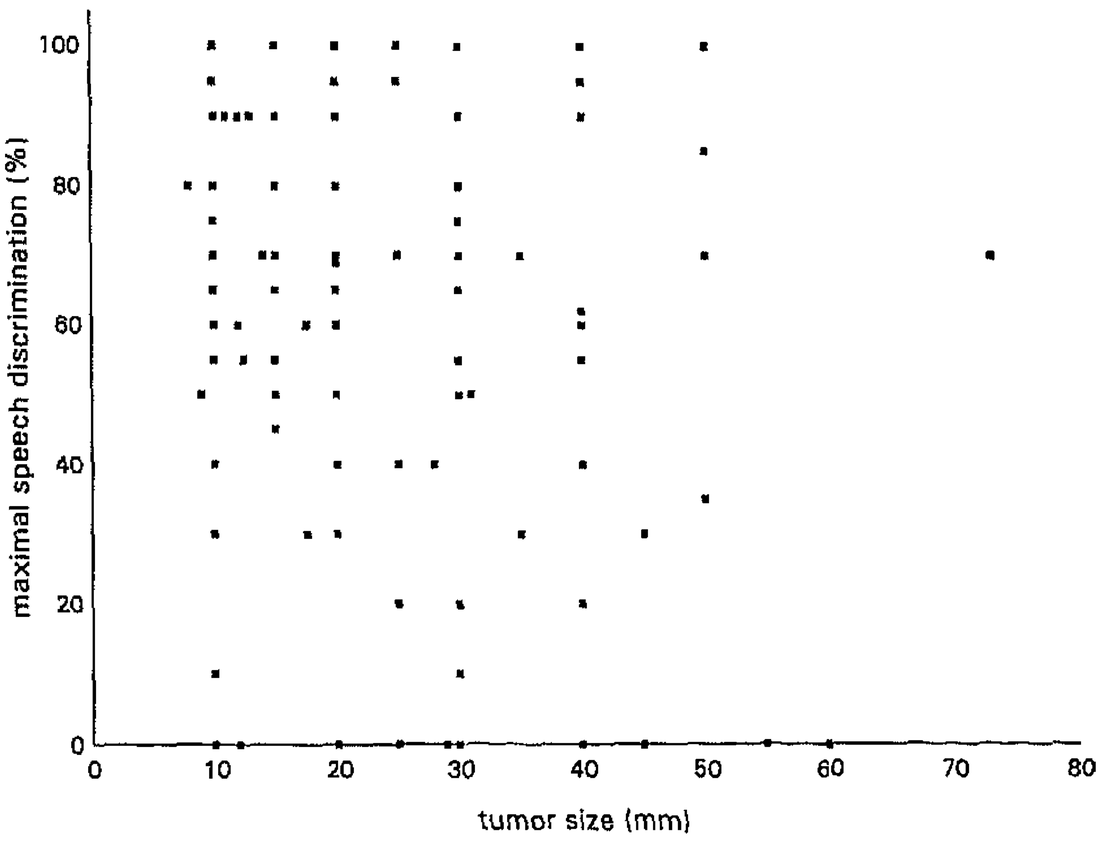

Fig. 6. Phoneme score related to tumor size in 122 of the 164 patients in the Nijmegen series.

at all ages, and it seems likely that varying growth rates can occur in a single patient. Table III shows that the average age of patients with a large tumor decreased gradually, although not nonsignificantly, against time. However, this study found no correlation between tumor size and patient age (Fig. 2).

It is possible that the growth rate varies, depending on whether the tumor has an isolated nongenetically determined etiology or an hereditary etiology, such as central neurofibromatosis type I or II. In light of recent genetic study results,[13] it has become reasonable to assume that a larger proportion of isolated cases of acoustic neuroma can be attributed to a chromosomal defect than would be expected on the basis of

clinical symptoms or family studies. Future genetic studies may provide information that will help predict the expected growth rate of an acoustic neuroma.

The symptoms of an acoustic neuroma vary, and in a retrospective review it is not always possible to distinguish clearly between the presenting symptom and all the other symptoms. The presenting symptom is usually unilateral deafness—but not in all cases. In addition, the percentage of patients with impaired hearing as their main symptom was found to decrease as tumor size increased (Fig. 3). Therefore, tumor size appeared to influence the average complaint pattern. Classifying the symptoms of an acoustic neuroma into an audiovestibular stage, a trigeminal stage, or a brainstem stage is too absolute.[11] It would be better to speak in terms of a gradual shift in symptoms (Fig. 3). In the present study, no correlation was found between tumor size and the duration of symptoms (Fig. 4). In fact, some of the patients with very short-term symptoms had large tumors, while some of the patients with long-term symptoms had tumors that were mainly restricted to the intrameatal site. In contrast, the Copenhagen study[2] reported a significant relationship between tumor size and symptom duration ($P < .05$).

Wiegand and Fickel[9] surveyed members of the American Acoustic Neuroma Association. Therefore, their study subjects were recruited using a procedure that was different from that employed in other studies (*i.e.*, subjects were members of a patient association as opposed to patients operated on by the authors of the study).

The incidence of hearing loss in the comparison studies (67% to 75%)[2,5–7] was very similar to that in the present series. The symptom distribution in the other studies was higher for tinnitus (2% to 36%) and vertigo (7% to 16%). Facial paresthesia was only observed in 1% to 3% of patients, while sudden deafness and headaches were not always mentioned. Some symptoms were mentioned infrequently in the literature. For instance, ataxia occurred in 33% of the patients in this series, but in only 8% of the patients in the study by Mathew, *et al.*[10] Symptoms such as sudden deafness occurred in only 3% to 4% of patients; however, in one study,[14] sudden deafness was listed as the presenting symptom for small tumors in 19% of patients. If each of the possible symptoms of an acoustic neuroma were considered an indication for MRI, these tumors could be diagnosed much earlier. However, it is questionable whether the cost-benefit ratio would remain acceptable in view of the number of negative diagnoses.

Unilateral hearing loss is the most frequent symptom of an acoustic neuroma, but no correlation was found between tumor size and the level of hearing loss. Deafness was found in patients with tumors of all sizes, but relatively good hearing could also be present on the affected side. Figure 5 shows that all combinations of tumor size and hearing loss are possible. The findings of this study disagreed with those in the Copenhagen study,[2] which reported a relationship between tumor size and hearing loss for large tumors ($P < .001$).

The authors of the present study did find asymmetry in the hearing loss of the pure-tone audiogram of at least 20 dB (average: 57.7 dB). Asymmetrical perceptive hearing loss without any other symptoms is a strong indication for further otoneurological tests to look for an acoustic neuroma, even though a small proportion of patients with such a tumor will have a normal pure-tone audiogram. These findings agree with those reported in a study performed in Seattle.[15] The authors of the Seattle study recommended that if the average threshold difference at 1 to 8 kHz was 20 dB or greater, MRI should be performed on the suspicion of an acoustic neuroma. Brainstem evoked response audiometry should suffice in patients with an average threshold difference of less than 20 dB.

CONCLUSION

Expected correlations among tumor size, symptoms, and patient age could not be demonstrated. Questions regarding tumor growth rate and the distribution in growth rates remain unanswered. It is not possible to say whether there is a relationship between the moment that a tumor starts to develop and the age of the patient; symptoms do not give any reliable indication. Since the authors of the present study could not demonstrate any of the correlations formerly assumed to exist, it would seem appropriate not to base the answers to any remaining questions about variation in tumor growth rate and the age of the patient on similar provisional assumptions. This would obviously have consequences on otoneurological diagnosis and would necessitate repeated cost-benefit analyses. Tumor growth rate is still unknown and therefore remains a problem in designing the treatment plan for a patient with an acoustic neuroma.

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