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The Course of Hearing Loss in Patients With a Progressive Vestibular Schwannoma

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Abstract

Objective. This study evaluates the natural course of hearing loss (HL) prior to treatment in patients with progressive tumors and an indication for active intervention. Evaluating this patient group specifically can put hearing outcomes after vestibular schwannoma therapy into an adequate context.

Study Design. Retrospective cohort study.

Setting. Tertiary referral center.

Methods. Inclusion criteria comprised unilateral vestibular schwannomas prior to active treatment, with ≥2 mm extracanalicular (EC) tumor growth and ≥2 audiograms. We performed a comprehensive assessment of hearing using multiple outcome parameters including (the annual decrease in) pure-tone averages (PTAs; an average of 0.5, 1, 2, and 3 kHz). Predictors for HL were evaluated (patient age, tumor size/progression, follow-up duration, baseline hearing).

Results. At presentation, 86% of patients suffered from sensorineural HL on the affected side (≥20 dB PTA) with a median of 39 dB (interquartile rate [IQR]: 27-51 dB). The median follow-up duration was 21 months (IQR: 13-34 months), after which 58% (187/322) of patients experienced progressive HL (≥10 dB), with a median increase of 6.4 dB/year. At the last follow-up, the median PTA was 56 dB (IQR: 37-73). Median speech discrimination scores deteriorated from 90% (IQR: 70%-100%) to 65% (IQR: 35%-100%). Tumor progression (maximal EC diameter) was significantly correlated to the progression of sensorineural HL, corrected for follow-up ($F(2,228) = 10.4$, $p < .001$, $R^2 = 8\%$).

Conclusion. The majority of patients (58%) with radiologically confirmed progressive vestibular schwannomas experience progressive sensorineural HL during observation. Tumor progression rate, EC tumor extension, and longer follow-up are factors associated with more sensorineural HL.

Keywords

hearing, hearing disorders, natural history, observation, sporadic, unilateral, vestibular schwannoma, wait-and-scan

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One of the main indications for active treatment of unilateral vestibular schwannomas (ie, radiotherapy or surgery) is tumor progression.[1] Because vestibular schwannoma treatment is effective, with tumor control rates between 90% and 95% for both surgery and radiotherapy, research now focuses on the reduction of the sequelae of the tumor and side effects of therapy, such as sensorineural hearing loss (HL). Both radiotherapy and surgery confer a risk to sensorineural hearing, even with hearing preservation strategies. Preferably, the effect of different treatment modalities on hearing should be compared to the natural course of hearing in patients with progressive tumors, and not, as often is the case, be compared to hearing of small, stable schwannomas that have no treatment indication.[2,3]

Patients with progressive tumors are underrepresented in the literature on vestibular schwannomas and HL over time, as reports tend to be skewed towards nonprogressive tumors with longer follow-up duration.[4,5] As a result, HL after vestibular schwannoma treatment is now frequently compared to hearing outcomes of untreated patient cohorts that comprise large numbers of nonprogressive tumors. This comparison is biased because nonprogressive tumors in general do not require therapy and may have a better and more stable hearing over time.[6,7]

Comparisons of hearing results between vestibular schwannoma studies or treatment groups are further hampered by differences in patient selection (eg, in pretreatment hearing levels, the average patients' age, or

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tumor size), different follow-up durations, and different standards for reporting on hearing (eg, the Gardner-Robertson Classification, the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS), or hearing presented as a binary outcome, as either "serviceable" or "non-serviceable," using the "50/50 rule").[8-10] As a result, the reported rates of patients experiencing significant HL after vestibular schwannoma treatment range widely between 10% and 100%.[11] An additional disadvantage of using binary outcomes for hearing is that the hearing of patients with slightly better speech discrimination than 50% is classified as "serviceable," while their hearing performance is actually severely diminished. Conversely, hearing levels may be deemed as "non-serviceable" while they still attribute to binaural hearing and hearing performance in background noise and thus still can be of value to the patient.[12]

This longitudinal study aims to assess the HL at presentation and during follow-up in vestibular schwannoma patients with documented tumor progression prior to active treatment. A comprehensive assessment of hearing is performed in order to gain a nuanced insight into the natural course of hearing in progressive vestibular schwannomas. In addition, the effect of factors that have been reported to affect the patients' hearing outcomes such as the follow-up duration, tumor progression rate, tumor size, and hearing at diagnosis is evaluated.

Methods

Subject Selection

Patients with a unilateral vestibular schwannoma with demonstrated tumor progression were included. Patients presented between 2000 and 2019 at the Leiden University Medical Center, a tertiary referral center in The Netherlands. All patients underwent concurrent audiometry and magnetic resonance imaging (MRI) at presentation and at least once during follow-up. Exclusion criteria included prior vestibular schwannoma therapy, and neurofibromatosis type 2. Patients with profound HL at baseline (0% speech discrimination score [SDS]) were not followed, as their HL was already so profound that further deterioration is not measurable (nor clinically relevant). Follow-up was terminated when patients started active treatment (radiotherapy/surgery).

Treatment decisions were made by a dedicated multidisciplinary team. Our local protocol is largely in line with a recently published modified Delphi consensus.[1] Treatment decisions are made in close consultation with the patient: especially with small-to-medium-sized tumors, where both the timing and the type of intervention are a shared decision. The active surveillance protocol consists of MRI and audiometry 6 to 12 months after diagnosis. Subsequent follow-up intervals are determined by the occurrence and rate of tumor progression and tumor size (more information in Supplemental Material A, available online).

Audiometry

Audiometry data collection was limited to the period of the reported tumor progression, including the last MRI and audiogram before tumor progression started. The protocol for the speech audiometry is described in Supplemental Material B, available online; maximum values were reported. Pure-tone averages (PTAs) were calculated by averaging the air-conduction thresholds of 500, 1000, 2000, and 3000 Hz in dB hearing level; if 3000 Hz is absent, the average of 2000 and 4000 Hz suffices.[13,14]

HL was defined as a sensorineural HL on the affected side using the cutoff values of the World Health Organization (20 dB PTA).[15,16] Asymmetrical HL was defined as a left-right PTA difference ≥15 dB. Significant HL was defined as a PTA difference ≥10 dB between audiograms.[17] For the contralateral ear, a definition of HL >25 dB was used to allow for a direct comparison to a previous study.[18] The annual hearing decrease rate (AHDR) was defined as the PTA difference per year.[19] As PTA values cannot exceed 120 dB (ceiling effect) while follow-up durations can extend, the AHDR has the disadvantage that extending follow-up always leads to lower AHDRs. The AHDR should, therefore, be viewed within the context of the follow-up duration, and we present AHDR values with a follow-up limited to 2 years. For the binary classification of "serviceable" or "non-serviceable" hearing (also called useful and nonuseful or preserved and nonpreserved hearing) the thresholds of >50% SDS and/or <50 dB PTA (ie, "50/50 rule") were used to define "serviceable" hearing.

Tumor Measurements

A neuroradiologist and an ENT surgeon measured the maximal extracanalicular (EC) tumor diameter during multidisciplinary meetings. No diameter (0 mm) was reported when a tumor was limited to the internal auditory canal.[20] Tumor progression was defined as an increase of ≥2 mm in the maximal EC diameter between 2 MRIs. Patients were selected based on this definition of (EC) tumor progression. However, some of them started out with intracanalicular (IC) tumors at diagnosis. As a result, tumor progression that remained confined to the internal auditory canal (purely IC tumors) was not included, but IC tumors that later progressed beyond the internal acoustic canal were. Rapid-growing tumors were defined as tumors gaining >2.5 mm/year in the maximal EC diameter.[21]

Statistical Analysis

Results were divided between short-term (<2 years) and longer-term follow-up (≥2 years), to show the effect of follow-up durations. Differences were assessed using an unpaired *t* test or Wilcox rank-sum (nonparametric data). Linear regression models were calculated for baseline PTA and for differences in PTA (between 2 audiograms of 1

patient); residuals were checked for normality. Parameters included the patient's age, baseline tumor diameter, the difference in tumor diameter, and follow-up duration and were added in a forward stepwise approach.[21] To assess the value of baseline hearing for the prediction of HL during follow-up, hazard ratios (HRs) and 95% confidence intervals (CIs) for "non-serviceable" hearing rates were assessed using Cox proportional hazards regression models.[5] In order to prevent bias and loss of statistical power, multiple imputations with predictive mean matching were performed for missing data (presumed at random) using (baseline) PTA, tumor diameter, and/or SDS as covariates.[22,23] No correction for multiple testing was performed. Statistical significance was set at $p < .05$. Analyses were performed using RStudio Inc, v.1.2.1335. The study was performed with the consent of the local medical ethical committee (Medisch-Ethische Toetsingscommissie Leiden Den Haag Delft), who waived the need for informed consent.

Results

Patient Selection and Baseline Characteristics

Tumor progression was seen in 433 vestibular schwannoma patients prior to active treatment. Excluded were 37 patients with missing baseline audiometry, 28 with no measurable SDS at diagnosis, and 46 due to missing follow-up assessments. This resulted in 322 patients eligible for longitudinal assessment (**Table 1**), of which 84% had an HL exceeding 20 dB (affected ear) and 66% had asymmetrical hearing. The median maximum EC diameter was 10 mm (interquartile rate [IQR]: 8-15 mm). The mean age was 55 years (range 24-82) and 53% of patients were male.

Follow-Up Results

In total, 747 audiograms were available from 322 patients with tumor progression, including >2 audiograms in 84 patients. The median follow-up duration at the last available audiological assessment was 21 months (IQR: 13-34). The median tumor progression was 4 mm (IQR: 2-6) for tumors followed <2 years and 7 mm (IQR: 5-10) for tumors followed ≥2 years. The median tumor progression rate was 3 mm/year (IQR: 1-4).

As a reference, according to the Common Terminology Criteria for Adverse Events version 5, hearing impairment at the last follow-up would be classified as Grade 0 (no HL) in 35% (113/322), Grade 1 in 27% (87/322), Grade 2 in 15% (48/322), Grade 3 in 23% (74/322), and Grade 4 in 0% (**Table 1**).[24]

Scattergrams demonstrate progressive HL over time (**Figure 1**). In 187 of 322 (58%) patients, the PTA HL was

Table 1. Hearing Results for Patients at Diagnosis, at Short-Term Follow-up (<2 Years), or at Longer-term Follow-up (≥2 Years)

	At diagnosis	Short-term follow-up	Longer-term follow-up
Follow-up, mo	-	13 (10-18)	37 (29-50)
PTA,[a] dB (HL)	39 (27-51)	52 (34-66)	61 (45-75)
	n = 316	n = 226	n = 139
The difference in PTA, dB (HL)	-	+8 (2-18)	+18 (7-30)
Significant (PTA) threshold shift[b]	-	46%	68%
Maximum SDS	90% (70%-100%)	74% (40%-91%)	60% (35%-90%)
	n = 297	n = 214	n = 134
The difference in max. SDS	-	−10% (−35% to 0%)	−20% (−40% to −5%)
The shift in dB (SPL) at max. SDS	-	+5 (−10 to + 15)	+10 (0-20)
Annual hearing decrease rate since diagnosis	-	6.9 (1.7-18.7) dB/year	4.6 (2.0-8.9) dB/year
AAO-HNS classification[c]	A: 32% (102)	A: 19% (43)	A: 15% (21)
	B: 34% (110)	B: 22% (50)	B: 16% (22)
	C: 23% (75)	C 30% (67)	C 30% (42)
	D: 11% (35)	D: 29% (66)	D: 39% (54)
CTCAE grading[d]	-	0: 46% (104)	0: 26% (36)
	-	1: 31% (70)	1: 21% (29)
	-	2: 9% (20)	2: 22% (30)
	-	3: 14% (32)	3: 32% (44)

Medians and interquartile rates are presented, unless otherwise specified.

Abbreviations: AAO-HNS, American Academy of Otolaryngology–Head and Neck Surgery; CTCAE,Common Terminology Criteria for Adverse Events; HL, hearing loss; n, number; PTA, pure-tone average; SDS, maximum speech discrimination score; SPL, sound pressure level.

[a]PTA is defined as the average dB HL hearing loss at 0.5, 1, 2, and 3 kHz (including the average of 2 and 4 kHz, if 3 was not measured).

[b]Significant (PTA) threshold shift defined as at least 10 dB difference in PTA between 2 audiograms.

[c]AAO-HNS classification: A: PTA ≤ 30 dB and SDS ≥ 70%, B: PTA >30 and ≤50 dB, and SDS ≥ 50%, C: PTA > 50 dB and SDS ≥ 50%, and D: PTA any level, SDS < 50%.

[d]Hearing impairment according to the CTCAE version 5, no patients demonstrated a Grade 4 hearing impairment.[24]

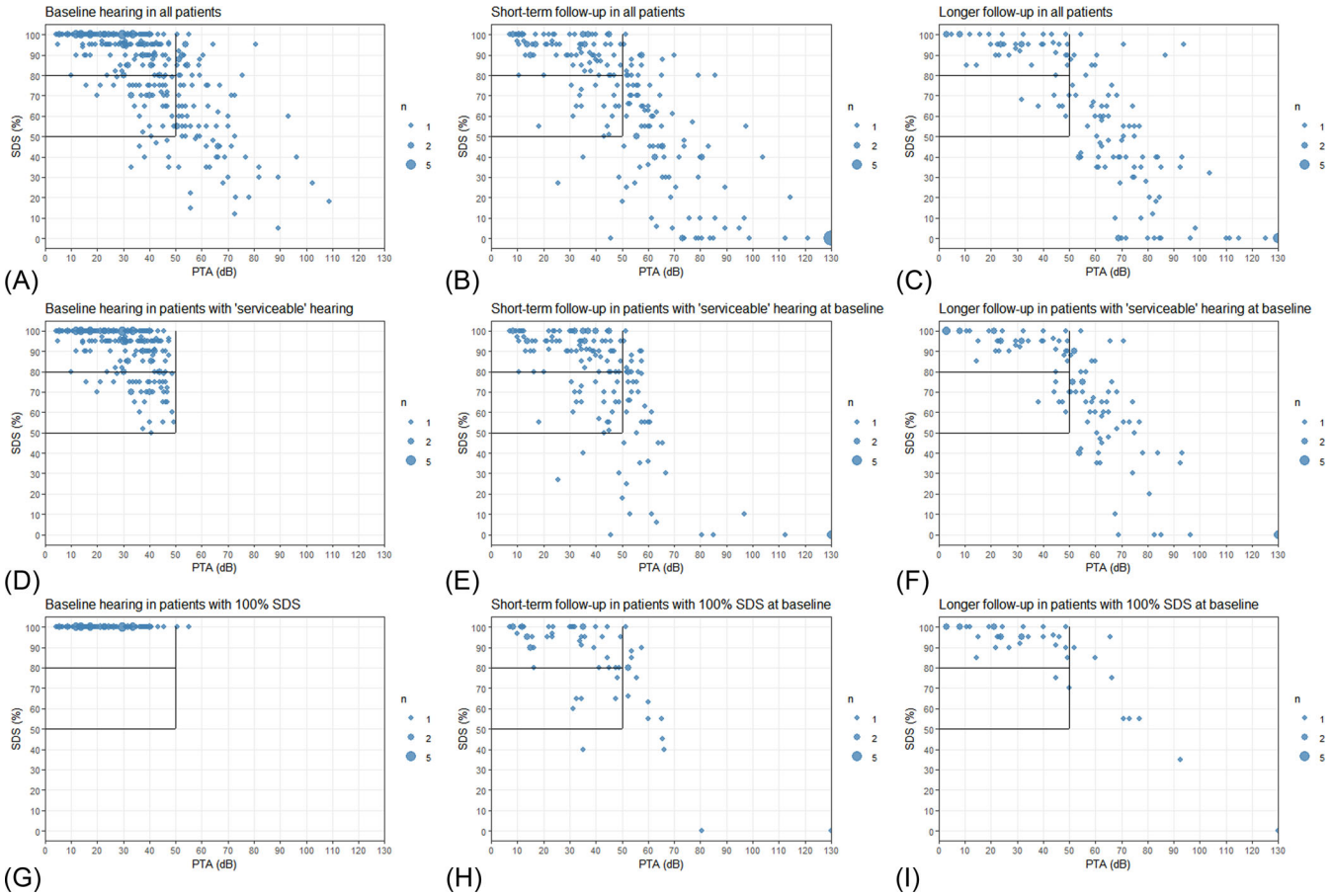

Figure 1. Adjusted version of the standardized AAO-HNS format for reporting hearing outcomes in clinical trials.[9,13] Top-left corner represents perfect hearing and the lower-right corner equates deafness. (A, D, G) At baseline; (B, E, H) <2 years; and (C, F, I) ≥2 years follow-up. AAO-HNS, American Academy of Otolaryngology–Head and Neck Surgery; PTA, pure-tone average; SDS, speech discrimination score.

Table 2. Multivariate Linear Regression Models for the Difference in PTA in dB HL During Follow-Up (Longitudinal Analysis)

Linear regression model	Covariate	Coefficient	95% CI	*p* value
Multivariate Adjusted R^2 = 4%[a]	Intercept	12.8	8.9-16.7	-
	Follow-up duration, mo	0.1	−0.1 to 0.3	.11
	Intracanalicular tumor at diagnosis	8.2	2.9-13.5	.002
Multivariate[b] Adjusted R^2 = 8%	Intercept	8.7	3.4-14.0	-
	Follow-up duration, mo	−0.1	−0.3 to 0.1	.26
	The difference in tumor diameter,[b] mm	1.7	0.9-2.5	<.001
Multivariate Adjusted R^2 = 1%	Intercept	12.8	6.5-19.2	-
	Follow-up duration, mo	0.1	0.0-0.2	.02
	Baseline PTA, dB	0.0	−0.1 to 0.2	.58

Abbreviations: CI, confidence interval; HL, hearing loss; PTA, pure-tone average.
[a]One outlier was removed to improve model fit.
[b]This model only included extracanalicular tumors.

at least 10 dB. Within 2 years, median PTA HL increased by 8 dB (IQR: 2-18 dB) and median SDS decreased by −10% (IQR: −35% to 0%). With longer-term follow-up (≥2 years), the median PTA deteriorated by an additional 18 dB (IQR: 7-30), and the median SDS deteriorated by an additional −20% (IQR: −40% to −5%).

Follow-up duration only had a small (but significant) effect on the PTA in a linear regression model (**Table 2**). The relative percentage of patients with "serviceable hearing" decreased with time (**Table 1**). The AHDR was higher within the first 2 years of follow-up (6.9 dB/year) (**Table 3**).

Table 3. Median and Interquartile Rates of the AHDRs and Follow-Up Duration (in Months) of Patients With Progressive Vestibular Schwannomas, Reported for Different Factors Known to Impact on Hearing

	Overall patients			Short-term follow-up		
Factor	Number of patients	AHDR	Follow-up	Number of patients	AHDR	Follow-up
Overall	314	6.4 (2-14)	21 (13-34)	218	6.9 (2-19)	13 (10-18)
Intracanalicular tumor at diagnosis	90	6.9 (4 -14)	26 (14-49)	51	9.4 (4-20)	14 (11-16)
Extracanalicular tumor at diagnosis	224	6.2 (2-13)	19 (13-31)	167	6.4 (1-7)	13 (9-18)
100% SDS at diagnosis	104	5.4 (2-12)	22 (12-32)	61	7.2 (1-14)	13 (9-19)
Growth ≤ 2.5mm/year[a]	103	4.4 (1-9)	27 (16-37)	56	4.7 (−1 to +12)	15 (11-18)
Growth > 2.5mm/year[a]	121	7.2 (2-18)	15 (9-21)	111	6.9 (2-19)	13 (9-18)

By evaluating the degree of hearing loss per year, the AHDR is especially useful when comparing patient cohorts with different or wide-ranging follow-up durations. Columns on the right present short-term follow-up (<2 years) results; AHDR should be viewed in the context of follow-up duration, because extending follow-up always leads to lower AHDRs.

Abbreviations: AHDR, annual hearing decrease rates; SDS, speech discrimination score.

[a]Only tumors with an extracanalicular component at presentation were included for this calculation.

Table 4. Uni- and Multivariate Linear Regression Models for Baseline PTA in dB HL (Cross-Sectional Analysis)

Regression model	Covariate	Coefficient	95% CI	*p*
Univariate Adjusted R^2 = 5%[a]	Intercept	18.1	7.7-28.5	-
	Age at diagnosis (y)	0.4	0.2-0.6	<.001
Univariate Adjusted R^2 = 1%	Intercept	41.0	38.7-43.4	-
	Intracanalicular tumor at diagnosis	−4.3	−8.8 to 0.2	.07
Univariate[b] Adjusted R^2 = 1%	Intercept	36.6	30.7-42.5	-
	Extracanalicular tumor diameter[b] (mm)	0.4	0.0-0.8	.11
Multivariate[b] Adjusted R^2 = 6%	Intercept	13.4	−0.3 to 26.5	-
	Age at diagnosis, years	0.4	0.2-0.6	<.001
	Extracanalicular tumor diameter[b] (mm)	0.3	− 0.1 to 0.8	.12

Abbreviations: CI, confidence interval; HL, hearing loss; PTA, pure-tone averages.

[a]As a reference, the patients' age accounted for 19% of the variation (adjusted R^2) for the contralateral ear (PTA).

[b]Model included the maximum diameter; only in extracanalicular expanding tumors (N = 234).

Factors that Potentially Affect the Hearing

Tumor Size at Presentation

A greater EC tumor size at diagnosis was significantly correlated to more severe baseline HL (PTA) (**Table 4**).

Patients presenting with IC tumors (28%) showed slightly better baseline hearing than EC tumors; this difference was borderline significant for PTA (37 vs 41 dB, $p = .05$, t test) and nonsignificant for speech discrimination (90% vs 85%, $p = .1$, Wilcoxon rank sum). During follow-up, patients with a progressive IC tumor demonstrated the fastest rate of HL (AHDR 9.4 dB/year) and the lowest hearing level at the end of follow-up (**Figure 2**, **Tables 2** and **3**).

Tumor Progression (Rate)

A higher tumor progression rate (≥2.5 mm/year) was associated with a faster deterioration of hearing (**Table 3**). In a linear regression model, the increase in tumor diameter was also significantly correlated with the increase in PTA between 2 audiograms and this remained the case when corrected for follow-up duration ($R^2 = 8\%$) (**Table 2**).

Hearing at Diagnosis

The patients' baseline hearing (PTA) was not significantly correlated with the difference in PTA during follow-up (**Table 2**).

Hundred Percent SDS at Diagnosis

Patients presenting with 100% SDS already showed HL to varying degrees on PTA (**Figure 1G**; N = 78). During follow-up, 55% experienced significant PTA HL (41 of 75 patients with complete audiometric data) (**Figure 1H** and **I**). Only 19 patients (25%) maintained 100% SDS, while 57 patients (73%) maintained "serviceable" hearing (≥50% SDS). The patients presenting with 100% SDS showed the highest AHDR within the first 2 years after diagnosis compared thereafter (**Table 3**).

"Serviceable" Hearing at Diagnosis

Of the 222 patients presenting with "serviceable" hearing, 50% (111 patients) lost "serviceable" hearing during

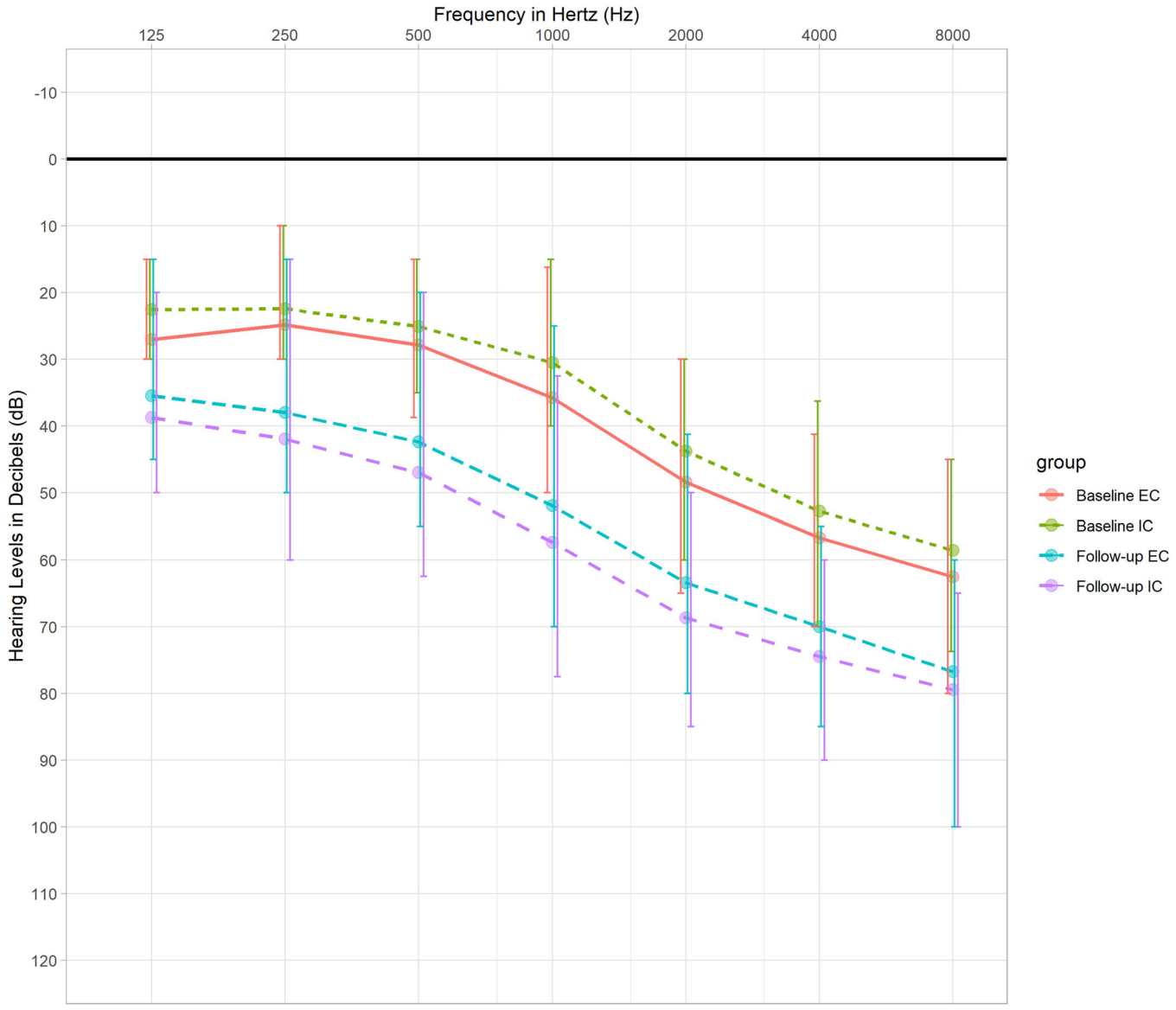

Figure 2. Mean audiograms at diagnosis and at last evaluation, for patients presenting with an intracanalicular (IC) or extracanalicular (EC) tumor.[25]

Table 5. Change in Hearing Between Diagnosis and Last Evaluation (After a Median of 21 Months [IQR: 13-34]) According to the AAO-HNS Classification of Hearing (N = 322)[10]

		At last evaluation				
AAO-HNS classification of hearing		A	B	C	D	Total
At diagnosis	A	50	24	16	12	102
	B	2	31	47	30	110
	C	2	2	31	40	75
	D	-	-	-	35	35
Total		54	57	94	117	322
Duration of follow-up, median (IQR) months		20 (12-34)	23 (15-37)	17 (13-31)	18 (14-25)	21 (13-34)

Abbreviations: AAO-HNS, American Academy of Otolaryngology–Head and Neck Surgery; IQR, interquartile rate.

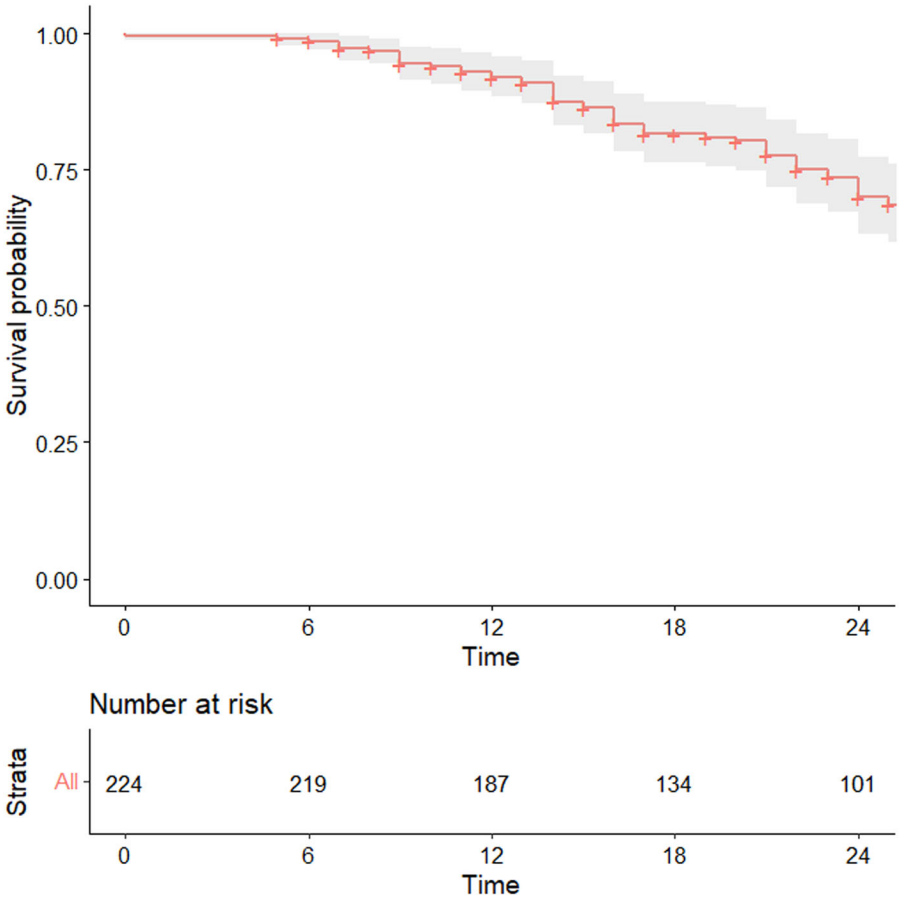

Figure 3. Kaplan-Meier curve for the preservation of "serviceable" hearing.

follow-up (**Table 5**). **Figure 3** presents a Kaplan-Meier curve for maintaining "serviceable" hearing.

Cox-estimated survival rates for maintaining "serviceable" hearing were 93% (95% CI 90%-97%) at 1 year, 63% (95% CI 55%-71%) at 3 years, and 30% (95% CI 21%-43%) at 5 years. In a univariate survival model for maintaining "serviceable" hearing during active surveillance, there was an HR of 1.37 (1.18-1.59) per 10-unit decrease of SDS at diagnosis, and 1.44 (1.19-1.75) per 10-unit increase in PTA at diagnosis (both $p < .001$). In a multivariate model combining SDS and PTA, the HR was 1.23 (1.04-1.46; $p = .02$) per 10% decrease of SDS at diagnosis and 1.29 (1.04-1.59; $p = .02$) per 10 dB increase in PTA.

Patients' Age

While the patients' age was correlated with the hearing level at diagnosis ($R^2 = 5\%$), there was no evidence of a risk of an increased rate of HL for older patients during follow-up (linear regression model; data not shown).

Contralateral Hearing

The median PTA for the contralateral ear was 14 dB (IQR: 8-22 dB) at diagnosis and remained stable during short- and longer-term follow-up (<2 years of follow-up: 14 dB [IQR: -1.5 to +2.8]; ≥2 years 15 dB [IQR: 10-23 dB]). The median maximum SDS was 100% and remained stable during follow-up. Baseline HL in the contralateral ear (defined as PTA > 25 dB; N = 96) did not predispose to increased HL in the contralateral ear during follow-up (Wilcoxon rank $p = .4$).

Discussion

This study presents longitudinal hearing data for patients with progressive vestibular schwannomas that eventually required treatment. The majority of these patients experienced HL during observation prior to active treatment, which seems to deteriorate faster than in patients with nonprogressive tumors.[7,19,26-28] This should be taken into account when comparing hearing results between studies, and when assessing the effect of different treatment modalities on hearing.

Effect of Tumor Progression on Hearing

During active surveillance, 58% of included patients experienced additional HL. We calculated the AHDR to be 6.4 dB/year. Although the relationship between tumor progression and HL might seem intuitive, it is not

commonly considered when comparing hearing results between studies or treatment groups.[2,3,11,29,30]

Of the evaluated variables that may affect hearing (baseline hearing, EC tumor extension, follow-up duration, and age at diagnosis), tumor progression rate (EC part in mm) showed the strongest correlation with HL during follow-up. Hearing furthermore declined faster in patients with rapidly growing tumors (AHDR 7.2 dB/year) compared to slower-growing tumors (AHDR 4.4 dB/year) (**Table 3**). This is in agreement with a review that compared hearing in 982 observed patients from 34 studies, where it was found that patients with slower-growing tumors had a better chance of preserving "serviceable" hearing than those with a faster-growing tumor (75% vs 32%, respectively).[21]

AHDR

The AHDR allows for an evaluation of factors that may impact HL other than follow-up and is especially useful in comparing studies with different or wide-ranging follow-up durations. Previously reported AHDRs (3-5 dB/year, mean follow-up between 22 and 121 months) are lower compared to this study (6.4 dB/year).[19,28] This can probably be explained by differences in patient selection, with other studies also including nonprogressive tumors. Studies reporting solely on nonprogressive vestibular schwannoma patients showed lower AHDRs between 2 and 4 dB/year.[26,28] We found that in contrast to the reported low rate of HL in stable IC tumors (±2.3 dB/year), IC tumors that over time progress extracanalicularly show a particularly rapid deterioration of hearing (6.9 dB/year).[7,26]

The Predictive Power of Hearing Levels at Diagnosis

Excellent baseline hearing levels are reported to be prognostic for future hearing preservation in previous cohorts comprising both progressive and nonprogressive tumors. In this study, baseline hearing levels were also significantly predictive for future HL, but the prediction was less strong than previously published (the previous study also included nonprogressive tumors).[5] For example, a 10 dB increase in baseline PTA, provided an HR of 1.44 (to develop "non-serviceable" hearing), while the HR in a previously performed study was 2.67. This is likely explained by tumor progression having a larger impact on hearing deterioration than baseline hearing levels.

Risk of Losing "Serviceable" Hearing

Although the dichotomic hearing outcome measure of "serviceable" versus "non-serviceable" hearing is deemed insensitive to changes in hearing performance by the AAO-HNS consensus, it is the most commonly used outcome metric for hearing data in vestibular schwannoma patients and therefore a current unfortunate necessity when comparing hearing across vestibular schwannoma studies.[13] A recent systematic review evaluated the survival rates for maintaining "serviceable" hearing: 96% at 1 year, 77% at 3 years, 62% at 5 years, and 42% at 10 years following diagnosis.[27] The included studies did not specifically include progressive tumors and are likely skewed towards nonprogressive tumors. Survival rates for maintaining "serviceable" hearing were 96% at 1 year, 77% at 3 years, 62% at 5 years, and 42% at 10 years following diagnosis. Compared to these previous results, our study shows a higher risk of maintaining "serviceable" hearing in patients with progressive tumors: 93% at 1 year, 63% at 3 years, and 30% at 5 years after presentation. Another factor that may attribute to a faster deterioration of "serviceable" hearing is the rate of PTA and SDS decline during the initial period of observation.[31]

Hundred Percent SDS

Excellent SDS at baseline did not seem to protect the majority of patients from further HL in this specific cohort. This is in contrast to previous observations in cohorts also including nonprogressive tumors.[4,28] Patients that maintained 100% SDS in this study, still showed a median PTA shift of 5 dB. Thus, even when speech discrimination is stable and excellent, this does not necessarily mean that there is no HL (audiometry or self-perceived).[32]

IC Versus EC Extending Tumors

Patients with a progressive tumor that was IC at presentation, showed more severe and more rapid HL than patients presenting with EC tumors, even when corrected for follow-up duration (**Tables 2** and **3**, and **Figure 2**). The IC patient group also demonstrated more growth than patients who presented with EC tumors, which could explain this variation (IC: median 10 mm, IQR: 0-23 mm vs EC: median 4 mm, IQR: 3-23 mm). This may in part be a reflection of the study's selection criteria and local treatment protocols resulting in IC tumors being followed for longer even after demonstrating growth. On the other hand, a previous study also found that tumors that progressed purely IC demonstrated faster HL.[7]

Contralateral Hearing

A previous study longitudinally followed the contralateral hearing in 534 vestibular schwannoma patients and compared this to age-/sex-matched nonvestibular schwannoma controls.[18] They found that vestibular schwannoma patients presenting with abnormal contralateral hearing at baseline (PTA > 25 dB HL) showed more contralateral HL during follow-up for their vestibular schwannoma than expected. In the current study, however, there was no significant difference in AHDR between patients with or without contralateral HL at presentation. We found an overall stable contralateral hearing in vestibular schwannoma patients.

Mechanisms of HL

The exact mechanisms behind sensorineural HL in untreated vestibular schwannoma patients remain unclear and its pathogenesis is likely multifactorial. Compression by the tumor on the cochlear nerve or vasculature could lead to retrocochlear HL or cochlear dysfunction. A second hypothesis states that HL could be the result of inflammatory processes that seem to be associated with vestibular schwannoma progression.[33,34] Both these hypotheses could explain why progressive tumors cause increased ipsilateral HL although they are somewhat contradicted by the occurrence of large vestibular schwannomas that do not cause severe HL and very small tumors that do. Finally, elevated protein levels in the perilymph on the affected side, effects on brain plasticity contributing to HL, and different genetic and molecular changes have also been suggested as possible factors influencing HL in patients with vestibular schwannomas.[35-38]

Strengths and Limitations

The rationale for focusing on the natural course of HL in patients with progressive vestibular schwannomas who required active treatment is that this provides an adequate reference to HL following an intervention. However, as a result of this selection, follow-up duration is inevitably shorter than the reported follow-up of cohorts that also comprised nonprogressive tumors.[4,5,7,19,21,31] Second, large progressive tumors are less likely managed by active surveillance and are underrepresented in this study. Likewise, tumors with IC progression only were not included because in general they do not (yet) qualify for active treatment according to the local protocols. Third, volumetric assessments may provide more assessment of growth.

Conclusions

The majority of progressive vestibular schwannoma patients experienced HL during observation prior to active treatment. Hearing seems to deteriorate faster in patients with progressive tumors than in patients with nonprogressive tumors. Tumor progression showed a significant correlation with HL over time, but baseline characteristics (such as excellent hearing at presentation or small tumor size) did not seem indicative of better hearing outcomes. This should be taken into account when comparing hearing results between studies and when assessing the effect of different treatment modalities on hearing.

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Author Contributions

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Supplemental Material

Additional supporting information is available in the online version of the article.

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