Vestibular schwannoma treatment : patients' perceptions and outcomes

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Chapter 3

Conservative treatment of vestibular schwannoma: a follow-up study on clinical and quality of life outcome

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Abstract

Objective: To determine the natural history and long term quality of life outcome following conservative treatment for vestibular schwannoma.

Study Design: Prospective study conducted in a university-based tertiary referral centre.

Patients: A total of 70 vestibular schwannoma patients who were initially included in the wait and scan protocol between January 2002 and December 2003 were followed with a mean observation time of 43 months. All patients had small- or medium-sized tumors when they were included in the protocol. Quality of life was measured at diagnosis and at the end of follow-up in those patients who were still conservatively treated using the SF-36. The study group was characterized by non-growing small tumors and relatively stable symptoms over time.

Main outcome measures: Clinical, audiometric, radiological and quality of life results.

Results: In 44 patients (63%), growth of the tumor was not observed, and 25 (36%) tumors did grow. Of the 70 included patients, 27 patients (39%) ultimately required treatment. Forty-one patients (59%) were still conservatively treated at the end of follow-up (mean, 47 ± 16 mo). Hearing was preserved in 16 (57%) of the 28 patients with useful hearing at diagnosis. At the end of follow-up, SF-36 scores were only slightly deteriorated for almost all subscales when compared to scores at diagnosis; however, differences were statistically not significant ($p > 0.05$). There was no significant correlation between the presence of cochleovestibular symptoms and quality of life scores ($p > 0.05$).

Conclusion: Conservative observation of small vestibular schwannomas may be regarded as a reasonable management option because the majority of these tumors do not grow during an initial period of observation. Conservative treatment of this subset of patients with small, non-growing tumors does not significantly affect life functioning, as reflected in SF-36 survey data. However, hearing loss did progress in this population. Thus, patients should be counseled regarding this risk and generic quality of life measures such as the SF-36 should be used with caution in future assessments. This study emphasizes the importance of combining generic and disease-specific quality of life measures in future studies of protocols of vestibular schwannoma management.

Introduction

Traditionally, treatment of vestibular schwannomas consists of microsurgical excision or stereotactic irradiation therapy. However, conservative management has increasingly become a treatment option in appropriate cases (1-5). The criteria used for recommendation of wait and scan include the patient's age and health status, tumor size and location, hearing status, and the patient's preference. The rationale for a wait and scan policy in vestibular schwannoma (VS) is the indolent growth pattern and static presentation in most cases (6,7). Improved magnetic resonance imaging (MRI) techniques now allow for an early diagnosis and exact measurement of growth, which has led to an increased number of patients with small and minimally symptomatic tumors suitable for conservative treatment. In a recent meta-analysis on conservative management, it was stated that wait and scan may be regarded as a safe approach for selected patients because most of the observed tumors (57%) did not grow, and only a minority of patients (20%) required treatment (i.e., microsurgery or stereotactic irradiation). However, the authors also concluded that there is a lack of prospectively designed studies with a clinical, radiologic, and audiometric follow-up beyond 3 years (8).

Over the past decades, quality of life (QoL) has increasingly become an important outcome measure for both patients and clinicians when discussing treatment options for VS. Several articles have been published on the patients' perspective of what constitutes a (radio)surgical success (9-14). It is now well recognized that microsurgical treatment of VS affects the patients' QoL significantly, and a trend toward more inferior QoL has been reported after stereotactic irradiation or radiosurgery. However, patient outcomes after conservative treatment have been scarcely described, and reports are often limited by the retrospective design or poorly described reference data (13,15).

A wait and scan policy implies that VS patients have to undergo periodic MRI and clinical evaluation to assess growth or progression of symptoms at least for several years after the diagnosis. In our opinion, to have a VS can therefore be considered as a chronic illness, which may be life-threatening in some cases. So far, it remains unclear how patients experience this kind of conservative approach for intracranial tumors such as VS; the effects of this treatment on QoL over time also remain to be elucidated. In this study, therefore, our first aim was to determine the natural course of VS and to identify and follow those patients who did not require treatment over

time. Second, QoL and possible correlations with cochleovestibular symptoms were prospectively studied with a follow-up of almost 4 years.

Materials and Methods

Patients

Between January 2002 and December 2003, 82 newly diagnosed VS patients were included in our wait and scan protocol. Inclusion criteria for conservative management were minimal symptoms, small- or medium-sized tumors, advanced age, poor general health, or patient preference. Patients were excluded from the study if they had neurofibromatosis type 2 (n = 1), previous surgical, or radiosurgical therapy (n = 5). Patients who were lost to follow-up (n = 2) or had less than 2 MRIs (n = 4) were also excluded. This resulted in 70 patients (29 men and 41 women) who were included in this study; they were followed until April 2008. The clinical data were obtained from the patients' clinical charts and our prospectively generated VS database (16). Patients remained included in the wait and scan protocol if surgical or radiosurgical intervention was not required. The decision for conversion to active treatment was based on the following criteria: significant tumor progression on repeated MRI, objectively quantified hearing deterioration, or the patient's preference for active treatment (e.g., in case of increase in cochleovestibular symptoms). In case of the need for surgical treatment, the surgical approach was based on the patient's hearing and the surgeon's preference for an approach technique. Facial nerve outcome was assessed according to the House-Brackmann classification (Grades I to VI) (17). In case of radiosurgical intervention, patients received stereotactic irradiation or radiosurgery.

Neuroradiologic Assessment

All patients underwent periodic gadolinium-enhanced MRI to determine tumor size or growth. In our clinic, imaging is generally performed at 12-month intervals within the first 4 years after the diagnosis. The scanning interval after this period was dictated by the clinical status of the patient or the patients' preference regarding the duration of the interval, tumor growth rate, or size of the tumor. The duration of follow-up was defined as the interval between the first and last MRI within the observation period. Tumor size was determined using the guidelines of the

American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS) (18). The extracanalicular component of the tumor was determined as follows: the maximum tumor diameter was measured on T1-weighted axial MRI images with gadolinium enhancement. The measurement was calculated parallel to the petrous bone and perpendicular to it. The size of tumors limited to the internal auditory canal was calculated on T1-weighted axial MRI images with gadolinium enhancement, and the total length of the tumor along the axis of the internal auditory canal from the porus to the fundus was measured.

Tumor growth or shrinkage was considered significant in case of an increase or decrease of 2 mm or more in comparison with the previous MRI scan, as proposed by Fucci et al. (3) and Stangerup et al. (19). The growth rate was calculated by dividing the difference in tumor size between the initial and the last available MRI scan by the overall follow-up time (in months) and by multiplying the obtained figure by 12.

Audiometric Assessment

Audiometric assessments were periodically performed during conservative management. In this study, the audiometric results were recorded at diagnosis and at last clinical evaluation. The pure-tone average (PTA) was calculated as the mean sum of 0.5, 1, 2, and 4 kHz hearing thresholds. Speech discrimination scores (SDSs) were obtained in quiet conditions using word list scoring by phonemes and recorded according to the guidelines of the AAO-HNS (18). Hearing was classified (according to AAO-HNS): Class A, PTA less than or equal to 30 and SDS greater than or equal to 70%; class B, PTA less than or equal to 50 dB and SDS greater than or equal to 50%; class C, PTA greater than 50 dB and SDS less than 50%; and class D, SDS less than 50%.

QoL Assessment

The SF-36 was used to measure QoL during the observation period. All the included patients filled out the SF-36 questionnaire at the time of their diagnosis, and the patients who were still included in the wait and scan protocol at the end of the observation period filled out the same questionnaire again (April 2008). The mean scores at time of diagnosis and at the end of the observation period were then compared with each other. Furthermore, relationships between QoL scores and cochleovestibular symptoms or change in symptoms were analyzed. The SF-36 is widely used and validated as a generic outcome measure in a variety of diseases throughout different patient populations (20, 21). It has also been extensively used

in measuring QoL in VS patients (9-16). The SF-36 assesses QoL in the following 8 domains: physical functioning, social functioning, physical role functioning, emotional role functioning, mental health, vitality, bodily pain, and general health. For each domain, there is a series of itemized questions that are scored. Each score is coded, summed, and presented on a scale of 0 to 100, where 0 implies the worst possible health status and 100 the best possible (22).

Statistical Analysis

Statisical analysis was performed using SPSS version 14.0 for Windows. The 2-tailed independent t-test was used for comparison between groups and the paired t-test for comparison within groups with a 95% level of significance ($p < 0.05$). Correlations between variables were analyzed using the Pearson correlation coefficient. Nonparametric equivalents were used in case of not normally distributed data.

Results

Clinical Results

The patients' characteristics are shown in Table 1. The overall average tumor size at presentation was 10 mm (range, 2-27 mm). There were 30 intracanalicular tumors and 40 extrameatal tumors (mean, 7 ± 2 mm and 12 ± 5 mm, respectively), and groups did not differ significantly in age or sex ($p = 0.4$ and $p = 0.6$, respectively). The presenting symptoms are shown in Table 2. Unilateral hearing loss, tinnitus, and balance problems were the 3 most common presenting symptoms. For most of the patients (64%), the duration of their (cochleovestibular) symptoms was 6 to 24 months until diagnosis. There was no significant correlation between presenting symptoms and initial tumor size or intracanalicular or extracanalicular tumors ($p = 0.4$).

Tumor Growth

In 44 (63%) patients, no tumor growth was observed during the entire observation period. In 1 (1%) patient, tumor shrinkage occurred. At a mean follow-up of 32 months (range, 11-67 mo), tumor growth occurred in 25 patients (36%). Within the group of extrameatal tumors (n = 40), 22 tumors (55%) did not grow, whereas 17 tumors (43%) did grow. In 1 tumor (2%) within the extrameatal tumor group, tumor

shrinkage was observed after 36 months of follow-up. In 8 tumors (27%) within the intracanalicular group (n = 30), tumor growth was observed, and the remaining 22 tumors (73%) did not show tumor growth. Among the extrameatal tumors, a larger number of tumors showed enlargement when compared with the intracanalicular tumors. However, this difference was statistically not significant (p = 0.3). The mean growth rate of the growing tumors (both intracanalicular and extrameatal) was 1.5 mm/yr, and the overall growth rate was 0.45 mm/yr. There was no significant relation between patient's age, sex, initial tumor size, or presenting symptoms and growth rate (all p > 0.05). Tumor growth rate also did not significantly differ between intracanalicular or extrameatal tumors (p = 0.1).

Table 1. Patient characteristics (n = 70).

No. of patients	70
Age at diagnosis, yr	60 (35-82)
Male/female	29: 41
Follow-up, mo	40 (11-73)
Initial tumor size, mm	10 (2-27)

Table 2. Presenting symptoms (n = 70).

Symptom	**No. of patients (%)**
Unilateral hearing loss	69 (99)
Tinnitus	38 (54)
Dizziness	31 (44)
Vertigo	18 (26)
Other*	3 (4)

*Trigeminal neuralgia, facial nerve paralysis.

Treatment Group (Failure of Conservative Management)

A total of 27 patients failed (39%) conservative management during the observation period after a mean follow-up of 31 months (median, 30 mo; range, 11-67 mo) because in these patients, microsurgery or radiosurgery was required. Patients were followed for an average of 11 months postsurgery (median, 11 mo; range, 8-12 mo). Nineteen patients (76%) underwent microsurgery and 5 patients (30%) received radiosurgery because of tumor growth. One patient (4%) with tumor

growth remained included in the wait and scan protocol (because of inconsistent tumor growth). Three patients without tumor growth, but with a significant increase in cochleovestibular symptoms during the observation period, also underwent surgical treatment. Two of these patients were operated via the translabyrinthine (TL) approach, and 1 patient underwent successful hearing preservation surgery via the middle fossa (MF) approach. The surgical outcome of these patients is presented in Table 3. Facial nerve outcome was favorable (House-Brackmann Grades I and II) in all operated patients, and there were no major postoperative complications. Two patients died during follow-up because of medical reasons not related to VS.

Table 3. Surgical outcomes of 22 primarily conservatively treated patients.

Patient	Surgical approach	Hearing function at diagnosis*	Preoperative hearing function preoperatively*	Postoperative hearing function postoperatively*
1.	TL	D	D	D
2.	TL	D	D	D
3.	TL	D	D	D
4.	TL	D	D	D
5.	TL	D	D	D
6.	TL	C	C	D
7.	TL	C	C	D
8.	TL	C	C	D
9.	TL	C	C	D
10.	TL	C	C	D
11.	TL	C	C	D
12.	TL	B	D	D
13.	TL	B	B	D
14.	TL	B	C	D
15.	TL	B	B	D
16.	TL	B	D	D
17.	TL	C	D	D
18.	TL	B	C	D
19.	TL	A	B	D
20.	TL	A	D	D
21.	TL	A	B	D
22.	MF	A	A	A

* American Academy of Otolaryngology Head and Neck Surgery hearing classification (18). TL indicates translabyrinthine surgery; MF, middle fossa surgery.

Nontreatment Group (Nonfailure of Conservative Treatment)

At the end of the observational period, a total of 41 patients (59%) were still included in the wait and scan protocol (mean, 47 ± 16 mo; range, 12-73 mo). The patients' characteristics are presented in Table 4. The overall average tumor size was 10 mm (range, 2-27 mm). There were 20 intracanalicular tumors and 21 extrameatal tumors (mean, 7 ± 3 mm and 14 ± 6 mm, respectively), and groups did not significantly differ in age or sex ($p = 0.2$ and $p = 0.4$, respectively). The presenting symptoms in these patients and subsequent symptoms at the end of the observation period are presented in Table 5. Of the presenting symptoms, hearing loss worsened in 20 (49%) of the 41 patients. Patients presenting with balance problems reported improvement of dizziness and vertigo in 5 (26%) of the 19 patients and in 5 (42%) of the 12 patients, respectively. Dizziness and vertigo worsened in 3 (16%) of the 19 patients and in 2 (17%) of the 12 patients, respectively. Symptoms in 2 patients presenting with a trigeminal neuralgia and 1 patient with a mild facial nerve paralysis did not change. There was no significant correlation between presenting symptoms or change in presenting symptoms and initial tumor size or intracanalicular or extracanalicular tumors (all $p > 0.05$). The score distribution on the SF-36 dimensions is listed in Table 6. At follow-up, the SF-36 scores of the 41 patients had slightly deteriorated compared with the scores at baseline some 4 years earlier except for social functioning, which was slightly improved. However, the SF-36 scores at follow-up did not significantly differ when compared with scores at baseline (all $p > 0.05$). Baseline and follow-up SF-36 scores did not correlate significantly with cochleovestibular symptoms or tumor size (all $p > 0.05$).

Table 4. Patient characteristics for the nontreatment group (n = 41).

No. of patients	41
Age at diagnosis, yr	63 (40-79)
Male/ female	16:25
Follow up, mo	47 (12-73)
Initial tumorsize, mm	10 (2-27)

Table 5. Presenting symptoms and change at the end of observation (n = 41).

Symptom	No. of patients (%) reporting symptoms at baseline	No. of patients reporting symptoms at follow-up		
		No change	Better	Worse
Unilateral hearing loss	41 (100)	21	0	20
Tinnitus	26 (63)	24	0	2
Dizziness	19 (46)	11	5	3
Vertigo	12 (29)	5	5	2
Other*	3 (7)	3	0	0

*Trigeminal neuralgia, facial nerve paralysis.

Table 6. Quality of life scores of the conservatively treated patients (n = 41).

	At diagnosis		End of observation	
Short Form-36 scales	Mean	SD	Mean	SD
PF	81.0	23.9	80.3	23.3
SF	74.3*	28.3	77.1*	22.7
RP	73.6	39.7	72.6	40.3
RE	82.4	31.0	78.9	33.1
MH	70.0*	15.7	69.4*	16.5
VT	66.8	15.8	63.6	18.8
BP	86.3*	18.8	84.8	18.3
GH	57.4*	18.3	56.6*	20.6

PF indicates physical functioning; SF, social functioning; RP, role-physical functioning; RE, role-emotional functioning; MH, mental health; VT, vitality; BP, bodily pain; GH, general health; SD, standard deviation; * $p < 0.05$.

Audiometric Results

At their diagnosis, 33 patients (47%) presented with useful hearing on the tumor ear (Classes A and B of the AAO-HNS classification), whereas 37 patients (53%) had no serviceable hearing on the tumor ear (Classes C and D of the AAO-HNS classification) (18). In 5 (15%) of the 33 patients with useful hearing, follow-up audiometry was not available. During the observation period, 12 patients (43%) of the remaining 28 patients within the useful hearing group lost their (useful) hearing, and in 16 patients (57%), useful hearing was maintained. Of the 12 patients who lost their

useful hearing, 4 patients lost their hearing because of TL surgery resulting in permanent hearing loss in the tumor ear. A total of 5 patients who underwent TL surgery during the observational period lost their useful hearing before the surgery was performed (Table 3). In the remaining 3 patients, useful hearing was lost during the observational period. No significant difference was found in loss of useful hearing between intracanalicular and extrameatal tumors ($p = 0.2$). Nearly half of the patients with useful hearing and with a growing tumor lost their hearing because of the TL surgery. A correlation between tumor growth and hearing loss could not be adequately interpreted because of the bias caused by the inevitable hearing loss after TL surgery.

Discussion

This study reported on 1 of the few follow-up studies in VS patients, with a set of outcome variables that encompasses clinical and QoL data. We described the natural course of VS in a prospective manner and with a focus on the long term QoL in those patients who were still conservatively treated after almost 4 years of observation.

During the observational period, the vestibular schwannomas seemed to be nongrowing in most patients (63%). This finding is in line with earlier studies in which absence of growth has been reported in 40% to 76% of cases (1-6,23-26). Furthermore, these results are underlined by the data of a recent meta-analysis performed by Smouha et al. (8); they found that in 1,345 VS patients, 57% of tumors were nongrowing, whereas 43% showed positive growth during a mean follow-up of 3.2 years. The observed nongrowth rate of 57% was likely to be overestimated according to the authors because of the relatively short duration of follow-up. Nonetheless, several studies, including our study with longer follow-up periods ranging from 3 to 7 years, still report high nongrowing tumor rates (24-26). We also observed tumor involution during the observational period in 1% of cases, which is also in line with reported tumor regression rates. The observed spontaneous involution of vestibular schwannomas may be explained by tumor necrosis caused by intratumoral thrombosis and may be part of normal involution of tumors that have reached their maximum growing potential (27). The growth patterns of VS may vary from spontaneous involution to rapid growth, and unfortunately, not many clinical or radiologic factors predicting tumor growth have been found so far. Intracanalicular

tumors are thought to display less growth than extracanalicular tumors, and younger age is associated with more rapid growth and the presence of intratumoral cysts (25,26,28). Although we observed an increased number of growing tumors in the extracanalicular tumor group compared with intracanalicular tumors, this difference was not statistically different. Other patient or tumor factors (i.e., age, presenting symptoms, tumor size) were also not significantly related to observed growth.

In the current study, failure was defined as conversion from wait and scan to active treatment, which occurred in 39% of patients. Various studies report a percentage of failure between 0 and 50% (26). As in most of these studies, our decision for definitive treatment was mostly based on significant tumor growth observed on MRI. However, in our study, not all patients with tumor growth received treatment. For instance, in 1 patient, the inconsistent tumor growth was observed for several years, and there was no increase of symptoms or deteriorated QoL. In this patient, therefore, treatment was successfully postponed. In 3 patients, however, a significant increase in cochleovestibular symptoms occurred, and finally, patients preferred to undergo microsurgical treatment. One of these patients underwent hearing preservation surgery using the MF approach, and useful hearing was postoperatively maintained (Table 3). The other 2 patients underwent TL surgery and subsequent vestibular neurectomy because of the disabling character of their vertigo. Postoperatively, there were no major complications, and facial nerve function was favorable for all 22 operated patients.

Consistent data concerning hearing loss or other cochleovestibular symptoms after conservative treatment is still scarcely found (8). We found that useful hearing was maintained in 57% of patients after almost 4 years of follow-up. However, one should be cautious while interpreting these data because in some patients, recent audiometric data were not available (15%). Furthermore, a relationship between tumor progression and hearing loss could not be established because nearly half of the patients with useful hearing and with a growing tumor lost their hearing because of the TL surgery. Other authors have reported on hearing loss in 50 to 67% of cases after conservative treatment and regardless of tumor progression (29). Studies concerning hearing preservation surgery have claimed some degree of preserved hearing in 35 to 60% of cases, and similar results are reported after radiosurgery (30). When considering these results, hearing preservation, therefore, could still be a matter of debate when discussing treatment options for small- and medium-sized vestibular schwannomas.

VS may be regarded as a chronic illness, which causes discomfort and may lead to unilateral hearing loss, tinnitus, or balance problems. Moreover, patients treated conservatively have to undergo periodic radiologic, audiometric, and clinical assessment for a prolonged period after their diagnosis. Therefore, information regarding QoL during the course of conservative treatment is of great importance for this group of patients. Of the 70 patients initially included in the wait and scan protocol, 41 patients (59%) were successfully treated with a mean follow-up of 47 months. As expected from earlier studies, conservative treatment did not significantly affect our patients' QoL (1-5,13, 15,25,26,31). We performed an observational study in a population of patients with small, nongrowing tumors for which symptoms were likely to remain stable over time. Furthermore, QoL scores seemed not to be influenced by the presenting symptoms or change in symptoms during the follow-up period. Of the main symptoms, deterioration of hearing loss was reported mostly by the patients, but the loss of hearing did not seem to affect QoL. A possible explanation might be the gradual character of the hearing loss or the fact that most patients already had nonserviceable hearing at diagnosis (21 of the 41 patients). Almost one third of patients with balance problems at diagnosis reported improvement over time, which may be explained by the gradual dysfunction of the vestibular nerve from the VS accompanied by vestibular compensation in the central nervous system. Two patients reported that their vertiginous complaints had worsened, but without significantly affecting their QoL, and therefore, they did not receive treatment yet. However, it is now well recognized that the SF-36, a widely used generic questionnaire, has limitations with respect to otolaryngologic interventions or auditory and vestibular functioning (32,33). In our opinion, the interpretation of QoL results should therefore be done with caution. When compared with other published results from our center in which QoL was measured in VS patients before treatment decision or proposal, our patients had better QoL scores (16). Again, this illustrates the patient selection in our sample.

Although this study was conducted using a prospective design, there are a number of limitations to this study of which some are already mentioned earlier. The interpretation of our QoL results is hampered by lack of data of the treated patients. We have not investigated QoL in these patients because of the relatively small patient subgroups (microsurgery and radiosurgery; n = 22 and n = 5, respectively). Patients were followed-up for almost 1 year postsurgery. We are aware that these data are preliminary, and longer and more profound follow-up is needed of the entire

cohort. Furthermore, with regard to the use of the SF-36, it should have been more preferable to combine generic with disease-specific measures of QoL. However, until now, no validated questionnaire is available for assessing VS-specific QoL. We have therefore, in our opinion, used the best methods available. We acknowledge the importance of combining generic and disease-specific QoL measures for future research projects. The results of this study may be valuable for counseling patients with small- or medium-sized vestibular schwannomas.

Conclusion

Conservative management is increasingly adopted as an initial treatment option for VS. As shown in previous reports, our study shows that conservative management of small tumors is a reasonable option because most tumors do not grow. Useful hearing was preserved in half of the patients, which is in line with existing literature. Conservative treatment does not seem to worsen the patients' QoL over time. However, in this study, patients with nongrowing small tumors and with stable cochleovestibular symptoms were prospectively followed. Of the symptoms, hearing loss deteriorated most frequently during follow-up, and QoL does not seem to meaningfully deteriorate due to hearing changes in the involved ear. However, it should be taken into account that the SF-36 has its limitations with regard to assessing QoL in otolaryngologic interventions and sensitivity to symptoms such as hearing loss or balance problems. It should therefore have been preferable to combine generic with disease-specific measures of QoL.

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