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ORIGINAL ARTICLE

Conservative Management of Vestibular Schwannoma☆

Ricardo José González-Orús Álvarez-Morujo,* Itziar Álvarez-Palacios, Carlos Martin-Oviedo, Bartolomé Scola-Yurrita, Miguel Ángel Arístegui-Ruiz

Servicio de ORL, Hospital General Universitario Gregorio Marañón, Madrid, Spain

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KEYWORDS
Vestibular schwannoma;
Acoustic neuroma;
Observation;
Conservative management

Abstract
Introduction: Vestibular schwannoma (VS) is a benign, slow-growing tumour originating in the 8th cranial nerve. The treatment includes microsurgery, stereotactic radiotherapy and conservative management of tumours with periodic radiological tests.
Methods: This was a retrospective study of patients with VS following conservative management in a tertiary hospital between 1993 and 2013. A total of 73 patients were enrolled in our protocol. The mean age at diagnosis was 59.7 years. The average size was 11.9 mm (4–27 mm); 58.9% of the tumours were intracanalicular and 41.1%, extracanalicular. The mean follow-up period was 35.75 months.
Results: In 87.7% of patients there was no evidence of tumour growth. A total of 9 tumours (12.3%) increased in size. The average growth rate was 0.62 mm/year. The percentage of extracanalicular tumours that grew (20%) was higher than that of intracanalicular tumours (7%). Seven patients (9.5%) experienced significant changes in their symptoms and 6 of these (8.2%) experienced a loss of useful hearing. Six patients (8.2%) left follow-up and underwent surgery.
Conclusions: Periodic monitoring of vestibular schwannomas with magnetic resonance imaging represents an option for management, because most small tumours experience little or no growth over time.
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PALABRAS CLAVE
Schwannoma vestibular;
Neurinoma del acústico;

Manejo conservador del schwannoma vestibular

Resumen
Introducción: El schwannoma vestibular (SV) es un tumour benigno de lento crecimiento originado en el VIII par craneal, en cuyo tratamiento entran a formar parte la microcirugía, la radioterapia estereoatáxica, y el manejo conservador de los tumores con controles radiológicos periódicos.

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* Corresponding author.
E-mail address: ricardomorujo@hotmail.com (R.J. González-Orús Álvarez-Morujo).

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Observación;
Manejo conservador

Material y métodos: Estudio retrospectivo de pacientes con SV siguiendo un manejo conservador en un hospital de tercer nivel entre los años 1993–2013.

Un total de 73 pacientes fueron incorporados a nuestro protocolo de seguimiento de SV. La edad media al diagnóstico fue de 59,7 años. El tamaño medio de 11,9 mm (4–27 mm), siendo el 58,9% intracanaliculares y el 41,1% extracanaliculares. El periodo de seguimiento medio fue de 35,75 meses.

Resultados: En el 87,7% no hubo evidencia de crecimiento tumoral. Un total de 9 (12,3%) tumores incrementaron sus dimensiones. La velocidad media de crecimiento fue de 0,62 mm/año. El porcentaje de tumores extracanal que crecieron (20%) fue mayor que el de los tumores intracanal (7%). Siete pacientes experimentaron cambios significativos en su sintomatología (9,5%) y 6 de estos una pérdida de la audición útil (8,2%). Seis pacientes salieron del seguimiento y fueron intervenidos quirúrgicamente (8,2%).

Conclusión: El seguimiento del SV con controles periódicos de resonancia magnética nuclear representa una opción válida de manejo, dado que la mayoría de los tumores de pequeño tamaño experimentan poco o nulo crecimiento a lo largo del tiempo.

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Introduction

Vestibular schwannoma (VS) is a benign slow-growing tumour originating in the eighth cranial nerve. VS treatment traditionally consisted of microsurgical resection or stereotactic radiotherapy.[1–4] However, the therapeutic approach to these tumours has recently changed and conservative management has become a valid option in appropriate cases.[5–8] Surgery has traditionally been the chosen option, the primary objective of which was the complete extirpation of the tumour, and, where possible, the complete preservation of the facial nerve and in some cases, hearing. Results have improved immeasurably through the refinement of surgical techniques, the monitoring of cranial nerves, the improvement in anaesthetic assistance, and the accumulated experience of surgeons. Treatment related morbidity does, however, continue to be unavoidable. Notwithstanding, since this type of benign tumour often shows little or even no growth, conservative management may be considered an option in selected cases.

There were several reasons for including certain patients in periodic VS follow-up treatment, using a ''wait and scan'' approach. These included: the patient's age, general patient condition, size and location of tumour, vestibular clinical history, hearing level, and patient preference. Logical defence of this treatment is the fact that these tumours often growth slowly over many years, with no substantial alterations in symptoms.[9,10] The improvement in MRI techniques has led to earlier diagnosis and appropriate growth monitoring, enabling patients with small tumours and minimal symptoms to receive conservative management.

The aim of this study is to determine the natural course of the acoustic neuroma, progression frequency, and mean growth, as well as determining the factors that could lead to potential growth.

Materials and Methods

A retrospective study of patients with VS, diagnosed in a tertiary hospital between 1993 and 2013, was performed. Out of a total of 428 cases of acoustic neuromas, 73 (17%) patients chose follow-up therapy. Patients who had received radiosurgery, who had undergone previous surgery and those diagnosed as neurofibromatosis type II were excluded.

Follow-up protocol consisted of each patient being carefully informed regarding the different treatment options, which included surgery, observation and radiosurgery, with an explanation of the possible risks and complications of each one of them.

Patients who received fewer than 2 MRIs were excluded from the study. One or several of the following factors led to the adoption of a follow-up strategy using periodic magnetic resonance imaging: tumour size, the patient's age, general patient condition, neurotological symptoms, level of hearing and patient preference.

The study group consequently included 73 patients. The mean age at diagnosis was 59.7 ± 11.9 years, ranging between 33 and 86 years. 76.7% of patients who were monitored were over 50, and 23.3% were over 70. Thirty-nine schwannomas were at the left side (53%) and 34 at the right (47%). Gender distribution was as follows: 41 (56%) women and 32 (44%) men.

Radiological Study

All the patients were radiologically assessed using MRI scans with paramagnetic contrast (axial, coronal) to determine tumour size. When determining tumour size, the intracanalicular and extracanalicular sections were analysed separately. To do this, the maximum diameter of all sections was included. The intracanalicular size primarily corresponded to the internal ear canal (IEC) save in exceptional cases. In solely intracanalicular tumours the extracanalicular diameter was considered to be 0.

The tumour size at diagnosis varied between 4 and 27 mm (considering both intra and extracanalicular sections), with a mean of 11.9 ± 6.9 mm. Forty-three were intracanalicular (58.9%) while the other 30 (41.1%) were extracanalicular (Fig. 1a). The mean diameter of the intracanalicular tumours at diagnosis was $7.84\,\text{mm} \pm 3.4\,\text{mm}$, and $17.1\,\text{mm} \pm 8.1\,\text{mm}$ for extracanalicular (Fig. 1b). A large

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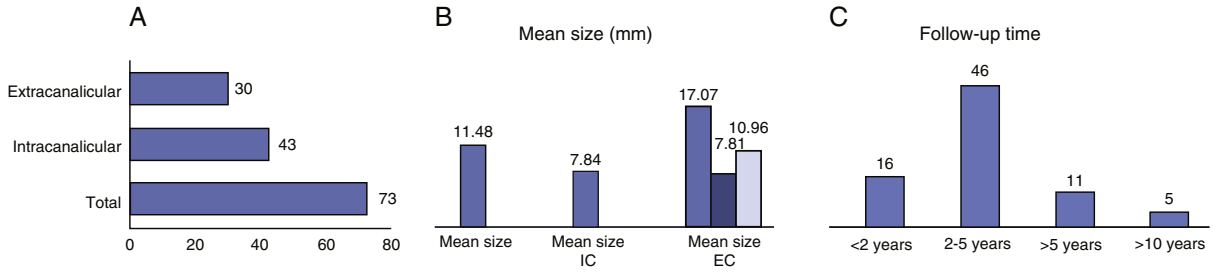

Figure 1 (A) Distribution of incranalicular and extracanalicular VS. (B) Mean VS size: overall mean size, mean size of intracanalicular (IC) tumours, means size of extracanalicular (EC) tumours, differentiating between intra and extrameatal sections. (C) Mean follow-up time in years.

majority of the tumours (85%) were under 15 mm. Tumour growth was defined as a two dimensional increase of 2 mm or more, compared with the previous MRI. Growth below this figure was considered to be absence of growth. A second MRI was performed 6 months after patient follow-up began. If no significant change in size was observed, radiological testing was reduced to 12-month intervals. However, if there was a higher than 2 mm growth and the patient wished to continue under observation, new MRI controls were performed every 6 months. The average/mean follow-up period was 35.8 months, with variation between a minimum of 12 and a maximum of 240 months. Of the 73 tumours, a great majority of them (85%) were followed up for 2 or more years (Fig. 1c).

Audiometric Study

In all patients tonal audiometries were performed to assess hearing function. If a deterioration of tonal levels was discovered in some of the successive controls, a speech audiometry was performed to verify whether discrimination ability had been affected.

Statistical Study

Statistical analysis was made using a data base created in the SSSP programme for version 15.0 with Fisher's exact test. $P<.5$ values were considered statistically significant.

Results

The mean speed of tumour growth incorporated into our follow-up protocol was 0.62 mm per year. The mean growth of extracanalicular tumours was almost 3 times higher than intracanalicular ones (Fig. 2a). Mean growth speed varied according to the tumour size, increasing in accordance with the extracanalicular size of the same (Fig. 2b). In 64 (87.7%) out of 73 cases, there was no evidence of tumour growth during the observation period (Fig. 2c). In a total of 9 cases (12.3%) the tumour grew, the mean speed of tumour growth being 5.1 mm/year, with variation between a minimum of 2 mm/year and a maximum of 8 mm/year. This resulted in a much higher overall mean speed. Mean follow-up of tumours which had grown was 39.7 months. Mean tumour size at the beginning of follow-up was 12.3 mm, and 20.7 mm on termination (mean growth higher than 8 mm). There was no evidence of tumour regression in any of the patients. In the intracanalicular neurinomas group, 40 (93%) remained stable, and 3 (7%) experienced growth. In tumours with intra and extrameatal components, 24 (80%) stayed the same size and 6 (20%) increased in size (Fig. 3a). We noted there was a higher percentage of tumours which increased, the larger the extracanalicular component size of the tumour (Fig. 3b). Of the tumours which grew, 5 opted for surgical treatment and 4 continued under observation, 3 due to age and one for personal reasons.

The clinical manifestations of the study group included: hearing loss in 53 patients (72.6%), tinnitus in 27 (36.9%), instability in 13 (16.4%), vertigo in 6 (8.3%), and sudden deafness in 4 cases (5.5%) (Fig. 4a). The most frequently associated symptoms patients presented were hearing loss and tinnitus. A total of 7 patients (9.5%) experienced significant alterations in their symptoms, while the great majority remained stable (90.5%) (Fig. 4b). Hearing was not substantially altered except in the case of 6 patients (8.2%), who experienced deterioration and lost discrimination ability

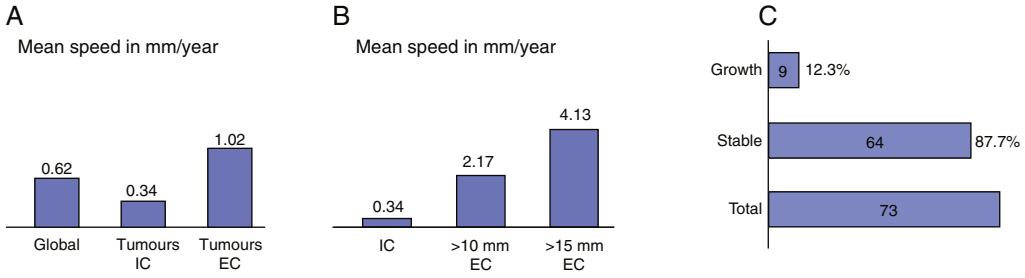

Figure 2 (A) Mean growth speed of tumours, differentiating between intracanalicular (IC) and extracanalicular (EC) tumours. (B) Mean growth speed compared with regarding extracanalicular (EC) component size. (C) Stable tumours and with growth.

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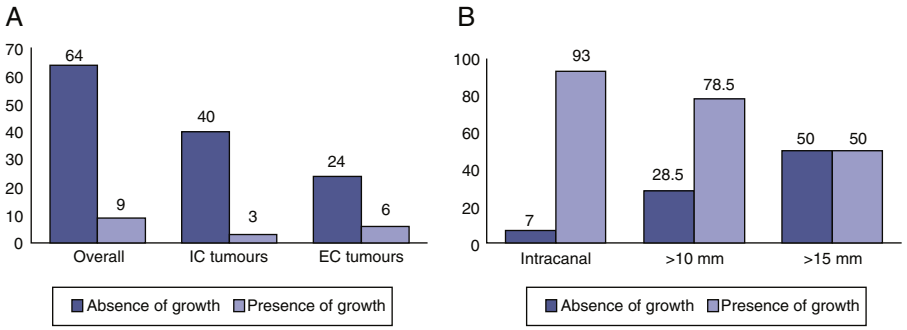

Figure 3 (A) Incranalicular (IC) and extracanalicular (EC) tumours which grew. (B) Percentage of tumours which grew according to extracanalicular (%) size.

previously held. Two patients also stated an increased instability: repetitive episodes of vertigo in one and increased tinnitus in the other (Fig. 4c).

Radiological testing showed cystic components in 3 tumours. Two patients presented VS in one ear only. Other associations included 1 patient with neurofibromatosis type I criteria, 1 patient with microtia-agenesis of the external auditory canal in the contralateral ear where an osseointegrated implant was installed, and one case of osteosclerosis where both ears had been operated on. Schwannoma was diagnosed in 2 patients when hearing loss in the ear contralateral to that of the tumour was examined. In 4 cases schwannoma was discovered coincidentally when other processes were being studied. These included 1 meningioma of the radiated sphenoid wing, 1 parasagital cerebral lesion, 1 epileptic focus, and 1 case of headaches.

Out of the total 73 tumours being monitored, 6 (8.2%) had surgery performed on them. In 5 of these cases the tumour size increased. Two patients also presented changes in symptoms: in one, instability increased and in another there was a loss of hearing intelligibility. The therapeutic approach was chosen according to the patient's hearing level, the size and penetration of the tumour in the back of the internal auditory canal, and surgeon's preference. In 5 of the 6 cases the extended translabyrinthine approach was used. The other patient was operated on using the retrolabyrinthine approach, since the tumour had not reached the back of the canal and useful hearing was intact. Facial function was good or very good (equal to or higher than grade II level according to the House-Brackman classification) in all patients operated on.

Discussion

Treatment options in VS patients include microsurgical resection (total or subtotal), radiosurgery and conservative management of tumours with periodical ''wait and scan'' imaging. Based on these options, several factors become essential in determining the most appropriate treatment. These are: the age of the patient, tumour size at diagnosis, symptoms, or growth pattern.

Thanks to the development and improvement of new MRI techniques over the last 20 years, plus their greater availability and higher application, the rate of VS incidence has increased. Several authors state there has been an increase in diagnosed schwannomas of 7.8–17.4 cases per million inhabitants/year as a consequence of the development and extension and diffusion of modern imaging techniques.[11] The increase in the detection of small tumours where several different treatment approaches may be adopted, each with its individual advantages and drawbacks (surgery, radiotherapy, and observation), has often led to dilemmas. Notwithstanding, surgery continues to be the treatment of choice in those neurinomas where maximum extracanalicular diameter is above 25 mm, the tumour tightly compresses the brainstem, or the patient presents vestibular symptoms which affect his or her well-being. The primary aim in these cases is to perform a complete resection of the tumour whilst preserving facial nerve anatomy and function. In several cases it is also possible to preserve hearing, although satisfactory results are infrequent and a high postoperative level of useful hearing is rarely obtained.[12,13] Furthermore, despite a general major

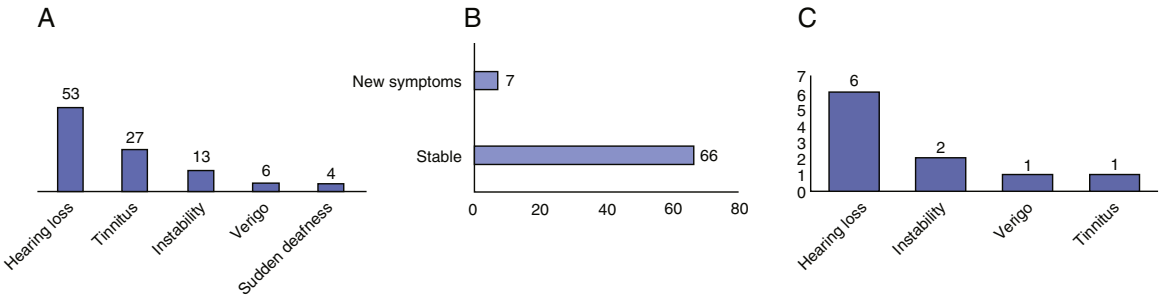

Figure 4 (A) Initial clinical manifestations. (B) Patients with changes in initial symptoms. (C) Symptoms which changed.

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improvement in surgical results over the last few decades, we should consider that these are benign, slow-growing tumours which often do not affect the patient's daily activities to any degree. On the contrary, the consequences from VS surgery may do so to a high degree (headache, instability, tinnitus, facial paralysis, unilateral cofosis or more serious conditions). Several studies show how quality of life may potentially deteriorate following surgery.[14–16]

Radiosurgery offers tumour growth control in a high percentage of cases with lowered rate of complications (trigeminal neuralgia, vertigo, hearing loss, facial paralysis, and hydrocephalus being the most representative). However, long-term studies are still needed to confirm these results and they do not exempt the patient from having to continue making periodical radiological controls following radiation.[17] The surgeon may also have difficulties in operating on a previously irradiated tumour without sufficient control of it growth. This generally leads to impaired surgical results, particularly relating to the facial nerve function,[18,19] and to rare cases of malignantly transformed schwannoma resulting from radiation.[20,21]

Increasingly more centres are adopting observation policies for eighth cranial nerve schwannomas, since these are benign tumours which often grow very slowly or not at all. The great majority of cases (87.7%) out of a total of 73 included in our follow-up protocol remained stable with no presence of growth. These figures coincide with other studies where the percentage of tumours which do not grow are around 50%.[7–9,22,23] Smouha et al. carried out a meta-analysis study with a total of 1345 VS patients and found that growth was absent in 57% of cases, present in 43%, with a mean follow-up period of 3.2 years.[24] The follow-up period, initial tumour size at diagnosis, tumour growth percentages and surgical intervention rates were very similar to those of other controlled neurinoma series (Fig. 5). If we consider a higher follow-up period, above 5 years, the total of tumours with no growth continues to be high (84.5%), as occurs in other published works. This explains the long-term conservative treatment viability.[25] In fact, one of our patients presents a case of intracanalicular acoustic neurinoma monitored over 20 years without any considerable alterations to size. In our study, no cases of tumour involution were noted. These were noted in other studies and varied between 4% and 17%.[7,26] Spontaneous involution of an acoustic neurinoma may be explained by the necrosis resulting from intratumoral thrombosis and may form part of the normal regression of those tumours which have already grown to their maximum proportions.[27]

Radiological assessment was carried out using two-dimensional measurements, as used by many other authors.[1,7,26,28] Although tumour size was generally measured by maximum diameter of its extracanalicular component, in the case of our follow-up protocol, we determined this by calculating the sum of the intra and extrameatal section, both measured separately. This was due to the fact that the majority of the monitored schwannomas were purely intracanalicular and the aim of the study was not only to determine the changes in extracanalicular tumour size but also changes where only intracanalicular tumours existed. Other studies state that three-dimensional volumetric measurements are the most appropriate,[29,30] and in the MRI series controlled with volume measurements there are higher percentages of tumour growth, indicating that this is the most suitable method for early detection of tumour progression.[31,32] We have defined tumour growth, as have other authors,[1–7] as a two-dimensional increase of 2 mm or more, compared with the previous MRI, since an increase of less than 2 mm may be due to an overestimation and preempt a hasty therapeutic decision.

One of the main problems in adopting a follow-up protocol for acoustic neurinomas is the impossibility of predicting tumour growth over time. The aim of all research is usually therefore to become aware of the predictive factors which determine VS progression or stability. In general, age and gender do not usually have any significant correlation with tumour growth, as most studies show.[7,26,29] However, other factors, such as initial symptoms do appear to be predictive factors of progression. Tschudi et al.[33] found that patients with progressive hearing loss as a primary symptom usually have a lower growth rate than those other patients who present instability, tinnitus and sudden deafness on initial diagnosis. It is suggested that tinnitus is an indicator of the biological activity of structures which include the inner ear, the cochlear nerve or the brainstem, and tinnitus as an initial symptom may be an indication of a greater tendency for tumour progression.[25] In our study those patients who presented changes to initial symptoms had tumour growth in 28.5% of cases, while those for whom symptoms were stable only had growth in 10.6% of cases, indicating that clinical changes were usually associated with tumour progression (P=.4). In our series, tumours associated with tinnitus, instability and sudden deafness at initial diagnosis grew more than those where progressive hearing loss was the only initial symptom, although the differences were not statistically significant (Fig. 5b). The size and the tumours with an extrameatal component are mentioned in many studies as factors which are related to growth. Although there are many authors who find no significant correlation between tumour size and growth, Fucci et al.[7] state that tumours over 20 mm tend to grow more than small ones, and there is a statistically significant relationship. The differentiation between intracanalicular and extracanalicular tumours, and their different susceptibility to growth, is present in many of the works on neurinomas in control. Walsh et al.[28] analysed 552 patients, finding that just 17% of intracanalicular tumours had grown, while there had been a extracanalicular tumour growth in 29% of cases. In our study, of the 9 patients with tumour growth, only 3 were intracanalicular tumours, whilst the other 6 presented extrameatal components. Tumour progression only occurred in 7% of our intracanicular tumours, in comparison with 20% in extracanalicular, indicating almost 3 times higher frequency in the latter tumour growth, with no statistically significant results (P=.19) (Fig. 3a). Furthermore, the percentage of tumours with recorded growth was higher among larger tumours (Fig. 3b). This indicates that the initial sizes and the component in the cerebellopontine angle (CPA) are factors which may determine tumour progression. Other authors state that growth during the first year is predictive of future progression in later years. Tschudi et al.[33] state they did not record any tumour growth after the first year of observation. However, in our patients, only 33.3% of tumours which grew did so during year one. The majority grew in size later. We also observed tumour progression in one patient even after

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A

Reference, year	Patients number	Mean follow-up time (years)	Initial mean size (mm)	Tumours grow >2 mm (%)	Intervention (%)
Glasock et al. 1997	48	2.4	8	32	59
Fucci et al. 1999	119	2.5	10	30	18.5
Modugno et al. 1999	47	3.0	11	No figure	19
O´Reilly et al. 2000	30	2.5	No figure	No figure	No figure
Raut et al. 2004	72	6.7	9.4	13	10
Battaglia et al. 2006	111	3.1	8.9	13	8
Bakkouri et al. 2009	325	No figure	No figure	12	18
Suryanarayanan et al. 2010	327	3.6	5.1	32	18.3
Mara˜ nón	73	3.0	11.5	12.3	8.3

B

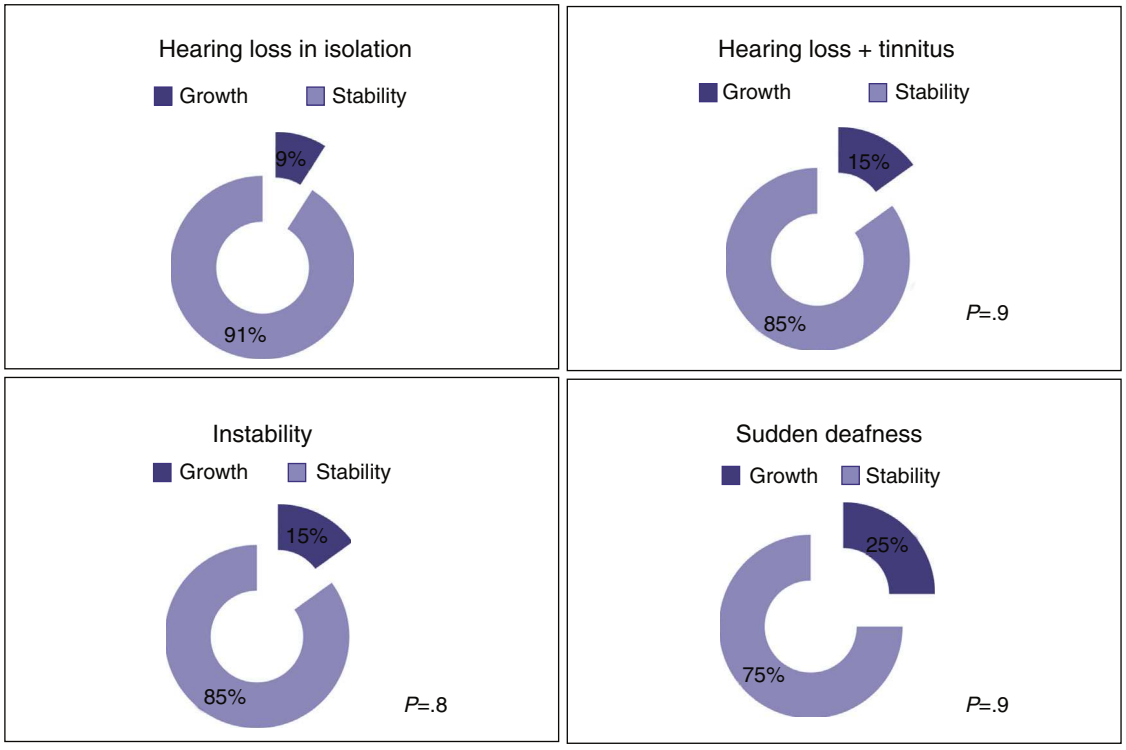

Figure 5 (A) Series of other authors on VS follow-up strategy. (B) Tumour progression relating to symptoms.

10 years of remaining stable under observation, which leads to the conclusion that potential growth is unpredictable and may occur many years after diagnosis.

In general, our indications for adopting a wait-and-see approach in VS treatment include the existence of patients of advanced age, with a bad general state of health, small tumours with few symptoms, a presence of useful hearing, and patient preference towards this approach. In the case of schwannomas with cystic components, which may suddenly lead to faster and less predictable growth, our

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recommendation is to perform surgery as soon as possible, or, alternatively maintain strict surveillance. In our series there are 3 patients with controlled cystic neurinoma. All of them present an extracanicular component and are under observation, 2 due to advanced age and another from personal preferences. There have been no significant changes to tumour size. In single ear tumours one option is follow-up, although contralateral ear rehabilitation or auditory rehabilitation option on the schwannoma side are options to consider. Extended translabyrinthine resection may be carried out in these tumours and if the cochlear nerve is preserved, a cochlear implant may be inserted in the same operation.[34] Among our patients were 2 with single ear tumours, which we kept under observation for years without growth or significant hearing deterioration. In general, if the patient is young and the tumour has grown, or useful hearing has been lost, we prefer to perform surgery as soon as possible since surgical results and facial nerve function is usually better with smaller tumours. If the tumour is intracanalicular, has not extended in the CPA, and tonal and verbal hearing levels are usable, a cranial excision of the middle fossa may be considered. Furthermore, if hearing is useful, the tumour has not extended to the back of the IAC and anatomical conditions are favourable, a retrolabyrinthine approach offers a relatively broad CPA access with the possiblity of auditive preservation. Equally, retrosigmoid resection offers the possibility of preserving hearing. However, it must be noted that these results are not frequently obtained and the percentage of usable postoperative hearing with this type of technique is usually very low.[12,13] If hearing is lost, the tumour is large, and has extended to the back of the IAC, we prefer the extended retrolabyrinthine approach, which offers greater tumour control, many possibilities of complete resection, and facial function is usually improved in our experience. Of the 6 tumours operated on after follow-up, 5 were performed using the translabyrinthine approach and one using the retrolabyrinthine approach. In general, the delay in surgery after the period of observation did not essentially alter results if the tumours had not grown significantly,[25] although it could mean losing hearing rehabilitation options. Another factor to consider is the patients with neurofibromatosis type II (NF2), who should sporadically be relieved of tumours because their histological characteristics and their growth pattern are different. Pre-emptive strategies are essential.

Conclusions

The ''wait and scan'' approach is adopted increasingly frequently in the initial management of a VS patient. Akin to other studies, ours shows that the conservative management of this type of tumour is a local alternative in the case of small neurinomas, since over time the majority of them grow only slightly or not at all. In our opinion, the patient should be informed of the possible therapeutic options (surgery, radiotherapy, observation), with an explanation of all risks and benefits. If observation is adopted as the approach, periodical check-ups of the patient should be made using audiometric controls and radiological testing to examine tumour behaviour and limit any possible complications. Familiarity with predictive factors in tumour growth will be essential in the future for wait-and-see VS management.

Conflict of Interests

The authors have no conflict of interest to declare.

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