Should Initial Surveillance of Vestibular Schwannoma Be Abandoned?

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ABSTRACT

Early diagnosis of vestibular schwannoma (VS) has increased in recent years because of increased longevity and availability of magnetic resonance imaging (MRI). Initial conservative radiological surveillance is often requested by patients and physicians to establish whether these tumors are growing before embarking on intervention. Initial observation of at least 1 year in all small VS was therefore recommended by some authors. We evaluated our prospective skull base database of VSs that were managed with initial radiological surveillance to establish when this policy should be abandoned and what predicts future growth. Fifty-four consecutive patients with VS in our institution who were managed by initial yearly MRI scanning were studied. The MRI data were collected prospectively and analyzed by Kodak CareStream viewing software where VS maximum diameters in three perpendicular planes and volume were calculated. One patient was excluded from the analysis as he had only one MRI follow-up. The median age of the 53 patients was 59 years (range, 26 to 86 years), 25 were males and 28 were females, and 33 were under 65 years of age; 18 VSs were extracanalicular, 18 were intracanalicular, and 17 extended both inside and outside the canal; 21 VSs were 1.2 cm³ or less, 22 were 1.2 to 4 cm³, and the rest were >4 cm³. Using volumetric analysis, 29.72% of conservatively managed VS grew by at least 2 mm per year, and 70.82% did not grow in 5 years. Age, gender, symptoms, and side did not predict future growth. However, growth in the first year was a strong predictor of future growth ($p < 0.001$) and initial volume was also a strong predictor of future growth ($p < 0.05$). Twenty-nine percent of observed VSs grew by at least 2 mm per year in the first 5 years of surveillance. As the growth rate is slow, initial radiological surveillance is justified in elderly patients and patients with small VSs and nonserviceable hearing. Growth in the first year was a strong predictor of future growth. The reported treatment effect should be interpreted in the light of 70.24% of VSs that either shrink or do not change in the first 5 years.

KEYWORDS: MRI, microsurgery, radiosurgery, schwannoma, vestibular

Vestibular schwannomas (VSs) represent ~6% of all intracranial tumors. They are benign, slow-growing tumors, arising from Schwann cells of nerve sheaths

of vestibular nerves, particularly the superior vestibular nerves. VS usually manifests as ipsilateral hearing impairment, which may go ignored by patient or dismissed

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by doctors. VS growth is difficult to predict in individual patients; however, continued growth of these tumors ultimately results in brain stem compression and gives rise to increased intracranial pressure. Early diagnosis offers patients a range of management options and may significantly reduce morbidity. These options vary from initial radiological surveillance, stereotactic radiosurgery, stereotactic radiotherapy, to microsurgery. The advent of magnetic resonance imaging (MRI) resulted in the diagnosis of asymptomatic VSs in patients who were scanned for other unrelated conditions.¹ The incidence of VS is around 13 cases per million people per year.² However, the incidence was reported to have increased over the past 20 years.³ This increased incidence is probably a reflection of better diagnostic methods, the aging population, and availability of MRI technology, rather than a true increase in VS incidence. Therefore, many VSs are discovered very small and in elderly patients and a dilemma of how best to manage these patients has arisen. We reviewed our prospective database to establish when initial radiological surveillance should be abandoned and to determine the predictors of future growth in VS.

PATIENTS AND METHODS

The prospectively collected data on patients with radiological diagnosis of VS were retrospectively analyzed to establish those who had initial radiological surveillance. These patients consisted of those who refused intervention (12) and those who either opted for or were advised initial radiological and clinical surveillance. Fifty-four patients were found in the database since the Kodak Carestream PACS (Kodak Carestream V1.01, Chicago, IL) system of MRI images was established in our institution. One patient had only one MRI in 2008 and had not had a second scan yet, and therefore he was excluded from this analysis, leaving 53 patients who had been followed for a minimum of 12 months. The decision of whether intervention or surveillance was adopted in each patient depended on tumor size, hearing function, comorbidity, and patient preference. Forty-one patients had no useful hearing at the time of presentation; 31 had tumors 4 cm³ or less in volume and decided to pursue radiological surveillance in preference

of intervention. Although 10 patients had tumors >4 cm³, 12 patients who had serviceable hearing were advised radiosurgery or microsurgery for management, and the pros and cons of each intervention was discussed with each patient, these 22 patients decided against intervention and elected to have initial surveillance. Of the 53 patients, 11 had intervention after the first year, leaving 42 patients who had 24 months of MRIs. Two of these had intervention after 2 years of observation and 11 are still waiting for their third MRI, leaving 29 patients who had 3 years of MRI. Two of the 29 patients had intervention after 3 years, and five were yet to have their fourth MRI, leaving 22 patients who completed 4 years of follow-up. Eleven of these patients have not had their fifth MRI scan, leaving 11 with 5 years of MRI. At the end of 5 years, one required intervention and seven were yet to complete their sixth year of MRIs (Table 1).

We collected information about the initial tumor size, volume, side, site in relation to the internal auditory canal, age, gender, and symptoms. We analyzed these results using linear and logistic regression methods to determine which factors predicted tumor growth. Growth was defined as an increase in diameter of VS by at least 2 mm between subsequent MRI scans in any three perpendicular planes. The 2-mm cutoff was to avoid the effect of MRI slice thickness and partial volume effects. Similarly, tumor shrinkage was defined as tumor-size reduction in any plane by at least 2 mm. MRI scans were performed on 1.5-T machines with 1-mm thickness without any slice gap using 512 × 512 matrix. T1-weighted, T2-weighted, three-dimensional magnetization prepared rapid-acquisition gradient echo and constructive interference steady-state sequence imaging protocols were used. In addition, each patient had T1-weighted imaging with gadolinium enhancement in axial and coronal planes.

The size of VS was measured using Kodak Carestream PACS software. The measurements were expressed in millimeters. We measured the anteroposterior diameter (*A*), medial-to-lateral diameter (*B*), and vertical diameter (*C*) in each MRI scan (Figs. 1 and 2). VS volume was calculated in cubic centimeters using the formula (*A* × *B* × *C*)/2. The first MRI scan measurements of the VS were used as a reference point for future comparisons.

Table 1 53 Vestibular Schwannomas Managed by Initial Radiological Surveillance

Months	Total	Grew* (%)	Shrank* (%)	Same (%)	Treated (%)	Censored
12	54	13 (24.5)	4 (7.5)	36 (67.9)	11 (29.8)	1
24	42	10 (23.3)	7 (16.7)	25 (59.5)	2 (4.8)	11
36	29	7 (24.1)	5 (17.2)	17 (58.6)	2 (6.9)	5
48	22	9 (40.9)	5 (22.7)	8 (36.4)	0	11
60	11	4 (36.4)	2 (18.2)	5 (45.5)	1 (9.1)	7

*Growth and shrinkage were defined as an increase or decrease in diameter by at least 2 mm in any dimension; growth and shrinkage in each 12-mo interval included new growth and continued growth. On average, vestibular schwannomas grew by ~29.8% per year in 5 y. Growth in the first year was strong predictor of future growth (*p* < 0.01).

Figure 1 Axial T1-weighted magnetic resonance image with gadolinium of vestibular schwannoma measuring 17.52 mm in maximum transverse diameter.

RESULTS

The median age was 59 years (range, 26 to 86 years), and there were 25 males and 28 females; 33 were under 65 years of age. Twenty-five of the VSs were right sided; 18 were totally intracanalicular; 18 were extracanalicular; and 17 extended inside the internal auditory canal and into the cerebellopontine angle. The initial maximum VS diameter and volume and the first-year follow-up data are illustrated in Table 2.

All 53 patients were followed for at least 1 year: in the first year, 24.5% of the VSs grew, 69.8% remained unchanged, and 5.7% shrank (Fig. 3). Eleven patients had intervention after the first year, leaving 42 patients followed for a second year: 9.5% of VSs grew, 35.7% remained unchanged, 16.7% shrank, and 14.3% continued to grow (Table 3). Two patients were treated at the end of the second year, and 11 had not yet had third MRIs by the time this review was undertaken, leaving 29 patients with a third-year follow-up: 10.3% of VSs grew, 44.8% remained unchanged, 19% shrank, and 11.9%

Figure 2 Magnified view of vestibular schwannoma shown in Fig. 1.

continued to grow (50% of those that grew or continued to grow in second year). Two patients had been treated after 3 years, and five had not had their fourth MRI, leaving 22 with fourth-year follow-up: none of the VSs grew, 36.4% remained unchanged, 22.7% shrank, and 40.9% continued to grow (all those grew or continued to grow during third year = 9). Eleven patients had not had fifth MRIs, and 11 had fifth-year follow-up: 9% of VSs grew, 45.5% remained unchanged, 18.2% shrank, and 27.3% continued to grow (one-third of those continued to grow during the fourth year; Fig. 3). No further growth or shrinkage was noted after the fifth year of those that did not grow in previous years (Fig. 3). Age, gender, side, and symptoms did not predict future growth ($p > 0.05$). However, growth in the first year was a strong predictor of future growth ($p < 0.001$), and VS volume $> 1.2 \text{ cm}^3$ at presentation was also a predictor of future growth ($p = 0.02$).

In addition to MRI follow-up, those who presented with serviceable hearing and 50/50 speech discrimination ($n = 12$; 22.6%) were also followed by yearly pure-tone audiograms. These 12 patients had decided against intervention and wanted initial radiological and clinical surveillance. Five of these patients had worsening hearing during the follow-up period (41.6%). Further

Table 2 53 Vestibular Schwannoma Managed by Initial Radiological Surveillance According to Their Initial Volumes

Outcome	$<1.2 \text{ cm}^3$	$1.2-4 \text{ cm}^3$	$>4 \text{ cm}^3$	Total	Number Treated
Unchanged	16 (76.2%)	13 (59.1%)	8 (80%)	37	8 (21.6%)
Grew $>2 \text{ mm}$	4 (19.1%)	7 (31.8%)	2 (20%)	13	8 (61.5%)
Shrank $>2 \text{ mm}$	1 (4.8%)	2 (9.1%)	0	3	0
Total	21	22	10	53	16 (30.2%)

Volume was significant predictor of vestibular schwannoma growth: the larger the volume, the more likely that the VS will grow in first year ($p = 0.03$).

Figure 3 Growth pattern of 53 vestibular schwannomas (VSs) managed initially with radiological surveillance demonstrating that the majority of VSs did not grow in the first 12 months. Y1 (year 1), 53 patients followed for 12 months; Y2 (year 2), 42 patients followed for 24 months; Y3 (year 3), 29 patients followed for 36 months; Y4 (year 4), 22 patients followed for 48 months; and Y5 (year 5), 11 patients followed up for 60 months.

growth of VS was associated with hearing deterioration in all these patients.

DISCUSSION

The management of small and asymptomatic VS is determined by patient factors, tumor factors, and availability of treatment options: microsurgery, stereotactic radiosurgery, stereotactic radiotherapy, or annual MRI. The latter has become more popular as many studies have demonstrated that these tumors grow slowly and may spontaneously shrink in size.⁴⁻⁶ Our study had demonstrated that VSs stayed the same size in 69.8% and shrank in 5.7% in the first year and that 24.5% grew by 2 mm in the same period, none of the tumors grew by more than 2 mm in the first 12 months, and there was no significant predictor of which VS will grow except initial VS volume of 1.2 cm³ or more. Therefore, initial conservative radiological surveillance with MRI is justifiable in all patients with small VSs (1.2 cm³) that present with nonserviceable hearing loss only. However, these patients should be warned that further tumor growth occurs in at least 24% of patients in 12 months and further growth is associated with hearing deterioration (41.6% in our study). Recent prospective, nonrandomized, matched controlled studies demonstrated better facial and hearing outcome following gamma knife radiosurgery.^{7,8} However, neither microsurgery nor ra-

diosurgery has been proven superior in a prospective, multicenter, randomized, controlled trial setting. Furthermore, no such studies have been published comparing either intervention technique against clinical and radiological surveillance.

In 1998, radiological surveillance literature was reviewed using MEDLINE from 1966 to 1997.⁹ The authors found 571 VSs that were followed up by imaging; 54% of the VSs grew within an average of 3 years. Based on this finding, the authors recommended radiological surveillance should be reserved to those who refuse intervention, those who have VS on the only hearing ear, or those who were unfit to have intervention. However, this was a retrospective review of published retrospective noncontrolled studies with short-term follow-up, without detail of how VS growth was assessed. Our study was prospective and used sophisticated software to measure VS growth; this is the first study to use VS volume rather than maximum diameter. Our study demonstrated 24.5% of VSs grew in the first year, another 9.5% grew in the second year, and 10.4% grew in the third year. By the end of 3 years, 44.4% grew compared with the 54% reported in the review.⁹ Flint et al reported 100 VSs less than 24 mm in maximum diameter followed for a mean of 25.5 months¹⁰; 36% grew, and there were no predictors of growth. However, 80% of VSs that grew did so in the first year; 22% of patients were eligible for hearing preservation with only 5/15 losing hearing after treatment.

Our study demonstrated that growth in the first year was a strong predictor of future growth. We also found that VS volume of 1.2 cm³ or more was associated with future growth. Future growth of VS can lead to hearing loss; 5 of 12 patients in our study lost eligibility for hearing preservation intervention because of tumor growth. Nevertheless, careful radiological and clinical surveillance is safe in patients with small VSs and does not result in more morbidity.¹⁰ We agree with other authors, who recommended an initial 1-year radiological surveillance in small VSs,⁴ but we propose that small VSs are those of <1.2 cm³ in volume, and we only recommend 1-year surveillance to those who present with nonserviceable hearing, as those who present with serviceable hearing are eligible for hearing preservation of up to 70% or more should they choose to be treated.

If the VS grows by more than 2 mm in any dimension in the first year, intervention is recommended.⁴ However, we propose that volume of the VS

Table 3 The Outcome of Vestibular Schwannomas That Grew in Previous Years

Year of Follow-up	Grew in Past Years	Treated (%)	Stopped Growing (%)	Continued to Grow (%)
2	13	4 (13.8)	3 (23.1)	6 (46.2)
3	10	2 (20)	3 (30)	5 (50)
4	7	2 (28.6)	0	5 (71.4)
5	9	0	0	9 (100)

also be measured using readily available software, and if the initial VS volume is $>1.2 \text{ cm}^3$, interventions should be considered. We also agree with those who recommended that surveillance should be abandoned in favor of intervention if the tumor grows by 2 mm or more in the first year.^{5,6} Our study also found that the most reliable predictor of future VS growth is growth in the first year: 46.2% of VSs that grew in the first year also grew in the second year, and 60% of those that grew in second year also grew in the third year.

Another group of authors recommended intervention for VSs of 15 mm or bigger and that radiological surveillance could be stopped if tumors were unchanged after 3 years.¹¹ We observed no shrinkage in any of the tumors that were $>4 \text{ cm}^3$ in volume (10 patients); however, most of these patients had intervention after 1 year of follow-up (two had radiosurgery and eight had microsurgery). However, VS volume of 1.2 cm^3 or more was associated with future growth. We observed no further growth of tumors that were stable for 3 years, supporting the notion that if the VS was stable for 3 successive years, radiological surveillance could be spaced to one MRI every 2 to 3 years. However, this recommendation could not be justified in patients who had larger VSs ($>1.2 \text{ cm}^3$) or those who present with serviceable hearing loss. In our series, we had only 12 patients with serviceable hearing because it was our policy to offer treatment options to those who present with serviceable hearing loss. These 12 patients represent less than 12% of those who presented with serviceable hearing loss and were offered therapy in our institution. We offer such patients up-front intervention because of the higher chances of hearing preservation with early intervention and smaller VSs reported in the literature.^{12–18} Samii and Matthies reported the largest series treated with microsurgery with hearing preservation rate of 47 to 88%.¹² Glasscock et al reported a hearing preservation rate of 35% after stereotactic radiosurgery in 1993,¹⁶ and Thomassin et al reported 70% hearing preservation rate in those who had normal hearing before treatment and 50% rate in those who had serviceable hearing loss using gamma knife radiosurgery.¹⁷ An extensive review of the radiosurgery literature was performed in 2009 by Yang et al and published in 2010;¹⁸ the authors concluded that hearing preservation rate depended on tumor size and preoperative hearing loss.

CONCLUSION

Initial radiological surveillance is justified in patients with small VS $<1.2 \text{ cm}^3$ and nonserviceable hearing loss. Yearly MRI needs to be continued for at least 3 years in these patients as long as the VS size remains stable. The main predictors of VS future growth is growth in the first year of follow-up and initial tumor volume of 1.2 cm^3 or more. The outcome of interventions in small

VSs needs to take into consideration that $>40\%$ of VSs do not grow and up to 20% shrink in the first 5 years after diagnosis without treatment.

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