Incidental vestibular schwannomas: a review of prevalence, growth rate, and management challenges

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With the relatively recent increase in the use of MRI techniques, there has been a concurrent rise in the number of vestibular schwannomas (VSs) detected as incidental findings. These incidental VSs may be prevalent in up to 0.02%–0.07% of individuals undergoing MRI and represent a significant portion of all diagnosed VSs. The management of these lesions poses a significant challenge for practitioners. Most incidental VSs tend to be small and associated with minimal symptoms, permitting them to be managed conservatively at the time of diagnosis. However, relatively few indicators consistently predict tumor growth and patient outcomes. Furthermore, growth rates have been shown to vary significantly over time with a large variety of long-term growth patterns. Thus, early MRI screening for continued tumor growth followed by repeated MRI studies and clinical assessments throughout the patient’s life is an essential component in a conservative management strategy. Note that tumor growth is typically associated with a worsening of symptoms in patients who undergo conservative management, and many of these symptoms have been shown to significantly impact the patient’s quality of life. Specific indications for the termination of conservative management vary across studies, but secondary intervention has been shown to be a relatively safe option in most patients with progressive disease. Patients with incidental VSs will probably qualify for a course of conservative management at diagnosis, and regular imaging combined with the expectation that the tumor and symptoms may change at any interval is crucial to ensuring positive long-term outcomes in these patients. In this report, the authors discuss the current literature pertaining to the prevalence of incidental VSs and various considerations in the management of these lesions. It is hoped that by incorporating an understanding of tumor growth, patient outcomes, and management strategies, practitioners will be able to effectively address this challenging disease entity.

Key Words • incidental lesion • vestibular schwannoma • vertigo • acoustic neuroma • tumor growth • conservative management • hearing preservation • quality of life

Abbreviation used in this paper: VS = vestibular schwannoma.
We reviewed the latest research with regard to the prevalence and presentations of incidental VSs. In this paper, we discuss how tumor growth rates and clinical outcomes relate to the management of these lesions, including the benefits and pitfalls of conservative management techniques. Our goal is to elucidate how the latest research can help to guide the clinician to effectively manage the increasing number of patients likely to present with incidental VSs.

**Epidemiological Data**

Early attempts to define the prevalence of VSs in the general population were made in cadaveric studies in both the pre- and post-MRI era. These studies involved the serial dissection of numerous temporal bones from deceased patients and ultimately suggested a prevalence of around 0.8%–2.4% (Table 1). Since VSs had not been diagnosed in these patients’ lifetimes and the patients may not have undergone a workup for symptoms related to VSs, in theory these early study results could correlate well with the actual prevalence of asymptomatic incidental VSs. However, the numerous limitations in studying only cadavers make it difficult to generalize these results to the entire population. Primarily, the fact that these studies were conducted in patients who were no longer living results in an obvious selection bias for older patients with other significant comorbidities. Furthermore, cultural differences, changes in the practice of medicine, and changes in our understanding of VSs throughout the time periods in which these studies were conducted probably meant that a number of these tumors were undiagnosed in life, adding further bias to the results. As a consequence, these values probably represent a gross overestimation of the actual prevalence of incidental VSs within the current population. Regardless, the relative consistency of these findings suggests that the results are not entirely baseless and may represent a close estimate of the prevalence of VSs in older populations at the time that these studies were conducted.

In contrast to those early cadaveric studies, more recent attempts to elucidate the prevalence of VSs in patients not suspected of having the disease have taken advantage of modern advances in imaging technology. With the advent of MRI, researchers can retrospectively analyze large imaging databases, enabling them to include a wider variety of patients and yield sample sizes significantly greater than what was possible with cadaveric studies (Table 2). It has been shown that VSs account for approximately 0.2% of incidental MRI findings. Two studies in particular have provided the best illustration of the prevalence of incidental VSs in patients not suspected of having the disease. In the first of these studies, Anderson et al. found 17 patients with unsuspected VSs after reviewing 24,246 MRI studies obtained for reasons other than ruling out a VS or evaluating patients with tinnitus, sensorineural hearing loss, or vertigo. This yielded a VS prevalence of 0.07% in patients in whom no VS was suspected. More recently, Lin et al. analyzed 46,414 MR images obtained for reasons other than audiovestibular signs, revealing a much lower prevalence of 0.02%, or only 8 patients with a positive reading. These latter authors determined that the difference between the two studies was statistically significant, ultimately attributing the discrepancy to numerous factors. They cited the increase in the number of MRI studies, the shorter time period analyzed by Anderson et al., and differences in the criteria of accepted MRI studies as possible reasons for this discrepancy. Moreover, Lin and colleagues specifically excluded studies on the internal auditory canal, whereas Anderson and associates did not. Imaging studies of the internal auditory canal are usually conducted to rule out a VS, even though it may not have been specified in the imaging database. Thus, the prevalence of 0.02% proposed by Lin et al. probably represents the best estimation of incidental VSs to date.

Interestingly, the study by Lin et al. also revealed a number of other patient variables associated with finding a VS on MRI. The number of patients presenting with VSs, whether symptomatic or not, was not statistically significant for a sex difference; however, when the study was limited to just those patients with an incidental finding, men represented a significantly larger proportion of the study group. The authors postulated that this could be the result of behavioral differences; that is, men may be less likely to seek treatment or consult a physician for audiovestibular concerns. This point was illustrated by a male patient who presented with an incidental finding but later reported profound unilateral deafness on further questioning after receiving the MRI results. Actually, 5 of the 8 patients determined to have incidental findings later reported significant audiovestibular symptoms that were not initially related when their histories were taken. This finding implies that while the Lin et al. study shows a lower prevalence of incidental VSs as compared with that in the Anderson et al. study, the actual number of truly asymptomatic patients with positive findings could be even lower than suggested if one assumes that all patients with symptoms can be ruled out by taking a thorough history. Regardless, both of these studies were within a...
Incidental vestibular schwannomas

similar order of magnitude compared with the cadaveric studies and probably represent a closer assumption of the real prevalence of incidental VSs.

Despite the prevalence of incidental VSs within the general population, in neurosurgical practice these lesions represent a significant fraction of the patients presenting with positive MRI findings. In a study conducted by Jeyakumar et al., among 121 patients with diagnosed VSs, the lesions were incidentally discovered in 15 (12.3%) of them. In direct contrast to the findings of Lin et al., Jeyakumar and colleagues showed that incidental VSs were diagnosed 4 times as many women than men, although the authors did not offer an explanation for this finding. Additionally, they showed that there was no age difference between those presenting with symptomatic VSs and those with incidental VSs. By putting all of these studies in the context of neurosurgical practice, it can be determined that patients with incidental VSs represent a significant portion of the neurosurgery patient base and that a diagnosis of VS will probably result from an incidental finding in a notable percentage of patients with VS. Therefore, neurosurgeons must have an intimate understanding of the tumor characteristics and treatment choices for incidental VSs, as they are likely to encounter this disease entity in their practice.

Growth Patterns and Natural History

Recently, an extensive body of literature has emerged discussing the natural history and growth patterns of VSs in both symptomatic and asymptomatic patients. A thorough understanding of the variety of characteristics associated with tumor progression is crucial in determining the proper care of patients who are asymptomatic with incidental findings. We are not aware of any studies specifically focused on the growth rates of incidental or asymptomatic tumors by themselves; however, numerous studies have been conducted to characterize the natural history and growth patterns of VSs that were not subjected to any initial intervention. An understanding of growth patterns in these tumors is paramount to guiding long-term treatment and follow-up decisions.

In general, VSs tend to be a relatively slow-growing lesion as compared with other more malignant intracranial tumors, with many showing little to no growth after diagnosis. A recent meta-analysis conducted by Nikolopoulos et al. showed that the rate of tumor growth varies significantly among patients who undergo conservative management. In 41 of the studies included in that review, the number of tumors demonstrating growth varied from 6% to 73%, with the rate of individual tumor growth varying significantly as well, from 0.3 to 4.8 mm/year. While the mean growth rate varied between 1 and 2 mm/year for all tumors, the growth rate was between 2 and 4 mm/year when only tumors that grew were considered. Moreover, some studies in the meta-analysis documented exceptional growth rates in excess of 15 mm/year. Nikolopoulos and colleagues also demonstrated that tumors showing only continuous growth represented a minority of the lesions, accounting for only 15%–25% of the tumors across the studies. Another meta-analysis conducted by Yoshimoto also reported a wide range of variability among studies, with 15%–85% of tumors showing growth. This author also demonstrated an overall growth rate of 1.2 mm/year. Taking into consideration all studies in the meta-analysis, he established that an average of 46% of tumors showed growth. However, he also indicated that the percentage of tumors that were determined to grow was greatly affected by the type of study conducted. The average percentage of growing tumors was 39% in the studies in which MRI alone was used and only 29% when considering only prospective studies. This finding suggests that the number of tumors that grow may actually be lower than initially predicted, as higher-quality studies are likely to be more representative of real growth characteristics. Interestingly, both of these reviews also showed that a significant portion of tumors actually regress, which occurred in 8%–22% of tumors.

Studies have shown that “tumor growth” is a broad descriptive term used to identify what is actually a largely heterogeneous group of tumor growth patterns. Three studies in particular have attempted to characterize VSs into specific groups based on their growth patterns (Table 3). What these studies have shown is that there is not a one-size-fits-all description that characterizes tumor growth patterns. Furthermore, how the growth rate at one interval fits into the entire natural history of the tumor is largely unpredictable. Thus, it is crucial that practitioners appreciate the variability in individual tumors and do not use a growth rate from one interval to define the rate for future intervals. For example, just because a patient presents with a small incidental tumor that reduced in size on the first follow-up scan does not mean that future scans are unnecessary. At any moment the growth rate of that tumor can change.

There have also been attempts to define independent patient and tumor characteristics that can predict tumor growth. For example, Yoshimoto proposed that larger tumors represent a lower risk for future VS enlargement. Solares et al. also suggested that tumor size plays a role in defining tumor growth, showing that 5-year no-growth rates vary significantly among intracanalicular, Grade I tumors.

<table>
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<tr>
<th>Growth Pattern</th>
<th>Shin et al., 2000</th>
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* Values expressed in %. Note that the specific radiological definitions used for growth varied slightly among the studies. Moreover, the exact names for growth patterns were altered for simplification, and not all patterns were accounted for in every study. Abbreviation: NA = not applicable.
tumors, and tumors above Grade I (89.8%, 73.9%, and 45.2% respectively). These latter authors also suggested that when analyzed separately based on tumor size, women had a significant difference in growth rates, showing growth in 90.9% of VSs smaller than 10 mm, as compared with 62.3% of VSs larger than 10 mm. However, as illustrated in the extensive meta-analysis conducted by Nikolopoulos et al.,22 there is marked variability in the significance and outcomes associated with independent predictive variables across studies. While some indicated that the growth pattern within the 1st year was a significant indicator of tumor behavior, other studies directly contradicted this assertion.5,24 The same was true when initial tumor size was used to predict growth, that is, with contradictory evidence suggested across studies.7,18,22,23,25 However, Nikolopoulos and colleagues did assert that cystic tumors tend to have a higher growth rate (approximately 3.7 mm/year) as compared with solid tumors. Regardless, no other consistent indicators of growth were revealed across the multiple studies: not age, initial lesion size, duration of symptoms, tumor laterality, or patient sex. However, the authors did admit that there were several limitations to their review, including variability in follow-up, different use of imaging studies, multiple publications from different institutions, and even the inclusion of patients with neurofibromatosis Type 2 in some studies in which a clear distinction was not specified. Thus, further large-scale prospective studies are needed to effectively elucidate possible predictors of growth as well as potential mechanisms leading to growth or regression.

Management Selection Strategies

Currently, 3 basic options exist for managing newly diagnosed VSs: 1) microsurgical removal; 2) radiation therapy, including stereotactic radiosurgery and stereotactic radiotherapy; and 3) conservative management. Specific treatment decisions at the time of VS diagnosis are poorly standardized at this point, with extensive variation in protocols among practice settings, but in general they have been determined based on tumor size, associated symptoms, and specific patient indicators. Details on the efficacy of and outcomes for primary interventional therapies, namely the use of microsurgery and radiation therapy at the time of diagnosis, have been well characterized in the literature.19,20,34,36 Recently, however, conservative management via serial radiological studies has become increasingly popular in patients with smaller tumors, especially when they are minimally or completely asymptomatic.22,34,41 The reasoning behind adopting a “wait-and-scan” approach is based on two fundamental ideas. First, a high proportion of the tumors do not grow following diagnosis. Second, there is sparse evidence to indicate that the treatment of a nongrowing lesion is beneficial. In contrast, surgery or radiotherapy can result in significant complications and is best avoided when unnecessary.20 Therefore, conservative treatment in patients with smaller tumors ultimately enables them to avoid the possible complications of primary intervention while allowing practitioners to closely monitor their status over time.

As discussed above, existing data on tumor growth rates, growth patterns, and predictors of growth suggest that there is extensive variability in tumor behaviors across patient populations and that there are few indicators that can accurately predict tumor growth. Given the dearth of consistent evidence, it is difficult to provide specific recommendations on who should undergo conservative management and how they should be monitored. However, a few protocols have been suggested to determine which patients should be conservatively monitored.3,29,30,32 One of the most cited studies used the following criteria to select patients for conservative management: advanced patient age (> 60 years), poor health or significant medical risks for surgery, risk of further hearing loss (American Academy of Otolaryngology–Head and Neck Surgery Level A or Level B), small tumor size (Koos Grade I or 2), minimal or no incapacitating symptoms, and patient preference.3 Other protocols have generally used similar selection criteria, including symptoms, patient age, and size of the tumor.

By definition, incidental VSs tend to be associated with few if any symptoms, with rare exceptions.1,14 Additionally, these lesions tend to be smaller than symptomatic VSs, with one study showing a significant size difference of 1.09 versus 1.50 cm between asymptomatic and symptomatic lesions, respectively.13 Furthermore, it has been suggested that small and medium-sized incidental VSs tend to have a more benign course and ultimately require less intervention (47% vs 76%, small and medium versus larger lesions).11 Therefore, the majority of incidental VSs will likely qualify for conservative management according to the above criteria. As mentioned, a few exceptions do exist, including instances in which symptoms are elucidated with further history taking after a positive imaging study44 or a large high-risk tumor is discovered. Asymptomatic VSs have been reported to be as large as 5 cm.11

Specific strategies for follow-up have also been recommended. Martin et al.16 suggested an initial rescan with MRI at 6 months posttreatment followed by scans annually for 2 years and then every 5 years for the remainder of the patient’s life. They recommended reassessment if growth > 2 mm occurs at any interval. The rationale behind their protocol was based on their findings that 90% of the patients demonstrating tumor growth did so before 3 years elapsed and the remaining 10% manifested growth within 6 years. Furthermore, the necessity of MRI as opposed to other screening options was emphasized. Such screening options included hearing tests, which were reported to be equivocal between lesions that grew and those that did not.29,31,32 Interestingly, in line with the findings of Nikolopoulos et al.,22 Martin and colleagues16 also suggested that cystic tumors should be followed more closely, as they represented a disproportionate percentage of the tumors that grew, especially in cases in which a solid tumor converted into a cystic one.

The protocol established by Martin et al.16 contrasts with the one proposed by Strangerup et al.,32 who suggested annual scans for 5 years after treatment and then follow-up scans at 7, 9, and 14 years after treatment. Smouha et al.29 proposed a different strategy, suggesting that those selected for conservative management should undergo MRI studies at 6 months after treatment and ev-
Incidental vestibular schwannomas

ery year thereafter. Regardless of the specific regimen, all of the studies agree that most tumors showing growth will do so early in the follow-up period. However, the lack of predictability for long-term growth or changes in growth patterns throughout the natural history of individual tumors requires extended follow-up of patients via serial imaging, and practitioners should anticipate growth at any interval.

While we do not specifically endorse one protocol over another or propose our own protocol for conservative management, we do believe that patients should be monitored at regular intervals throughout the course of their lives. Additionally, we support the notions of Nikolopoulos et al., who emphasized the significance of educating and counseling patients with incidental VSs about the lack of predictability in tumor growth and the importance of patient compliance. A thorough discussion about the method and frequency of follow-up should take place, and any barriers in the patient’s life that can lead to poor compliance should be thoroughly explored. The insufficient follow-up of patients undergoing conservative management to monitor growth can result in catastrophic consequences and increase the risks associated with secondary intervention.

Outcomes of Conservative Management

It is postulated that all symptomatic VSs probably have a silent asymptomatic period before presentation to a physician, providing the conceptual rationale for the existence of asymptomatic patients who present with incidental findings. The evolution of symptoms and neurological deficits in initially asymptomatic or minimally symptomatic patients with conservatively managed VSs, while varying significantly from patient to patient, tends to follow certain patterns that correlate with certain stages of increasing lesion size as well as with the location of the lesion. Given that most patients with incidental VSs probably qualify for conservative management, an understanding of how these tumors progress, the effect that this form of management has on the later development of symptoms, and how conservative management affects long-term quality of life is paramount to the successful long-term management of these lesions.

One of the most heavily studied outcomes in regard to conservative management is its effect on long-term hearing preservation. Hearing loss has been suggested to be an integral part of the natural history of VSs, possibly as a result of ischemia of the inner ear or protein shedding from the tumor. Prior studies have shown that hearing may be preserved in up to 49% of individuals undergoing conservative management, while hearing preservation rates vary between 17% and 68% in patients undergoing primary microsurgery. Whitmore et al. suggested that conservative management is associated with a significantly higher incidence of functional hearing loss; however, at this point, the comparison of hearing outcomes between conservative management and other forms of therapy is largely inconclusive. The latest prospective study on conservative management by Breivik et al. suggested that hearing deteriorates in patients over time, regardless of treatment or tumor growth.

Multiple attempts have been made to elucidate the risks for hearing loss based on various tumor and patient characteristics. Sughrue et al. reported an overall hearing preservation rate of 54% in patients undergoing conservative management, showing that tumors with a slower growth rate (≤ 2.5 mm/year) were associated with a significantly higher rate of hearing preservation as compared with lesions that grew faster (75% vs 32%, respectively). However, other studies have suggested that tumor growth is not a reliable indicator of hearing loss. Furthermore, Bakkouri et al. attempted to classify risk factors based on initial tumor size. These authors reported that patients with preserved hearing tended to have larger initial tumor sizes (11.5 vs 9.3 mm). Taken together, these studies suggest that the impact of specific tumor factors, such as initial size and growth rates, is highly variable.

The relationship between hearing loss and quality of life in the context of other complications is also an important parameter requiring discussion. Breivik et al. showed that hearing deterioration actually had little impact on quality of life, except in terms of social functioning in those with complete unilateral hearing loss. In contrast, previous retrospective analyses suggested that the negative impact of hearing loss was greater than all other complications, including weakness, numbness, spasm, pain, tinnitus, or even hydrocephalus. However, these findings do not necessarily mean that the effect of hearing loss on the quality of life was a significant change from the baseline status of the patient since the study was conducted retrospectively. Again, these data show conclusions in this regard are highly variable. In general, we suggest taking a case-based approach to patients with incidental VSs, focusing on both the hearing status at various intervals and how it affects patients’ quality of life and perception of their illness, ultimately using their subjective hearing experience combined with radiological indicators to guide further management.

Other symptoms besides hearing loss have also been discussed in terms of long-term outcomes of conservative management and patient quality of life. Of these symptoms, tinnitus, vertigo, and balance disturbances have been the most heavily studied. Whitmore et al. suggested that the incidence of tinnitus and vertigo is significantly higher in patients undergoing conservative management as opposed to primary intervention. Tinnitus was also shown to be significantly associated with tumor size and type of hearing loss. Interestingly, however, Breivik et al. suggested that, after a period of conservative management, tinnitus was not significantly associated with a reduced quality of life as compared with baseline conditions. Additionally, they showed a significant reduction in the number of patients experiencing vertigo after a period of conservative management. However, the presence of vertigo was also associated with a significant reduction in quality of life. While it is clearly important to follow hearing loss and tinnitus as possible indicators of worsening clinical progression, the presence of vertigo may have the greatest impact on patient quality of life since it is often a debilitating symptom. Thus, the discussion of vertigo in addition to tinnitus and hearing loss is a vital part of patient follow-up in conservative management.
Conversion to Active Treatment

Understanding the frequency of treatment failure as well as when to intervene is an integral aspect of adopting a conservative management strategy. The overall failure rate, defined as conversion to an active treatment, has been found to be 15%–50%.5,21,29,30 Smouha et al.29 reported that 43% of patients undergoing conservative management ultimately demonstrate positive tumor growth. However, only 20% of the patients undergoing a conservative regimen required definitive treatment, suggesting that treatment failure is not directly linked to tumor growth. When analyzed prospectively, the likelihood of requiring treatment is 13.3% at 2 years and 41.3% at 5 years, suggesting that during a longer follow-up period more patients will require secondary intervention.3 Fortunately, secondary intervention has been shown to be relatively safe. Numerous studies have also demonstrated that the incidence of postoperative complications is similar between patients undergoing primary surgery and those undergoing surgery due to failure of conservative management.4 Note, however, that there was an increased risk of hearing deterioration with delayed surgery.3 Furthermore, up to 83% of patients in whom conservative therapy fails will disproportionately undergo microsurgery.30 This finding is interesting, suggesting that further investigation into factors determining the selection of microsurgery versus radiotherapy in secondary management, as well as the outcomes that these two strategies have on these patients, would be useful in guiding future management decisions.

Numerous indicators suggest the failure of conservative management and the commencement of secondary intervention. Overt clinical deterioration is a clear indicator to cease conservative management and implement secondary treatment. However, other less obvious indicators can be used as well. Currently, tumor growth rate is a commonly used parameter to indicate the failure of conservative management. Most studies suggest that in patients with small conservatively managed tumors, growth rates > 2–3 mm/year or significant worsening of symptoms should signal the need for treatment.10,16,35 Bakkouri et al.3 found that conservative management failed in 23.7% of their patients. They characterized treatment failure by a tumor growth rate ≥ 3 mm between two consecutive MRI studies, disabling vertigo, hearing deterioration, patient choice, or seeking a second opinion from another provider. When utilizing hearing loss as a parameter of failure, it has been suggested that a growth rate > 2.5 mm/year is a strong predictor of failed conservative management at the 3-year follow-up in patients with tumors < 25 mm on presentation.36 However, it was shown that regardless of the presentation, more than half of the patients managed with observation did not show tumor enlargement (52%–57%), and only 16%–21% required therapy within a period of 3 years.41 In general, secondary intervention was required in only a minority of patients managed conservatively and tended to be successful in most of these patients. Thus, we suggest that conservative management with careful follow-up is an appropriate therapy in almost all cases of incidental VSs.

Conclusions

With the advent of advanced imaging technologies, an increasing number of patients have been diagnosed with VSs as incidental findings on studies conducted for alternate reasons. These patients probably represent a significant fraction of all patients presenting for the management of VSs. Because these lesions are smaller, produce minimal symptoms, and are relatively indolent, a trial of conservative management is probably appropriate in the majority of cases. And although current data indicate that tumor growth occurs in a minority of patients, long-term growth is largely unpredictable and may follow a wide variety of specific patterns. Furthermore, patients undergoing conservative management can later present with symptoms that significantly affect their quality of life and everyday functioning. Numerous protocols for the selection of and follow-up in conservative management have been proposed, but no large-scale multiinstitutional prospective studies have compared the various options or addressed specific risk factors for tumor growth, symptom onset, or overall treatment failure. Thus, we recommend that practitioners take an individualized approach with early initial follow-up and continued lifelong management, emphasizing the importance of continued contact and observation for both clinical and radiological deterioration.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Liu, Schmidt, Boghani. Acquisition of data: Schmidt. Analysis and interpretation of data: Schmidt, Boghani, Choudhry. Drafting the article: Schmidt, Boghani. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Administrative/technical/material support: Liu, Choudhry, Eloy. Study supervision: Liu.

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Incidental vestibular schwannomas


