Acoustic neuroma observation associated with an increase in symptomatic tinnitus: results of the 2007–2008 Acoustic Neuroma Association survey

Clinical article

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Object. Tinnitus is a known presenting symptom of acoustic neuromas, but little is known about the impact of observation or treatment on tinnitus. Most patients experience improvement with treatment, while others may worsen. Therefore, this study was designed to assess the overall impact of observation and treatment on tinnitus outcome in patients with acoustic tumors.

Methods. Data from the 2007–2008 Acoustic Neuroma Association survey were used. Tinnitus severity was graded both at presentation and at last follow-up for all patients questioned. This data set was analyzed using the Student t-test and a linear regression model adjusted for possible confounders.

Results. Overall there were more patients receiving intervention (n = 1138) for their acoustic neuromas than observation (n = 289). Presenting tumor size positively correlated with tinnitus severity score. Regardless of treatment (microsurgery or stereotactic radiosurgery), tinnitus improved at last follow-up and worsened in those who were observed (p = 0.02). When comparing microsurgical options, retrosigmoid and translabyrinthine resection improved tinnitus symptoms (both p < 0.01). Stereotactic radiosurgery had a treatment effect similar to microsurgery.

Conclusions. Presenting tinnitus severity correlates strongly with tumor size. Furthermore, regardless of treatment, there appears to be an overall reduction in tinnitus severity for all forms of microsurgery and stereotactic radiosurgery. Importantly, observation leads to a worsening in symptomatic tinnitus and therefore should be weighed in the treatment recommendation.

Key Words • tinnitus • survey research • Acoustic Neuroma Association • oncology • skull base • vestibular schwannoma

In the famous court ruling of Jacobellis v. Ohio (1964), a phrase was made famous by Supreme Court Justice Potter Stewart to describe a threshold test for obscenity: “You know it when you see it.” Tinnitus can be described in a similar fashion, that is, you know it when you hear it. The word “tinnitus” is derived from a Latin term that means ringing, but is defined as the perception of sound within the ear in the absence of an external source. Tinnitus has a plethora of causes, but patients with acoustic neuromas commonly present with this symptom. Tinnitus is a presenting symptom in 73% of patients with radiographically confirmed acoustic neuroma according to the most recent ANA survey results, a rate that is increasing since the original survey results (57%) in 1983.1

Previously, microsurgery has been shown to improve tinnitus in relation to preoperative severity.2,6,7,10,12,15 Kam eda et al. reported in 2010 that in 242 patients undergoing retrosigmoid resection of their acoustic neuroma, tinnitus disappeared in 25% of patients, 33% improved, and only 10% worsened postoperatively.6 Furthermore, vestibulocochlear nerve sectioning did not impact postoperative tinnitus in this study.6 Stereotactic radiosurgery can similarly improve postoperative tinnitus and appears to be dose dependent.15 In contrast, current treatment strategies regarding acoustic neuromas guided by the Danish study by Stangerup et al. suggest that surgeons should observe small acoustic neuromas (those 1.5 cm or less).13,14 This

Abbreviation used in this paper: ANA = Acoustic Neuroma Association.
Tinnitus and acoustic neuroma treatment

recommendation is based solely on size progression with time, and excluded patients who underwent hearing preservation surgery.\textsuperscript{14} Therefore, although observation as suggested in this now-classic article guides intervention for patients based on radiographic measurements, we are left to wonder what we should do in the symptomatic patient?\textsuperscript{9--11} Furthermore, how do we counsel a patient with symptomatic tinnitus and a tumor who is about to enter observation? This study utilizes data accumulated in the 2007–2008 ANA survey,\textsuperscript{1} which asks patients to objectively grade their presenting symptoms (pertinent to this study, tinnitus) and compare them to their most current assessment of their tinnitus. Utilizing this data, we assessed the following question: does observation lead to a change in a patient's tinnitus with time?

**Methods**

The ANA is a nationwide organization, independent of treatment center, whose serial survey publications have offered insight into acoustic neuroma diagnosis and management since its initial publication in 1983. The 2007–2008 ANA online survey offers a patient-perspective view of current acoustic neuroma symptomatology and treatment trends. Email requests were sent to 4000 members of the ANA, of which 2004 responses (50\% response rate) were collected as of February 2008 (http://anausa.org/index.php/patient-surveys). Notably, the 2007–2008 survey results differentiated diagnosis of neurofibromatosis Type 2 patients or other lesions besides acoustic neuromas (most commonly meningioma), and only acoustic neuromas were analyzed in this study. The database provided primary and secondary treatments of these tumors, but only the index procedure was used in analysis (http://anausa.org/index.php/patient-surveys). Furthermore, only patients reporting tinnitus as a symptom, either at presentation or currently, were used. Finally, fractionated radiation was not assessed as this is typically not offered as a primary treatment modality in current practice, and if fractionated radiation is offered, there are often other factors driving this decision.

Tinnitus severity was used as a continuous variable by asking respondents at initial presentation, and presently, to grade their tinnitus on a 10-point scale, from 10 (most severe/disabling) to 1 (least severe/mild). Data were analyzed using JMP version 9.0, Prism version 5.0, and SAS version 9.3. The Student t-test for bivariate analysis and ANOVA for multivariate analysis were used. A linear regression model was used to study the relationship between the change of tinnitus severity from baseline to the most recent survey, and different treatments, adjusting for possible confounders (sex, race, tumor size at diagnosis, and others). A p value < 0.05 was considered statistically significant.

**Results**

**Tinnitus by Treatment**

Overall, there were 1138 patients reporting treatment and 289 patients reporting no treatment or observation in this study. Presentation tinnitus scores (3.7 ± 0.1, mean ± SEM) worsened compared with last follow-up tinnitus scores (mean 4.1 ± 0.2) when no intervention was undertaken (p = 0.018). However, regardless of treatment type, the presentation tinnitus score was 4.3 ± 0.1 (mean ± SEM) compared with the most recent tinnitus score (3.8 ± 0.1) in those who reported treatment; there was a general improvement in this score, which was significant (p < 0.001). These findings are summarized in Fig. 1. The linear regression model of the change of severity from baseline to follow-up yielded similar results, showing that treatment accounts for a significant reduction in tinnitus severity compared with observation (Table 1). Race and tumor size at baseline were not found to be significant in explaining the change in tinnitus severity from baseline to current state. The median follow-up duration from diagnosis was 5 years (mean 8.2 ± 1.0 years, range 1–34 years).

**Tinnitus and Microsurgery**

The overall distribution of patients undergoing microsurgery was 429 using a translabyrinthine approach, 249 using a retrosigmoid approach, and 122 using a middle fossa approach. When comparing tinnitus improvement by modality of treatment, all forms of microsurgical approaches (translabyrinthine, retrosigmoid, and middle fossa) produced significant improvement in postoperative tinnitus (p < 0.01; Fig. 1 right).

**Tinnitus and Stereotactic Radiosurgery**

Stereotactic radiosurgery was performed in 221 patients as primary treatment. When comparing all microsurgical options to stereotactic radiosurgery (Fig. 1 right), there was no difference between treatment groups (p = 0.60, ANOVA).

**Tumor Size at Presentation and Tinnitus**

Analysis of the acoustic neuroma size at presentation and the tinnitus severity score at presentation demonstrated a positive correlation (r = 0.01, p < 0.01) between these 2 variables (Fig. 2 left). Therefore, as the tumor size at presentation increases one observes the tinnitus severity score increasing. There is a substantial difference in mean presenting acoustic neuroma size in those undergoing observation compared with all patients undergoing treatment, and this significant difference was maintained in comparison with the translabyrinthine approach, retrosigmoid approach, and stereotactic radiosurgery (p < 0.01; Fig. 2 right). Tumors treated with a middle fossa approach had sizes similar at presentation to those that entered observation.

**Tinnitus and Presentation Epoch**

We investigated the presenting tumor size by year of presentation and found no change in acoustic neuroma size at presentation over the course of this study (Fig. 3 left). We then assessed patients by dividing them into epoch of presentation: between 1966 and 1988 (n = 54), 1989 and 1998 (n = 310), and after 1998 (n = 1063); we found a significant absolute reduction in overall improvement in tinnitus (Fig. 3 right).
Discussion

The message of this study is relatively straightforward: previously published studies support improvement of tinnitus with intervention (stereotactic radiosurgery or microsurgery), and this finding has been further supported by this study.\cite{3,4,5,6,7,8,9} Importantly, the question to be asked is whether observation is associated with a change in tinnitus. This is a more pressing issue in today’s management of acoustic neuromas as we begin to observe more small “asymptomatic” tumors, as suggested by the data of Stangerup et al.\cite{10,11} This knowledge would be useful in counseling patients who present with symptomatic tinnitus regarding their likely outcome if they elect to undergo an observation period. Symptomatic tumors may be driving care as was already observed with a paradoxical trend in treatment in the US, and may be one of many causes of overtreatment of smaller tumors (acoustic neuromas < 1.5 cm) in the US.\cite{12,13} In this study we demonstrate that in patients undergoing observation, there is a worsening of tinnitus during follow-up.

Although tinnitus is a complex symptom, in this study we attempt to distill its complexity by relying on patient reporting of the severity of tinnitus when they presented, compared with their most recent symptom severity; clearly this method is vulnerable to recall bias. However, this study asks the patient a basic question: do you think your intervention—whether it be a translabyrinthine approach, retrosigmoid approach, middle fossa approach, stereotactic radiosurgery, or observation—changed your tinnitus? In this respect, this data set should prove useful for gaining insight into this complex symptom. Again, regardless of intervention, there appears to be an improvement in postintervention tinnitus, and the magnitude of the effect is affected by preoperative tinnitus severity and acoustic neuroma size.

Although treatment appears to reduce tinnitus, the absolute tinnitus mean score appears to correlate with acoustic neuroma size. Moreover, larger tumors were commonly treated with a translabyrinthine approach or retrosigmoid craniotomy, therefore their presentation tinnitus scores were generally higher and there was more opportunity for treatment effect as the larger tumors seemingly were correlated with more preoperative tinnitus. Therefore, we investigated size as a confounder in this data set. In linear multivariate analysis, treatment or observation were found to strongly affect tinnitus while controlling for tumor size, and appear to be independent of the effect related to size. As described by Stangerup et al., roughly 20% of those with intracanalicular tumors and 30% of those with extrameatal tumors will grow with time.\cite{14} Although it may be conjecture, it is possible this proportion of growing tumors may account for the baseline increase in symptomatic tinnitus described in this study.

Finally, there appears to be an overall effect of time on the improvement of tinnitus. Those patients treated in an earlier epoch of this study demonstrated greater improvement than those more recently treated. This data can be seen in Table 1.

TABLE 1: Multivariate analysis of the change in tinnitus severity from initial diagnosis to current state

<table>
<thead>
<tr>
<th>Variable</th>
<th>Change in Tinnitus Severity</th>
<th>Estimate</th>
<th>SEM</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>nonwhite vs white race</td>
<td></td>
<td>0.11</td>
<td>0.42</td>
<td>0.79</td>
</tr>
<tr>
<td>treatment</td>
<td></td>
<td></td>
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</tr>
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<td>translabyrinthine vs no treatment</td>
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<td>-0.97</td>
<td>0.28</td>
<td>&lt;0.01</td>
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<tr>
<td>retrosigmoid vs no treatment</td>
<td></td>
<td>-0.95</td>
<td>0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>middle fossa vs no treatment</td>
<td></td>
<td>-0.72</td>
<td>0.37</td>
<td>0.04</td>
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<tr>
<td>tumor size at diagnosis</td>
<td></td>
<td>-0.03</td>
<td>0.04</td>
<td>0.47</td>
</tr>
</tbody>
</table>

FIG. 1. Graphs showing treatment impact on tinnitus severity. **Left:** Absolute change in tinnitus severity score (mean ± SEM) of treated patients (n = 1138) compared with those electing for observation (n = 289). There was a significant improvement in tinnitus after treatment, whereas observation lead to worsened tinnitus at follow-up (p < 0.0001, Student t-test). **Right:** Absolute change in tinnitus severity score (mean ± SEM) comparing the translabyrinthine (TL, n = 422), retrosigmoid (RS, n = 249), middle fossa (MF, n = 122), and stereotactic radiosurgery (SRS, n = 221) treatment categories. There were no significant differences between treatment groups (p = 0.60, ANOVA).
ultimately offers hope to our immediate postoperative patients still struggling with tinnitus, in that it should continue to improve with time. However, this phenomenon has not been previously described.

The 2007–2008 ANA survey data set and this paper do have multiple limitations. As indicated above, we relied on patient recall, which is clearly susceptible to recall bias. Furthermore, self-reported tinnitus severity is also subject to substantial measurement error, as the scale used here to study its effect is not validated. There are available validated inventories that attempt to objectify the symptom of tinnitus, but unfortunately, and restricted by the retrospective nature of the study, the ANA did not choose to use such an inventory in their analysis. There are further limitations to the study based on the nature of the ANA survey. The ANA survey results are known to be subjective. Inherent to the sample is a bias in those who participate in the ANA and those who respond to the survey; in other words, are those with remarkable symptomatology more apt to respond to a survey about their pre- or postoperative symptoms? A national tumor database examining symptoms as we have done would have the potential to provide data free from selection and reporting bias. However, because that is not available to us, the ANA database provides a large national reach covering many different locations and ages. Unlike a database based around a treatment center, the ANA data could have more low-severity patients who have yet to seek treatment from a specialized center. Finally, treatment in this data set is uncontrolled in treatment assignment; therefore the results between treatment options and tinnitus are correlational rather than causal. One major advantage to the survey data set is that it is driven by a patient-centered organization and not by physicians.

Conclusions

Tinnitus is an important presenting symptom in patients with acoustic neuroma. Currently, acoustic neuroma size at presentation, hearing, and patient preference drive
treatment decisions. In patients with tinnitus as a troubling symptom for whom watching and waiting is their treatment option, continued observation will likely worsen the patient’s tinnitus. However, intervention, whether it is microsurgery or stereotactic radiosurgery, may improve the patient’s tinnitus.

Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Agazzi, Van Gompel. Analysis and interpretation of data: Van Gompel, Patel, van Loveren. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Statistical analysis: Zhang. Study supervision: Agazzi.

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