How to Address Small- and Medium-Sized Acoustic Neuromas with Hearing: A Systematic Review and Decision Analysis

Weiming Liu[1], Ming Ni[1], Wang Jia[1], Dabiao Zhou[1], Qing Zhang[1], Yong Jiang[2], Guijun Jia[1]

OBJECTIVE: **Small- and medium-sized acoustic neuromas (ANs) increase in both number and proportion. Observation, radiosurgery, and microsurgery are all used to treat this disease; however, the appropriate treatment is controversial, especially in patients with hearing.**

METHODS: **We searched the MEDLINE, EMBASE, CENTRAL (Cochrane Central Register of Con-trolled Trials), LILACS (Latin American and Caribbean Center on Health Sciences Information), and CMB (Chinese Biomedical Database) databases without limits on the language and the time of publication. For the wait-and-scan strategy, we included the population-based prospective studies with sufficient follow-up time and information. We also attempted to locate high-level evidence that compared radiosurgery with microsurgery. The data were extracted from the studies to synthesize the probabilities. We surveyed 60 patients with small- and medium-sized ANs to plot the outcomes on a linear scale to measure the utility.**

RESULTS: **Eight studies met the inclusion criteria of the wait-and-scan strategy, and 3 grade II evidence studies were found that compared microsurgery with radiosurgery. After synthesizing the data in 3 groups, the preservation of useful hearing was 58.9%, 60.2%, and 4.3%, whereas the rate of tumor control was 71.1%, 97.0%, and 94.3%, respectively. The expected value for radiosurgery was 0.68, whereas the expected values for wait-and-scan and surgery were 0.64 and 0.28, respectively.**

CONCLUSION: **On the basis of the evidence, radiosurgery is the optimal choice for small- and medium-sized ANs. Because of the current difficulty with understanding the natural history of ANs, we suggest that there is a need for new evidence and a health economics assessment to update this result.**

INTRODUCTION

Acoustic neuromas (ANs), or vestibular schwannomas, is a type of benign brain tumor. ANs represent 8% of all primary brain neoplasms and approximately 16% of benign brain tumors (24). These tumors are usually slow growing, and there are even some reports that they may undergo long periods of stasis (14, 19, 21). Most patients with small ANs have slight or imperceptible symptoms. Presently, increasing numbers of ANs are being detected incidentally by magnetic resonance imaging for minor symptoms (14, 19). The treatment of this type of tumor continues to be controversial. Both intervention and wait-and-see strategies have been advocated by different experts (1, 16). Even with the use of intervention strategies, microsurgery and radiosurgery continue to be under debate (16, 27). Some systematic reviews have been performed to determine a suitable treatment (23, 29, 41), even proposing treatment algorithms (31). Because the inclusion criteria for the studies vary widely, and because there is a lack of available high-level evidence, their conclusions are not convincing.

Currently, decision-making has been based primarily on the doctor's experience and the patient's choice. On the basis of the results of previous studies, this study evaluates these treatment strategies using decision analysis in an attempt to determine the appropriate treatment.

METHODS

Ethical Considerations

This is an analysis primarily using the evaluation of anonymous data obtained from the published literature without requiring

Key words
- Acoustic neuromas
- Decision analysis
- Microsurgery
- Observation
- Radiosurgery
- Systematic review

Abbreviations and Acronyms
AN: Acoustic neuroma
QOL: Quality of life

From the Departments of [1]Neurosurgery and [2]Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

To whom correspondence should be addressed: Guijun Jia, M.D. [E-mail: jiaguijun@cssc.net.cn]

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additional consideration of ethics. The patients' survey was approved by the institutional review board of the local hospital (KY2014-022-01).

Definition

Definition of the Problem. The patient should have useful residual hearing, and the tumors should be no more than 3.0 cm in diameter or stages I, II, or III based on the Koos classification (17). Other than some hearing impairment and tinnitus, the patient should have no major tumor-related symptoms.

Definition of Interventions. *Wait-and-Scan.* The patient follow-up included an outpatient consultation and contrast axial and coronal, thin-slice magnetic resonance imaging studies. Each patient was followed up with magnetic resonance imaging for at least 2 years or until the observation was terminated because of treatment via surgery or radiosurgery.

Microsurgery. The goal of microsurgery is to remove as much of the tumor as possible without injuring the surrounding structures. A biopsy is not performed. The procedures are performed by a neurosurgical team or an otolaryngology team. Regardless of the surgical approach (retrosigmoid, translabyrinthine or middle fossa approach), all of the approaches are included in microsurgery.

Radiosurgery. The goal of radiation treatment is to stop tumor growth without injuring the important structures surrounding the tumor. Current radiosurgical approaches include gamma knife, fractionated stereotactic radiotherapy, and linear accelerator radiosurgery (CyberKnife) approaches. There is no clear advantage of one modality over another; therefore, all of the modalities were included in this study.

Definition of the Outcomes. *Hearing.* We evaluated hearing using the American Academy of Otolaryngology-Head and Neck Surgery hearing classification system (5) and the Gardner and Robertson (GR) Scale (7). Serviceable (useful) hearing was defined as patients having GR scale I or II hearing or American Academy of Otolaryngology-Head and Neck Surgery class A or B hearing. The outcome has the following 2 branches: hearing is preserved (with serviceable hearing) or there is a loss of hearing.

Tumor Control. A situation in which the tumor volumetric analysis or the diameter measurement increases on imaging (more than 1 mm each year) indicates definite tumor growth or a recurrence. We defined a tumor as controlled (no growth) if the tumor volume (diameter) was unchanged or had regressed during the follow-up.

Complications. Outcomes that included one or more of the following were identified as complications: the facial nerve function was worse than a House-Brackmann grade (11) of 1 or 2; a cerebrospinal fluid leak, meningitis, or hydrocephalus occurred after the interventions; survival with severe vertigo, unsteadiness, chronic headache, and tinnitus that was worse than when the status was diagnosed (include hear-losing); and serious complications meaning life-threatening complications or death. A systematic review and data synthesis is included in the PRISMA statement.

Search Strategy

We searched the CENTRAL (Cochrane Central Register of Controlled Trials), MEDLINE, EMBASE, LILACS (Latin American and Caribbean Center on Health Sciences Information), and CMB (Chinese Biomedical Database). The cut-off time for the retrieved documents was the end of May 2014. We used the search strategy described as follows. We searched for articles containing the keywords "neuromas, acoustic" as a medical subject heading or related words, such as "vestibular schwannoma," "cerebellopontine angle tumor," and others in the title field. We also searched Google Scholar on these issues to prevent omitting a grey paper or important studies.

Inclusion Criteria of the Studies. For the wait-and-scan strategy, we included studies with the following criteria: 1) population-based studies, with data from a country or regional report; 2) prospective study; 3) sufficient cases (more than 20 cases) and a sufficient follow-up time (a mean more than 2 years); and 4) sufficient information for extracting data.

For the intervention strategy (microsurgery or radiosurgery), we attempted to extract a high level of evidence and included studies with the following criteria: 1) we identified studies comparing microsurgery with radiosurgery in the treatment of ANs. We excluded case-series studies (level 4); 2) we sought high-level evidence. We attempted to find randomized controlled trials (level 1) on this subject. If no randomized controlled trial existed, prospective cohort studies (level 2) and retrospective cohorts (level 3) were considered; 3) sufficient cases (more than 20 cases) and a long enough follow-up time (a mean of more than 2 years); and 4) sufficient information for extracting data.

Data Collection and Analysis. Three authors (W.L., M.N., and G.J.) independently selected the trials for inclusion. The outcomes were cross-checked, and ambiguities or misinterpretations were resolved through discussion and consensus finding. Two of the authors (W.L., M.N.) independently used the QUADAS tool (38) to assess the quality of the included studies. Then, we extracted data from the selected studies for the synthesis of all types of probable outcomes.

Decision Analysis on Small ANs. *Decision Tree Structure.* TreeAge Pro 2012 (TreeAge Software Inc., Williamstown, Massachusetts, USA) was used to construct a decision tree. The root node (quadrangle) of the small ANs was branched into 3 treatment modalities, as noted previously. Chance nodes (round) followed each treatment outcome. The clinical outcomes of each treatment were categorized into the following 3 groups: (1) without complications, tumor control, and maintenance of useful hearing; (2) without complications, tumor control, and loss of useful hearing; (3) tumor growth or recurrence; and (4) complications. Each treatment was branched according to the presence of the procedures, and all of the branches reached the 4 clinical outcomes. The terminal node (triangle) at an end point is the "utility," which signifies a clinical outcome in the decision tree (see **Figure 1**).

Measurement of Utilities. The measurement of the outcome utilities was based on the patient's survey in our department (the premiere neurosurgical department in China, with approximately 200 AN operations each year). Sixty patients with AN were surveyed when diagnosed. A patient without complications, in whom the tumor is controlled, and whose useful hearing is maintained was considered to be a perfect outcome, with a score of 1.00. The worst outcomes were death or survival with severe complications, which were scored as 0 points. Other outcomes included tumor control