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Decision analysis of treatment options for vestibular schwannoma

Clinical article

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Object. Widespread use of MR imaging has contributed to the more frequent diagnosis of vestibular schwannomas (VSs). These tumors represent 10% of primary adult intracranial neoplasms, and if they are symptomatic, they usually present with hearing loss and tinnitus. Currently, there are 3 treatment options for quality of life (QOL): wait and scan, microsurgery, and radiosurgery. In this paper, the authors' purpose is to determine which treatment modality yields the highest QOL at 5- and 10-year follow-up, considering the likelihood of recurrence and various complications.

Methods. The MEDLINE, Embase, and Cochrane online databases were searched for English-language articles published between 1990 and June 2008, containing key words relating to VS. Data were pooled to calculate the prevalence of treatment complications, tumor recurrence, and QOL with various complications. For parameters in which incidence varied with time of follow-up, the authors used meta-regression to determine the mean prevalence rates at a specified length of follow-up. A decision-analytical model was constructed to compare 5- and 10-year outcomes for a patient with a unilateral tumor and partially intact hearing. The 3 treatment options, wait and scan, microsurgery, and radiosurgery, were compared.

Results. After screening more than 2500 abstracts, the authors ultimately included 113 articles in this analysis. Recurrence, complication rates, and onset of complication varied with the treatment chosen. The relative QOL at the 5-year follow-up was 0.898 of normal for wait and scan, 0.953 for microsurgery, and 0.97 for radiosurgery. These differences are significant ($p < 0.0052$). Data were too scarce at the 10-year follow-up to calculate significant differences between the microsurgery and radiosurgery strategies.

Conclusions. At 5 years, patients treated with radiosurgery have an overall better QOL than those treated with either microsurgery or those investigated further with serial imaging. The authors found that the complications associated with wait-and-scan and microsurgery treatment strategies negatively impacted patient lives more than the complications from radiosurgery. One limitation of this study is that the 10-year follow-up data were too limited to analyze, and more studies are needed to determine if the authors' results are still consistent at 10 years.
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Key Words • **acoustic neuroma** • **vestibular schwannoma** • **decision analysis** • **radiosurgery** • **microsurgery**

Vestibular schwannomas (acoustic neuromas) are benign tumors arising from the Schwann cells of the superior vestibular nerve. They represent 10% of all primary brain neoplasms and may be located intracanalicular, extracanalicular, or at the cerebellopontine angle.[151,165] These tumors are usually slow growing and are diagnosed either because of symptoms such as unilateral hearing loss, tinnitus, and vertigo or as the result of incidental detection by MR imaging.[72]

Abbreviations used in this paper: QOL = quality of life; SF-36 = 36-Item Short Form Health Survey; VS = vestibular schwannoma.

There are 3 treatment strategies available to patients with VS: "wait and scan" with serial MR imaging, microsurgical resection, or stereotactic radiosurgery.[158] Each treatment option has its own advantages and disadvantages, and most commonly the individual characteristics of a patient's presentation are used to tailor the appropriate therapy. Expectant management avoids the complications of surgery and radiosurgery at the risk of tumor progression and irreversible neurological injury. Microsurgery offers the greatest immediate chance for cure but is associated with CSF leakage, facial nerve injury, and infection. Finally, radiosurgery is a noninvasive

treatment option for tumor control but may come with delayed complications from radiation toxicity and the need for additional microsurgery.

The goal of this study was to determine which treatment strategy yielded the highest QOL after 5 and 10 years of follow-up. To account for the multiple possible outcomes of a patient's treatment course, we developed a decision analytical model. The data for this model were derived from a meta-analysis of reports on the treatment of VS and on QOL following treatment.

Methods

Base Case

Because of the great variety of tumors and patients, we elected to limit the tumors for which this model is to be applied to no more than 2.5 cm in diameter, extracanalicular, and extending into the posterior fossa in a patient with at least some residual useful hearing (Fig. 1). Other than some hearing impairment, the hypothetical patient has no major tumor-related symptoms. Since several options have been proposed for this population, a critical comparison is of some practical importance in guiding patient treatment.

Management Strategies

The 3 strategies proposed most commonly in the literature are those of watchful waiting, termed wait and scan, microsurgery by the posterior fossa route (suboccipital or retromastoid approach), and radiosurgery (Gamma Knife or linear accelerator). Microsurgery performed through a translabyrinthine or middle fossa route was not included in this analysis because too few cases have been reported for this type of patient to allow statistically valid comparisons. Radiotherapy included single-dose treatments and fractionated protocols.

Data Collection

We derived the data for our analysis from a literature search of articles published between 1990 and June 2008. We searched MEDLINE, Embase, and the Cochrane database for English-language articles containing the key words "neuroma, acoustic" as a medical subject heading or related words, such as "vestibular schwannoma," "cerebellopontine angle tumor," and others in the title field. The search was expanded to include the terms "surgery," "radiotherapy," "radiosurgery," "therapy," and "complications" as either subheadings or titles. This search was supplemented using the "related articles" links in PubMed and by searching selected bibliographies manually.

The search yielded 2748 abstracts, of which 2127 were excluded. The excluded abstracts either lacked any original data or dealt with subjects unrelated to treatment outcomes. The remaining 621 articles were reviewed by 3 of the coauthors. Excluded from the 621 were 508 case series that lacked follow-up or followed fewer than 7 patients, those that dealt with bilateral, large (> 2.5 cm), intracanalicular, or other unusual vestibular tumors, or those that included patients who lacked useful hearing. We also culled these cases from larger, more inclusive, series whenever possible. This left us with 113 articles, which provide the data for this decision analysis (Table 1 and Fig. 2).

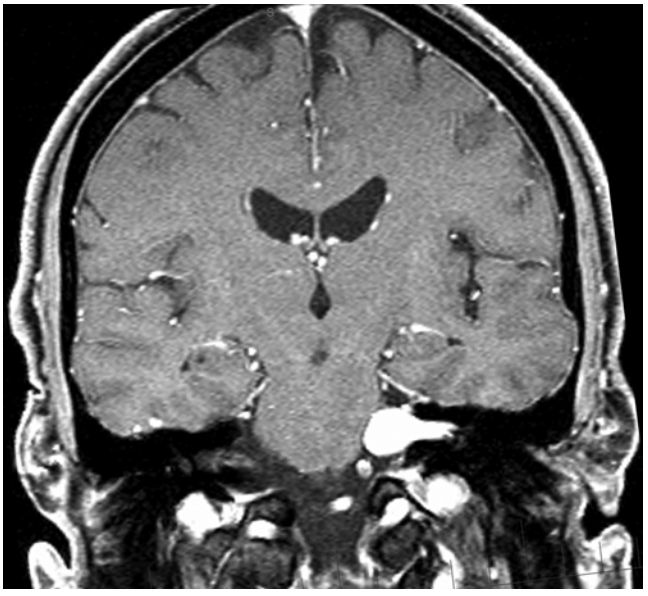

Fig. 1. Coronal T1-weighted Gd-enhanced MR image demonstrating a VS of dimensions consistent with our base case.

In addition, searches were performed for health-related QOL associated with the presence of various complications, using "quality of life," "neuroma, acoustic," or specific complications as either subheadings or titles. This search yielded 27 relevant studies, listed in Table 2. All series used in our analysis, including those comparing different therapies, are nonanalytical and considered Level III evidence.[53]

Decision Analytical Model

The decision analysis tree demonstrating the possible pathways and outcomes following treatment of a patient with VS is shown in Fig. 3. For a patient presenting with VS and fitting the definition of our base case, 1 of the 3 options is selected. Once treatment is chosen, the clinical course can be problem free, or complications can occur. We define complications as chronic or permanent, and ignore minor or transient difficulties encountered in the course of care (for example, hair loss). Complications, including death, can occur as the result of treatment or due to tumor growth or hemorrhage. The model ignores death due to other causes. Many studies documented asymptomatic tumor growth, but our model defines "recurrence" as growth that requires treatment by microsurgery or radiosurgery. Such "salvage" treatment is usually associated with poorer outcomes than outcomes associated with initial therapy.[39,133] After a given period of follow-up, the patient's health-related QOL is estimated, based on the effects of tumor recurrence or whatever complications may be present. The calculation of QOL is discussed below. Surgical complications are assumed to occur immediately; other complications are assumed to occur midway through the follow-up period.

The primary analysis involved calculating point esti-

TABLE 1: Complications after the wait-and-scan strategy, microsurgical treatment, and radiosurgical treatment for VS*

Complications	No. at Risk	Mean	95% CI	References
wait-and-scan strategy				
useful hearing loss	1427	0.528	0.40–0.64	10,14,19,36,43,45,60,88,89,98,103,106,110,120,136,139,144,152,160,164
facial numbness	168	0.016	0–0.02	45,152
vertigo, unsteadiness	617	0.225	0.16–0.26	43,45,111
tinnitus	199	0.176	0.10–0.24	111
hydrocephalus requiring shunt	317	0.038	0.02–0.04	20,112,123,162
other†	119	0.050	NC	45
required later treatment (≤5 yrs)	1842	0.238	0.17–0.30	2,10,14,19,36,43,45,47,60,88,89,98,101,103,105,110,112,121,123,126,136,138,139,145,147,152,161,164,167
likelihood later treatment is microsurgery	397	0.831	NC	
tumor-related deaths	2038	0.024	0.02–0.03	
microsurgical treatment				
useful hearing loss	1537	0.445	0,36–0.52	6,10,12,14,16,28,30,35,48,57,61,68–70,73,74,94,104,128,129,135,138,146
facial paralysis HB (Score VI)	2236	0.084	0.07–0.10	
facial weakness HB (Scores I–V)	2229	0.142	0.10–0.18	
vertigo, unsteadiness	508	0.008	0–0.05	128
tinnitus	508	0.030	0–0.10	10,128
hydrocephalus requiring shunt	234	0.004	0–0.03	35,128
other‡	3927	0.117	NC	14,16,28,35,48,128,130
recurrence needing treatment				
≤5 yrs	617	0.027	0–0.07	13,14,28,35,69,102
≤10 yrs	617	0.054	0–0.14	
likelihood later treatment is microsurgery	5	0.80	NC	
periop & tumor-related deaths	2660	0.004	0.002–0.006	5,10,12–14,16,28,29,35,48,57,61,68–70,73,74,94,102,104,128,129,135,138,146
radiosurgical treatment				
useful hearing loss	2817	0.281	0.18–0.37	3,4,17,18,22,23,25,26,31,37,44,54–56,63,65–67,74,77,78,80,89,90,95,97,107,109,116,119,132,134,141,143,151,154,157,159,169,170
facial paralysis (HB Grade VI)	1291	0.077	0–0.19	17,22,31,37,54,55,58,74,90,115,116,154,159,170
facial weakness (HB Grades I–V)	3515	0.048	0.04–0.06	4,11,17,22,24,27,37,44,54,55,58,66,74,80,85,86,90,115,116,119,132,134,143,154,157,159,168,170
facial numbness	4088	0.092	0.02–0.14	3,4,11,17,22,24,25,27,31,44,54–56,63,67,74,77–80,86,90,99,107,116,119,132,134,141,143,154,159,168,170
vertigo, unsteadiness	1919	0.057	0.055–0.059	3,4,58,67,79,86,141,154,159
tinnitus	1919	0.015	0.014–0.016	27,56,154
hydrocephalus requiring shunt	1919	0.040	0.016–0.058	3,17,27,54,56,67,86,109
other§	1919	0.022	NC	3,17,62,67,74,77,80,151,170
recurrence requiring treatment (≤5 yrs)	6044	0.035	0.023–0.046	3,4,11,17,18,24,25,27,31,37,41,42,44,54–56,58,63,65–67,74,77,80,82,84–86,89,90,95,97,99,107,109,115,116,119,131,137,141,143,149,151,154,157,159,168–170
likelihood that later treatment is microsurgery	273	0.773	NC	
tumor-related deaths	2672	0.010	0.003–0.013	3,4,17,18,22,24,27,37,41,44,54,63,65,66,74,77,86,95,108,109,115,132,143,154,157,159,168–170

* HB = House-Brackmann; NC = not calculated.
† Other complications for the wait-and-see strategy include the following: chronic severe headache and facial paresthesias.
‡ Other complications for microsurgical treatment include the following: CSF leak (with or without repair), bacterial or chemical meningitis, and chronic severe headache.
§ Other complications for radiosurgical treatment include the following: permanent facial spasms, facial and scalp pain, severe chronic headache, persistent nausea and vomiting, dysarthria, and dysphagia.

mates of QOL associated with using each of the 3 management strategies using the decision tree pictured in Fig. 3. One challenge involved estimating and calculating the effects of patients with multiple complications. By convention, QOL is scored proportionately between 1 (perfect health) and 0 (dead).[49] Without exception, series enumerated complications separately. None reported how many patients suffered multiple complications or which combinations occurred. However, the patient with several complications in addition to loss of useful hearing is likely to have a lower QOL than one in whom hearing loss is an isolated finding. To compensate for the lack of evidence

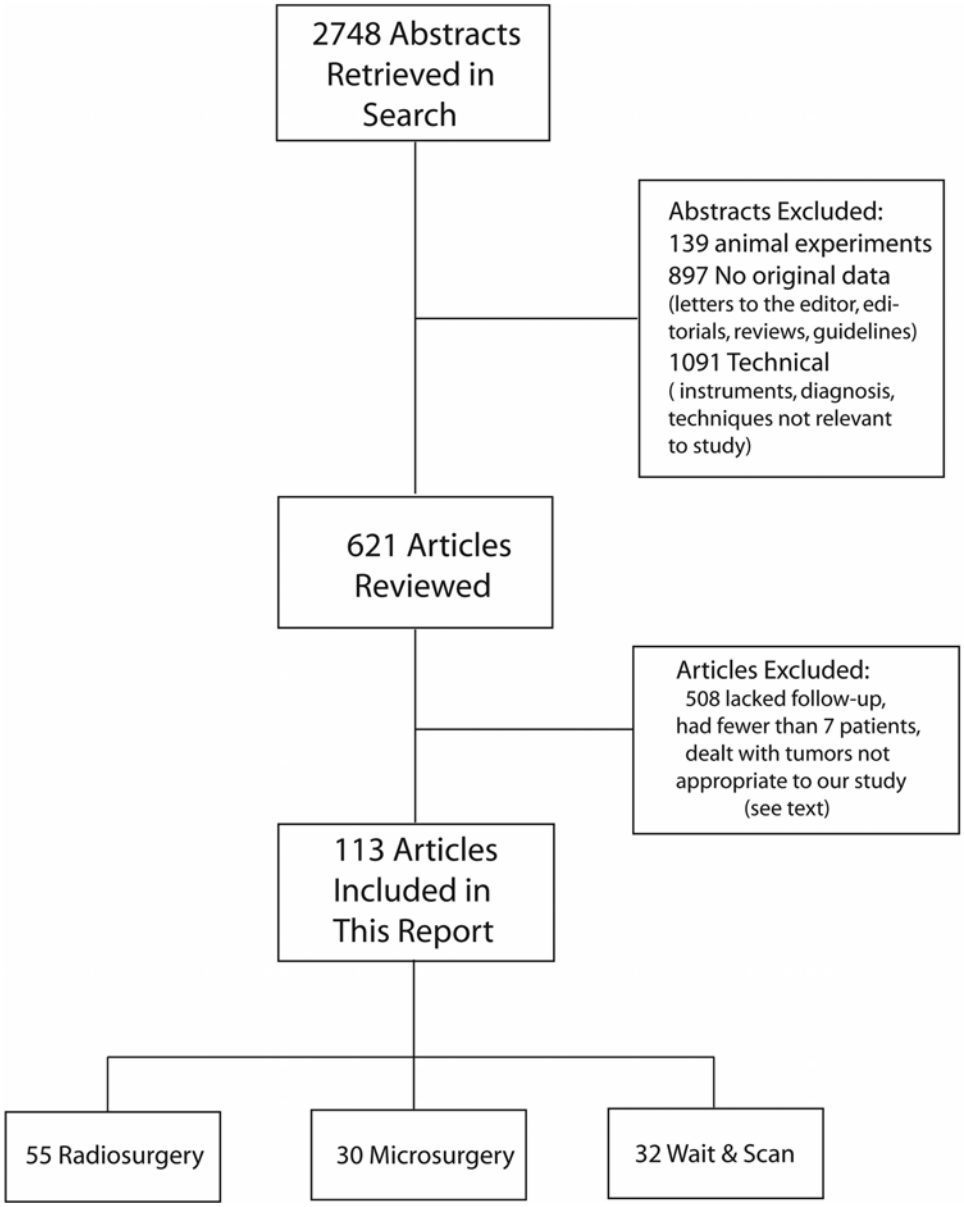

Fig. 2. Diagram summarizing the literature search. Note that the total number of articles in the 3 categories included in this report is more than 113, as some articles dealt with more than 1 treatment strategy.

regarding the likelihood of multiple complications, we ran 3 models. The first considered all patients as having at most a single complication. The second model considered as many complications as possible to be multiple. Since consensus is to weight individual complications less if they are combined than if each is isolated,[49] it is likely that the first model overestimates the importance of having complications and the second model underestimates their impact on QOL. The third model and the one used, treats half the complications as single and the other half as multiple. This is discussed in detail in the *Appendix*.

We performed sensitivity analysis for each parameter of the model within its 95% CI to determine its relative influence on outcomes and to test the robustness of point estimates. A further test of robustness of point estimates involved a 2D Monte Carlo simulation[32] (expected value for 1000 simulated trials, each made up of 1000 microsimulations). We used beta distributions for all probabilities. Analyses of the model employed TreeAge Pro 2009 (TreeAge Software, Inc.).

A final check of our results used external validation. Postoperative QOL was measured in several surgical series, using the SF-36,[163] considered by many to be a reasonable metric for health-related QOL. We compared our calculated postsurgical QOL with a pooled value obtained from global SF-36 scores obtained from the literature.[9,13,34,71,75,93,96,100,113,153,156,163] The individual domain scores of each study were converted to composite physical and mental QOL scores using an online calculator (http://www.sf-36.org/ [Accessed March 8, 2010]), and the composite scores were added. In addition, a small number of series reported numbers of patients in whom there were

TABLE 2: Health-related QOL associated with complications*

Complications	No. at Risk	Mean Utility	95% CI	References
no new symptoms	NA	1.0	NA	49
useful hearing loss	1705	0.929	0.89–0.97	8,21,50,52,140,148
facial paralysis (HB Grade VI)	16	0.924	0.88–0.96	33,87
facial weakness (HB Grades I–V)	36	0.983	0.96–10.0	33,87
facial numbness	156	0.960	0.96–0.96	142
facial spasm	131	0.958	0.94–0.98	59,124,150
facial pain, headache	928	0.935	0.90–0.97	125,127,166
vertigo, unsteadiness	456	0.890	0.87–0.91	1,38,91,92,110
tinnitus	879	0.957	0.91–1.0	7,110,114
hydrocephalus requiring shunt	115	0.965	0.90–1.0	46,83
meningitis	360	0.930	0.93–0.93	117,118
tumor-related death	NA	0.0	NA	49

* NA = not appropriate.

no complications. We compared the prevalence calculated by our model with reported values.

Data from multiple case series were pooled to calculate values for the means and 95% CIs using the random effects model of the metan function in Stata 9 (Stata Corp). For studies in which prevalence varied with time of follow-up, we used Stata 9's metareg function to determine mean prevalence and 95% CIs at a specified length of follow-up. A 2-tailed t-test was used to compare 2 means, and 1-way ANOVA, followed by post hoc Bonferroni tests for individual comparisons involving comparisons among multiple means. We considered differences for which the probability was < 0.05 to be significant.

Results

Pooled data from more than 71,000 cases in these 113 reports were used to create evidence tables, from which we calculated the incidence of complications and the recurrence and relative risks for the 3 management strategies. We abstracted estimates of the probabilities of tumor-related death, complications, and recurrence associated with each strategy (Table 1). For example, the 5-year rate of hearing loss is 53% with wait and scan, 44% with microsurgery, and 28% with radiosurgery. These probabilities represent the likelihood that a hypothetical patient travels along a particular pathway pictured in Fig. 3. The reported point estimates of pooled data represent variance-weighted means and were tested to exclude heterogeneity.[76]

The same procedures were followed to assign point estimates for expected QOL associated with each potential complication, and the results are reported in Table 2. Each management strategy was associated with different potential complications in different frequencies. For each strategy, we modeled an average risk of complications based on the reported frequencies and an average associated QOL.

Rates that were expected to increase over time, such as complications or tumor recurrence, were tested by meta-regression.[155] Variance-weighted rates were regressed against mean duration of follow-up of each series, and pooled values were calculated.

The incidence of each of the complications listed in Table 1 (for example, useful hearing loss, facial weakness, vertigo, and so on) was determined at 5 years using meta-regression analysis. Between the 3 treatment strategies (wait and scan, microsurgery, and radiosurgery) there were no significant differences in the incidence of each complication at 5 years with 1 exception. The only variable with a statistically significant temporal trend ($p < 0.05$) was tumor recurrence rates in the radiosurgery and the wait-and-scan groups compared with microsurgery. The tumor recurrence rate after radiosurgery is illustrated in Fig. 4.

Based on the results of second-order Monte Carlo simulation, health-related QOL at 5 years of follow-up is significantly greater with radiosurgery than with microsurgery. Both approaches are superior to the wait-and-scan strategy by a highly significant margin. These results are illustrated in Table 3, which also shows outcomes at 10-year follow-up. Here, there is a trend for higher QOL with microsurgery than with radiosurgery, but the difference is not significant. Both strategies remain significantly better than wait and scan.

Sensitivity analysis supported the results of the Monte Carlo simulation. All 3 models for dealing with multiple complications exhibited parallel results with little variation. The model we used gave results that were between those of the other 2 models, and not significantly different from them. One-way sensitivity analysis suggested the only parameter whose value might alter the choice of strategies was the complication rate of radiosurgery. When plotted against surgical complication rate in a 2-way sensitivity analysis of 5-year outcome, the decision in favor of radiosurgery is shown to be robust (Fig. 5).

Discussion

This study is the first quantitative and comprehensive decision analysis for treatment of VS. We established a base case as a patient with a schwannoma less than 2.5 cm in diameter and some useful residual hearing. The base case facilitates the comparisons within the decision analytical model. In practice, however, the treatment decision for VS is highly individualized according to patient/physician preferences and many clinical variables. Nevertheless, the base case is a common and relevant clinical scenario.

Wait-and-Scan Strategy

The wait-and-scan treatment strategy is generally used in patients in whom the tumor is minimally symptomatic because of its small size, or the patient is of advanced age or has significant comorbidities. In the largest meta-analytical retrospective review, Smouha et al.[139] found that the average tumor size for this strategy was 11.8 mm. The average follow-up in the studies examined

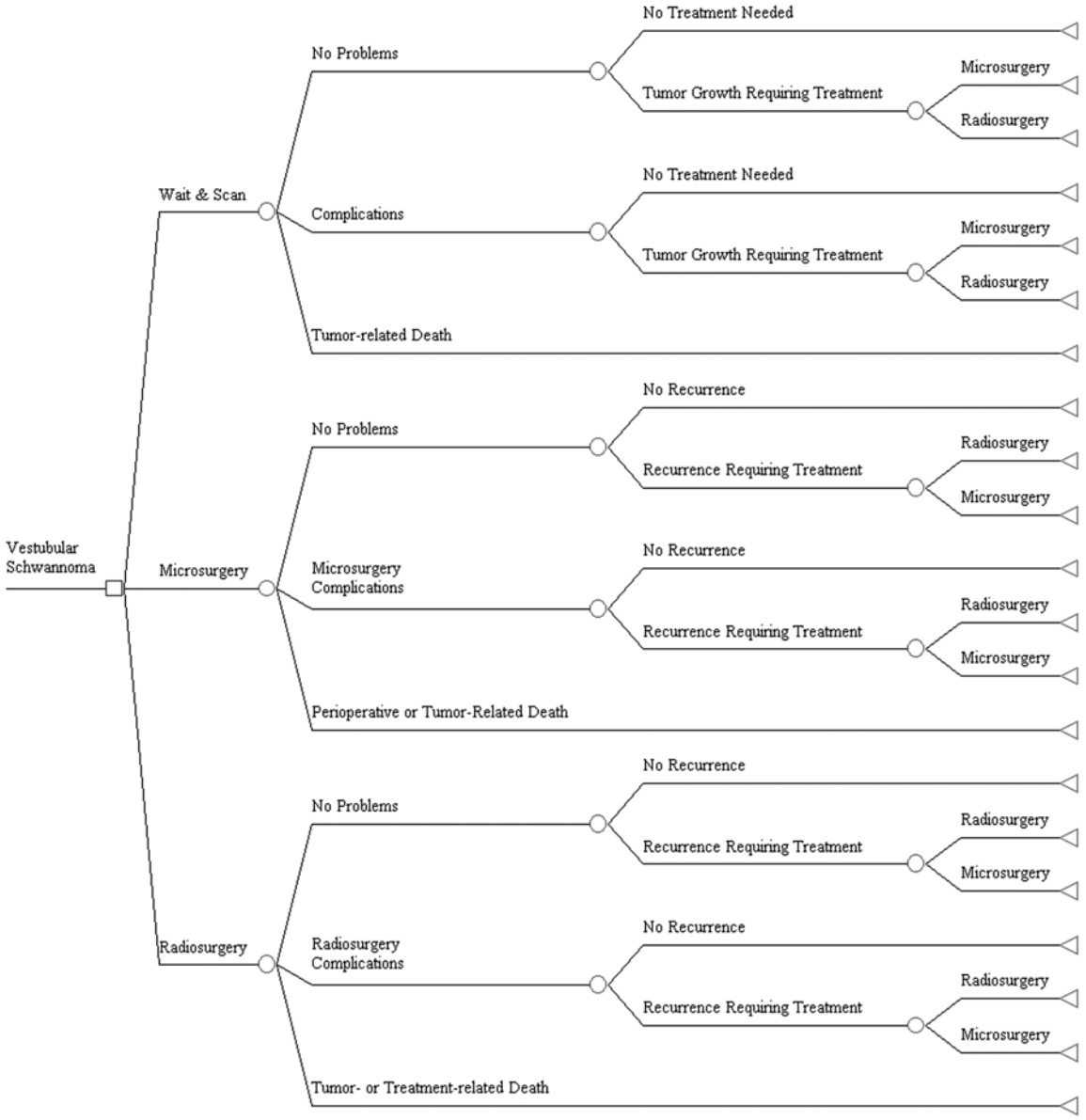

Fig. 3. Decision tree for comparison of outcomes. The 3 management strategies are shown, as are the possible pathways taken by a simulated patient after treatment. Each pathway has a calculated probability and is associated with a calculated outcome.

was 3.2 years and during this time, 57% (709 of 1244) of patients showed no tumor growth. Hearing loss occurred in 51% of patients, and the wait-and-scan strategy failed in 20%, who elected to have further treatment.

Our study reached similar conclusions about conservative management for VSs. By 5 years, hearing loss occurred in 53% of patients, and 24% of patients required additional treatment. Of those requiring additional treatment, 83% underwent microsurgical resection. This finding contradicts one of the initial rationales for using conservative management, namely that increased age or comorbidities increase the risk of surgical treatment. It is likely that by using a wait-and-scan strategy, the tumor progresses in size such that the window of opportunity for radiosurgery or microsurgery may be lost before the patient's symptoms necessitate treatment. Therefore, earlier radiosurgery may be optimal for those tumors that demonstrate radiographic growth in the wait-and-scan strategy.

Another important shortcoming of the wait-and-scan strategy is the high percentage of patients who lose useful hearing. A common assumption is that hearing loss is preferable to the complications related to surgical treatment or radiotherapy. However, the overall negative impact on QOL for hearing loss is greater than facial weakness, numbness, spasm, pain, tinnitus, or even hydrocephalus (Table 2). Hearing loss should not be considered an acceptable morbidity in the management of VS, and its impact on an individual should be discussed prior to choosing a treatment strategy.

The wait-and-scan strategy was shown to have the

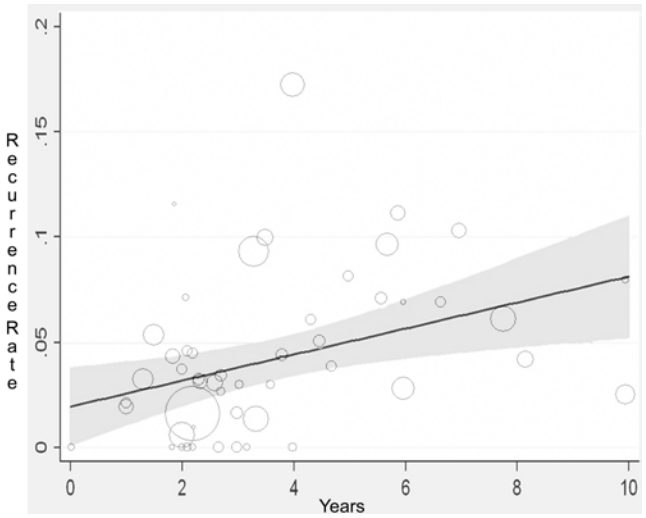

Fig. 4. Bubble diagram of meta-regression of tumor recurrence rate over time in the radiosurgery group. Each bubble represents 1 of the 50 case series reported. The center of each bubble is located at the mean length of follow-up for the series (x axis) and the reported recurrence rate (y axis). The size of the bubble is proportional to the number of cases reported in the series. The pooled mean incidence over time *(solid line)* is shown as well as 95% CIs in *gray*.

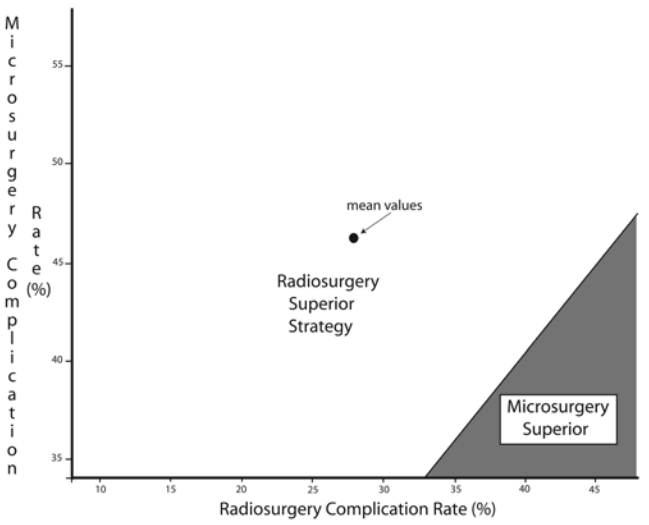

Fig. 5. Two-way sensitivity analysis comparing the 3 treatment options as both radiosurgery and microsurgery complication rates are varied. Each zone is labeled by the treatment that yields the best results for that combination of complication rates. The x and y axes represent the ranges of complication rates encompassed by the 95% CIs of the 2 parameters, and the dot in the center of the graph is the combination of the pooled mean rates from the literature. Radiosurgery is the best option for all combinations except very high radiosurgery and low microsurgery complication rates. Wait and scan is never the best strategy.

lowest QOL compared with radiosurgery and microsurgery at 5- and 10-year follow-up. The predominant reason is that the wait-and-scan strategy has a significantly higher incidence of functional hearing loss, tinnitus, and vertigo than either microsurgery or radiosurgery. The complications of this treatment strategy are perceived by patients as being more detrimental to QOL than any other treatment-related complication, such as facial weakness. In addition, for those patients who require later treatment, delaying microsurgery or radiosurgery may decrease the chances of success and increase the likelihood of complications.

Microsurgery for VS

Microsurgery for VS has been considered the gold standard of treatment. With improved techniques and neuromonitoring, vestibulocochlear and facial nerve preservation have become the measure of surgical success. Mortality from this procedure has been reported as less than 1% with a greater than 90% chance of preserved facial nerve function.[12,15,51] Despite these successes, the morbidity of surgery is not insignificant. Betchen et al.[12] investigated the rate of long-term hearing preservation in patients after microsurgery for VS and the factors contributing to hearing loss. Among 142 patients eligible for hearing preservation surgery, even despite the presence of an experienced surgeon and the use of neuromonitoring, only 20% of patients retained functional hearing. Tinnitus occurred in 51% of patients and dizziness in 31% of patients. Raut et al.[123] showed a correlation between the size of the schwannoma and preservation of functional hearing, with a 52% chance of preserved hearing if the tumor was less than 2 cm and 83% if the lesion was less than 1 cm.

TABLE 3: Health-related QOL after treatment of VS

Management Strategy	Mean QOL	95% CI	p Value*
5-yr follow-up			
radiosurgery	0.9699	0.9626–0.9772	0.0052
microsurgery	0.9526	0.9430–0.9622	NC
wait & scan	0.8978	0.8949–0.9007	<0.001
10-yr follow-up			
radiosurgery	0.9284	0.8929–0.9639	0.354
microsurgery	0.9515	0.9147–0.9883	NC
wait & scan	0.7825	0.7609–0.8041	<0.001

* Comparisons are made with microsurgery.

In this study, based on 1537 combined patients, 44.5% suffered loss of functional hearing after microsurgery. However, our rates of facial weakness (14%) and facial paralysis (8%) are far higher than those reported by some authors such as Betchen et al.[12] Although these morbidity rates are higher than the rate seen in certain centers, they represent the average complication rates reported in the literature.

Complete facial paralysis was associated with a negative impact on QOL, and compared with other possible complications, only vertigo was perceived as worse by patients. However, facial weakness without paralysis was not considered to impact QOL to a great extent when compared with other complications (Table 2). Our study found an equivalent rate of facial paralysis following either microsurgical (8%) or radiosurgical (7.7%) treatment of VS, but microsurgery had a greater incidence of facial weakness (14%) than radiosurgery (4.8%). At 5-year follow-up, the overall QOL after treatment is significantly higher for radiosurgery than that for microsurgery. However, the higher rate of facial weakness after microsurgery does not greatly

affect this finding, since the negative impact on QOL for facial weakness is relatively minor.

Similarly, the higher QOL associated with radiosurgery over microsurgery is not significantly related to the likelihood of tumor recurrence requiring treatment at 5 years. The rate of tumor recurrence was lowest with microsurgery (2.7%), but it did not differ significantly from the 5-year recurrence rate of radiosurgery (3.5%). In both cases, the treatment of the recurrence was resection in approximately 80% of cases. Therefore, it is the complications specific to microsurgery that significantly decrease the QOL at 5 years compared with radiosurgery. These complications include CSF leak and bacterial or chemical meningitis. The negative impact of meningitis on QOL was approximately equal to that of functional hearing loss.

Stereotactic Radiosurgery

One of the most influential studies supporting the use of radiosurgery for treatment of VS was written by Pollock et al.[122] In a prospective study of 82 patients with VSs less than 3 cm, Pollock investigated the outcome at the 42-month follow-up of microsurgery versus radiosurgery. The study found that patients treated with radiosurgery were more likely to maintain normal facial movement and functional hearing than those treated with microsurgery. The surgical arm of the study had significantly worse scores on physical functioning, energy/fatigue, and pain. Lastly, there was no difference in tumor control. Pollock et al. noted that 14% (30 of 208) of VS treated with radiosurgery showed a significant growth (> 2 mm). Of those that increased in size, 20% caused new symptoms, but only 14% required additional treatment.

The results from our study demonstrate a higher rate of complications and recurrence than that reported by Pollock et al.[122] Combining facial paralysis (7.7%) and facial weakness (4.8%) after radiosurgery, we found that normal facial movement was preserved in 87.5% of cases compared with 96% of cases in Pollock et al. Facial numbness occurred in 9% of radiosurgery cases compared with only 2% of those reported by Pollock et al. However, functional hearing was preserved in 72% of cases in our study versus only 63%. The difference between our study and the published results may be due to modern use of lower marginal doses than in the past. In both studies, the rate of tumor recurrence requiring treatment was approximately 4%. When compared with the other treatment strategies, radiosurgery had a higher incidence of facial numbness (9.2 vs 1.6% for wait and scan) and hydrocephalus requiring a shunt (4 vs 0.4% for microsurgery). Both of these complications are moderate in regard to their negative impact on QOL.

Comparison with Prior Studies and Current Limitations

External evidence also provides support for our findings. We found 12 case series reporting QOL in a total of 967 patients undergoing microsurgical treatment of VS, as measured by SF-36 scores. The pooled mean QOL was 0.952. Our model calculated an average QOL of 0.953. In addition, Kondziolka et al.[81] reported that 69% of 115 patients were complication free between 5 and 10 years after radiosurgery. Our model calculated the number to be 71% at 5 years. One series in the wait-and-scan category reported that 44.9% of its 49 patients developed neither new nor worsened symptoms during a mean follow-up of 3 years.[103] Our model calculated this number to be 44.5% at 5 years.

The literature contains a previous decision analysis on treatment of VS.[64] This study, while reaching the same conclusions about the superiority of radiosurgery over microsurgery, lacked a number of features critical to modern decision analyses. Outcomes were not quantified, making statistical comparisons and sensitivity analysis impossible. The diverse effect of time on the 2 groups in terms of recurrence and complication incidence was ignored. Complication and mortality rates reflect data from an earlier time period and are higher than in more recent reports. The present study is based on a more complex model with longer follow-up data.

Our study shares the potential drawbacks of all such decision analytical models. We made several simplifying assumptions, any of which may impact our results. The calculated values for microsurgery and radiosurgery are close to those of perfect health, and the differences between them quite small. A modest change in the model's assumptions might alter our conclusions. For example, we cannot be certain that our handling of multiple complications is accurate, although the external evidence tends to validate our choice. In addition, the SF-36 has been criticized as a measure of QOL in cases of VS, as well as other contexts.[40] We cannot dispute this assertion but could not find an alternative metric in the literature.

The fact that surgical complications tend to present immediately, whereas complications of radiosurgery and conservative management are delayed makes comparisons difficult. We have used meta-regression to help us overcome this obstacle. Intuition suggests that information on individual patients, which is rarely reported in case series, is needed to document appearance of delayed complications. However, for binary data such as recurrence and mortality, case numbers and mean follow-up duration are adequate. Our regression assumes that delayed complications accrue in a linear fashion. Although this is certainly an oversimplification, sensitivity analysis and external evidence suggest that this does not invalidate our findings.

Long-term follow-up studies are so sparse that data uncertainties accumulate as the model approaches 10 years. Although there is a much greater difference between outcomes in the micro- and radiosurgical groups at 10 years than at 5, the 95% CIs are so wide that this difference is no longer significant. Figure 4 is an example of this growing data uncertainty. The mean 10-year recurrence rate after radiosurgery is calculated at 8%, but the 95% CI is anywhere between 5 and 11%. Until more late-term data are collected, we cannot determine whether the apparent advantage of microsurgery over radiosurgery is valid.

Finally, we concede that a decision analysis cannot replace a well-controlled, randomized trial. At best, it can only approximate the outcome of such a trial. However, if our approximation is close to correct, it is extremely unlikely that the required trial is practical. For an expected difference in the primary end point (QOL) of 1–2% and standard statistical requirements for significance (power

of 80%, 2-tailed t-test, and $p < 0.05$), a sample size of more than 6700 cases would be needed for each group.

Conclusions

At 5 years, patients treated with radiosurgery have an overall better QOL than those treated with either microsurgery or those who undergo follow-up with serial imaging. Patients found that the complications associated with the wait-and-scan and microsurgery treatment strategies impacted their QOL more than the complications from radiosurgery. One limitation of this study is that the 10-year follow-up data were too limited to demonstrate whether a significant difference existed between the radiosurgery and microsurgery groups.

Appendix: Calculating Utilities in Patients with Post-Treatment Complications

As mentioned above, published series have not reported in what proportion of patients treatment complications are multiple, and they have not detailed which complications tend to occur together. We approached this obstacle by calculating overall complication rates and utilities using 3 separate theoretical models and choosing the one that resulted in outcomes that approximated most closely those in the literature.

For the purposes of illustration, we use 3 complications in an example and apply all 3 models. As can be seen in Table 4, complication A is the most common, occurring in 30% of cases. It is also the most serious, being associated with a utility of 0.7 (normal health carries a utility of 1). Model A treats the complications as mutually exclusive; a patient can have at most 1 complication. Model B treats the complications as maximally multiple. Thus, 10% of patients have all 3, 10% have complications A and B, and 10% have complication A alone. Model C is intermediate and treats one-half of the patients the same as Model A and the other half as Model B. These are illustrated in Fig. 6. Utilities of patients with multiple complications multiply. For example, a patient with both complications A and B has a utility of 0.7×0.8, or 0.56.

Table 5 reports the outputs of all 3 models. As discussed in *Methods*, Model A tends to overemphasize the effect of multiple complications on outcome, and Model B tends to do the opposite. Model C, which is what we used in our final calculations, yields intermediate results. As mentioned in *Results*, the model predicted overall QOL and complication-free rates quite accurately, and published results tend to support its validity.

TABLE 4: Complication rates and utilities

Complication	Frequency	Associated Utility
A	0.3	0.7
B	0.2	0.8
C	0.1	0.9

Disclosure

TABLE 5: Calculated total complication rates and utilities

Model	Total Complication Rate (%)	Mean Utility
A	60	0.860
B	30	0.876
C	45	0.868

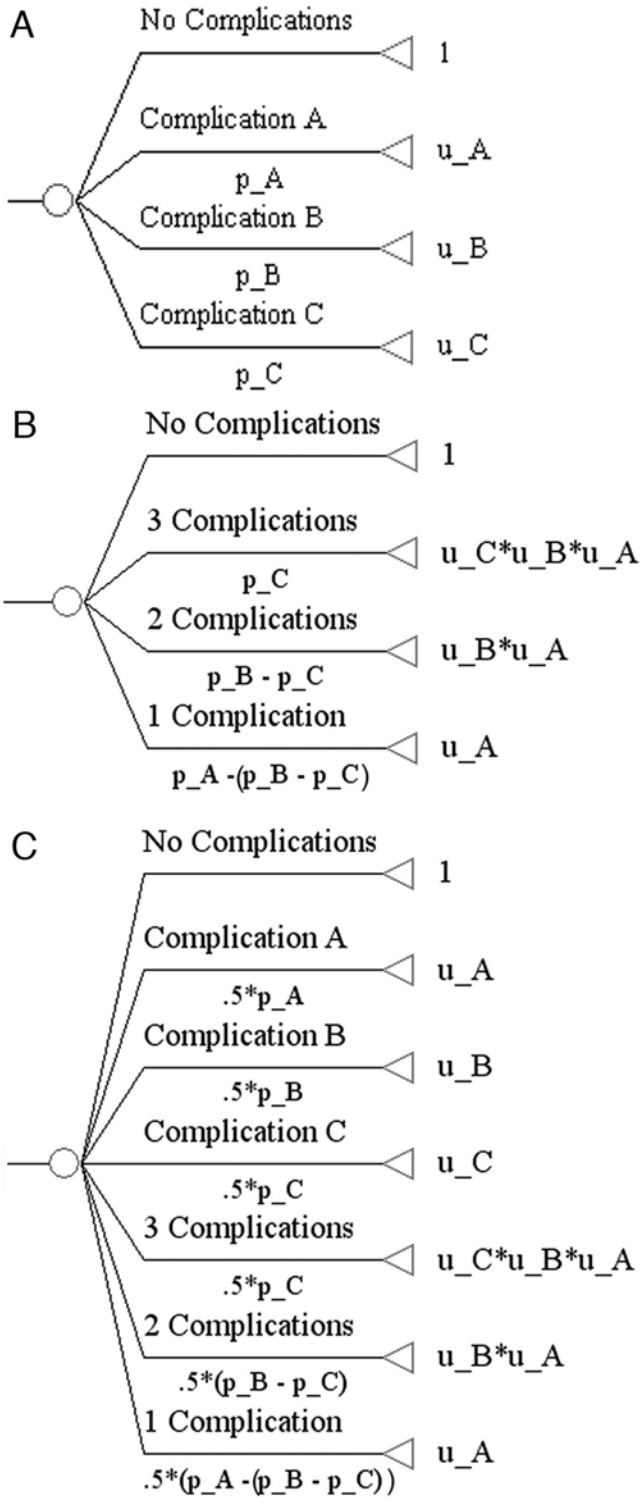

Fig. 6. Subtrees for calculating complication rates and utilities in the example. Panels A, B, and C represent the subtrees for Models A, B, and C, respectively. The p_A, p_B, p_C and u_A, u_B, u_C represent the probabilities and utilities associated with complications A, B, and C, respectively.

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

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