

# Long-Term Prospective Quality-of-Life Outcomes in 445 Patients with Sporadic Vestibular Schwannoma

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**Objective:** To evaluate the long-term changes in sporadic vestibular schwannoma (VS) disease-specific quality-of-life (QOL) outcomes.

**Study Design:** Prospective longitudinal study using the Penn Acoustic Neuroma Quality of Life (PANQOL) Scale.

**Setting:** National survey.

**Patients:** Patients with sporadic VS who completed a baseline survey before treatment and at least one follow-up survey recruited through the authors' center and through the Acoustic Neuroma Association.

**Interventions:** Observation, microsurgery, radiosurgery.

**Main Outcome Measures:** Changes in PANQOL scores from baseline to most recent survey.

**Results:** Among 445 eligible patients the mean duration of follow-up was 4.4 (SD, 2.3) years, including 122, 218, and 105 in the observation, microsurgery, and radiosurgery groups, respectively. Patients managed with observation ( $p = 0.03$ ) or microsurgery ( $p < 0.001$ ) demonstrated improvement in anxiety scores. Changes in facial function scores differed significantly by management group ( $p = 0.01$ ), with patients undergoing microsurgery

demonstrating a mean decline of 10 points in facial function scores compared with mean declines of 3 for those managed with observation or radiosurgery. Hearing loss scores decreased similarly over time for all three groups ( $p = 0.3$ ). There were minimal changes in total PANQOL scores over time across all management groups ( $p = 0.5$ ).

**Conclusions:** Long-term changes in total QOL among VS management groups are not significantly different. Microsurgery may continue to confer an advantage regarding improvement in anxiety postoperatively, but with a greater decline in facial function when compared to observation or radiosurgery. Long-term declines in hearing loss scores were not statistically significantly different among groups.

**Key Words:** Acoustic neuroma—Neurotology—Patient-reported outcome measure—Quality of life—Skull base surgery—Vestibular schwannoma.

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## INTRODUCTION

Corresponding to the widespread adoption of screening protocols for asymmetric and sudden sensorineural hearing loss, and increasing access to high-resolution neuroimaging, the lifetime prevalence of sporadic vestibular schwannoma (VS) now exceeds 1 in 500 persons (1–3). Paralleling these developments, the prototypical disease presentation has shifted from younger patients with sizeable, symptomatic tumors to an older demographic with less severe symptoms. In fact, a recent population-based study found that almost a quarter of patients were diagnosed incidentally after obtaining head imaging for seemingly unrelated indications (2,3).

Despite data documenting that an increasing proportion of newly diagnosed patients are pursuing initial wait-and-scan management, this shift toward conservatism is outpaced by the increasing rate of disease detection, such that the treatment incidence (i.e., number of treated patients per population) has not appreciably declined in the last 30 years, an indication of continued overtreatment (4,5). Paradoxically, overall, more patients are treated today than ever before at older ages, with smaller tumors and fewer symptoms (5). As VS does not significantly alter life expectancy and most people live decades after being diagnosed, aspects such as quality of life (QOL) become paramount (6).

QOL data offer insights into nuanced and often less tangible aspects of the patient care experience and disease journey that are frequently overlooked by physical examination and other traditional “objective” diagnostic tests. QOL data also contextualize these traditional outcome measures and their true effect on daily life in a way that challenges traditional medical viewpoints. For example, within the context of VS care, clinicians often consider functional or useful hearing to be a word recognition score above 50%. Yet, a recent study documents that most people

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do not consider their hearing useful if word recognition scores fall below approximately 70%, particularly when the contralateral ear has normal or near-normal hearing (7,8).

In 2021, the authors initially published prospective QOL outcomes among 244 subjects treated at our institution with a mean follow-up of 2.1 years (9). Herein, we report an expanded cohort of 445 subjects recruited through the authors' practice and through the Acoustic Neuroma Association (ANA) with an extended mean duration of follow-up of 4.4 years. Importantly, all subjects in these two studies had prospective QOL data available, including baseline pretreatment data, which is important given potential differences in starting points among management arms resulting from inherent selection biases.

## METHODS

In 2014, the investigators initiated a national survey study (Mayo Clinic Institutional Review Board protocol 14-009331), recruiting subjects to prospectively report longitudinal QOL outcomes using a validated disease-specific instrument, the Penn Acoustic Neuroma Quality of Life (PANQOL) Scale. Eligible subjects were recruited through the Mayo Clinic Rochester clinical practice and through the ANA web site. Subjects treated at other centers nationally have the opportunity to enroll in the study through the ANA web site. Thus, this study includes patients treated at Mayo Clinic and many other centers. To date, over 1,500 subjects have submitted QOL outcomes for at least one time point. The current report summarizes QOL outcomes for all subjects diagnosed with sporadic VS who completed a baseline survey before treatment and at least one follow-up survey after treatment. Specifically, to be included in the microsurgery or radiosurgery arms, patients must have completed a baseline survey and at least one follow-up survey after treatment. To be included in the observation arm, patients must have completed a baseline survey within 1 year of diagnosis and at least one follow-up survey. Patients who were treated with more than one intervention (e.g., radiosurgery after microsurgery or microsurgery after radiosurgery) were excluded.

The outcomes studied included changes in PANQOL scores for anxiety, facial function, general health, balance, hearing loss, energy, pain, and total QOL from the baseline survey to most recent survey. The independent variable was management group (observation versus microsurgery versus radiosurgery) and covariates of interest included source of patient enrollment (Mayo Clinic or ANA), age at the baseline survey, sex, self-reported tumor size at diagnosis, and years between the baseline and most recent surveys. Comparisons of covariates among the management groups were evaluated using analysis of variance, Kruskal–Wallis tests, and  $\chi^2$  tests. The effects of management group on the outcomes studied were evaluated using analysis of covariance and summarized with adjusted means and 95% CIs. Linear model diagnostics were evaluated to verify the underlying assumption of normality and check for multicollinearity and influential observations. Statistical analyses were performed using version 9.4 of the SAS software package (SAS Institute, Cary, NC). All tests were two-sided, and  $p$  values  $<0.05$  were considered statistically significant.

## RESULTS

A total of 445 patients were eligible for study, with a mean age at enrollment of 56 (SD, 13) years and a mean duration of follow-up of 4.4 (SD, 2.3) years. Altogether, 122 patients (27%) were managed with observation alone, 218 patients (49%) underwent microsurgery, and 105 patients (24%) received radiosurgery. A comparison of covariates studied by management group is shown in Table 1. Patients undergoing microsurgery were younger and had larger tumors compared to those receiving radiosurgery or observation alone. The duration of follow-up was not significantly different among management groups.

A summary of baseline and most recent PANQOL scores by management group after adjusting for the covariates of source of enrollment, age, sex, tumor size, and duration of follow-up is shown in Table 2. A comparison of changes in PANQOL scores from the baseline to most recent survey by management group is shown in Table 3. For example, after adjusting for the covariates listed above, including

**TABLE 1.** Comparison of covariates by management group,  $N = 445$

Feature <sup>a</sup>	Observation, n = 122	Microsurgery, n = 218	Radiosurgery, n = 105	$p^b$
Source of patient enrollment				
Mayo Clinic	88 (72)	174 (80)	76 (72)	0.17
ANA	34 (28)	44 (20)	29 (28)	
Age at baseline survey in years	59 (12)	52 (14)	62 (10)	<0.001
Sex				
Female	73 (60)	126 (58)	55 (52)	0.5
Male	49 (40)	92 (42)	50 (48)	
Tumor size at diagnosis in cm ( $n = 113:203:94$ )				
0–0.9	68 (60)	34 (17)	34 (36)	<0.001
1–1.9	36 (32)	81 (40)	46 (49)	
2–2.9	8 (7)	62 (31)	13 (14)	
$\geq 3$	1 (1)	26 (13)	1 (1)	
Years from baseline to most recent survey	4.2 (2.4)	4.4 (2.3)	4.6 (2.0)	0.5

<sup>a</sup>Features summarized with mean (SD) or n (%). Sample sizes for features with missing data are indicated in italics.

<sup>b</sup> $p$  value for whether the feature is statistically significantly different among management groups (observation versus microsurgery versus radiosurgery). ANA, Acoustic Neuroma Association.

**TABLE 2.** Summary of baseline and most recent PANQOL scores by management group

	Observation	Microsurgery	Radiosurgery
Baseline PANQOL score, mean (95% CI) <sup>a</sup>			
Anxiety	71 (66–77)	64 (60–68)	68 (63–74)
Facial function	85 (81–89)	84 (81–87)	85 (81–90)
General health	66 (62–70)	63 (60–66)	62 (57–66)
Balance	72 (66–78)	59 (55–63)	68 (62–74)
Hearing loss	63 (58–69)	55 (52–59)	57 (51–62)
Energy	67 (61–73)	56 (52–60)	61 (55–67)
Pain	72 (65–80)	60 (55–65)	68 (60–75)
Total	71 (67–75)	63 (61–66)	67 (63–71)
Most recent PANQOL score, mean (95% CI) <sup>a</sup>			
Anxiety	77 (71–83)	74 (70–78)	71 (65–77)
Facial function	82 (78–87)	74 (70–77)	83 (78–88)
General health	64 (59–68)	66 (63–69)	59 (54–63)
Balance	68 (62–73)	58 (54–62)	64 (58–70)
Hearing loss	59 (54–65)	49 (45–52)	48 (42–53)
Energy	68 (63–74)	57 (53–61)	58 (52–64)
Pain	78 (71–85)	60 (56–65)	71 (64–78)
Total	71 (67–75)	63 (60–65)	65 (61–69)

<sup>a</sup>Adjusted for source of patient enrollment, age, sex, tumor size, and years from baseline to most recent surveys.

PANQOL, Penn Acoustic Neuroma Quality of Life.

tumor size, the mean changes in anxiety scores on a 100-point scale from the baseline to most recent survey after multivariable adjustment were 6, 10, and 3 for the observation, microsurgery, and radiosurgery groups, respectively. All three management groups demonstrated improvement in anxiety scores, although the improvement was statistically significant for those managed with observation ( $p = 0.03$ ) or microsurgery ( $p < 0.001$ ) but not for those receiving radiosurgery ( $p = 0.3$ ). However, there was not enough evidence to conclude that the magnitude of improvement in anxiety scores differed significantly by management group ( $p = 0.07$ ). For context, changes in this domain of at least 11 points are considered clinically significant, whereas changes of at least 20 points for facial function, 15 points for general health, 16 points for balance, 6 points for hearing loss, 13 points for energy, 11 points for pain, and 11 points for total QOL scores are considered clinically significant (10). Changes in facial function scores differed significantly by

management group ( $p = 0.01$ ), with patients undergoing microsurgery demonstrating a mean decline of 10 in facial function scores compared with mean declines of 3 for those managed with observation or radiosurgery. Hearing loss scores decreased over time for all three groups, with mean declines of 4, 7, and 9 for those managed with observation, microsurgery, and radiosurgery, respectively ( $p = 0.3$ ). There were minimal changes in total PANQOL scores over time across all management groups, with mean changes of 0, -1, and -2 for those managed with observation, microsurgery, and radiosurgery, respectively ( $p = 0.5$ ).

The single-modality microsurgery and radiosurgery groups were further divided into those who underwent upfront treatment, defined as an interval between diagnosis and treatment of less than 6 months and those who underwent a period of observation for at least 6 months before treatment. The 218 patients who underwent microsurgery included 131 with upfront treatment and 87 with an initial period of observation, whereas the 105 patients who received radiosurgery included 26 with upfront treatment and 79 with an initial period of observation. Changes in PANQOL scores from the baseline to most recent survey for these four groups, as well as those who were managed with observation only, are shown in Table 4. Patients who underwent microsurgery, either upfront or after a period of observation, demonstrated similar improvements in anxiety scores and similar declines in facial function scores. Even when stratified into upfront versus delayed treatment, hearing loss scores declined during follow-up regardless of management modality, with several changes exceeding the published minimally clinically important difference of 6 points (10).

**DISCUSSION**

In this report, the authors describe long-term QOL outcomes using a validated disease-specific measure in a large national cohort of subjects encompassing all three management modalities, including pretreatment baseline data. When comparing management groups, extended follow-up becomes imperative because each treatment modality

**TABLE 3.** Comparison of changes in PANQOL scores from baseline to most recent by management group

Changes	Observation		Microsurgery		Radiosurgery		$p^c$
	Mean (95% CI) <sup>a</sup>	$p^b$	Mean (95% CI) <sup>a</sup>	$p^b$	Mean (95% CI) <sup>a</sup>	$p^b$	
Anxiety	6 (0 to 11)	0.03	10 (6 to 14)	<0.001	3 (-3 to 8)	0.3	0.07
Facial function	-3 (-8 to 2)	0.3	-10 (-14 to -7)	<0.001	-3 (-8 to 3)	0.3	0.01
General health	-2 (-8 to 2)	0.3	3 (0 to 6)	0.08	-3 (-8 to 2)	0.18	0.06
Balance	-4 (-10 to 1)	0.12	-2 (-5 to 2)	0.4	-4 (-9 to 2)	0.16	0.7
Hearing loss	-4 (-9 to 1)	0.09	-7 (-10 to -4)	<0.001	-9 (-14 to -4)	<0.001	0.3
Energy	1 (-4 to 6)	0.6	1 (-2 to 4)	0.6	-4 (-9 to 2)	0.17	0.2
Pain	6 (-2 to 14)	0.12	1 (-4 to 6)	0.8	4 (-4 to 11)	0.4	0.5
Total	0 (-3 to 3)	0.9	-1 (-3 to 2)	0.6	-2 (-6 to 1)	0.19	0.5

<sup>a</sup>Adjusted for source of patient enrollment, age, sex, tumor size, and years from baseline to most recent surveys.

<sup>b</sup> $p$  value for whether change in PANQOL scores from baseline to most recent survey is statistically significantly different from zero within each management group separately.

<sup>c</sup> $p$  value for whether change in PANQOL scores from baseline to most recent survey is statistically significantly different among management groups (i.e., observation versus microsurgery versus radiosurgery).

PANQOL, Penn Acoustic Neuroma Quality of Life.

**TABLE 4.** Comparison of changes in PANQOL scores from baseline to most recent by management group accounting for observation then treatment and upfront treatment

Changes	Observation		Observation Then MS		Upfront MS		Observation Then RS		Upfront RS	
	Mean (95% CI) <sup>a</sup>	p <sup>b</sup>	Mean (95% CI) <sup>a</sup>	p <sup>b</sup>	Mean (95% CI) <sup>a</sup>	p <sup>b</sup>	Mean (95% CI) <sup>a</sup>	p <sup>b</sup>	Mean (95% CI) <sup>a</sup>	p <sup>b</sup>
Anxiety	6 (0 to 11)	0.03	9 (3 to 15)	0.006	11 (6 to 16)	<0.001	1 (-6 to 7)	0.8	6 (-3 to 16)	0.2
Facial function	-3 (-8 to 3)	0.3	-12 (-18 to -6)	<0.001	-9 (-14 to -6)	<0.001	-2 (-8 to 4)	0.5	-5 (-14 to 4)	0.3
General health	-2 (-8 to 2)	0.3	1 (-5 to 6)	0.9	4 (0 to 8)	0.04	-3 (-9 to 2)	0.3	-5 (-14 to 3)	0.2
Balance	-4 (-10 to 1)	0.12	4 (-2 to 10)	0.16	-5 (-9 to 0)	0.04	-2 (-9 to 4)	0.5	-3 (-13 to 6)	0.5
Hearing loss	-4 (-9 to 1)	0.09	-4 (-10 to 1)	0.12	-8 (-12 to -4)	<0.001	-9 (-15 to -3)	0.005	-8 (-17 to 0)	0.06
Energy	1 (-4 to 6)	0.6	-1 (-7 to 4)	0.6	2 (-2 to 6)	0.3	-6 (-12 to 0)	0.07	-1 (-9 to 8)	0.9
Pain	6 (-2 to 14)	0.12	5 (-4 to 13)	0.3	-1 (-8 to 5)	0.7	4 (-5 to 13)	0.4	6 (-8 to 19)	0.4
Total	0 (-3 to 3)	0.9	0 (-4 to 4)	0.9	-1 (-4 to 2)	0.5	-2 (-7 to 2)	0.2	-2 (-8 to 4)	0.6

<sup>a</sup>Adjusted for source of patient enrollment, age, sex, tumor size, and years from baseline to most recent surveys.

<sup>b</sup>p value for whether change in PANQOL scores from baseline to most recent survey is statistically significantly different from zero within each management group separately.

MS, microsurgery; PANQOL, Penn Acoustic Neuroma Quality of Life; RS, radiosurgery.

introduces risk at different time points. For example, microsurgery presents the most risks upfront and provides a new stable baseline after approximately 1 year—a “new normal”—whereas radiosurgery and observation generally spread the risks and symptom evolution over many years in a protracted manner. The time-dependent nature of the QOL experience is also highlighted by a study indicating that, for many people, the worst QOL experienced occurs with the initial diagnosis of VS, particularly within the emotional domain, and this effect often settles with time as the patient reconciles with the diagnosis (11).

Several findings are worth highlighting from this study. First, on a large cohort level, treatment only modified total overall QOL scores by 0 to 2 points on a 100-point scale, which do not exceed previously published minimum clinically important differences for this instrument (10). This reinforces a concept brought forth in prior work that the patient condition (what they enter the treatment with) has a greater effect on outcome than the treatment itself (9,12). A second important point is that, for the most part, treatment does not improve QOL over natural history. Treatment is most commonly used to prevent potential complications associated with increasing mass effect but does not predictably reverse existing neurological dysfunction. For example, microsurgical resection has been historically recommended for people with prominent “dizziness,” yet patient-reported outcome data from this study and prior work indicate that, on the whole, microsurgery does not generally improve this symptom compared to other treatment options (13,14). Third, and as a caveat to the second point, microsurgery seems to confer a psychological or emotional benefit as evidenced by an improvement in the anxiety domain of the PANQOL postoperatively (9,12,15). Although not directly assessed in this study, it is possible that this improvement is driven by having the tumor physically removed, the only true “cure” in a sense. Indeed, a prior study found that the second most common motivating factor for patients choosing microsurgery after “physician recommendation” was “do not want tumor in head” (16). Interestingly, patients undergoing microsurgery received this benefit regardless of whether they underwent upfront microsurgery or microsurgery after a period of initial observation. Last,

during longer-term follow-up, the differences in hearing loss among treatment groups equalize. In other words, although microsurgery increases the risk of early hearing loss, declines associated with the natural history of the disease and radiosurgery become similar after approximately 5 years of follow-up. We also acknowledge that in our experience, the PANQOL and other patient-reported outcome measures of hearing loss do not always correlate well with hearing function in the setting of unilateral hearing loss. Thus, the results of the hearing domain may not necessarily parallel audiometric findings.

Since 2012, several studies have examined QOL outcomes in patients with VS using the PANQOL (Supplemental Table 1, <http://links.lww.com/MAO/B974>). Most of the recent literature has evaluated the complex interplay among symptoms, treatment modalities, and patient demographics in determining QOL outcomes. Various questionnaires have been used to assess patient QOL, with the 36-Item Short Form Health Survey (SF-36) being most common in older studies and the disease-specific PANQOL survey most common in recent studies.

The growing body of literature sheds light on the effect of various preoperative and postoperative factors on patient QOL, including balance, hearing status, tinnitus, facial nerve function, tumor size, and the need for salvage therapy. A general trend among these studies is the notion that the diagnosis itself has a greater effect on QOL than management pathway. As discussed earlier, the findings in the present study reinforce this concept, as minimal changes were observed in total PANQOL scores across all management groups. Moreover, in studies that included non-VS controls, those in the control cohort tend to have better overall scores than all VS cohorts, regardless of management strategy (12). As an extension of the current study showing greater improvement within the anxiety domain in the microsurgery arm, compared to other management groups, previous research shows that the extent of resection may affect perceived QOL, with those who receive gross total resection having better QOL outcomes (15).

From our experience researching QOL in VS using the PANQOL and other measures, and based on receiving thousands of comments volunteered from patients through our prospective survey study, we developed a new QOL measure, the Vestibular Schwannoma Quality of Life (VSQOL)

Index, added to our survey study in 2023 (15). As a future step, we plan to compare results of the PANQOL with the VSQOL Index within the same cohort. Limitations of the current study include lack of verifiable data pertaining to tumor characteristics, treatment details, and traditional outcome measures such as audiogram data or facial nerve grading assessments. For example, it is possible that millimeters or centimeters could be inadvertently interchanged when self-reporting tumor size. Second, enrollment through the ANA potentially introduces certain study biases, described previously (17). Specifically, patients interacting with the ANA generally have larger tumors and more severe symptoms compared to the population of patients seen at tertiary referral centers and the general U.S. VS population (17,18). The primary strengths of this study include the relatively large prospective cohort size, the extended follow-up duration, and the inclusion of all three management arms. By including subjects from across the United States who were treated by a wide range of centers, the generalizability of our findings is enhanced.

### CONCLUSION

Long-term changes in total QOL among VS management groups are not significantly different. Microsurgery may continue to confer an advantage regarding anxiety, but with a greater decline in facial function when compared to observation or radiosurgery. Long-term declines in hearing loss scores were not statistically significant among groups, emphasizing the value of longer-term follow-up.

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