ORIGINAL ARTICLE

What determines quality of life in patients with vestibular schwannoma?

Ineke M. J. Pruijn[1] | Wietske Kievit[2] | Mayke A. Hentschel[1] | Jef J. S. Mulder[1] | Henricus P. M. Kunst[1,3]

[1]Department of Otorhinolaryngology, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen, The Netherlands

[2]Department for Health Evidence, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen, The Netherlands

[3]Department of Otorhinolaryngology, Maastricht University Medical Center, Maastricht, The Netherlands

Correspondence
Ineke M. J. Pruijn, Radboud University Medical Center, P.O. Box 9101, 6525, EX Nijmegen, The Netherlands.
Email: Ineke.Pruijn@radboudumc.nl

Abstract

Objectives: Patients with a vestibular schwannoma (VS) experience a reduced quality of life (QoL). The main objective of this study was to determine the strongest predictors reducing physical and mental QoL from the disease-specific Penn Acoustic Neuroma Quality of Life (PANQOL) questionnaire in patients with VS.

Design: Observational study.

Setting: Radboudumc Skull Base Centre, Nijmegen.

Participants: Patients newly diagnosed with VS between 2014 and 2017 managed with either observation, stereotactic radiosurgery or microsurgery.

Main outcome measures: Quality of life was assessed using the disease-specific PANQOL and general Short-Form (36) Health Survey (SF-36). Multiple linear regression models with PANQOL domains as predictors were used to determine the strongest predictors for SF-36 QoL physical and mental health scores. Standardised beta coefficients (β) were used for ranking.

Results: A total of 174 patients (50% females, mean age 58.9 years) returned the questionnaires, providing a 69% response rate. Fifteen patients (9%) were treated with microsurgery, 29 (17%) with stereotactic radiosurgery and 130 patients (75%) were observed in a wait and scan strategy. A lack of energy ($\beta = .28$; $P \leq .001$), lower general health ($\beta = .22$; $P \leq .001$), headache ($\beta = .16$; $P \leq .001$), anxiety ($\beta = .15$; $P \leq .001$) and balance problems ($\beta = .10$; $P \leq .001$) are the strongest predictors affecting physical health, while mental health is most affected by anxiety ($\beta = .37$; $P \leq .001$), a lack of energy ($\beta = .34$; $P \leq .001$), facial nerve dysfunction ($\beta = .07$; $P \leq .001$), balance problems ($\beta = .04$; $P \leq .001$) and headaches ($\beta = .04$; $P \leq .001$).

Conclusion: A lack of energy, anxiety, headache and balance problems are the strongest predictors of both SF-36 physical and mental QoL in patients with VS. More awareness and supportive care regarding energy, anxiety, headache and balance in informing, evaluating and treating patients with VS could improve QoL.

1 | INTRODUCTION

Vestibular schwannomas (VSs) are benign, slowly growing tumours, arising from the eighth cranial (vestibulocochlear) nerve with an incidence of 34 VSs/million/year.[1] The most commonly known symptoms in patients with VS are asymmetrical hearing loss, tinnitus and dizziness or balance complaints.[2] Patients might, however, also experience anxiety, fatigue, headache and depression.[3] Aforementioned symptoms have a substantial impact on the patient's quality of life (QoL).

Current management strategies for VS comprise observation in a wait and scan (W&S) strategy with serial imaging, microsurgery (MS) or stereotactic radiosurgery (SRS).While currently, in management of VS, high tumour control rates and remarkably low mortality rates are already achieved,[4] preservation of QoL and possible improvement in QoL has become of paramount importance. Supportive care should therefore be aimed at treating symptoms that have a high impact on perceived QoL.[5]

Despite this, the majority of VS literature is focused on treatment outcomes such as tumour control rates, preservation of serviceable hearing and facial nerve outcomes, usually set by physicians.[6-8] There is, however, often a disparity between what physicians prioritise and what patients value.[4,9] Ongoing dizziness and headache for example, have shown to be stronger predictors for long-term reduced QoL than the impact of hearing loss, tinnitus and even facial paralysis.[3] The easy to use and disease-specific multi-domain Penn Acoustic Neuroma Quality of Life (PANQOL) questionnaire[10] makes it possible to measure and monitor QoL in patients with VS. Insight in the effect, weight and importance of factors affecting the patient perceived overall health-related QoL are therefore of major clinical importance to preserve and possibly improve this, yield targets for treatment outcomes, further improve patient outcomes and enhance patient counselling. For that purpose, the current study aimed to determine the strongest predictors affecting physical and mental QoL in patients with VS.

2 | MATERIALS AND METHODS

2.1 | Study cohort

For this analysis, we selected patients and data from the prospectively maintained Radboudumc VS database. This database contains all patients aged 18 years and older, with a newly diagnosed unilateral VS. This registry is approved by the Regional Review Board of the Radboud university medical center, Nijmegen, the Netherlands. Patients with neurofibromatosis type 2 or malignancies are excluded from the registry. Clinical data on age, sex, Koos classification[11] and treatment are regularly gathered from the electronic patient files and entered in the database. In the year 2017, all patients newly diagnosed with VS between 2014 and 2017 were invited to fill in the disease-specific PANQOL questionnaire[10] and general QoL Short Form (36) Health Survey (SF-36). Patients who received salvage treatment were excluded. These questionnaires were used in the current study.

Key points

1. Lack of energy, anxiety, headache and balance problems are the strongest predictors for SF-36 physical and mental health in patients with VS.
2. Overall, hearing- and tinnitus-related symptoms have no significant impact on SF-36 physical and mental health.
3. More awareness and supportive care regarding energy, anxiety, headache and balance in informing, evaluating and treating patients with VS could improve QoL.

Comparing PANQOL data of a VS population with a non-VS cohort could also give insight in those symptoms most affected by the disease; therefore, we compared our PANQOL results of patients with a VS to PANQOL data that was acquired from the general population. Two hundred study packages containing an informing letter and the PANQOL questionnaire were distributed in the mailbox of citizens in random streets in different neighbourhoods in Nijmegen and surroundings. Because it was unknown who the residents of the household were, we considered this a random selection. To improve comprehensiveness of the PANQOL questionnaire for non-VS participants, three questions were made clearer by leaving out the specific words "vestibular schwannoma": "I accomplish less than I would like," "I have problems with head pain on one side of the head" and "I often feel isolated," questions 13, 14 and 20, respectively (see PANQOL questionnaire[10]). Participants 18 years or younger, with a VS or with inconsistent answers (strongly disagreeing, claiming an excellent QoL (q1-24), but also strongly disagreeing with "My health is excellent" (q25)) were excluded from analysis.

2.2 | Quality of life assessment

The disease-specific PANQOL questionnaire[10] and general SF-36 were used to assess QoL. Results of the PANQOL and SF-36 in patients treated with W&S, SRS and MS were compared to non-VS controls for the PANQOL, and to a national Dutch non-VS cohort by Aaronson et al for the SF-36 scores.[12] The Minimal Clinically Important Difference (MCID),[13,14] defined as the smallest difference in scores that patients perceive as important, was used to interpret differences between cohorts.

2.3 | PANQOL

The disease-specific PANQOL consists of 26 questions on several domains with answer options on a Likert-scale ranging from strong disagreement (1) to strong agreement (5).[10] The translated and validated Dutch PANQOL version was used for this study.[15] The original domain "pain," measured with one item in the PANQOL ("I have problems with head pain on the side of my vestibular schwannoma")

actually questions the presence of headache. For that reason, the domain was renamed *"headache"* in this study. Scores were normalised to a 0-100 point scale to calculate domain scores on hearing, balance, facial function, headache, anxiety, energy and general health by averaging the scores corresponding to each domain, with higher scores indicating better QoL. The total PANQOL score was calculated by the mean score on these seven domains.

2.4 | SF-36

The general SF-36 health questionnaire contains 36 items corresponding to eight domains, that is Physical Functioning, Social Functioning, Physical Role limitations, Emotional Role limitations, Mental Health, Vitality, Bodily pain and General Health perceptions. Though the SF-36 is a general QoL questionnaire, with limited hearing- and vertigo-related measures, it is frequently used in VS QoL research, enabling comparison with other studies. It is a well-established instrument to measure HRQOL in many different diseases. Scores on a scale from zero to 100 were calculated for each domain with higher scores indicating better health and well-being. For each patient, the individual scores were summarised into the Mental Component Summary (MCS) score and Physical Component Summary (PCS) score.[16]

2.5 | Statistical analysis

To determine the symptoms with the strongest effect on QoL stratified by treatment strategy, we performed a multiple linear regression analysis with the PANQOL domain scores as predictors for both the SF-36 PCS and MCS scores. Standardised beta coefficients were used to compare and rank the influence of predictors. Patient and tumour characteristics of influence on QoL were compared between treatment groups to check for significant differences and added as covariates to the linear regression one by one. Covariates with a significant impact, defined as a difference of ≥10% on the beta-coefficient of the PANQOL domains, were included in the final model. Regression model diagnostics were used to check for multicollinearity. Statistical significance was defined as P-values ≤ .05. Variables were summarised with means, standard deviations (SD) and 95% confidence intervals (CIs), and compared using Student's t tests for continuous variables or chi-squared test for categorical data. Statistical analysis was performed using RStudio, version 1.1.463 (RStudio). The "mice" package was used for multiple imputation of missing answers which were missing at random.[17]

3 | RESULTS

Questionnaires were completed by 174 (69%) of the 252 invited VS patients. There were no statistical differences between responders and non-responders (data not shown). Of the 174 respondents, 50% was female, the mean age at time of the survey was 58.9 years (SD

11.7, range 22-89) and mean time between diagnosis and the questionnaire was 1.8 years (SD 0.9). The majority of patients (n = 112, 64.4%) had a VS extending into the cerebellopontine angle (Koos II-IV). One hundred thirty patients (75%) were observed in a wait and scan strategy while 29 (17%) were treated with stereotactic radiosurgery and 15 patients (9%) had received microsurgery. The mean time between treatment (SRS or MS) and survey was 13 months (SD 6.8 months) (Table 1).

3.1 | PANQOL

PANQOL scores were highest on the face, anxiety and headache domain, indicating better QoL, and lowest for the hearing, balance, general and energy domain. Mean scores and standard deviations of the current study, the national non-VS Dutch sample, and the MCID are presented in Table 2.

Of the 200 invited non-VS participants from the general population, 93 responded. One participant was excluded because of age <18 years and one participant was omitted due to inconsistent answers, leaving 91 participants (45.5%) for analysis. People from the VS and non-VS cohort were comparable in age (58.9 vs 61.1 years, P = .153, 95% CI = −5.1 to 0.8) and sex (50% vs 49.5% female, P = .918, 95% CI = −0.1 to 0.1). Figure 1 displays the mean PANQOL domain scores by treatment modality and the Dutch non-VS cohort. Similar to VS patients, the PANQOL scores in the non-VS cohort were highest on the headache, face and anxiety domain and lowest for the hearing, general, energy and balance domains, though with general significant higher scores than in the VS population. The mean differences between the VS cohort and general population did, however, not exceed the MCID[13] on the general domain for W&S and the face domain for W&S, SRS and MS.

3.2 | SF-36

In comparison with the national Dutch non-VS sample of Aaronson et al[12] (Figure 2) patients treated with SRS and MS had a PCS and MCS score lower than the MCID,[14] indicating clinically relevant lower scores (Table 3).

3.3 | Association of symptoms reducing QoL

The results of the developed multiple linear regression model using PANQOL domain scores to predict the SF-36 PCS and MCS scores are summarised in Table 4. In general, the PANQOL energy, general health, headache and anxiety domain were the four determinants with the highest influence on PCS outcomes ($F_{(8, 3584)}$ = 491.5; R^2 = .52; P ≤ .05). The face and hearing domain showed to have no significant influence on the PCS score in all patients together, but did prove to influence the PCS score when

TABLE 1 Patient characteristics

	W&S n = 130 (75%)	SRS n = 29 (17%)	MS n = 15 (9%)	Pairwise comparisons, P-value		
				W&S vs SRS	W&S vs MS	SRS vs MS
Age at survey, years (SD)	59.8 (11.1)	58.1 (10.2)	52.9 (15.7)	<.001	<.001	<.001
Diagnosis to survey, months (SD)	19.1 (9.4)	28.9 (7.3)	19.2 (5.0)	<.001	.746	<.001
Sex						
Female	61 (46.9%)	20 (69.0%)	6 (40.0%)	<.001	.020	<.001
Male	69 (53.1%)	9 (31.0%)	9 (60.0%)			
Side VS, right	75 (57.7%)	13 (44.8%)	7 (46.7%)	<.001	<.001	.595
Koos classification						
Koos I	68 (52.3%)	5 (17.2%)	2 (13.3%)	<.001	<.001	<.001
Koos II	31 (23.8%)	9 (31.0%)	0			
Koos III	17 (13.1%)	7 (24.1%)	0			
Koos IV	14 (10.8%)	8 (27.6%)	13 (86.7%)			
Management to survey, months (SD)	NA	12.6 (8.2)	14.4 (5.3)	NA	NA	.466

Note: Bold: $P \le .05$.

TABLE 2 Comparison of PANQOL scores

	All	W&S	SRS	MS	Non-VS		Pairwise comparisons, P-value		
	(n = 174)	(n = 130)	(n = 29)	(n = 15)	(n = 91)	MCID	Non-VS vs W&S	Non-VS vs SRS	Non-VS vs MS
Age, yr (SD)	58.9 (11.6)	59.8 (11.1)	58.1 (10.2)	52.9 (15.7)	61.1 (14.0)		.443	.289	.041
Gender (%)									
Female	87 (50%)	61 (46.9%)	20 (69.0%)	6 (40.0%)	45 (49.5%)		.711	.066	.497
Male	87 (50%)	69 (53.1%)	9 (31.0%)	9 (60.0%)	46 (50.5%)				
PANQOL, Mean (SD)									
Anxiety	69.2 (23.4)	71.3 (23.4)	65.5 (24.8)	58.1 (13.9)	87.3 (15.9)[a]	16	<.001	<.001	<.001
Balance	55.9 (25.5)	60.4 (25.3)	42.5 (23.0)	43.2 (17.9)	86.4 (21.4)[a]	14	<.001	<.001	<.001
General	56.0 (22.5)	56.9 (22.4)	53.8 (24.1)	52.3 (19.3)	66.9 (23.2)[b]	13	.002	.01	.023
Hearing	34.9 (20.6)	36.7 (20.9)	29.0 (20.9)	29.9 (14.2)	64.2 (29.7)[a]	13.1	<.001	<.001	<.001
Energy	60.0 (24.3)	63.6 (24.1)	50.5 (24.5)	47.0 (13.7)	82.9 (15.6)[a]	16	<.001	<.001	<.001
Headache	66.4 (31.0)	68.3 (30.8)	61.4 (31.5)	59.4 (29.2)	93.0 (18.1)[a]	21	<.001	<.001	<.001
Face	75.0 (23.1)	77.9 (22.8)	69.6 (24.0)	60.6 (15.9)	92.3 (12.1)	25	<.001	<.001	<.001
Total	59.6 (17.8)	62.2 (17.8)	53.1 (18.0)	50.0 (8.6)	81.8 (12.6)[a]	12.5	<.001	<.001	<.001

Note: Bold: $P \le .05$.
[a]Difference ≥ MCID compared to W&S, SRS & MS.
[b]Difference ≥ MCID compared to SRS and MS.

taking a closer look at the subgroups stratified by treatment modality. Almost similar to all patients together, the four most influencing domains on the PCS score in patients in a W&S strategy were a loss of energy, lower general health, anxiety and headache. For those treated with SRS, loss of energy, lower general health, balance problems and anxiety were the four domains with highest influence on PCS scores. In patients treated with microsurgery, though only 15 in our cohort, the strongest influencing domains

for PCS scores turned out to be balance problems, headache, loss of energy and anxiety.

In modelling the prediction of the MCS for the entire cohort, the PANQOL domains, anxiety, loss of energy, face, balance problems and headache turned out to have a significant impact $F_{(11, 3582)} = 294.9$; $R^2 = .47$; $P \le .05$. For patients in a W&S protocol, anxiety, energy, face and hearing were the domains with the strongest influence on the MCS score. In patients treated with SRS, energy,
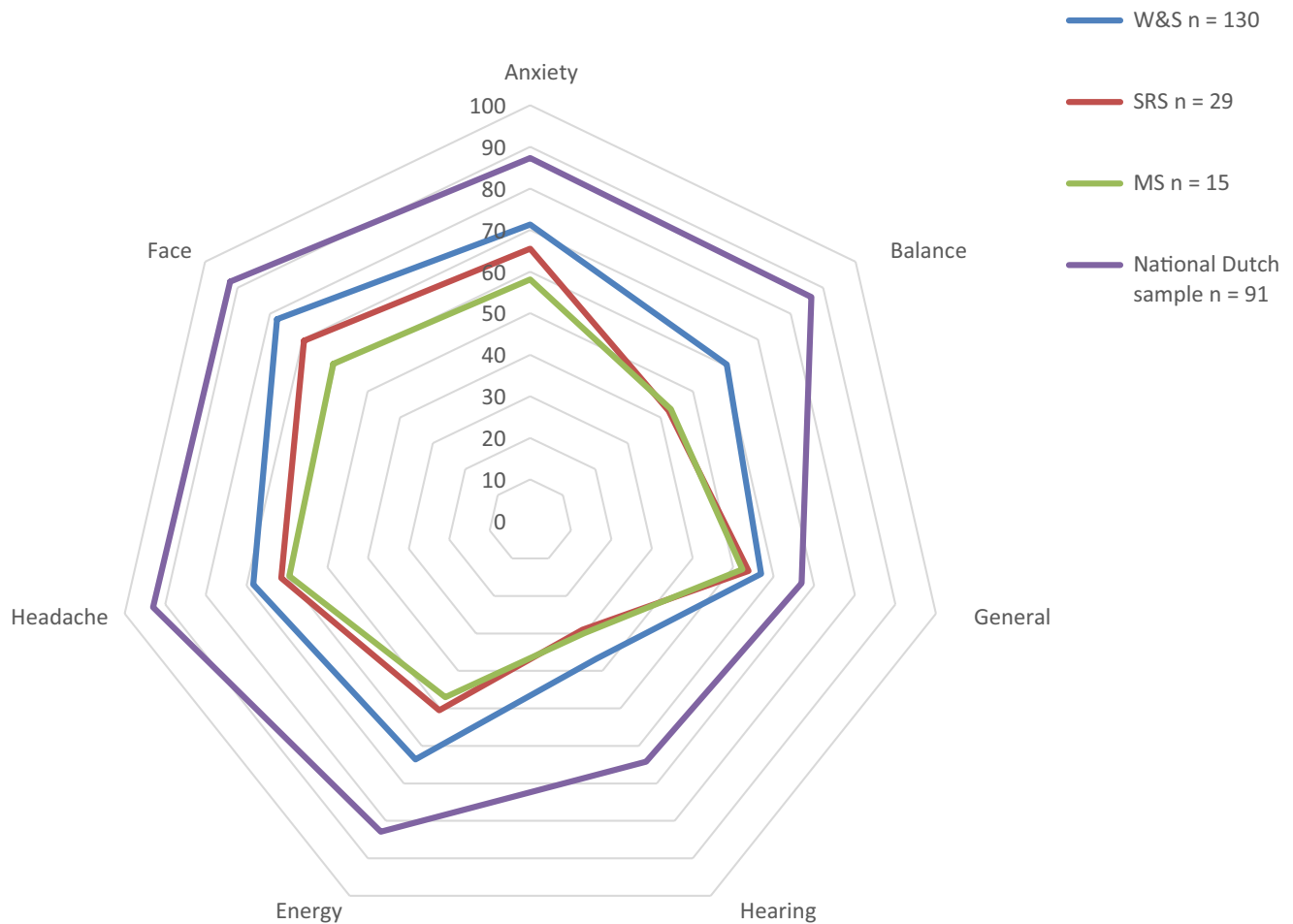
Comparison of PANQOL scores

FIGURE 1 Spider plot comparing PANQOL domain scores. Higher scores indicating better quality of life. MS, microsurgery; PANQOL, Penn Acoustic Neuroma Quality of Life questionnaire; SRS, stereotactic radiosurgery; W&S, Wait and scan

headache and general health had the strongest influence on their MCS score. For patients who underwent MS, headache was the strongest influencer on the MCS score, followed by hearing and general health (Table 4).

4 | DISCUSSION

In this study, we determined the strongest predictors affecting and reducing the SF-36 physical and mental QoL in patients with VS using the disease-specific PANQOL domains as predictors. A lack of energy, headache, anxiety and balance problems had the greatest impact on SF-36 QoL. Specified per treatment strategy, a lack of energy, anxiety and hearing problems have the strongest impact on SF-36 QoL in patients within a W&S protocol. For patients treated with SRS, a lack of energy, lower general health and headache have the greatest influence on QoL while in patients treated with MS, headaches, hearing loss and lower general health determine QoL the strongest. This is particularly interesting as these results show that though PANQOL scores for anxiety, headache, energy and balance are relatively high, indicating good

QoL, these domains had a greater impact on QoL than domains with lower scores for QoL.

4.1 | Comparison with other studies

Our results are in line with current literature. Carlson et al[3] evaluated the contribution of hearing loss, facial nerve paresis, dizziness, tinnitus and headache on the quality of life in 538 patients and found that ongoing dizziness and headache were associated with the greatest reduction in health-related quality of life using the PANQOL and SF-36 PCS and MCS scores. Likewise, Lloyd et al[18] showed dizziness to be the most significant audio-vestibular predictor of QoL in 165 conservatively managed patients when examining associations using the SF-36, Hearing Handicap Inventory, Tinnitus Handicap Inventory and Dizziness Handicap Inventory. Hearing loss on the contrary, did not seem to influence QoL, just like in our study. While the model of Lloyd et al[18] containing audio-vestibular factors only explained a small amount of the data, it was suggested that other factors such as illness perception might also play an important role in the QoL. This was
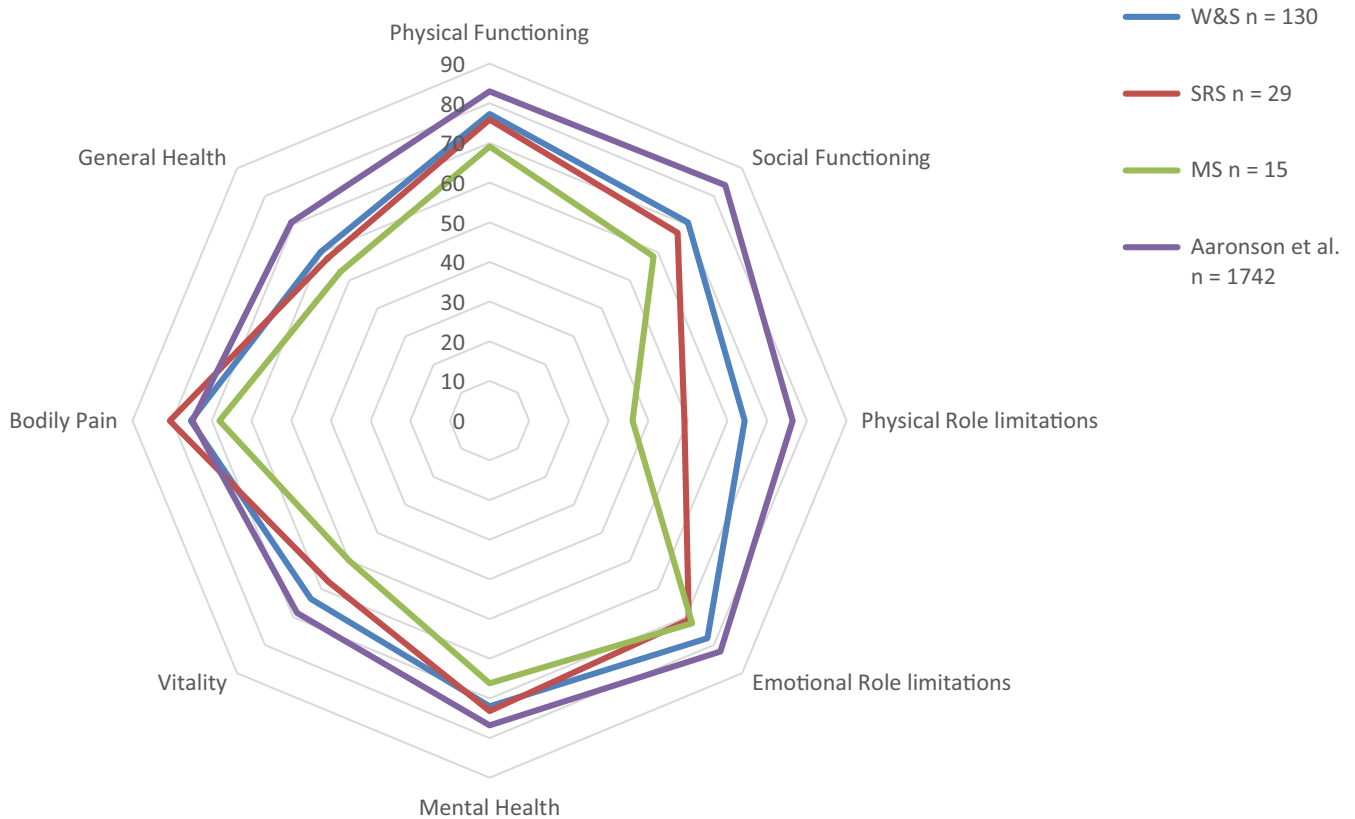
Comparison of SF-36 scores

FIGURE 2 Spider plot comparing SF-36 domain scores. Higher scores indicating better quality of life. MS, microsurgery; SF-36, Short Form 36 Health Survey; SRS, stereotactic radiosurgery; W&S, Wait and scan

confirmed by Carlson et al[19] who showed that VS patients had a significant poorer QoL during the first 6 months following diagnosis, particularly with regard to anxiety. In addition, Dhayalan et al[20] showed that 57% of 88 VS patients suffered from significant fatigue, compared to 25% in 49 matched non-VS controls. This fatigue, which was measured with the fatigue severity scale, had a strong negative correlation to the overall QoL as measured by the PANQOL. Depression, apathy and vertigo were predictors of the fatigue.

Anxiety, a key factor in deterioration of QoL, may derive from the diagnosis of VS as much as the treatment. A newly diagnosed VS imparts significant anxiety on the patient, leading to a reduction in QoL, which shows to be temporary as QoL scores, 6 months after diagnosis, are higher in all patients with VS, either observed in a W&S protocol, treated with SRS or with MS compared to shortly after diagnosis.[19] Anxiety may, however, also derive from the chosen treatment strategy as shown by our results in which anxiety is a significant predictor for physical and mental SF-36 QoL in patients observed with W&S. This may explain why some studies have shown an improved QoL after SRS or MS treatment despite reduced physical functioning.[21,22]

Headache, one of the significant strongest predictors for physical and mental health in our study, is a common symptom in patients with VS. It is usually described postoperatively after surgery or stereotactic radiosurgery and associated with a poorer QoL.[23,24] Carlson et al, however, found that 148 patients with VS, managed with observation,

were more than twice as likely to have severe headache disability than 103 non-VS controls.[25] They speculated dural traction in the internal auditory canal and at the porus acusticus to be the most plausible explanation for this, supported by the observation of the headache most commonly lateralising to the side of the VS.[26] Nevertheless, age, sex, emotional distress and pre-treatment headache were the strongest predictors for long-term headache disability at eight years, whereas treatment modality and tumour size had much less influence.[25]

4.2 | Strengths and limitations

Several strengths and limitations of the current study should be acknowledged. The utilisation of the validated disease-specific PANQOL and general SF-36 instrument for analysing associations and weighed correlations on the quality of life is a major strength. Even though previous studies used poorly discerning multipurpose instruments in assessing QoL in VS patients, such as the Glasgow Benefit Inventory, patient-reported symptoms and several Handicap Inventories,[4] this is the first study to determine the associations of the disease-specific PANQOL to the broadly utilised SF-36, improving generalisability and comparability of our results with other diseases and the general population. Nevertheless, a limitation of the use of these close-ended questionnaires is the absence of space for

TABLE 3 Comparison of SF-36 scores

	All	W&S	SRS	MS	Aaronson et al		Pairwise comparisons, *P*-value		
							Aaronson vs WS	Aaronson vs SRS	Aaronson vs MS
	(n = 174)	(n = 130)	(n = 29)	(n = 15)	(n = 1742)	MCID			
Age, yr (SD)	58.9 (11.6)	59.8 (11.1)	58.1 (10.2)	52.9 (15.7)	47.6 (18)		**<.001**	**.002**	.256
Gender (%)									
Female	87 (50%)	61 (46.9%)	20 (69.0%)	6 (40.0%)	766 (44%)		.513	**.007**	.758
Male	87 (50%)	69 (53.1%)	9 (31.0%)	9 (60.0%)	976 (56%)				
SF-36, Mean (SD)									
Physical functioning	76.3 (24.2)	77.3 (24.1)	75.9 (25.3)	69.1 (21.4)	83.0 (22.8)		**.006**	.097	**.019**
Social functioning	69.0 (26.3)	70.7 (26.9)	67.0 (25.1)	58.5 (19.8)	84.0 (22.4)		**<.001**	**<.001**	**<.001**
Physical role limitations	59.3 (41.2)	64.3 (40.4)	49.1 (41.7)	36.0 (34.9)	76.4 (36.3)		**<.001**	**<.001**	**<.001**
Emotional role limitations	76.0 (35.1)	77.6 (34.6)	71.0 (36.7)	72.2 (35.1)	82.3 (32.9)		.118	.067	.237
Mental health	71.7 (19.4)	72.0 (19.7)	73.2 (17.1)	66.2 (19.3)	76.8 (17.4)		**.003**	.269	**.019**
Vitality	61.4 (22.7)	63.6 (22.2)	57.4 (22.4)	50.0 (22.8)	68.6 (19.3)		**.005**	**.002**	**<.001**
Bodily pain	75.6 (26.4)	75.3 (26.5)	80.6 (25.0)	68.1 (26.1)	74.9 (23.4)		.852	.194	.263
General health	59.2 (21.3)	60.2 (20.2)	57.8 (27.7)	53.1 (13.9)	70.7 (20.7)		**<.001**	**<.001**	**.006**
PCS	67.6 (23.4)	69.3 (23.1)	65.8 (25.9)	56.5 (17.4)	76.3[a]	8	**<.001**	**.031**	**<.001**
MCS	69.5 (21.0)	71.0 (21.4)	67.1 (20.5)	61.7 (16.7)	77.9[a]	7	**<.001**	**.005**	**<.001**

Note: Bold: *P* ≤ .05

[a]Difference ≥ MCID compared to SRS and MS.

TABLE 4 Multiple regression models

	All (n = 174)		W&S (n = 130)		SRS (n = 29)		MS (n = 15)	
	PANQOL Domain	Standardised beta	PANQOL Domain	Standardised beta	PANQOL Domain	Standardised beta	PANQOL Domain	Standardised beta
Physical Component Summary score								
1	**Energy**	**0,2842954**	**Energy**	**0,314049**	**Energy**	**0,270761**	**Balance**	**0,571220**
2	**General**	**0,2191161**	**General**	**0,179516**	**General**	**0,268016**	**Headache**	**0,218785**
3	**Headache**	**0,1613398**	**Anxiety**	**0,115366**	**Balance**	**0,203982**	**Energy**	**0,215692**
4	**Anxiety**	**0,1505325**	**Headache**	**0,106984**	**Anxiety**	**0,190562**	**Anxiety**	**0,201998**
5	**Balance**	**0,0984835**	**Hearing**	**0,059826**	**Headache**	**0,182053**	**Hearing**	**0,141394**
6	Face	0,0086317	**Balance**	**0,045010**	**Face**	**0,068921**	**General**	**0,098737**
7	Hearing	0,0032588	Face	0,008882	Hearing	0,029312	Face	0,077398
Mental Component Summary score								
1	**Anxiety**	**0,370350**	**Anxiety**	**0,384317**	**Energy**	**0,430359**	**Headache**	**0,328616**
2	**Energy**	**0,340653**	**Energy**	**0,357059**	**Headache**	**0,193926**	**Hearing**	**0,133978**
3	**Face**	**0,065366**	**Face**	**0,118743**	**General**	**0,158083**	**General**	**0,103780**
4	**Balance**	**0,043759**	**Hearing**	**0,087625**	Anxiety	0,042201	Energy	0,096854
5	**Headache**	**0,042772**	Balance	0,026551	Face	0,023357	Face	0,075155
6	Hearing	0,024017	General	0,024688	Hearing	0,022302	Balance	0,054732
7	General	0,005424	Headache	0,006584	Balance	0,008204	Anxiety	0,026491

Note: Bold: *P* ≤ .05.

the patient to remark any other symptoms that the patient might experience which were not asked for in the questionnaire, but do influence the QoL. Another conceivable limitation of the study is the possible selection bias in the non-VS cohort as only citizens of Nijmegen, though randomly selected from different neighbourhoods, were invited to participate. Patients with VS referred to our centre, however, live in Nijmegen and surroundings and therefore are considered to be comparable. Moreover, while it is known that age and sex influence QoL scores, the non-VS and VS cohort were well matched for age and sex. Finally, the study cohort, mainly contains patients managed with observation (75%), with lesser patients treated with surgery (9%) or stereotactic radiosurgery (17%), limiting power in subgroup analysis.

4.3 | Clinical applicability

The literature clearly demonstrates that there is a focus on functional nerve preservation in vestibular schwannoma research[27-29] while less time is dedicated to the evaluation of the less tangible features that have shown to significantly influence QoL.[3,18,20] The recently published EANO guideline on the diagnosis and treatment of vestibular schwannoma acknowledges this lack of data on the value of supportive care in VS patients and suggests focusing care on clinical symptoms and treatment of complications.[5] Our results provide valuable information about the symptoms measured with the easy to use disease-specific PANQOL which have the strongest impact on SF-36 QoL and thus should be aimed for in supportive care to preserve and improve QoL in patients observed with W&S, treated with SRS or with MS.

To further improve patient care and QoL, more awareness, attention and resources should be awarded to the acknowledgement, prevention and rehabilitation of a lack of energy, anxiety, headache and balance complaints in patients with VS. While these symptoms may not be continuously present and may fluctuate over time, it is conceivable that patients forget to mention these as we tend to routinely perform MRI scanning, audiometric testing and facial nerve examination during follow-up,[5] making these symptoms easily overlooked. Integrating the routine use of QoL questionnaires, such as the PANQOL, in the follow-up, could be helpful to incorporate the well-being of patients in the outpatient consultation and is an important step towards personalised care. Actively addressing the well-being of patients and commencing the appropriate care either by counselling, rehabilitation, psychological support or multidisciplinary referral could be helpful, improving these symptoms,[3,4,19,30,31] and possibly improve quality of life in patients with VS.

5 | CONCLUSION

When analysing the contribution of all PANQOL domains (anxiety, balance, general health, hearing, energy, headache and facial nerve paresis) on the SF-36 QoL, a lack of energy, anxiety, headache and balance problems are associated with the greatest impact in SF-36 physical and mental QoL. While it is clear that hearing preservation and facial nerve preservation are important outcomes, our results suggest that the greatest potential opportunity to positively impact QoL in patients with VS may be expected from improvements in the counselling, prevention and rehabilitation of the lack of energy, anxiety, headache and balance problems.

CONFLICT OF INTEREST

All authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

IP, WK and DK: Research design. MH: Data collection. IP and WK: Data analysis and interpretation. IP, WK, MH, JM and DK: Manuscript writing and revising.

ETHICAL APPROVAL

The prospectively maintained Radboudumc VS registry is approved by the Regional Review Board of the Radboud university medical center, Nijmegen, the Netherlands.

DATA AVAILABILITY STATEMENT

Deidentified individual participant data will be made available to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to: ineke.pruijn@radboudumc.nl.

ORCID

Ineke M. J. Pruijn https://orcid.org/0000-0002-9439-5626
Mayke A. Hentschel https://orcid.org/0000-0001-6106-089X
Jef J. S. Mulder https://orcid.org/0000-0003-0676-3319

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