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ORIGINAL ARTICLE - TUMOR - SCHWANNOMA

Fatigue in patients with vestibular schwannoma

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Abstract

Background Patients with vestibular schwannoma (VS) often complain about tiredness, exhaustion, lack of energy, and strength, but such symptoms of fatigue have scarcely been objectified and analyzed in a VS population. We aimed to characterize fatigue in a cohort of patients with VS and compare such symptoms with a control group.

Methods All patients who attended an educational course for patients with VS were surveyed with validated tools for assessment of fatigue (fatigue severity scale), anxiety and depression (hospital anxiety and depression scale), sleepiness (Epworth sleepiness scale), and apathy (Starkstein apathy scale). Quality of Life was assessed with the disease-specific Penn Acoustic Neuroma Quality of Life (PANQOL). Symptom severity was estimated with a visual analog scale (VAS). The results have been compared to a control group consisting of patient companions.

Results Data from 88 VS patients and 49 controls were analyzed. The controls had similar age and sex distribution as patients. Fifty-seven percent of VS patients had significant fatigue, compared to 25% in the control group. The mean fatigue score was 4.1 for the patients, and 2.8 for controls. Patients with fatigue were more likely to have depression, anxiety, sleepiness, and apathy. No correlation of fatigue was found with age, gender, or treatment modality. Regression analyses revealed depression, apathy, and vertigo to be predictors of fatigue. Fatigue was strongly correlated to QoL.

Conclusion Almost six out of ten VS patients had fatigue, significantly higher than the control group. Interest and focus on fatigue in VS patients can improve the patient's QoL.

Keywords Vestibular schwannoma · Acoustic neuroma · Fatigue · Quality of life

Abbreviations

ANA	Acoustic Neuroma Association
CSF	Cerebrospinal fluid
Dept.	Department
ESS	Epworth sleepiness scale
FSS	Fatigue severity scale
HADS	Hospital anxiety and depression scale
MS	Microsurgery
PANQOL	Penn Acoustic Neuroma Quality of Life
PD	Parkinson's disease
PROM	Patient-reported outcome measures
QoL	Quality of life
REC	Research ethics committee
SAS	Starkstein apathy scale
SRS	Stereotactic radiosurgery
VAS	Visual analog scale
VS	Vestibular schwannoma

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Introduction

Vestibular schwannomas (VS) are benign and usually slow-growing neoplasms arising from the Schwann cells of the vestibulocochlear nerve [16]. With an incidence of approximately 1–2 per 100,000/year, they account for 6–8% of all intracranial neoplasms and 80–90% of all cerebellopontine angle lesions [2, 26, 31]. The hallmark symptoms of VS are the triad of unilateral hearing loss, tinnitus and vertigo [19]. However, large tumors which affect cerebrospinal fluid (CSF) diversion or compress cranial nerves, the brain stem and cerebellum can cause a much wider range of symptoms [11].

Depending on factors such as tumor size, growth, symptoms, comorbidities, and patient preferences, most tumors are treated by microsurgical resection (MS), stereotactic radiosurgery (SRS), or observation with serial imaging and clinical follow-up [5]. VS are considered to be benign tumor with good prognosis. As the mortality rate from tumor progression and treatment is reduced to a minimum, the importance of disease and treatment-related morbidity, quality of life (QoL) and post-treatment patient satisfaction have gained increasingly prominent roles in patient follow-up and choice of treatment strategy. This is evident from the literature in recent years, with an increasing number of publications focusing on patient-reported outcome measures (PROMs) and QoL [12].

In our practice, we have noted that VS patients frequently complain about fatigue. This complaint has received scarce scientific and therapeutic attention: There are virtually no studies that mainly focus on fatigue in patients with VS, but some have explored fatigue by non-validated methods [10, 23, 38]. To our knowledge, no publications have explored whether VS patients are more likely to suffer from fatigue than the rest of the population, nor are there any studies that seek to identify possible risk factors for fatigue. Mainly from oncological research, we have recognized that fatigue is associated with physical, emotional, psychologic, and social impairment [6, 8]. This could also be the case in patients with VS. Improvement of fatigue could improve QoL, which we know is reduced in VS patients compared to the general population [6, 35].

In the present study, we report prospectively collected data on fatigue in a series of VS patients responding to standardized and validated questionnaires. The patients' responses were compared with a group of individuals not diagnosed with VS. In addition, we analyzed the association between fatigue and clinical complaints caused by vestibular schwannoma.

Methods and materials

Patients and reference population

Our hospital is a tertiary treatment center, where two departments (Dept. of Neurosurgery and Dept. of Head and Neck Surgery) co-operatively share the national treatment responsibility for all patients with VS in Norway. As part of our service, we provide a 2-day educational course for VS patients, fully sponsored through the National Health Service. Each patient may bring one companion, usually the spouse.

During 2014 and 2015, we held five educational courses. All course participants and their companions were invited to take part in a prospective study on the educational course's impact on VS symptoms and QoL. The current study is part of this examination. The patients participating in the course constitute the study population; their companions, often the patient's spouse, constitute the reference population/control group. The study was approved by the regional committee for medical and health ethics (REC, 2014/1376).

Data collection and assessment

Baseline and follow-up clinical data were obtained from a prospectively maintained VS database. The study participants were requested to fill out a compilation of standardized questionnaires and assessment tools. The following questionnaires were utilized in Norwegian translated versions:

1) Fatigue was measured by the fatigue severity scale (FSS), a validated, nine-item questionnaire recommended for both screening and severity rating [20]. FSS was developed in 1989 to facilitate research in this field and is now the most commonly used fatigue specific questionnaire [14, 20, 36]. Each question is rated on a seven-point Likert scale where 1 implies "strongly disagree," and 7 implies "strongly agree." The total score is calculated as the mean score of all questions. A total FSS mean score ≥ 4 is recognized as a cut-off for clinically significant fatigue [20].
2) To distinguish fatigue from anxiety and depression, study participants filled out The hospital anxiety and depression scale (HADS); a self-assessment tool developed to detect states of depression, anxiety, and emotional distress [30, 39]. HADS has a total of 14 questions, 7 of which are related to anxiety and 7 are related to depression. With responses being scored on a scale of 0–3 (higher score, more symptoms), it generates an emotional distress total score (HADS-T), an anxiety score (HADS-A), and a depression score (HADS-D). Scores for each subscale (anxiety and depression) range from 0 to 21 with scores categorized as follows: normal 0–7, mild 8–10, moderate 11–14, and severe 15–21. The scale is not a clinical diagnostic tool. However, in a systematic review, Bjelland and coworkers identified 8/21 as a cut-off point for anxiety or depression [3]. For anxiety, this gave a specificity of 0.78 and a sensitivity of 0.90. For depression, this gave a specificity of 0.79 and a sensitivity of 0.83.
3) To differentiate tiredness and poor sleep from fatigue, sleep quality and daytime sleepiness were evaluated by the Epworth sleepiness scale (ESS); a validated questionnaire with 8 questions [17, 18]. Respondents were asked to rate, on a 4-point scale (0–3), their usual chances of dozing off or falling asleep while engaged in eight different activities. The ESS score equals the sum of 8 item scores and can range from 0 to 24. The higher the ESS score, the higher that person's average sleep propensity in daily life. A score of 9 or above is considered "abnormal (possibly pathologic) sleepiness" [17].
4) To distinguish fatigue from diminished motivation, we utilized the 14-item Starkstein apathy scale (SAS) to

screen for and measure the severity of apathy [32]. The questionnaire has primarily been used testing patients with Parkinson's and Alzheimer's disease [32, 33]. Respondents are asked to determine, on a 1–4 scale, whether or not (not at all, slightly, some, a lot) they lack or have diminished feelings, emotions, interest, or motivation. No cut-off score has been set to define pathological apathy, and for calculations in the current study—we defined a score of 16 (which was equal to the 75% percentile in responses) or above as significant apathy.

5) The Penn Acoustic Neuroma Quality of Life Scale (PANQOL) is a VS-specific QoL assessment tool shown to discriminate VS patients from controls better than the most utilized generic QoL tool (the 36-item short form survey: SF-36) [29]. PANQOL consists of 26 questions with responses ranging from 1 to 5, with 1 denoting strong disagreement through 5 indicating strong agreement. Symptom subscores for facial function, balance, hearing, pain, anxiety, energy, and general health are calculated by the average response of questions assigned to the symptom. A total score is calculated as the equal average of the 7 subscores. As such, the subscores and the total score can range from 0 to 100, with higher scores indicating better QoL.
6) The subjects were additionally asked to tick "yes" or "no" to whether or not they experienced potential VS-related symptoms (hearing, tinnitus, dizziness, balance problems, fatigue, headache, facial pain, taste, problems with tearing, and facial movement). If "yes," they were requested to address the severity by using visual analog scales (VAS) for each symptom.

Statistical analyses

Continuous features have been summarized with means, standard deviations, and medians depending upon data distribution. For the analyses of means between two groups, the Student's *t* test was used if data were normally distributed (e.g., age). For skewed data (e.g., FSS), the Mann-Whitney *U* test was utilized. For analyses of categorical values, two-tailed Fisher's exact test was used. In order to assess the relationship between fatigue and typical VS symptoms, we dichotomized the patients into either "significant fatigue" (FSS ≥ 4) or "no fatigue" (FSS < 4) and performed a logistic regression analysis that was supplemented with a Spearman's rank order correlation. Two-sided *p* values less than 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (Version 22.0. Armonk, NY: IBM Corp.).

Results

Baseline data

A total of 360 VS patients were invited to the courses, of whom 90 (25.0%) patients took part. Eighty-eight (97.8%) agreed to participate by written approval. In addition to the patients, 55 caretakers took part in the educational course of whom 49 (89.1%) agreed to participate in the study as controls. Eleven patients failed to return a completed questionnaire and were omitted from some analyses.

The patients and controls had a comparable age and sex distribution (Table 1). The majority of patients was being treated with observation through serial imaging (46.6%) or had been treated with SRS (38.6%). Thirteen patients (14.8%) had been treated by microsurgical resection. The most common indication for active treatment was tumor growth (40.4%), indicating that many treated patients first had gone through a period of observation. Typically for VS patients, the majority reported the presence of unilateral hearing loss (94.2%), tinnitus (81.6%), vertigo (75.0%), and balance problems (83.0%).

Table 1 Population description

Feature	Mean (median; range) or *N* (%)	
	VS patients	Controls
	(*n* = 88)	(*n* = 49)
Gender, *n* (%) female	51 (58.0)	29 (59.2)
Age at survey (years)	56.0 (55; 35–87)	59.0 (61; 31–83)
Age at Dx (years)	53.5 (53; 25–83)	–
Dx to survey (years)	2.5 (1; 0–23)	–
Tx to survey (years)	1.2 (0.4; 0.0–22.3)	
Tx modality		
Observation	41 (46.6)	–
SRS	34 (38.6)	–
Microsurgery	13 (14.8)	–
Age at first Tx	54.1 (51; 34–87)	–
Indication for first Tx		
Growth	19 (40.4)	–
Size	14 (29.8)	–
Symptoms	14 (29.8)	–
VS symptoms		
Hearing loss	82 (94.2)	–
Balance	73 (83.0)	–
Tinnitus	71 (81.6)	–
Vertigo	66 (75.0)	–
Headache	47 (54.0)	–
Facial palsy	14 (16.1)	–
Trigeminal neuralgia	14 (16.1)	–

Fatigue outcomes

VS patients had a significantly higher (worse) mean FSS total score than the control group; 4.1 versus 2.8 respectively (Table 2). The same applied for all FSS subquestions, except one (fatigue interferes with my physical functioning). Overall, 50 VS patients (56.8%) had a total FSS score of ≥ 4 indicating "significant fatigue." This applied to only 25% of the non-VS population.

Clinical features

In order to examine what clinical features were related to fatigue, we dichotomized the total FSS score in (1) patients with a score ≥ 4 and (2) patients with a score < 4 (Table 3). Age, gender, treatment, time from diagnosis, and time from treatment were equally distributed between the two populations. Although most patients with fatigue did not have depression or anxiety; these issues were more often featured in patients with fatigue as almost 1/3 of patients with fatigue reached clinically significant thresholds, versus close to 0% in patients without fatigue. The majority of patients with fatigue experienced problems with daytime sleepiness (71%)—whereas, in patients with no fatigue, only 40% had such problems. Apathy was also observed more often in patients with fatigue (45%) compared to patients without fatigue (5.6%).

Other questionnaire outcomes

Results from hospital anxiety and depression scale, Epworth sleepiness scale, and Starkstein apathy scale are presented in Table 4. Overall, patients scored significantly poorer than the controls.

Predictors of fatigue

In order to determine clinical predictors for fatigue, we ran a binomial logistic regression analysis with the nine VS symptom VAS scores as independent variables (Table 5). Although the model itself was statistically significant ($p = 0.013$), none of the symptoms were statistically significant predictors for fatigue. We then included HADS-A, HADS-D, SAS, and ESS in the model, and the model was statistically significant ($p < 0.001$). The model explained 64.0% (Nagelkerke R^2) of the variance in fatigue and correctly classified 55.8% of cases. Of the thirteen predictor variables, three were statistically significant: vertigo, depression, and apathy. In a third model which also included age at the time of the study, time from diagnosis to survey, time from treatment to survey, and PANQOL total score—neither of these variables were found significant.

Quality of life

The PANQOL total score revealed a strong and negative correlation with the total score of the fatigue severity scale (Pearson correlation, $r = -0.603$, $p < 0.001$), implicating that fatigue was strongly related to the overall QoL. This was also documented by the mean PANQOL score and subscores in VS patients with or without fatigue, which overall (except "general health") was poorer in patients with fatigue.

Figure 1 compares the mean PANQOL scores in the current study with three other publications on VS and QoL [6, 24, 29]. Overall, respondents in the current study evaluate their disease-related QoL poorer than the respondents in the comparing studies. For question 23 (energy, vitality), the mean difference between the current study population and that of the 2015 Carlson et al. study was significant ($p < .001$) [7].

Table 2 Fatigue severity scale (FSS)

		VS patients ($n = 87$)		Controls ($n = 49$)		95% CI of the Difference	
		Mean	SD	Mean	SD	Lower	Upper
FSS 1	My motivation is lower when I am fatigued	4.9*	(1.9)	4.1	(1.9)	.06	1.40
FSS 2	Exercise brings on my fatigue	4.2*	(1.9)	2.8	(1.7)	.77	2.05
FSS 3	I am easily fatigued	3.8*	(1.8)	2.4	(1.7)	.77	2.05
FSS 4	Fatigue interferes with my physical functioning	4.2	(1.9)	3.6	(1.8)	− .07	1.24
FSS 5	Fatigue causes frequent problems for me	3.5*	(1.9)	2.2	(1.5)	.62	1.92
FSS 6	My fatigue prevents sustained physical functioning	4.0*	(2.0)	2.7	(1.9)	.60	2.02
FSS 7	Fatigue interferes with duties and responsibilities	4.1*	(2.0)	3.0	(1.9)	.34	1.74
FSS 8	Fatigue is among my three most disabling symptoms	3.8*	(2.2)	2.1	(1.7)	.94	2.42
FSS 9	Fatigue interferes with my work, family or social life	3.9*	(2.1)	2.4	(1.8)	.79	2.23
FSS	Total score	4.1*	(1.9)	2.8	(1.5)	.45	1.81

*Significant differences between VS patient and controls ($p < 0.05$)

Table 3 Descriptive data for VS patients with or without fatigue

	VS patients with FSS ≥ 4 (n = 50)	VS patients with FSS < 4 (n = 38)	p value
Gender, n (%) female	32 (66.7)	19 (50.0)	.20 †
Age at survey (year), mean (SD)	55.0 (12.2)	57.2 (9.4)	.37 ‡
Age at Dx (year), mean (SD)	53.0 (12.4)	54.3 (10.3)	.62 ‡
Age at first Tx (year), mean (SD)	54.5 (13.5)	53.5 (11.2)	.79 ‡
Active treatment, n (%)	27 (54.0)	20 (52.6)	1.00 †
PANQOL, mean (SD)	52.9 (12.7)	72.0 (10.6)	.0001 *†
Depression, n (%)	13 (27.1)	0 (0.0)	.0004 *†
Anxiety, n (%)	16 (33.3)	2 (5.3)	.0013 *†
Sleepiness, n (%)	34 (70.8)	15 (39.5)	.0046 *†
Apathy, n (%)	21 (44.7)	2 (5.6)	.0001 *†

*$p < 0.05$

† Two-tailed Fisher's exact test

‡ Simple t test

Discussion

Fatigue in patients with VS is scarcely studied. No prior studies have examined the incidence and severity of fatigue in a VS population by validated methods. We found that more than half of VS patients suffer from significant fatigue and that the mean level of fatigue was almost double compared with the non-VS control group. Unsurprisingly, we found that fatigue was associated with depression, anxiety, daytime sleepiness, and apathy—but also one of the hallmark symptoms of VS; vertigo.

Our study is the first to document fatigue in VS patients by utilizing a standardized instrument, as well as the first to compare with a control group. Nonetheless, fatigue is not entirely unknown territory in VS. In the making of the disease-specific PANQOL instrument, the authors decided to include "concentration and energy level" as an individual topic in the questionnaire [20]. Perhaps the most extensive documentation of fatigue in VS patients is the Ryzenman 2004 publication where all members of the acoustic neuroma association (ANA) were requested to name the "most difficult aspect of the acoustic neuroma experience" [28]. Hearing loss was the most difficult symptom in the majority of patients (25.8%), but 5.1% of patients reported fatigue to be the most challenging symptom. Wiegand et al. reported the subjective assessment of 541 members of the same association in 1989, and 26% of the respondents reported fatigue as a disability [38]. In a United Kingdom cohort of 465 VS patients, Leong et al. explored the issues patients wanted to discuss during their clinic consultation [21]. Tinnitus was the most frequently selected issue (46%), followed by fatigue/tiredness (43%). Brooker et al. investigated the psychological and functional impact attributed to different VS symptoms [4]. The symptoms with the highest prevalence last 4 weeks prior to the questionnaire were hearing loss (95.1%) and fatigue (80.4%). Noticeably, fatigue was the symptom that was most often reported as having a functional impact and was also one of the symptoms most frequently reported to have a severity of "moderate" to "severe" (51.7%). Our results are in line with the indications from the previous studies; fatigue is a significant struggle for VS patients.

Table 4 Depression, anxiety, sleepiness, and apathy in patients and controls

	Patients (n = 88)	Controls (n = 49)
HADS depression, mean (median)	3.59 (2.0)	2.15 (1.0)*
HADS anxiety, mean (median)	4.46 (4.0)	3.71 (3.0)*
HADS total, mean (median)	8.09 (7.0)	5.80 (5.0)*
Epworth sleepiness scale, mean (median)	8.83 (9.0)	6.65 (6.0)*
Starkstein apathy scale, mean (median)	13.10 (13.0)	11.29 (11.0)*

*$p < 0.05$

Herlofsen et al. studied fatigue in a Norwegian cohort consisting of 66 patients with Parkinson disease (PD) [13]. When comparing our VS patients with PD patients, we surprisingly found the mean FSS to be similarly poor. We must take into account the age difference between the two groups; PD patients were even significantly older (71 years) compared to our VS patients (56 years, $p < 0.001$). However, their study excluded patients with depression and dementia. Thus, the actual prevalence of fatigue in PD patients might be higher. Regardless, it is noteworthy that our study population of VS patients has a comparable level of fatigue as the older PD population.

In VS patients without hydrocephalus, it is problematic to relate fatigue and the lack of energy to nearby anatomical structures; fatigue is by all pathogenetic logics a secondary symptom. We first postulated that fatigue was a consequence

Table 5 Logistic regression predicting likelihood of fatigue based on typical VS symptoms ($n = 77$)

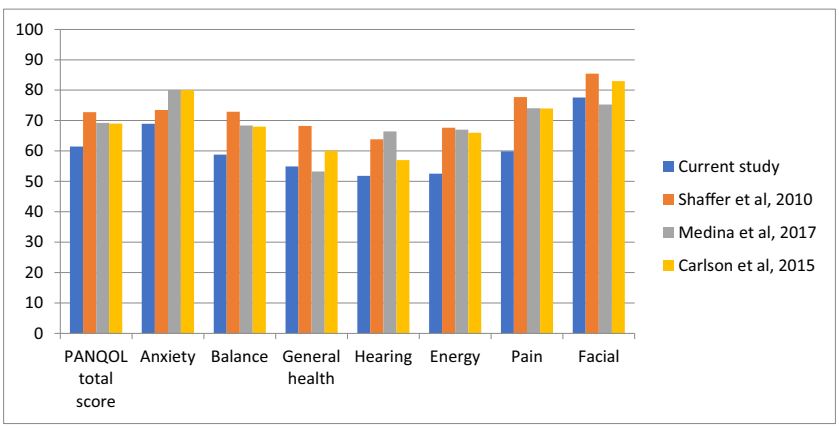
	p	Odds ratio	95% CI for odds ratio	
			Lower	Upper
Hearing	.80	.96	.73	1.28
Tinnitus	.98	1.00	.76	1.31
Vertigo	.05*	1.60	.99	2.58
Balance	.74	1.09	.64	1.88
Headache	.96	.99	.72	1.36
Facial pain	.46	1.35	.61	2.96
Taste problems	.59	.88	.55	1.41
Eye problems	.80	.93	.52	1.65
Facial palsy	.33	1.30	.76	2.22
Anxiety (HADS-A)	.12	1.24	.95	1.62
Depression (HADS-D)	.05*	1.51	1.00	2.27
Apathy (SAS)	.05*	1.24	1.00	1.54
Sleepiness (ESS)	.31	1.12	.90	1.41

of impaired hearing, loss of audiological sense of direction, and so forth. The majority of VS patients have impaired hearing, and it is reasonable to believe that such symptoms require an additional concentration to participate in social settings and that this additional effort results in fatigue. The same logic could be applied to imbalance. Indeed, this coexistence of symptoms has already been suggested in a recent publication by Alhanbali et al. [1]. The authors suggest that hearing loss may increase listening-related effort and fatigue due to increased mental exertion. However, in our study, no correlation was found between hearing loss and fatigue. Indeed, we found vertigo to be the only VS-related symptom that was a predictor for fatigue. This is coherent with our earlier report demonstrating that among vestibulocochlear symptoms, vertigo is the main contributor to reduced quality of life in VS patients [25]. We have also demonstrated a close relation between fatigue and other subjective symptoms such as depression, anxiety, and apathy. The overlap of symptoms and similarities of questions on the questionnaires, possibly explain these close relations [34]. Unsurprisingly, many patients with fatigue also struggle with daytime sleepiness.

We found a strikingly high proportion of patients with "significant" fatigue (56.8%), which might indicate that the cut-off score for fatigue is set too low—and surely this question has been previously debated [22]. Nonetheless, our results are comparable to that of previous studies: In a 2008 validation of the FSS on more than 1300 subjects—with the same cut-off score, Valko et al. found fatigue in 18% of healthy controls, 69% of multiple sclerosis patients, 49% of stroke patients, and 62% of patients with sleep-wake disorders [36].

The relatively high number of patients with fatigue may also in part be explained by the short interval between diagnosis, treatment, educational course, and time of the survey. It is imaginable that the psychological impact of being diagnosed for VS and treated for such can cause fatigue—meaning that we might have witnessed other results if we conducted a similar study at a later stage. Regardless, time between diagnosis, treatment and follow-up, did not correlate to fatigue in our study and were not found to be confounding factors. Neither did age, gender or treatment modality. These finding can be due to a type II statistical error. However, not surprising, as they correspond well to a comparable study where Carlson et al. found small differences in QoL outcomes following observation, SRS and microsurgery—including the PANQOL subdomain "energy" [6].

In closing, we would like to mention the limitations of this study. We suspect the results in part can be explained by potential selection bias as our study population is based exclusively on teaching course participants. All patients with VS at our tertiary treatment center were invited; however, only 25% attended the course. Although we are unable to analyze how representative the responders were for the study population, we must assume that patients who struggle with their disease



Comparison of PANQOL outcomes in four different studies.

Fig. 1 Differences in PANQOL distribution, current study versus previous studies. Comparison of PANQOL outcomes in four different studies

are more likely to participate than patients with less intimidating symptoms. We are concerned about whether fatigued, depressed, and anxious patients are overrepresented in our VS population. This hypothesis is backed by the comparison of PANQOL scores in the current study population versus previous studies: Our VS population consistently have poorer PANQOL scores. Our reference group consists of accompanying guests, mainly spouses. Caretaker stress is a topic of interest, and we are concerned whether this could affect our results. Conversely, we can speculate whether the fatigued caretakers have less energy to bring their spouses to the seminar and whether those who attend might underreport their fatigue when comparing themselves to their spouse with VS. However, Herlofsen et al. assessed fatigue in a cohort consisting of 131 individuals randomly chosen by the Norweigan Central Bureau of Statistics utilizing the FSS and found a mean FSS score at 2.7, which is comparable to our control group of caretakers (2.8) [13]. In both studies, 25% had significant fatigue (total FSS > 4). In future studies, we should avoid course participants and caretakers. Utilizing a general VS population and an independent non-VS control group, would make the results more generalizable.

The subjective nature of fatigue makes it challenging to understand, define, and measure. The anatomical site of the VS and its benign biological characteristics perhaps makes it difficult to acknowledge fatigue as an independent symptom. This is a contradiction to several comparable neurological diseases, such as Parkinson disease, multiple sclerosis, and glioblastoma, where fatigue is acknowledged as a prevalent symptom, and the pathogenesis is well examined [13, 15, 27, 37]. Nonetheless, we have documented fatigue as a symptom in VS, and that its substantial impact on the patients QoL. Given the increasing focus on QoL in VS treatment, fatigue should also be investigated, and if present, attempted treated. As of now, there is probably a communication gap between the patient and the treating doctor. In an oncology setting, it has been shown that patients may benefit from a doctor initiation of discussion of fatigue [9]. It is hard to believe that this would be different in a VS setting.

Conclusion

We have identified that a large proportion of VS patients struggle with fatigue and that fatigue in VS patients is comparable to that of other chronic illnesses such as PD. Vertigo, depression, and apathy were predictors of fatigue, but the overlap of symptoms can explain much of this calculation. One of the primary goals of VS treatment is the maintenance and improvement of QoL. In an effort to reach such goals, fatigue should also be of the doctor's concern and interest. There might be an inclusion bias in our findings. Future studies should investigate fatigue in unselected VS patients.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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