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Quality of Life of Patients With Bilateral Vestibulopathy

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Objectives: Currently, there is no evidence of an effective treatment for patients with bilateral vestibulopathy (BV). Their main complaints are oscillopsia and imbalance. Opinions about the impact of BV on their quality of life are controversial, and their handicap is not always recognized, even among otoneurologists. The aim of this study was to objectively assess the health status of BV patients in order to evaluate the need for pursuing efforts toward the development of new treatments.

Methods: The Short-Form Health Survey (SF-36), the Dizziness Handicap Inventory (DHI), the Short Falls Efficacy Scale–International (Short FES-I), and an oscillopsia severity questionnaire were submitted to 39 BV patients. The SF-36 scores were compared to the scores of a general Dutch population. The DHI scores were correlated to the oscillopsia severity scores. The Short FES-I scores were compared to scores in an elderly population. Residual otolithic function was correlated to all scores, and hearing to SF-36 scores.

Results: Compared to the general Dutch population, the BV patients scored significantly worse on the "physical functioning," "role physical," "general health," "vitality," and "social functioning" SF-36 variables ($p < 0.05$). The DHI scores were strongly correlated with the oscillopsia severity scores ($r = 0.75$; $p < 0.000001$). The Short FES-I scores indicated a slight to moderate increase in the patients' fear of falling. No significant score differences were found between BV patients with residual otolithic function and patients with complete BV. There was no correlation between hearing status and SF-36 scores.

Conclusions: The results correlate with our clinical impression that BV has a strong negative impact on physical and social functioning, leading to a quality-of-life deterioration. There is a clear need for a therapeutic solution. Efforts toward the development of a vestibular implant are justified.

Key Words: bilateral vestibulopathy, oscillopsia, quality of life, VEMP, vestibular evoked myogenic potential, vestibular implant.

INTRODUCTION

The vestibular system enables automatization of balance control, automatization of spatial orientation, and automatization of image stabilization during head movements, allowing the simultaneous performance of various cognitive tasks. For example, under normal conditions, one of the main tasks of the vestibulo-ocular reflex (VOR) is to automatically execute adequate compensatory eye movements during head movements. The semicircular canals' system registers 3-dimensional (3-D) angular accelerations and provides the central nervous system with information about angular head velocity via the vestibular nerve. In case of a bilateral failure of the system, the angular VOR can no longer be elicited. The subject is therefore no longer able to maintain sharp vision on a fixed target during high-frequency head movements, having oscillopsia and reduced visual acuity. It has recently been shown that it is possible to partially restore the angular VOR in animals.[1] In humans, it is possible to control eye movements by selective acute electric stimulation of the vestibular nerve branches. Chronic electric stimulation of the ampullary nerves allows restoration of a baseline firing rate that can be modulated to generate controlled eye movements.[2-6] Those major findings indicate the feasibility of restoring an angular VOR with a vestibular implant that would artificially register 3-D angular accelerations by use of gyroscopes and accelerometers, process the information, and transmit it to the brain via electrodes implanted in the vicinity of the vestibular nerve branches in a way similar to that of a cochlear implant. Patients with bilateral vestibulopathy (BV) would be first-choice candidates. Bilateral vestibulopathy is a chronic condition of which the causes can be ototoxic, infectious, traumatic, autoimmune,

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or congenital, but in approximately 50% of cases, no cause can be found.[7] Currently, there is no clear evidence of an effective treatment for BV patients, and in the long term there is no improvement of the condition for the majority of them, despite vestibular exercises and balance training.[8] The prevalence of BV has been estimated at 81 in 100,000 persons, corresponding to 500,000 patients in Europe and the United States and as many as 3 million worldwide.[9] With progressive aging of the populations of developed countries, presby-vestibulopathy, a progressive neurosensory degeneration that is generally bilateral, could affect an increasing number of patients in the future.[10] Patients with BV complain mainly of oscillopsia (a sensation that the visual environment is moving when it is not) and of imbalance. Symptoms related to vestibular function impairment, such as vertigo, dizziness, headache, nausea, double vision, photophobia, ataxia, and light-headedness, have also been reported in BV patients.[11,12] Those symptoms were rarely mentioned spontaneously by our BV patients and were very heterogeneous among them. Moreover, it can be difficult to accurately define those symptoms. We therefore decided to focus mainly on oscillopsia. Additionally, BV can also induce neuropsychological modifications of body perception in space.[13] As to how BV affects patients' quality of life, otoneurologists differ greatly. Some would say that BV patients adapt very well to the absence of vestibular cues by relying mainly on visual and proprioceptive information and by an increase of their tolerance to oscillopsia,[14] undergoing a minor impact on their quality of life. Our experience tends to show the opposite. Indeed, most of our BV patients mention a decrease of their physical performance, and also complain that their condition is not understood and acknowledged by others. The data on BV patients' quality of life are sparse and are limited to a small number of patients.

Health-related quality-of-life measurements are widely used to assess the burden of a chronic disease, to compare treatments, and to evaluate the efficacy of treatment. They could also be useful tools for justifying the development of new treatments by providing a more objective evaluation of a disease's impact on patients' quality of life. A multidimensional approach, combining a validated general health survey and a validated disease-specific questionnaire, has been chosen to assess the impact of BV on patients' lives. As there is not any standardized way to evaluate oscillopsia, a new questionnaire was developed. The aim of this study was to assess the quality of life, the self-perceived handicap, the "fear of falling," and the severity of oscillopsia in BV patients. As moderate and severe bilateral hearing impairments have a significant impact on general health survey scores,[15] audiometric evaluation was systematically performed. The causes of bilateral vestibular function loss were documented.

TABLE 1. DEMOGRAPHIC VARIABLES IN BV PATIENTS AND IN GENERAL DUTCH POPULATION

	BV Patients (N = 39)	*Normal Population (N = 1,742)*
Age (y)		
Mean ± SD	57.0 ± 10.9	47.6 ± 18.0
Range	29-83	16-94
Gender		
Male	56%	56%
Female	44%	44%

BV — bilateral vestibulopathy.

MATERIALS AND METHODS

BV PATIENTS

Thirty-nine BV patients (22 male and 17 female; mean age, 57 years; age range, 29 to 83 years) who were investigated at the Division of Balance Disorders at Maastricht University Hospital between October 2009 and April 2011 were prospectively included in the study (Table 1). A search of the 2006 to 2009 (January 2006 to September 2009) department database was performed with the first criteria listed below. Eighty-one subjects were found. Of them, 48 accepted our invitation. The remaining 33 could not be reached or declined our invitation. Of those 48 patients, 25 fulfilled the second and third criteria listed below and were included in the study. Fourteen BV patients had diagnoses made between October 2009 and April 2011 and fulfilled all 3 inclusion criteria.

The 3 inclusion criteria were 1) mean peak slow phase velocity of no more than 5°/s in bilateral bithermal caloric irrigations, 2) gain of less than 15% on rotatory chair tests, and 3) pathological head impulse test results for the horizontal and vertical canals. Electronystagmography was used for vestibular testing. Bilateral bithermal (30°C and 44°C) caloric irrigations with water were performed by experienced technicians under standard conditions. Rotatory chair tests consisted of horizontal and vertical torsion swings (0.11 Hz; ω_{max} of 100°/s) and bilateral velocity steps (ω of 250°/s). Manual head impulse test results were recorded with a high-speed camera (Casio Exilim, Pro EX-F1, 12× optical zoom, high speed camera, 300 frames per second) in the 3 semicircular canal planes. Presence of correction saccades in all 6 directions was considered as pathological. All recordings were analyzed by an experienced otolaryngologist.

Assessment of the otolithic function consisted of cervical vestibular evoked myogenic potentials (cVEMPs; Nicolet, Viking IIIP). The active electrodes were placed on the main belly of the sternocleidomastoid muscle, equidistant from the mastoid process and the sternum. The reference electrodes were placed on the superior part of the sternum, and the ground electrode was placed on the forehead. The patients were in the supine position; they were instructed to turn the head contralateral to the stimulation side and then to lift it in order to contract the sternocleidomastoid muscle ipsilateral to the stimulation. The electromyographic results were recorded, amplified, and rectified. Tone bursts (500 Hz at 130 dB sound pressure level stimulus repetition rate of 5.1 Hz, rise time of 2 ms, plateau of 2 ms, and fall time of 2 ms) were transmitted unilaterally via headphones to the right and left ears. Signals of 150 stimuli were averaged. Cervical vestibular evoked myogenic potentials were considered present when unilateral or bilateral positive (P1) and negative (N2) peaks could be identified. The presence of cVEMPs indicated at least a residual otolithic function, of saccular origin.[16] Patients with bilateral absence of cVEMPs and the presence of an air-bone gap were omitted from the calculation.

The hearing assessment consisted of a pure tone air and bone conduction audiogram. Average air conduction thresholds of more than 25 dB hearing level (HL) at the frequencies 0.5, 1, 2, and 4 kHz were considered to show hearing impairment. Thresholds between 26 and 45 dB HL were defined as mild hearing loss, thresholds of 46 dB to 65 dB HL as moderate loss, and thresholds above 65 dB HL as severe loss. The level of hearing loss was defined according to the best ear in patients with bilateral impairment, and according to the worst ear for patients with unilateral impairment.

All patients had a neuro-ophthalmologic examination. The oculomotor function was normal in all BV patients. Polyneuropathy was reported in 1 BV patient. All patients were investigated on a volunteer basis and gave their written informed consent. The investigations were conducted according to the principles expressed in the Declaration of Helsinki.

TABLE 2. OSCILLOPSIA SEVERITY QUESTIONNAIRE

Oscillopsia Severity Questionnaire
1. Do you have the sensation that the visual environment is moving when it's not?
2. By dim light, do you have the sensation that what you see is not stable?
3. Is it difficult for you to recognize known faces when you are walking?
4. When you are reading, do you have the sensation that the text is not stable?
5. When you are watching television, do you have the sensation that the image is not stable?
6. When you are driving your car, do you have the sensation that what you see is not stable?
7. As a car passenger, do you have the sensation that what you see is not stable?
8. When you are riding a bicycle, do you have the sensation that what you see is not stable?
9. When you are walking on uneven ground, do you have the sensation that what you see is not stable?
always = 5, often = 4, sometimes = 3, seldom = 2, never = 1

QUESTIONNAIRES

The questionnaires were submitted to patients during an interview at the Division of Balance Disorders at Maastricht University Hospital.

SF-36. The Short-Form Health Survey (SF-36) is a validated short-form health questionnaire composed of 36 items grouped into 8 variables: "physical functioning," "role physical," "bodily pain," "general health," "vitality," "social functioning," "role emotional," and "mental health," assessing both mental and physical health.[17,18] For each variable, item scores are coded, summed, and transformed on a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state). It is a generic health measure, rather than disease-specific. The validated Dutch version of the SF-36 was used in the present study.[19] The SF-36 scores of the BV patients were compared to scores of a general Dutch population.

DHI. The Dizziness Handicap Inventory (DHI) is a validated 25-item, self-perceived handicap scale designed to assess the effect of dizziness and unsteadiness on quality of life. The items are grouped into 3 subscales evaluating the effects of dizziness and unsteadiness on emotional, functional, and physical aspects of daily living. For each item, there are 3 possible answers: no, sometimes, and yes, giving, respectively, 0, 2, and 4 points. A total score of 100 corresponds to the worst self-perceived disability handicap, and a total score of 0 to an absence of handicap.[20] As it might not be adequate to use the 3 subscales separately, only the total DHI score was used for interpretation.[21,22]

Short FES-I. The Short Falls Efficacy Scale–International (Short FES-I) is a validated questionnaire. It has been implemented to evaluate the fear of falling, especially in elderly persons.[23]

Oscillopsia Severity Questionnaire. A questionnaire assessing oscillopsia severity was developed for the purpose of the study. Oscillopsia was defined as a "sensation that the visual environment is moving when it's not." The 9 questionnaire items investigated oscillopsia frequency in different situations encountered in daily life (Table 2).

TABLE 3. CAUSES OF BV

Cause	Patients (N = 39) No.	%
Idiopathic	18	46.15
Ototoxic	7	17.96
Positive family history for inner ear disease	4	10.26
COCH gene mutation (DFNA9)	4	10.26
Infectious	3	7.69
Wegener's granulomatosis	1	2.56
Meniere's disease	1	2.56
Traumatic	1	2.56

Each item was scored 1 (never), 2 (seldom), 3 (sometimes), 4 (often), or 5 (always). The mean scores gave an oscillopsia severity score ranging from 1 to 5. Mean scores of 3 or more were considered as indicating moderate to extreme oscillopsia severity. The internal consistency of the questionnaire was measured with Cronbach's α. The coefficient α would be 1 if the questionnaire items were perfectly correlated, and 0 if they were independent. Cronbach's α was 0.88 in the group of BV patients. Values above 0.7 are generally considered acceptable.[24]

STATISTICAL ANALYSIS

Means and standard errors were obtained for all SF-36 variables. For each variable, expected SF-36 scores were computed from age- and sex-specific equations obtained in the general population, provided by Aaronson et al[19] (also Aaronson, personal communication, 2010). The differences between actual and expected scores were tested by means of 2-tailed paired *t*-tests. A Mann-Whitney U test was used to compare SF-36 scores, DHI scores, and oscillopsia severity scores between BV patients with and without residual otolithic function. A Mann-Whitney U test was further used to compare the SF-36 scores of BV patients with moderate or severe bilateral hearing loss with the SF-36 scores of BV patients with mild bilateral hearing loss, unilateral hearing loss, or normal hearing. The Pearson product-moment correlation coefficient between DHI scores and oscillopsia severity scores was determined. For all tests, statistical significance was defined as a p value of no more than 0.05.

RESULTS

The cause of bilateral vestibular function loss was ototoxicity in 7 patients (17.96%; due to systemic gentamicin treatment in 6 and cisplatin in 1), related to a *COCH* gene mutation (DFNA9) in 4 (10.26%), and infectious in 3 (2 patients or 5.13% with positive serologic tests for *Borrelia burgdorferi* and 1 patient or 2.56% who had meningitis at the age of 1 year). One patient (2.56%) reported the first symptoms to have occurred after a severe head trauma without fracture (a fall on stairs). One patient (2.56%) had bilateral Meniere's disease, and in 4 patients (10.26%), a positive family history for inner ear disease was known. One patient (2.56%) was known to have Wegener's granulomatosis. In 18 patients (46.15%), no cause could be found (Table 3).

TABLE 4. SF-36 SCORES OF BV PATIENTS COMPARED TO PREDICTED SCORES, COMPUTED FROM AGE- AND SEX-SPECIFIC EQUATIONS OBTAINED IN GENERAL DUTCH POPULATION

SF-36 Variables	Scores of BV Patients (N = 39) Mean	SE	Predicted Scores of Normal Population (N = 1,742) Mean	SE	p
Physical functioning	54.7	4.3	76.8	1.2	<0.001
Role physical	51.9	6.2	71.3	1.1	0.005
Body pain	76.5	3.8	72.1	0.7	0.267
General health	57.5	3.5	67.0	0.7	0.014
Vitality	57.1	2.8	67.1	0.7	0.003
Social functioning	67.3	3.9	81.9	0.5	0.001
Role emotional	75.2	5.4	80.7	0.6	0.342
Mental health	72.1	2.4	75.7	0.5	0.174

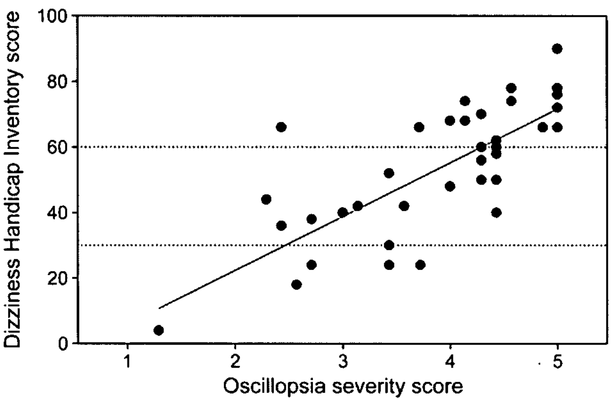
SF-36 — Short-Form Health Survey.

Five of the 8 SF-36 variable scores were significantly lower ($p < 0.05$) than predicted, adjusted scores from the general Dutch population. The 5 SF-36 variables concerned were "physical functioning," "role physical," "general health," "vitality," and "social functioning." There was no significant difference for the other 3 SF-36 variables ($p > 0.05$; Table 4). The presence of cVEMPs could be identified in 20 patients. Two patients with audiometric tests showing an air-bone gap of more than 10 dB over 0.5, 1, 2, and 4 Hz and absent cVEMPs were not included for calculation. The SF-36 scores, DHI scores, and oscillopsia severity scores were not significantly different between BV patients with residual otolithic function and BV patients without residual otolithic function ($p > 0.05$).

The DHI scores were strongly correlated to the oscillopsia severity scores ($r = 0.75$; $p < 0.000001$). DHI scores from 30 to 60 indicate a moderate self-perceived handicap, and scores above 60 indicate a severe handicap.[25] Thirty-three patients (85%) had a score of 30 or above, and 17 patients (44%) had a score of 60 or more (see Figure).

The Short FES-I scores corresponded to a slight to moderate fear of falling for 29 of 39 patients (74%). Three patients (8%) had severe fear of falling, and 7 (18%) had no fear of falling[23] (Table 5).

A pure tone audiogram was performed in 38 of



Dizziness Handicap Inventory (DHI) scores versus oscillopsia severity scores in patients with bilateral vestibulopathy. Self-perceived handicap is considered moderate for DHI scores between 30 and 60, and severe for DHI scores above 60.

the 39 patients. A bilateral hearing impairment was found in 17 patients (44.7%). Among them, 4 (10.5% of 38 patients) had mild hearing loss, 3 (7.9%) moderate, and 10 (26.3%) severe. Unilateral hearing loss was present in 6 patients (15.8%), and 15 (39.5%) had normal hearing (Table 6). No significant differences in the SF-36 scores were found between BV patients with moderate or severe bilateral hearing loss and BV patients with mild bilateral hearing loss, unilateral hearing loss, or normal hearing ($p > 0.05$).

DISCUSSION

The SF-36 scores correlate quite well with our clinical impression. Patients with BV progressively reduce their physical activities. In the Netherlands, a country with about 16 million inhabitants, over 14 million persons ride a bicycle every day, to go to work or social events. Not being able to ride a bicycle anymore is perceived as an important handicap. Most of our BV patients are affected; as a consequence, they have to modify their professional and social activities. As we learned from the different questionnaires, most of our BV patients also have important difficulties with simple tasks such as taking a shower, taking care of the household, going up stairs, or putting on clothes. The scores obtained for "physical functioning" and "social functioning" correlate very well with those observations. The "vitality" variable reveals that they feel less enthusiastic and energetic and are more often tired. The "general health" variable indicates that the BV patients perceive their health as worse than the health of most persons living in their social environment, and that they are not optimistic about improvement of their condition in the future.

TABLE 5. SHORT FES-I SCORES OF BV PATIENTS

Fear of Falling	Patients (N = 39)
None	7
Slight	12
Moderate	17
Severe	3

FES-I — Short Falls Efficacy Scale–International.

TABLE 6. AUDIOMETRIC FINDINGS IN BV PATIENTS

	Patients (N = 38)	
	No.	%
Bilateral hearing loss		
Mild (26-45 dB HL)	4	10.5
Moderate (46-65 dB HL)	3	7.9
Severe (>65 dB HL)	10	26.3
Unilateral hearing loss (>25 dB HL)	6	15.8
Normal hearing (<25 dB HL)	15	39.5

HL — hearing level.

Residual otolithic function of saccular origin was found in 20 BV patients (51%). In contrast, in a study including 84 BV patients, of whom only 48% showed "complete" BV, cVEMPs were present in all patients, with bilateral pathological amplitudes in 61% of the cases.[26] This difference could be explained by the fact that the criteria for defining BV patients differed. In our study, the inclusion criteria were stricter regarding semicircular canal function, which might be associated with poorer otolithic function. No significant score differences (SF-36, DHI, and oscillopsia severity) were found between BV patients with residual otolithic function and BV patients without identifiable otolithic function. This finding is in accordance with a study including 5 BV patients with preserved saccular function who reported oscillopsia while walking.[27]

The results indicate that 34.2% of the BV patients had moderate to severe bilateral hearing impairment. The SF-36 scores of the BV patients with moderate or severe bilateral hearing loss and the BV patients with mild bilateral hearing loss, unilateral hearing loss, or normal hearing were not significantly different, indicating that hearing level was not a relevant factor among our BV patients. The prevalence (44.7%) of bilateral hearing impairment among the BV patients in this study is at least twice as high as that reported for an age-matched general population.[15] Normal hearing was found in 39.5% of BV patients; this percentage is slightly above the 34% reported in 50 BV patients by Rinne et al[11] and the 27% reported by Vibert et al[28] in a study of 52 BV patients. In a large study including 255 BV patients, based on bedside hearing tests and subjective hypoacusis, audiometry was only performed in 80 BV patients, and hearing loss was found in 78 of them.[8] Most likely, no significant hearing loss would have been found in the remaining two thirds of BV patients. As the definition of BV is not uniform and the hearing testing differs in different studies, interpretation of those results is limited. Interestingly, all 5 BV patients with an ototoxic cause due to gentamicin who completed audiometry had normal hearing. This finding is probably due to a higher gentamicin sensitivity on the part of the vestibular hair cells compared to the cochlear hair cells.[29]

The strong correlation with the DHI scores shows that the oscillopsia severity questionnaire can be used to assess oscillopsia severity in BV patients. The DHI scores indicate that the handicap was perceived as severe by 17 BV patients (44%) and as moderate by 16 (41%). It is interesting to see that in a study of 19 patients with superior semicircular canal dehiscence, the mean DHI score was 44.[30] Leaving patients with such a handicap without treatment was not even an option; indeed, they all benefited from surgical treatment with a middle fossa approach despite potential severe complications.[30] In our BV patient group, 26 patients (67%) had a DHI score higher than 44, without having any effective treatment option. Likewise, for most subjects in a group of patients with unilateral vestibular loss with a mean DHI score of 40, there were effective medical, surgical, or rehabilitative treatments available.[25] This finding shows clearly the need to propose therapeutic solutions to BV patients.

Patients with BV can modify their activities and the way they function according to symptom severity, preventing falls efficiently. Of 39 BV patients, only 3 (8%) mentioned having fallen sporadically (results not documented). Fear of falling can be maintained at a low or moderate level, but at a cost, as indicated clearly by the negative impact on quality of life and patients' high ratings of self-perceived handicap.

Efforts to develop a vestibular implant to restore the vestibular reflexes are worthwhile to pursue in order to propose a potential therapeutic solution to BV patients in the future. The SF-36, DHI, Short FES-I, and oscillopsia severity questionnaire could be very useful tools for monitoring BV patients after vestibular implantation.

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