Research article

Clinical characteristics and otolith dysfunction in presbyvestibulopathy: A retrospective cross-sectional analysis

Thanh Tin Nguyen [a,c], Jin-Ju Kang [a,b], Thi Thuy Nguyen [d], Sun-Young Oh [a,b,*]

[a] Department of Neurology, Jeonbuk National University Hospital & School of Medicine, Jeonju, South Korea
[b] Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute, Jeonbuk National University Hospital, Jeonju, South Korea
[c] Department of Pharmacology, Hue University of Medicine and Pharmacy, Hue University, Hue, Viet Nam
[d] Department of General Internal Medicine, Vinh City General Hospital, Nghe An, Viet Nam

ARTICLE INFO

ABSTRACT

Objective: The Bárány Society recently established diagnostic criteria for presbyvestibulopathy, an age-related bilateral vestibular impairments in older individuals. Drawing upon a cross-sectional database, this study delves into the demographic and clinical features of presbyvestibulopathy patients and investigates the implications of otolith dysfunction.

Methods: The study retrospectively analyzed 1218 patients aged 60 years or older who visited the tertiary dizziness clinic in 2020, due to symptoms of dizziness or instability. By reviewing medical records, we gathered clinical information and laboratory vestibular test results, such as cervical and ocular vestibular evoked myogenic potentials, and subjective visual vertical.

Results: Out of 1218 patients aged 60 and above who reported dizziness or unsteadiness, 33 patients (2.7 %, with an average age of 74.2 ± 9.2 years) were diagnosed with presbyvestibulopathy. Deficiencies in horizontal angular vestibulo-ocular reflex were found in caloric tests (75 %), video head impulse tests (51.7 %), and rotatory chair tests (47.8 %), respectively. Otolith dysfunction was also observed, as shown by abnormal ocular and cervical vestibular evoked myogenic potentials in 62.96 % and 51.85 % of patients, and abnormal subjective visual vertical in 45.8 % of the cases.

Conclusions: Among elderly patients experiencing consistent dizziness or instability, the incidence of presbyvestibulopathy was approximately 2.7 % over one year. Alongside the abnormalities detected in the horizontal angular vestibulo-ocular reflex, significant changes were also noted in the ocular and cervical vestibular evoked myogenic potentials, as well as in the subjective visual vertical tests. As a result, it's vital to underscore the significance of both otolithic function and vestibulo-ocular reflex in the fundamental mechanisms of presbyvestibulopathy.

1. Introduction

Presbyvestibulopathy (PVP) is a recently defined term that characterizes long-term, bilateral deficits in the vestibular system associated with aging. Frequent symptoms include dizziness, disturbances in gait, a sense of instability, and recurrent falls.

---

* Corresponding author: Department of Neurology, Jeonbuk National University Hospital and School of Medicine, Jeonbuk National University, 20 Geonji-ro, Deokjin-gu, Jeonju-city, Jeonbuk, 561-712, South Korea.
E-mail address: ohsun@jbnu.ac.kr (S.-Y. Oh).

Examinations reveal that PVP patients exhibit mild bilateral peripheral vestibular deficits, with results falling between the standard normal ranges and the defined boundaries for bilateral vestibulopathy (BVP) [1–3]. Numerous studies have established a correlation between vestibular impairment in older adults and a decline in cognitive function, postural control, gait speed, and daily tasks, as well as an increased risk of falls and the need for medical attention. These factors ultimately affect their physical and mental quality of life [1,4]. While PVP is age-related rather than strictly age-dependent, significant evidence suggests that endogenous factors, exposure to infection, inflammation, medications, and trauma contribute to the age-related decrease in both structural and physiological vestibular function [1,5]. Research has noted age-related declines in vestibular sensory epithelia (hair cells, otoconia), vestibular ganglion cells, vestibular afferents, and vestibular nucleus cells populations [6–8].

The Bárány Society established diagnostic criteria for PVP in 2019, based on patient history, bedside examinations, and laboratory evaluations (Table 1) [1]. The current criteria do not sufficiently assess the severity of vestibular-related symptoms such as postural imbalance, abnormalities in gait, dizziness, recurrent falls, and potential cognitive impairment. Moreover, the laboratory evaluations only focus on the angular vestibulo-ocular reflex (VOR), which can show mild bilateral hypofunction across high, middle, and low-frequency ranges [1]. Consequently, the current criteria primarily emphasize the role of the semicircular canals (SCCs) in PVP's pathophysiology [6,9–12]. Although the diagnostic criteria do not include otolith function, studies suggest that this function diminishes with age and that the otolith organs may deteriorate earlier than semicircular canals (SCCs) [12–15]. The reasons for the frequently observed absence of vestibular-evoked myogenic potentials (VEMPs) in older adults remain unclear, but growing clinical evidence suggests a need to reassess the role of otolith function in PVP [16]. Therefore, this cross-sectional, database-driven study aims to examine the prevalence and characteristics of PVP while exploring the functions of both otoliths and SCCs in PVP diagnosis [1,16].

2. Materials and methods

2.1. Study design

In this retrospective cohort study, we reviewed 1218 patients' medical records who reported chronic dizziness or unsteadiness visited the tertiary dizziness clinic at Jeonbuk National University Hospital between January 1, 2020, and December 31, 2020. The study design, illustrated in Fig. 1, followed the Declaration of Helsinki and received approval from the Institutional Review Boards of Jeonbuk National University Hospital (no. 20220404500).

To identify patients with PVP who met the Bárány Society diagnostic criteria outlined in Table 1[1], the following exclusion criteria were applied sequentially: (1) having a diagnosis of other causative diseases (n = 737), (2) having a disease duration of less than three months (n = 44), (3) experiencing only one of the four key symptoms, including postural imbalance or unsteadiness, gait disturbance, chronic dizziness, or recurrent falls (n = 77), (4) absence of vestibular function data, such as results from the bithermal caloric test, video head-impulse test (vHIT), or rotatory chair test (n = 219); and (5) patients either showing normal vestibular function outcomes (n = 84) or demonstrating bilateral vestibulopathy (BVP, n = 24). Consequently, only 33 patients (2.7 %), with a mean age of 74.2 ± 9.2 years and including 18 females, fulfilled the PVP criteria and were selected for further analysis (Fig. 1).

Patient data was collected by examining medical records, which contained demographic information, clinical symptoms, and laboratory results of the caloric test [17,18], rotatory chair test [19], vHIT [20,21], pure tone audiometry (PTA) [20], subjective visual vertical test (SVV) [22–24], and cervical and ocular VEMPs [20,21,24].

2.2. Vestibular function tests

2.2.1. Bithermal caloric test

The patient was subjected to a caloric irrigation test while lying down with a head elevation of 30°. Closed-loop water irrigators were used at temperatures of 30 °C and 44 °C, with each irrigation lasting 30 s and a rest interval of 5 min between each. Induced binocular nystagmus was captured using Video-Oculography (VOG, SLMED, Seoul, Korea). The total mean speed of the slow phase of the nystagmus, at the maximum response peak for each side, was recorded in degrees per second across the four different stimulation conditions [17,18].

Table 1
Diagnostic criteria of presbyvestibulopathy by the classification committee of the Bárány Society.

A. Chronic vestibular syndrome (at least 3 months duration) with at least 2 of the following symptoms:
1. Postural imbalance or unsteadiness
2. Gait disturbance
3. Chronic dizziness
4. Recurrent falls
B. Mild bilateral peripheral vestibular hypofunction documented by at least 1 of the following:
1. VOR gain measured by video-HIT between 0.6 and 0.8 bilaterally
2. VOR gain between 0.1 and 0.3 upon sinusoidal stimulation on a rotatory chair (0.1 Hz, Vmax = 50–60°/sec)
3. Reduced caloric response (sum of bithermal maximum peak SPV on each side between 6 and 25°/sec)
C. Age ≥60 years
D. Not better accounted for by another disease or disorder

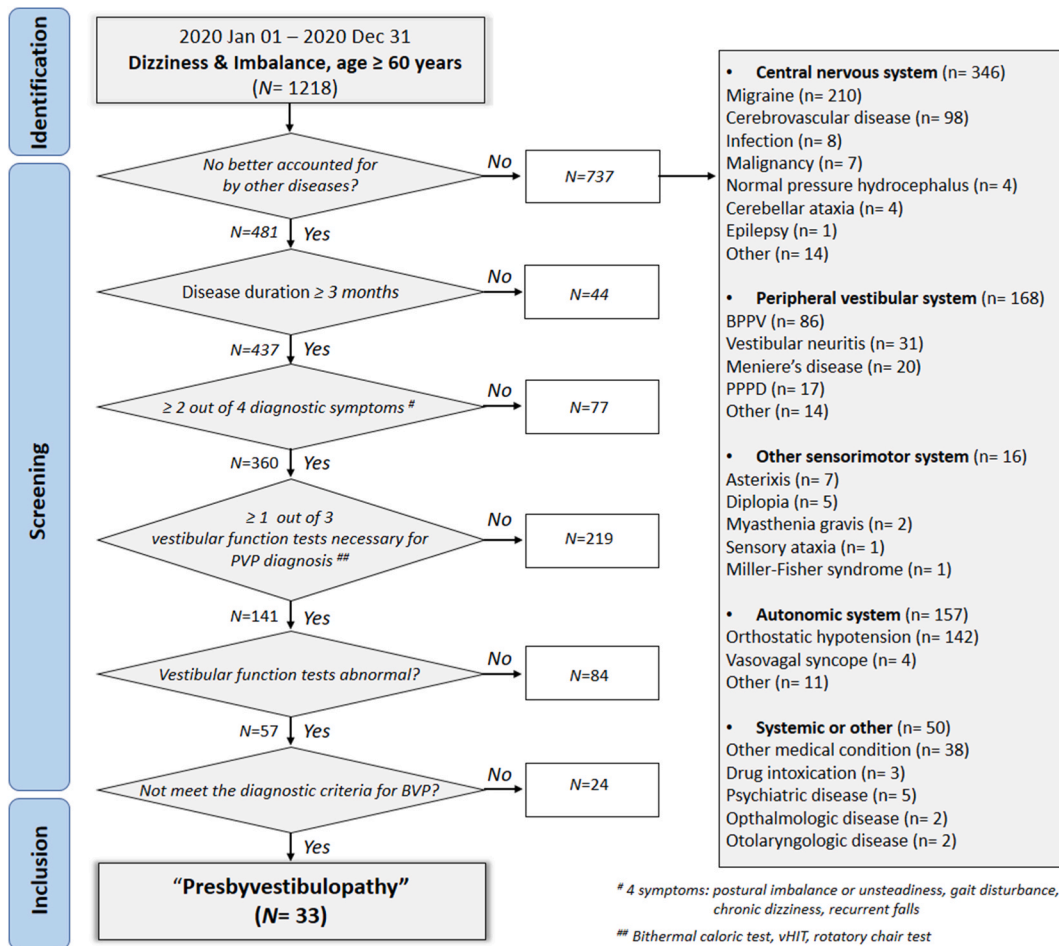SPV: slow phase velocity, VOR: vestibulo-ocular reflex.

Fig. 1. Flowchart outlining study selection process. The study process is comprised of three steps: identification, screening, and final inclusion. Identification of patients was conducted through a search of electronic data stored in the hospital information system. BPPV = benign paroxysmal positional vertigo; PPPD = persistent postural perceptual dizziness; vHIT = video head impulse test.

2.2.2. Rotary chair test

The patients underwent sinusoidal rotation around a vertical axis at a harmonic frequency of 0.1 Hz, achieving a peak angular speed between 50 and 60°/s. While conducting the VOR test (CHARTR® rotary vestibular test system, ICS Medical, IL, USA), the patient's head was positioned forward at a 30° angle from the vertical plane. The VOR gain, the measure of the vestibular system's output in response to an input, was calculated by determining the ratio between the slow-phase eye velocity induced by the test and the stimulus velocity (velocity of the rotating chair) [19,25].

2.2.3. Video head-impulse test (vHIT)

Patients, while seated in an adjustable chair, were asked to keep their eyes on a target placed at eye level on a wall 1 m away. vHIT was carried out over 20 times (with head rotation spanning 15–20°, duration lasting 150–200 ms, and peak velocity exceeding 150°/s) on each side of every plane, and the results were evaluated using oculography (SLMED, Seoul, Korea) [20,21]. After calibrating the eye position, an experienced and well-trained technician administered random horizontal head impulses in both right and left directions to facilitate unpredictable assessment. For the evaluation of the anterior and posterior semicircular canals, head rotations were executed in the planes of these vertical canals, specifically in the left anterior-right posterior (LARP) and right anterior-left posterior (RALP) directions. The patient's head was angled approximately 30–40° to either side, aligning the targeted vertical canal plane closely with the body's sagittal plane. This positioning allowed for diagonal head movements along the vertical canal plane, while the patient's gaze was eccentrically directed along the rotational plane. During each impulse, the examiner, with one hand atop the head and the other beneath the chin, rapidly moved the head through a small, unpredictable angle (about 10–20°) either upward or downward. The patient endeavored to maintain visual fixation on a stationary target throughout this process. The VOR gain was quantified by calculating the ratio of the area under the eye velocity curve to that under the head velocity curve during these head impulses [26].

2.2.4. Cervical and ocular VEMPs

For the cervical VEMP tests [27], active electrodes were placed over the middle or upper portion of the sternocleidomastoid muscle. For ocular VEMP tests [28], electrodes were placed on the infraorbital margin 1 cm below the center of the contralateral lower eyelid. The VEMP results were interpreted based on the presence or absence of a response, the amplitude measured from peak-to-peak, and the n10 peak latencies for oVEMP and p13 for cVEMP [29]. Stimuli were generated by customized software (Cadwell Laboratories, Kennewick, WA). We used unilateral 500 Hz air-conducted short tone bursts at an intensity of 100 dB normalized hearing level (nHL). The specific parameters of these bursts included a rise and fall time of 2 ms and a plateau time of 1 ms. A total of 100 trials were conducted at a frequency of 5 Hz. The auditory stimuli were delivered through calibrated headphones, also sourced from the same manufacturer, ensuring consistent and accurate sound delivery for the VEMP testing [20,30].

2.2.5. Subjective visual vertical (SVV)

Seated upright with their chins on a chin rest in a darkened room, patients focused on a rod displayed on a computer screen positioned 1 m away, using a joystick to align the target rod to the vertical position at the center of the monitor. The static SVV was determined by taking the average of 10 adjustments made from a randomly offset position while keeping the monitor stationary. This assessment was conducted under both binocular and monocular viewing conditions [22–24].

2.3. Data availability statement

All of the individual participant data that underlie the results reported in this article (manuscript, tables, and figures) will be shared after deidentification.

Table 2
Demographic and clinical characteristics of patients with presbyvestibulopathy (n = 33).

Characteristics	Presbyvestibulopathy (n = 33)
Gender	
Male: Female, n (%)	15 (45.5 %): 18 (54.5 %)
Current age, years	74.21 ± 9.23
60-69, n (%)	11 (33.3 %)
70-79, n (%)	11 (33.3 %)
80-89, n (%)	9 (27.3 %)
≥90, n (%)	2 (6.1 %)
Onset age, years	70.55 ± 8.87
50-59, n (%)	4 (12.1 %)
60-69, n (%)	12 (36.4 %)
70-79, n (%)	13 (39.4 %)
≥80, n (%)	4 (12.1 %)
Symptoms, n (%)	
Rate of each individual symptoms	
Chronic dizziness	33 (100 %)
Postural imbalance or unsteadiness	27 (81.8 %)
Gait disturbance	15 (45.5 %)
Recurrent falls	7 (21.2 %)
Rate of combination of 4 symptoms above	
2 symptoms	20 (60.6 %)
3 symptoms	10 (30.3 %)
4 symptoms	3 (9.1 %)
Symptoms duration, years	2.62 ± 3.29
3 months to 1 year, n (%)	15 (45.5 %)
1 year to 5 years, n (%)	11 (33.3 %)
≥5 years, n (%)	7 (21.2 %)
Comorbidities, n (%)	29 (87.9 %)
Hypertension	13 (39.4 %)
Diabetes mellitus	5 (15.2 %)
Dyslipidemia	6 (18.2 %)
Cardiac arrhythmia	3 (9.1 %)
Stroke	3 (9.1 %)
Bronchial asthma	1 (3 %)
Chronic kidney disease	3 (9.1 %)
Ophthalmic disease	3 (9.1 %)
Osteoporosis	2 (6.1 %)
Herniation of lumbar/cervical disc	2 (6.1 %)
Cancer	5 (15.2 %)
No identified disorders	4 (12.1 %)

Values are presented as number (percentage) or mean ± standard deviation (SD).

Table 3

Laboratory characteristics in the patients with presbyvestibulopathy.

	Presbyvestibulopathy (n = 33)	Healthy subjects over 60 years of age in our dataset (n = = 60)
Video-Head impulse test, n	29	60
Horizontal angular VOR gain		
VOR gain (0.6–0.8), n (%)	15/29 (51.7 %)	0.93 ± 0.17
Mean ± SD, Right	0.73 ± 0.1	0.91 ± 0.19
Mean ± SD, Left	0.74 ± 0.11	0.94 ± 0.12
Vertical angular VOR gain		
Anterior semicircular canals		
Mean ± SD, Right	0.95 ± 0.19	0.96 ± 0.11
Mean ± SD, Left	0.96 ± 0.15	0.95 ± 0.23
Posterior semicircular canals		
Mean ± SD, Right	0.88 ± 0.23	0.89 ± 0.18
Mean ± SD, Left	0.89 ± 0.22	0.90 ± 0.19
Caloric test, n	28	
Caloric response (6–25°/s), n (%)	21/28 (75 %)	
Mean ± SD, Right (°/s)	18.93 ± 6.06	
Mean ± SD, Left (°/s)	18.91 ± 6.37	
Rotatory chair test, n	23	
VOR gain (0.1–0.3), n (%)	11/23 (47.8)	
Mean ± SD	0.27 ± 0.13	
Pure tone audiometry, n	27	60
Mean ± SD (dB), Right/Left	27.52 ± 15.37/29.72 ± 15.95	16.12 ± 11.31
PTA (dB), average[1]		
Normal (<26), n (%)	13 (48.2 %)	–
Mild (26–40), n (%)	7 (25.9 %)	–
Moderate and severe (>40), n (%)	7 (25.9 %)	–
Cervical vestibular-evoked myogenic potential, n	27	60
No response, n (%)	2 (7.4 %)	0
Bilateral/Unilateral	0/2	–
Peak-to-peak amplitude (μV)		
Mean ± SD, Right/Left	215.13 ± 120.39/210.5 ± 131.58	398.4 ± 25.μV
Decreased, n (%)	11 (40.7 %)	–
Right (<124 μV)/Left (<147 μV)/Both	7 (25.93 %)/8 (29.63 %)/3 (11.11 %)	–
p13 latency (ms)		
Normal[4] (<17.4), n (%)	24 (88.9 %)	12.8 ± 2.5 ms
Increased (≥17.4), n (%)	1 (3.7 %)	–
Bilateral/Unilateral	0/1	–
Normal: Abnormal cVEMP	*13 (48.15 %): 14 (51.85 %)*	-
Ocular vestibular-evoked myogenic potential, n	27	60
No response, n (%)	9 (33.3 %)	0
Bilateral/Unilateral	3/6	–
Peak-to-peak amplitude (μV)		
Mean ± SD, Right/Left	3.86 ± 2.44/4.25 ± 5.55	6.74 ± 5.20 μV
Decreased,[2] n (%)	12 (44.4 %)	–
Right (<2.4)/Left (<2.4)/Both	7 (25.93)/9 (33.33)/4 (14.81)	–
n10 latency (ms)		
Normal[3] (<12.5), n (%)	16 (59.3 %)	9.4 ± 1.8 ms
Increased (≥12.5), n (%)	2 (7.4 %)	–
Bilateral/Unilateral	1/1	–
Normal: Abnormal oVEMP	*10 (37.04 %): 17 (62.96 %)*	-
Subjective visual vertical test, n	24	60
Normal[5] (<3.11°), n (%)	13 (54.2)	−0.2±0.9°
Abnormal (≥3.11°), n (%)	11 (45.8)	–
Binocular/Right/Left	4/8/4	–
Normal: Abnormal SVV	*13 (54.2 %): 11 (45.8 %)*	-

Values are presented as number (percentage) or mean ± standard deviation (SD). dB = decibel; μV = microvolt, ms = millisecond.

[1] Normative values were referenced to {Oh, I.-H. et al. (2014). "Hearing loss as a function of aging and diabetes mellitus: a cross sectional study." PLoS one 9(12): e116161.}

[2] Normative values were referenced to {Oh, S.-Y. et al. (2018). "Simultaneous recording of cervical and ocular vestibular-evoked myogenic potentials." Neurology 90(3): e230-e238.}

[3] Normative values were referenced to {Kim, J.-S. and H. J. Kim (2012). "Inferior vestibular neuritis." J Neurol 259: 1553–1560. Mean = 1.09 s, SD = 0.8.}

[4] Normative values were referenced to {Oh, S.-Y. et al. (2013). "Cervical and ocular vestibular-evoked myogenic potentials in vestibular neuritis: comparison between air-and bone-conducted stimulation." J Neurol 260: 2102–2109. Mean latency = 15.4 s, SD = 1. Mean oVEMP amplitude = 5.4 ± 5 on the right, 5.5 ± 5.8 on the left}.

[5] Normative values were referenced to {Yang, T.-H. et al. (2014). "Topology of brainstem lesions associated with subjective visual vertical tilt." Neurology 82(22): 1968–1975. Mean = 1.51°.
SD = 0.8}.

2.4. Statistical analyses

SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA) was utilized to analyze the data, with a variety of statistical tests employed depending on the nature of the variables. Mean ± standard deviation (SD) was used to present parametric data, while nonparametric data was presented as median (95 % confidence interval- CI). Frequency variables were expressed as numbers (percentages) and evaluated with either the one sample binomial test (for 2 subgroups) or the Chi-square test (for >2 subgroups). All tests were performed at a significance level of 0.05.

3. Results

3.1. Prevalence, clinical characteristics, and comorbidities

Between January 1, 2020, and December 31, 2020, 33 out of 1218 elderly patients (aged 60 years or above) who visited a tertiary dizziness clinic with symptoms of chronic dizziness or unsteadiness were identified as patients with PVP. This accounts for 2.7 % of total cases (33 out of 1218) and 6.86 % (33 out of 481) of cases with unknown causes for dizziness and imbalance. Numerous etiological disorders of dizziness have been identified, involving the central nervous system (n = 346, including migraine, cerebrovascular disease, cerebellar ataxia, infection, or malignancy), peripheral vestibular disorders (n = 168, including vestibular neuritis, benign paroxysmal positional vertigo (BPPV), Meniere's disease, or persistent postural-perceptual dizziness), autonomic disorders (n = 157, including orthostatic hypotension or vasovagal syncope), systemic diseases (n = 50, including psychiatric, ophthalmologic, or otolaryngologic disorders, or drug intoxication), and other sensorimotor systems (n = 16, including diplopia, asterixis, myasthenia gravis, Miller-Fisher syndrome, or sensory ataxia) (Fig. 1).

The mean age of the PVP patients was 74.21 ± 9.23, and the percentage distribution across age subgroups of 60–69, 70–79, 80–89, and ≥90 showed no significant variation (p = 0.084, Chi-square test) (Table 2). Gender distribution was not significantly skewed, with 15 male and 18 female patients (p = 0.728, one sample binomial test). Based on clinical data, the average disease duration was 2.6 ± 3.3 years, with no significant differences observed between subgroups divided by duration (p = 0.234, Chi-square test). Primary symptoms reported by patients included chronic dizziness (100 %), postural imbalance (81.8 %), gait disturbance (45.5 %), and recurrent falls (21.2 %). Among patients, 60.6 % presented two symptoms simultaneously, while 30.3 % and 9.1 % exhibited three and four symptoms concurrently, respectively. Comorbidities reported among PVP patients included hypertension (39.4 %), dyslipidemia (18.2 %), diabetes mellitus, cancer (15.2 %), cardiac arrhythmia, stroke, chronic kidney disease, ophthalmic disease (9.1 %), osteoporosis, herniation of lumbar/cervical disc (6.1 %), and bronchial asthma (3 %). Only four patients (12.1 %) had isolated PVP.

3.2. Vestibulo-ocular reflex and otolith function tests

Laboratory test outcomes demonstrated a decrease in bilateral horizontal angular VOR gain, within the diagnostic range for PVP, in 75 % (21/28) of caloric tests, 51.7 % (15/29) of vHIT cases, and 47.8 % (11/23) of rotatory chair tests (Table 3). The prevalence of "positive results" didn't significantly differ among these three tests (p = 0.095, Kruskal-Wallis test). Among the 19 cases with complete data for the bithermal caloric test, rotatory chair test, and vHIT, three cases (15.8 %) met all three criteria of the Bárány Society, seven cases (36.8 %) met two criteria, and nine cases (47.4 %) met only one criterion (Fig. 2). The average VOR gain for the right and left side was 0.73 ± 0.1 and 0.74 ± 0.11, respectively, for vHIT, and caloric responses were 18.93 ± 6.06°/s and 18.91 ± 6.37°/s, respectively. The mean VOR gain for the rotatory chair test was 0.27 ± 0.13. Vertical VOR gain, as evaluated through vHIT, didn't display a decrease, in both the anterior canals (0.95 ± 0.19 for the right, 0.96 ± 0.15 for the left) and posterior canals (0.88 ± 0.23 for the right,
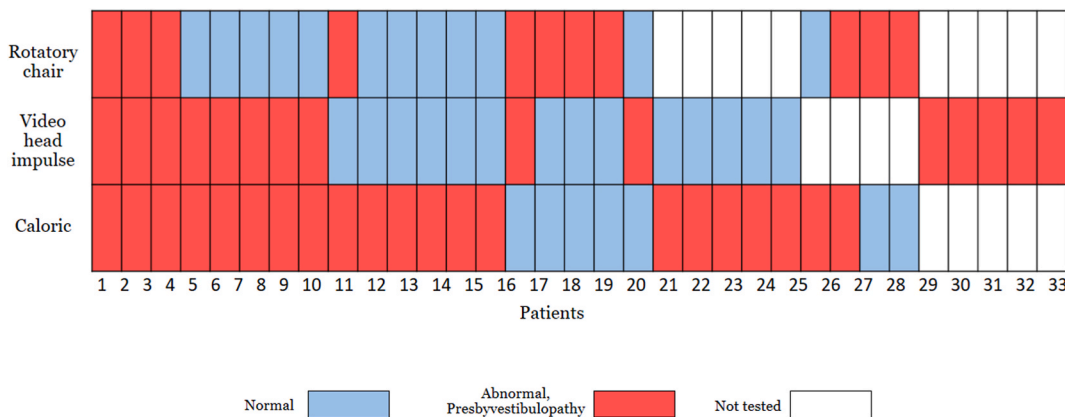

Fig. 2. Distribution of vestibular function tests results meeting the objective diagnostic criteria for presbyvestibulopathy (PVP), including caloric bithermal test (n = 33), video head impulse test (n = 33), and rotatory chair test (n = 27). Blue = normal, red = abnormal, compatible for PVP, white = not tested.

0.89 ± 0.22 for the left) (Table 3). Mild auditory impairment, characterized by threshold levels of 26–40 dB [31], was detected in 25.9 % (7/27) of the cases, while moderate to severe impairment (threshold levels >40 dB) was present in another 25.9 % (7/27).

Regarding otolithic function, when compared to our institutional normal dataset of individuals over 60 years of age (n = 60), abnormalities were observed in 45.8 % (11/24) of the cases, as indicated by the SVV test results (Table 3) [22]. The oVEMP findings revealed non-responsiveness in 33.33 % (9/27, with 22.22 % unilateral and 11.11 % bilateral), or decreased peak-to-peak amplitude in 44.4 % (12/27, with 25.93 % [7/27] on the right, 33.33 % [9/27] on the left, and 14.81 % [4/27] bilaterally) [32], or increased n10 latency in 7.4 % (2/27) [33]. The average oVEMP amplitude was 3.86 ± 2.44 μV for the right and 4.25 ± 5.55 μV for the left. However, fewer abnormalities were noted in the cVEMP, including non-responsiveness in 7.4 % (2/27, all bilateral), decreased peak-to-peak amplitude in 40.7 % (11/27, with 25.93 % [7/27] on the right, 29.63 % [8/27] on the left, and 11.11 % [3/27] bilaterally), or increased n10 latency in 3.7 % (1/27) [30]. The average cVEMP amplitude was 215.13 ± 120.39 μV for the right and 210.5 ± 131.58 μV for the left (Table 3). There was no correlation observed between the occurrence of ocular (Fig. 3A and B) and cervical (Fig. 3C and D) VEMP abnormalities and auditory status as determined by PTA (Pearson correlation). Similarly, no significant association was discerned between the outcomes of cervical/ocular VEMP tests and the magnitude of VOR gain, as detailed in Table 4. Furthermore, analysis elucidated no meaningful correlation between the presence of four diagnostic indicators of presbyvestibulopathy and VEMP or VOR gain results, as shown in Supplementary Table 2.

4. Discussion

This retrospective study investigated the demographic, clinical characteristics, and laboratory tests in patients with PVP, which had not been previously studied. Among elderly patients who visited our tertiary vertigo clinic due to persistent dizziness or unsteadiness in
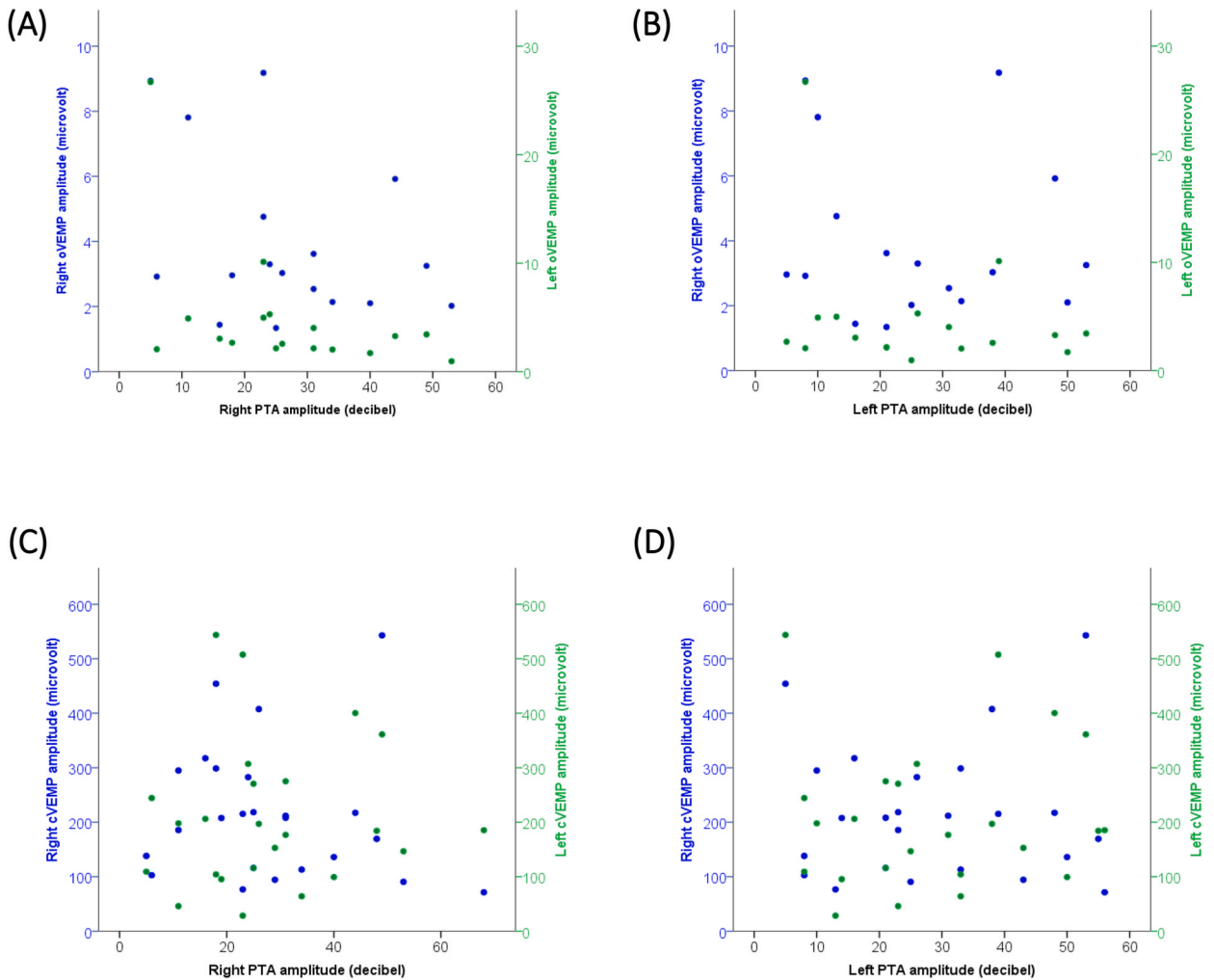

Fig. 3. Correlation between ocular (A, B) and cervical (C, D) vestibular evoked myogenic potential (VEMP) peak-to-peak amplitude and pure tone audiometry (PTA) amplitude.

Table 4

Pearson correlation analysis of vestibulo-ocular reflex (VOR) responses and vestibular evoked myogenic potentials (VEMPs) results.

			Vestibular evoked myogenic potentials (VEMPs)							
			cVEMP				oVEMP			
			Right		Left		Right		Left	
			coefficient	p	coefficient	p	coefficient	p	coefficient	p
VOR Responses	vHIT									
	Anterior SCC	*Right*	0.384	0.078	0.023	0.917	−0.008	0.973	0.113	0.665
		Left	0.307	0.165	0.202	0.368	0.29	0.228	0.281	0.274
	Posterior SCC	*Right*	0.116	0.609	0.012	0.958	−0.107	0.662	−0.081	0.756
		Left	0.278	0.21	0.109	0.628	−0.037	0.88	0.082	0.755
	Horizontal SCC	*Right*	0.132	0.559	0.068	0.764	−0.124	0.613	−0.266	0.301
		Left	0.087	0.699	0.066	0.771	−0.194	0.427	−0.169	0.517
	Rotatory test		−0.131	0.572	−0.07	0.763	−0.386	0.14	−0.261	0.296
	Caloric test	*Right*	0.083	0.692	0.148	0.489	0.193	0.415	−0.065	0.787
		Left	−0.312	0.129	0.031	0.886	0.321	0.168	0.125	0.599

VOR = vestibulo-ocular reflex; cVEMP = cervical vestibular evoked myogenic potential; oVEMP = ocular vestibular evoked myogenic potential; SCC = semicircular canal.

2020, the prevalence of PVP was approximately 2.7 % (33 out of 1218) of total cases and 6.86 % (33 out of 481) of cases with an unknown cause, which is consistent with recent research [2,34]. Although the vast majority of patients reporting dizziness symptoms were primarily diagnosed with neurological or vestibular disorders other than PVP, however, among our subset of elderly patients experiencing dizziness or imbalance, PVP emerged as the fifth most common diagnosis, after migraine, orthostatic hypotension, cerebrovascular disease, and benign paroxysmal positional vertigo (BPPV), in terms of prevalence (Supplementary Table 1). This suggests that the frequency of PVP diagnoses may be relatively higher among elderly patients with dizziness who are referred to a tertiary healthcare center.

In our study found no significant variations in the prevalence of PVP across gender or different age brackets, segmented by decade. Aligning with previous research [2], we discovered that a substantial majority of patients with PVP (87.9 %) also had comorbidities, while a smaller group (12.1 %) had PVP as an isolated condition. Intriguingly, previous studies have highlighted that PVP frequently coincides with other gait-related sensorimotor deficits (96.9 % of cases), and about 56.3 % of PVP patients demonstrated impairments in two or more systems [2]. This could be explained by the age-related decline in vestibular function, typical of PVP, often appearing within the broader spectrum of the body's aging processes. Such processes are marked by physiological decline across multiple systems like presbyopia (age-related vision loss), presbycusis (age-related hearing loss), and age-related deterioration of peripheral sensory structures [1]. While hypertension was observed in 39.4 % of the PVP cases, our study didn't establish a significant association between PVP and the prevalence of other co-existing conditions (each less than 20 %). This research is the first to document the prevalence of PVP (2.7 %) in the elderly alongside primary symptoms including chronic dizziness (100 %), postural imbalance (81.8 %), gait disturbance (45.5 %), and recurrent falls (21.2 %). Furthermore, we found that 60.6 % of patients were grappling with two concurrent symptoms, whereas 30.3 % and 9.1 % of patients presented three and four simultaneous symptoms, respectively. This suggests that the chance of fulfilling diagnostic criterion A during the first consultation is not particularly high.

In adhering to the diagnostic criteria, our laboratory evaluations scrutinized the outcomes of tests typically considered to be current indicators of PVP, including the bithermal caloric test, vHIT, and rotatory chair test, both individually and collectively. Our research indicated that an impaired horizontal VOR, registering results higher than those for bilateral vestibulopathy (BVP) and beneath the lower thresholds of standard normal ranges, was detected in 75 % of cases for the caloric test, 51.7 % for the vHIT, and 47.8 % for the rotatory chair test. These tests assess different frequencies of the VOR: the caloric test is used for low frequency (<0.01 Hz), the rotatory chair test for low to medium frequency (0.01–0.64 Hz), and the vHIT for high frequency (1–10Hz) [1]. Amid the ongoing debate surrounding proposed subtypes of PVP as well as BVP based on low-frequency versus high-frequency vestibular impairment [1,13], our study didn't uncover any conspicuous difference in the prevalence of low-frequency impairment versus high-frequency impairment among PVP patients. Recent hypotheses have posited that vestibular impairments related to aging, particularly PVP, may predominantly manifest as high-frequency dysfunctions rather than low-frequency ones [6,10]. This conjecture is underpinned by parallels drawn with presbycusis, an age-related auditory decline predominantly characterized by high-frequency hearing loss, which exhibits a notable correlation with PVP. Deterioration in vestibular hair cells, integral to sensory processing, is not homogenous across the vestibular system. Histological studies have revealed that age-related degeneration predominantly impacts type I hair cells, which are crucial for the irregular/phasic afferent pathway, responsible for encoding high-frequency stimuli and demonstrating nonlinear response characteristics [35–40]. In contrast, type II hair cells, forming the regular/tonic afferent pathway for encoding low-frequency stimuli with linear response properties, are less affected by aging [35–40]. Specifically, the decline in type I hair cells is uniformly observed across all three semicircular canal (SCC) cristae, proceeding at a notably faster pace compared to their counterparts in the striola of the otolithic macula [37,41–43]. In comparison, type II hair cell loss is consistent across all five sensory epithelia, with a similar rate of degeneration [37]. The saccule and utricle exhibit an approximate 25 % reduction in hair cell counts with aging, whereas the SCCs experience a loss of around 40 % of hair cells [41–44]. Utricular hair cells are more susceptible to age-related degeneration than saccular hair cells [42].

An additional interesting element in this study was the examination of all three semicircular canals (SCCs), not just limiting the

focus to the horizontal SCC [1,13]. Contrary to the detected impairments in the horizontal SCC, no deficits were found in either the anterior or posterior vertical SCC. This outcome corresponds with previous research, which reported a considerably lower prevalence of abnormalities in the vertical SCCs compared to the horizontal SCC when conducting a vHIT [45]. According to another study, the VOR gain in the horizontal canal showed a decline at age 70, whereas the VOR gain in the vertical canals declined after the age of 80 [46]. Our findings are corroborated by an earlier study which reported a considerably lower occurrence of anterior canal hypofunction relative to horizontal and posterior hypofunction in the context of BVP. Specifically, the preservation of anterior canal function was noted in cases associated with aminoglycoside vestibulotoxicity, Menière's disease, and undetermined causes, whereas it was not observed in instances related to inner-ear infections, cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS), and sensorineural hearing loss [47]. Nevertheless, additional morphological research examining the aging patterns of hair cells in all three canals is necessary to elucidate the reasons behind the superior preservation of VOR gain in the vertical canals as opposed to the horizontal canals.

Experimental evidence supports the association between aging and decreased blood flow to the utricle and saccule, leading to otolith demineralization, a reduction in hair cell count, and a weakened neural response to otolith stimulation [48]. This is validated by the diminished otolith-ocular responses observed in older individuals when subjected to linear acceleration stimuli [49,50], reduction in ocular counter-rolling function (the modulation of ocular torsion during sinusoidal roll tilt) during $\pm20°$ roll tilt at 0.005 Hz, and an increase in postural sway which are risk factors for falls [48]. Considering the significant contribution of otolith function to balance and coordination of body movements, the presence of otolith hypofunction negatively impacts gait (shortening stride length and reducing gait speed, while increasing variability in stance, rotation, and support duration) particularly when there is an increase in gait speed, leading to vertical displacement of both the body's center of mass and the head [51]. In our exploration of VEMP testing, we observed that oVEMP impairments were more prevalent compared to cVEMP, evidenced by higher instances of both non-response and reduction in peak-to-peak amplitude. This observation indicates a potential predilection for utricular dysfunction over saccular dysfunction. Given the indisputable evidence of age-related deterioration in otolith structure and function [1,7,8,16], there is a compelling argument to contemplate the integration of otolith function in future revisions of the diagnostic criteria for PVP. Considering past research which underscores a stronger link between postural abnormalities, spatial deficits, and otolith dysfunction as opposed to canal dysfunction [52], the incorporation of otolith assessments is indeed justified. Furthermore, the inclusion of otolith function evaluations along with semicircular canal function carries considerable implications for the management and treatment of PVP [10].

Given the retrospective nature of our study, conducting additional behavioral correlation tests to further assess otolith dysfunction and the impact of PVP on disability or quality of life measures was not feasible. Moreover, potential selection bias, stemming from patient referrals to a tertiary healthcare center, constrains the generalizability of our findings to the Korean population and patient cohorts in geriatric or general practices, and may not accurately represent the true prevalence of PVP. Lastly, as our study involved a limited patient pool from a single center, our findings should be validated through larger, multi-center studies to draw more robust conclusions.

Our investigation not only revealed the prevalence of PVP and its associated primary clinical symptoms, but also highlighted distinct changes in VOR gains and otolithic functions. The substantial alterations observed in ocular and cervical VEMPs, in conjunction with the SVV outcomes, underscore the importance of examining the role of otolith function in PVP's pathophysiology and the diagnostic value of otolith function assessment.

Funding

CRediT authorship contribution statement

Thanh Tin Nguyen: Writing – original draft, Investigation, Formal analysis, Data curation. **Jin-Ju Kang:** Investigation, Formal analysis, Data curation. **Thi Thuy Nguyen:** Writing – original draft, Investigation, Data curation. **Sun-Young Oh:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Sun-Young Oh reports financial support was provided by Korea Ministry of Science and ICT. Sun-Young Oh reports a relationship with Korea Ministry of Science and ICT that includes: funding grants.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32536.

References

[1] Y. Agrawal, R. Van de Berg, F. Wuyts, et al., Presbyvestibulopathy: diagnostic criteria Consensus document of the classification committee of the Bárány Society, J. Vestib. Res. 29 (2019) 161–170.

[2] K.J. Müller, S. Becker-Bense, R. Strobl, E. Grill, M. Dieterich, Chronic vestibular syndromes in the elderly: presbyvestibulopathy—an isolated clinical entity? Eur. J. Neurol. 29 (2022) 1825–1835.

[3] A. Soto-Varela, M. Rossi-Izquierdo, M. del-Río-Valeiras, et al., Presbyvestibulopathy, comorbidities, and perception of disability: a cross-sectional study, Front. Neurol. 11 (2020) 582038.

[4] N. Herssens, D. How, R. van de Berg, C. McCrum, Falls among people with bilateral vestibulopathy: a review of causes, incidence, injuries, and methods, JAMA Otolaryngol Head Neck Surg 148 (2022) 187–192.

[5] E.J. Pröpper, H.M. Koppelaar-van Eijsden, T.R. Schermer, T. Bruintjes, Bilateral vestibular hypofunction in a tertiary dizziness center: occurrence and etiology, J Int Adv Otol 18 (2022) 327.

[6] S. Iwasaki, T. Yamasoba, Dizziness and imbalance in the elderly: age-related decline in the vestibular system, Aging Dis 6 (2015) 38.

[7] G.A. Gabriel, L.R. Harris, J.J. Gnanasegaram, et al., Age-related changes to vestibular heave and pitch perception and associations with postural control, Sci. Rep. 12 (2022) 6426.

[8] J.M. Furman, Y. Raz, S.L. Whitney, Geriatric vestibulopathy assessment and management, Curr. Opin. Otolaryngol. Head Neck Surg. 18 (2010) 386.

[9] S.R. Wiener-Vacher, Wiener Sijfin, Video head impulse tests with a remote camera system: normative values of semicircular canal vestibulo-ocular reflex gain in infants and children, Front. Neurol. 8 (2017) 434.

[10] M.C. Schubert, A.A. Migliaccio, New advances regarding adaptation of the vestibulo-ocular reflex, J. Neurophysiol. 122 (2019) 644–658.

[11] T. Raphan, B. Cohen, The vestibulo-ocular reflex in three dimensions, Exp. Brain Res. 145 (2002) 1–27.

[12] M.J. Kobel, A.R. Wagner, D.M. Merfeld, J.K. Mattingly, Vestibular thresholds: a review of advances and challenges in clinical applications, Front. Neurol. 12 (2021) 643634.

[13] M. Strupp, J.-S. Kim, T. Murofushi, et al., Bilateral vestibulopathy: diagnostic criteria consensus document of the classification committee of the Bárány society, J. Vestib. Res. 27 (2017) 177–189.

[14] Y.S. Jang, C.H. Hwang, J.Y. Shin, W.Y. Bae, L.S. Kim, Age-related changes on the morphology of the otoconia, Laryngoscope 116 (2006) 996–1001.

[15] L. Walther, M. Westhofen, Presbyvertigo-aging of otoconia and vestibular sensory cells, J. Vestib. Res. 17 (2007) 89–92.

[16] L. Ji, S. Zhai, Aging and the peripheral vestibular system, J. Otolaryngol. 13 (2018) 138–140.

[17] J.H. Choi, H.-S. Park, M.S. Song, et al., Age-related differences of vestibulo-ocular reflex gains based on presbyvestibulopathy objective criteria, Korean J Otorhinolaryngol-Head Neck Surg 65 (2022) 752–757.

[18] K.D. Choi, S.Y. Oh, H.J. Kim, J.W. Koo, B.M. Cho, J.S. Kim, Recovery of vestibular imbalances after vestibular neuritis, Laryngoscope 117 (2007) 1307–1312.

[19] S.-H. Jeong, S.-Y. Oh, H.-J. Kim, J.-W. Koo, J.S. Kim, Vestibular dysfunction in migraine: effects of associated vertigo and motion sickness, J. Neurol. 257 (2010) 905–912.

[20] S.-Y. Oh, M. Dieterich, B.N. Lee, et al., Endolymphatic hydrops in patients with vestibular migraine and concurrent Meniere's disease, Front. Neurol. 12 (2021) 594481.

[21] S.-H. Jeon, Y.-H. Park, S.-Y. Oh, et al., Neural correlates of transient mal de debarquement syndrome: activation of prefrontal and deactivation of cerebellar networks correlate with neuropsychological assessment, Front. Neurol. 11 (2020) 585.

[22] T.-H. Yang, S.-Y. Oh, K. Kwak, J.-M. Lee, B.-S. Shin, S.-K. Jeong, Topology of brainstem lesions associated with subjective visual vertical tilt, Neurology 82 (2014) 1968–1975.

[23] B.-S. Shin, S.-Y. Oh, J.S. Kim, et al., Cervical and ocular vestibular-evoked myogenic potentials in acute vestibular neuritis, Clin. Neurophysiol. 123 (2012) 369–375.

[24] H.-J. Kim, S. Kim, J.H. Park, J.-S. Kim, Altered processing of otolithic information in isolated lateral medullary infarction, J. Neurol. 263 (2016) 2424–2429.

[25] D. Starkov, M. Strupp, M. Pleshkov, H. Kingma, R. van de Berg, Diagnosing vestibular hypofunction: an update, J. Neurol. 268 (2021) 377–385.

[26] G.-S. Nam, H.-J. Shin, J.-J. Kang, N.-R. Lee, S.-Y. Oh, Clinical implication of corrective saccades in the video head impulse test for the diagnosis of posterior inferior cerebellar artery infarction, Front. Neurol. 12 (2021) 605040.

[27] J.A. Honaker, R.N. Samy, Vestibular-evoked myogenic potentials, Curr. Opin. Otolaryngol. Head Neck Surg. 15 (2007) 330–334.

[28] K. Ochi, T. Ohashi, S. Watanabe, Vestibular-evoked myogenic potential in patients with unilateral vestibular neuritis: abnormal VEMP and its recovery, J. Laryngol. Otol. 117 (2003) 104–108.

[29] T.D. Fife, J.G. Colebatch, K.A. Kerber, et al., Practice guideline: cervical and ocular vestibular evoked myogenic potential testing: report of the guideline development, dissemination, and implementation subcommittee of the American academy of Neurology, Neurology 89 (2017) 2288–2296.

[30] S.-Y. Oh, J.-S. Kim, T.-H. Yang, B.-S. Shin, S.-K. Jeong, Cervical and ocular vestibular-evoked myogenic potentials in vestibular neuritis: comparison between air- and bone-conducted stimulation, J. Neurol. 260 (2013) 2102–2109.

[31] I.-H. Oh, J.H. Lee, D.C. Park, et al., Hearing loss as a function of aging and diabetes mellitus: a cross sectional study, PLoS One 9 (2014) e116161.

[32] S.-Y. Oh, H.-J. Shin, R. Boegle, et al., Simultaneous recording of cervical and ocular vestibular-evoked myogenic potentials, Neurology 90 (2018) e230–e238.

[33] J.-S. Kim, H.J. Kim, Inferior vestibular neuritis, J. Neurol. 259 (2012) 1553–1560.

[34] Y. Agrawal, Dizziness demographics and population health, in: A.T. Gleason, B.W. Kesser (Eds.), Dizziness and Vertigo across the Lifespan, Elsevier, 2018, pp. 1–7.

[35] U. Rosenhall, Degenerative patterns in the aging human vestibular neuro-epithelia, Acta Otolaryngol. 76 (1973) 208–220.

[36] S.N. Merchant, K. Tsuji, I.I.I.C. Wall, L. Velázquez-Villaseñor, R.J. Glynn, S.D. Rauch, Temporal bone studies of the human peripheral vestibular system: 1. Normative vestibular hair cell data, Ann. Otol. Rhinol. Laryngol. 109 (2000) 3–13.

[37] S.D. Rauch, L. Velazquez-Villaseñor, P.S. Dimitri, S.N. Merchant, Decreasing hair cell counts in aging humans, Ann. N. Y. Acad. Sci. 942 (2001) 220–227.

[38] I.S. Curthoys, A.M. Burgess, S.C. Goonetilleke, Phase-locking of irregular Guinea pig primary vestibular afferents to high frequency (>250 Hz) sound and vibration, Hear. Res. 373 (2019) 59–70.

[39] I.S. Curthoys, Concepts and physiological aspects of the otolith organ in relation to electrical stimulation, Audiol. Neurootol. 25 (2020) 25–34.

[40] I.S. Curthoys, The anatomical and physiological basis of clinical tests of otolith function. A tribute to yoshio uchino, Front. Neurol. 11 (2020) 566895.

[41] M. Anniko, The aging vestibular hair cell, Am. J. Otolaryngol. 4 (1983) 151–160.

[42] M. Gleeson, H. Felix, A comparative study of the effect of age on the human cochlear and vestibular neuroepithelia, Acta Otolaryngol Suppl 436 (1987) 103–109.

[43] S.D. Rauch, L. Velazquez-Villasenor, P.S. Dimitri, S.N. Merchant, Decreasing hair cell counts in aging humans, Ann. N. Y. Acad. Sci. 942 (2001) 220–227.

[44] A.J. Matheson, C.L. Darlington, P.F. Smith, Dizziness in the elderly and age-related degeneration of the vestibular system, N. Z. J. Psychol. 28 (1999) 10–16.

[45] M. Davalos-Bichara, Y. Agrawal, Normative results of healthy older adults on standard clinical vestibular tests, Otol. Neurotol. 35 (2014) 297–300.

[46] T.H. Kim, M.B. Kim, Effect of aging and direction of impulse in video head impulse test, Laryngoscope 128 (2018) E228–E233.

[47] A.A. Tarnutzer, C.J. Bockisch, E. Buffone, S. Weiler, L.M. Bachmann, K.P. Weber, Disease-specific sparing of the anterior semicircular canals in bilateral vestibulopathy, Clin. Neurophysiol. 127 (2016) 2791–2801.

[48] J.M. Serrador, L.A. Lipsitz, G.S. Gopalakrishnan, F.O. Black, S.J. Wood, Loss of otolith function with age is associated with increased postural sway measures, Neurosci. Lett. 465 (2009) 10–15.

[49] J.M. Furman, M.S. Redfern, Effect of aging on the otolith-ocular reflex, J. Vestib. Res. 11 (2001) 91–103.

[50] J.-R. Tian, I. Shubayev, R.W. Baloh, J.L. Demer, Impairments in the initial horizontal vestibulo-ocular reflex of older humans, Exp. Brain Res. 137 (2001) 309–322.

[51] A.J. Layman, C. Li, J.P. Carey, Y. Agrawal, Influence of age-related loss of otolith function on gait: data from the Baltimore longitudinal study on aging, Otol. Neurotol. 36 (2015) 260.

[52] Y. Agrawal, T. Bremova, O. Kremmyda, M. Strupp, Semicircular canal, saccular and utricular function in patients with bilateral vestibulopathy: analysis based on etiology, J. Neurol. 260 (2013) 876–883.