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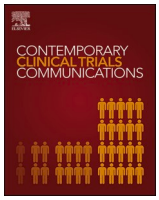

Supervised multicomponent exercise as an adjuvant program for people with unilateral and/or bilateral chronic vestibular hypofunction: EXERVEST study protocol

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ABSTRACT

Background: Unilateral and bilateral peripheral vestibular hypofunction (UVH and BVH) often complains of dizziness, gaze, and balance disturbances. There is a lack of evidence on exercise intervention in UVH and BVH patients. To investigate the effect of an eight-week supervised multicomponent exercise program in people suffering from UVH or BVH in comparison with a control group doing conventional vestibular rehabilitation at home.

Methods: This longitudinal, controlled, randomized, prospective, single-blinded, two-arm, parallel intervention study will include 66 adults (≥18 years old) with chronic UVH or BVH. Participants will be randomly assigned to an exercise intervention group or an attention control group. Participants will be assessed at baseline, after a two-month intervention period, and after a six-month follow-up. The primary variable will be the balance, measured by the dynamic posturography sensory organization test and the Modified Dynamic Gait Index test. Secondary outcome variables will include cardiorespiratory fitness (peak cardiopulmonary exercise test), body composition (bioimpedance and anthropometric variables), physical activity level and sleep quality (accelerometry), health-related quality of life (Dizziness Handicap Inventory questionnaire), emotional state (Beck Depression and Anxiety Inventory questionnaires), and blood pressure monitoring.

Discussion: This study will try to answer whether in people with UVH/BVH, an adjuvant program of multi-component exercise will help the prognosis of this population.

Trial registration: ClinicalTrials.gov, identifier [NCT05192564]. Verification date: April 2023.

1. Background

The vestibular system is a sensory system that encodes linear and angular acceleration of the head in three different dimensions and provides the brain with information about self-motion, which is important for maintaining clear vision and balance [1]. Thus, vestibular hypofunction (VH) is a partial or complete deficit of function of the central (brain) or peripheral (inner ear) system affecting both the vestibulo-ocular reflex and the vestibulo-spinal reflex which maintains stable gaze and posture [2]. There are two types of VH (unilateral-UVH, and bilateral-BVH), being the more common UVH, which only affects one side of the vestibular system because it is replicated symmetrically in the periphery [3]. Although levels of functional impairment can vary considerably among individuals, people with BVH, are usually more severely affected than those with UVH, presenting a reduced or absent function of both vestibular organs, vestibular nerves, or a combination of both [2,4].

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Abbreviations

AC	Attention Control group
ABPM	ambulatory blood pressure monitoring
BP	blood pressure
BAI	Beck's Anxiety Inventory
BDI	Beck's Depression Inventory
BVH	bilateral vestibular hypofunction
CPET	cardiopulmonary exercise testing
DHI	Dizziness Handicap Inventory
EX	EXercise group
EXERVEST	EXERcise VESTibular
FITT	Frecuency, Intensity, Time, Type
HIIT	High Intensity Interval Training
IPAQ	International Physical Activity Questionnaire
HR	heart rate
MDGI	Modified Dynamic Gait Index
UVH	unilateral vestibular hypofunction
VH	vestibular hypofunction
VO_{2peak}	peak oxygen uptake
VR	vestibular rehabilitation
VT	ventilatory threshold

Vestibular hypofunction leads to many direct and indirect consequences on functioning and daily life. Mostly, it causes subjective complaints of persistent dizziness with or without vertigo, oscillopsia (visual disturbance), ataxia (difficulties in balance and walking), and consequently, an increased risk of falls [5]. This chronic dizziness interferes also with worsened depressive symptoms, self-reported health, and decreased confidence in performing social activities [6]. Moreover, balance impairment caused by VH is related to developing psychiatric disorders such as anxiety or, avoiding behaviors and environments that can provoke the symptoms, and consequently, individuals suffering from VH become less active and sedentary [7]. Therefore, people with VH may fall into a vicious cycle of dizziness, anxiety, and physical inactivity, which may negatively impact vestibulopathy [7]. Physical activity levels of people with VH are lower compared to those of healthy, and less active people showed decreased postural stability [7].

The management of VH is an important issue in primary care because of its impact on the individual's health and quality of life, apart from its large economic burden [8]. For people with VH, it has been ascertained that exercise-based vestibular rehabilitation (VR) is effective in ameliorating persistent dizziness and function, reducing disability, and improving their daily living [9,10]. Indeed, VR is designed to adapt the central nervous system to diminished vestibular input and to compensate for vestibulo-ocular reflex and vestibulo-spinal reflex losses [11,12]. The physiological principle to work on the VR program is gaze stability, which is classified into adaptation (*i.e.*, head movements while fixating on a small stationary target) and substitution (*i.e.,* different sensory inputs) exercises [5]. Further, body control or posture stability is one of the main difficulties faced by this population [5]. Therefore, although balance training using static and dynamic exercises is recommended, the quality of evidence and level of recommendation is not strong, and the optimal specific doses of this type of training are still unknown [9]. Besides, endurance training and gait technique exercises have been proven to be well-founded exercise strategies for improving the quality of life of VH patients, along with a graduated walking program for endurance [9]. In this sense, the World Health Organization states that ≥18-year-old adult people must perform 150–300 min per week of moderate-intensity physical activity, and/or 75–150 min per week of high-intensity physical activity or an equivalent combination of both. It is also recommended moderate-to-vigorous muscle-strengthening activities on two or more days per week [13]. According to that, interventions combining High-Intensity Interval Training (HIIT) and resistance training exert beneficial effects that are superior to any other exercise modality at increasing lean body mass and cardiorespiratory fitness [7]. Thus, low-volume HIIT is nowadays considered one of the most time-efficient methods for improving cardiorespiratory fitness and metabolic function and, hence people's health-related quality of life [14–17]. The question is-why deny the benefits of this training modality to a population that needs to improve their physical condition to transfer it to other capabilities? Therefore, although previous studies indicate that exercise-based VR shows benefits [8], there is an absence of studies determining an adequate protocol considering the FITT (Frequency, Intensity, Time, Type) principle and the latest scientific advance in terms of exercise training. It is therefore deemed necessary to further explore exercise-based training strategies considering the FITT principle in this VH population.

In light of the above, the EXERVEST study has been designed to investigate the effect of an eight-week supervised EXERcise multicomponent program (*i.e.,* aerobic, resistance, and balance exercises in the same session) in people suffering from unilateral or bilateral peripheral VESTibular hypofunction in comparison with an attention control (AC) group doing conventional VR at home. Thus, the overall aims of this randomized controlled trial will be to analyze: 1) the effects of a multicomponent exercise program on balance in people with a diagnosis of both UVH and BVH, compared to an AC group, and 2) the effect of six months follow-up without professional supervision, but with general physical activity recommendations. The specific secondary objectives will be: 1) to assess changes in quality of life and psychological well-being, 2) to analyze changes in balance and risk of falls according to the etiology that caused the VH and the time elapsed after the establishment of VH, 3) to analyze the effect on cardiorespiratory fitness, body composition, physical activity level, sedentary behavior, and sleep quality, and blood pressure (BP); and 4) to evaluate the association between changes in balance and the rest of the analyzed variables.

2. Methods

2.1. Study design

EXERVEST is a controlled, randomized, prospective, single-blinded (staff of the otorhinolaryngology department of the hospital), two-arm, parallel intervention study (ClinicalTrials.gov ID: NCT05192564), and fulfills the Proper Reporting of Evidence in Sports and Exercise Nutrition Trials (PRESENT 2020) checklist. The protocol (Clinical Trials.gov ID: NCT05192564) and informed consent procedures of the EXERVEST study were approved by the Ethics Committee of Investigation of Alava University Hospital (January 19, 2023, Certificate No. 2021-095). Participants will be fully informed of the aims and procedures of the research before collecting their informed consent and before the clinical and physiological examination.

After baseline measurements, the participants will be included in the trial by being given a trial-specific identification (*i.e.,* EXERVEST-001) number (ID). They will be followed for eight weeks and after the intervention, they will be assessed again in a six-month time. All follow-up measurements will be performed in the same laboratory and by the same researchers. Allocation consignment will be performed by a technician from Bioaraba Research Institute (http://aleatorizacion.bioaraba.org/) using the technique of stratified randomization (1:1) by sex (men/women), established chronic instability vs critical instability with acute punctual vertiginous crises (Meniere); and age (<60 years vs > 60 years), because at older age, worse physiological balance associated with age is more common, as well as other multifactorial elements and higher risk of falls. The participants will be randomized to one of the two groups of intervention: 1) exercise + conventional rehabilitation treatment (EXercise group, EX) and 2) conventional rehabilitation treatment (AC). The flow diagram of the study can be seen in Fig. 1.

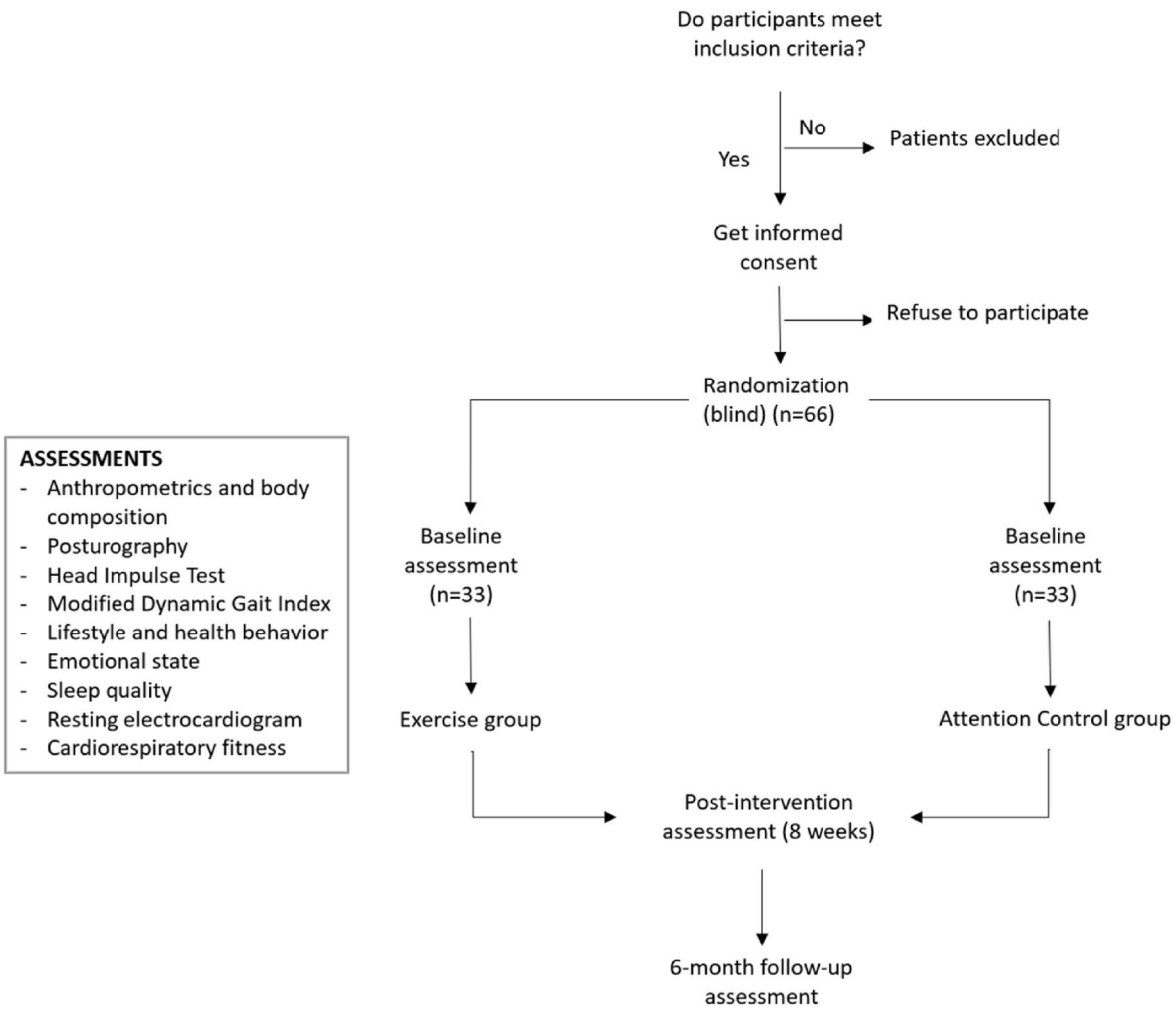

Fig. 1. Flow diagram of the EXERVEST study.

2.2. Participants and selection criteria

The sample will include 66 adults (≥18 years old) with chronic UVH or BVH attending the Otoneurology Department of the local hospital.

The inclusion and exclusion criteria for the EXERVEST study are shown in Table 1.

Participants will be free to withdraw from the study at any time. The main reason for withdrawal will be recorded on the corresponding page of the data collection form. The medical doctor responsible for the research will also withdraw participants from the study for the following reasons:

- Failure of the participant to comply with procedures and recommendations, including procedures related to the administration of study medication.
- Any significant history that limits the patient's ability to participate in the study.
- Pregnancy.
- Administration of excluded treatments.
- Loss of contact during follow-up.
- A decision by the person responsible for the research that continuation in the study is not in the best interest of the participant (e.g., intercurrent disorder or disease requiring the use of prohibited drugs or treatments). At the time of withdrawal, all study termination procedures must be performed.
- Occurrence of serious or life-threatening reactions.
- Non-attendance for more than two weeks in a row to the exercise program.
- An injury that prevents continuation of the exercise treatment.

At the time of withdrawal from the study, the main reason for withdrawal should be collected and, if possible, the participant will be assessed again.

2.3. Measurements

Assessments used in the protocol will be evaluated before (T0), after an eight-week intervention period (T1), and after a six-month follow-up period (T2). Participants from the two groups will be evaluated at the same time.

The primary variable will be the equilibrium (balance), measured by the dynamic posturography sensory organization test and the Modified Dynamic Gait Index (MDGI). Secondary outcome variables will include cardiorespiratory fitness, quality of life, body composition, physical activity level, sleep quality, and emotional state. Sociodemographic, etiological, and clinical health values will be collected only before the intervention. The Recommendations for Interventional Studies (SPIRIT) figure showing the time points for assessments and intervention is apportioned in Fig. 2.

2.3.1. Degree and type of vestibular hypofunction

Participants will be measured by the video Head Impulse Test (ICS Impulse USB, Natus hearing and balance, USA) to determine their

Table 1
Inclusion and exclusion criteria for the EXERVEST study.

Inclusion criteria
- Patient with UVH or BVH. - More than 6 months since the onset of VH (chronic instability). - ≥18 years old. - No previous rehabilitation treatment for VH other than home exercises.
Exclusion criteria
- Fluctuating instability (not presented every day). - Recent onset instability (less than six months old, susceptible to complete clinical recovery). - Current neurological pathology. - History of neurosurgical disease, cerebrovascular disease, neurodegenerative disease, or central nervous system sequelae. - Uncorrected ocular disorders. - History of peripheral neuropathy in the lower extremities. - Arthropathy or motor defects in lower limbs. - Prolonged use of sedatives or vestibular suppressant medication. - Significant medical disorders: including uncontrolled arterial hypertension, chronic or recurrent respiratory, neuromuscular, or psychiatric diseases; musculoskeletal problems that interfere with exercise; immunodeficient diseases or a positive video Head Impulse Test; anemia, blood disorders, chronic thrombotic disorders or hyper coagulant states; malignant tumors within the last five years, except for therapeutically controlled skin cancer; any other disease that may be affected or aggravated by exercise. - Being pregnant or breastfeeding. - Being physically active. - Have plans to be out of town for more than two weeks.

≥, greater than or equal to; BVH, bilateral vestibular hypofunction; UVH, unilateral vestibular hypofunction; VH, vestibular hypofunction.

degree and type of VH. This hypofunction must be chronic, maintained over time, therefore fluctuating cases are discarded. This test collects computerized vestibulo-ocular reflex, measuring the speed of head movement and the ocular response. Two parameters will be measured: the gain (ratio between cephalic and ocular movement, which should be close to 1 and is pathological if it is less than 0.8) and the occurrence of saccades (late responses produced by the central neuronal system indicating pathology) [18,19].

2.3.2. Primary outcome assessment. Instability, balance, and risk of falls

The participant's instability will be assessed by a dynamic posturography (dynamic SPS system, Synapsys, France) [20]. The sensory organization test will be studied, where six different sensory conditions provide an opportunity to measure the contributions of the general balance and the one purely dependent on somatosensory, visual, and vestibular information, evaluating them separately on a scale from 0 to 100. It also measures 0 to 100 the degree of dependence on visual information, which indicates pathology, but adequate compensation at a central level. The first three conditions will be performed on a fixed platform where first, the eyes are opened, second, the eyes are closed, and third, the eyes are opened in a sway-referenced visual enclosure. In conditions 4, 5, and 6, the platform may move and the eyes will be opened, closed, and opened in a sway-referenced visual enclosure respectively [21].

The balance and risk of falls will be measured by the MDGI. It has a scoring system based on three facets of performance, such as level of assistance, gait pattern, and time. It is composed of eight exercises through which they measure the time needed to complete 6.1 m of distance; level of assistance, which is scored using a 3-level scale (2 = no assistance, 1 = uses an assistance device, 0 = requires the physical assistance of another person); and 2gait patterns, which are scored on a 4-level scale (4 = normal, 3 = mild impairment, 2 = moderate impairment, 0 = severe impairment). The maximum score is 64 points [22]. Further, on the first day, during the physical examination, three questions will be included to assess each participant's fall history [23]: 1) Have you fallen in the past year? If yes ask: how many times? Were you injured? 2) Do you feel unsteady when standing or walking? 3) Are you worried about falling?

2.3.3. Anthropometry and body composition

Anthropometry measurements will be taken following the guidelines from the International Society for the Advancement of Kinanthropometry [24] and include the stature (SECA 213, Hamburg, Germany), total body mass (SECA 869, Hamburg, Germany), Body Mass Index calculated as [total body mass (kg)/stature (m^2)], and waist and hip circumferences (SECA 200, Hamburg, Germany) to calculate waist/hip ratio. In addition, fat-free mass, fat mass, and total body water will be assessed with bioelectrical impedance analysis (Tanita, BF 350 and Tanita, BC-418 MA, Amsterdam, The Netherlands).

2.3.4. Lifestyle and health-related quality of life

Physical activity and sedentary behavior will be measured in two different ways: 1) the short-form International Physical Activity Questionnaire (IPAQ) collecting information about household maintenance, occupational, transportation, leisure, and sedentary activities [25]; and 2) a 3-axis accelerometer (ActiGraph wGT3X-BT, Pensacola, FL, USA) will be worn on the non-dominant wrist for a whole week by the participants as proposed in the practice guidelines for research [26]. Each participant will be given oral instructions on how to wear the accelerometer and how to complete the diary log. On the eighth day after the accelerometers are distributed, both accelerometers and diaries will be collected.

All participants will answer the Dizziness Handicap Inventory questionnaire for the assessment of health-related quality of life [27]. This is a specific and validated questionnaire for vestibular pathology with 25 items, with possible answers of 'yes' (4 points), 'sometimes' (2 points), and 'no' (0 points). The questions are divided into physical (11 questions), functional (16 questions), and emotional (10 questions) groups. The scoring of the results is done in the following way: 0–14 points indicate a normal handicap, 16–34 mild, and 36–52 moderate, while a score over 54 points severe quality of life worsening.

Psychological evaluation protocols will include the Beck's Depression Inventory (BDI) [28] and Beck's Anxiety Inventory (BAI) [29]. Both BDI and BAI are 21 Likert-type items, multiple-choice, and self-reported inventories. Each item is scored 0 to 3 points for a maximum score of 63 points. For BDI, scores between 0 and 13 indicate minimal depression, 14–19 mild depression, 20–28 moderate depression; and 29–63 severe depression. For BAI, scores between 10 and 16 indicate mild anxiety, 17–29 moderate anxiety, and scores above 30 represent severe anxiety.

2.3.5. Resting cardiovascular measurements

Since the assessment of cardiorespiratory fitness will be performed with a maximal test and the exercise intervention includes high intensity, resting cardiovascular measurements will be performed as a check to avoid risks. A 12-lead electrocardiogram will be performed at rest with the wireless device of the Ergo CarMedisoft S.S, Belgium Ref. USM001 V1.0 system and the data will be analyzed by a blind medical specialist. The assessment of BP will be carried out in line with the guidelines set by European societies [30]. Ambulatory blood pressure monitoring (ABPM) will be conducted for 24 h using the ABPM 7100 (Welch Allyn, New York City, NY, USA). The device will measure the BP at 30-min intervals during the daytime, and at 60-min intervals during the nighttime. Values will be registered from the recorder as mean values of systolic and diastolic BP for both periods.

2.3.6. Cardiorespiratory fitness

A peak, symptom-limited cardiopulmonary exercise test will be performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands) to determine peak oxygen uptake (VO_{2peak}) and ventilatory thresholds (VT) in laboratory-controlled conditions. The protocol will start at 40 W (~70 rpm), with gradual increments of 10 W every minute to exhaustion. Continuous electrocardiogram monitoring will be conducted throughout each test using the instrument abovementioned. During the test, participants will be encouraged by the exercise specialist. The gas and ventilatory

Activity/Assessment	Study period		
	Pre-intervention	Post-intervention (8 weeks)	Follow-up (6 months)
TIMEPOINT	T0	T1	T2
Eligibility screen	X		
Informed consent	X		
Clinical and physical examination	X		
Randomization	X		
INTERVENTIONS:			
Attention Control (AC)			
Exercise Group (EX)			
ASSESSMENTS:			
Anthropometry: Stature, body mass, waist/hip ratio, fat-free mass, fat mass, total body water	X	X	X
Degree and type of VH and instability: Posturography, Head Impulse Test, Modified Dynamic Gait Index	X	X	X
Lifestyle and health behavior: IPAQ, DHI, BAI, BDI, Accelerometry.	X	X	X
Resting electrocardiogram	X	X	X
CPET	X	X	X

Fig. 2. SPIRIT *figure* showing an overview of the assessment schedule at baseline and follow-up in the EXERVEST study. BAI (Beck's Anxiety Inventory), BDI (Beck's Depression Inventory), CPET (Cardiopulmonary Exercise Test), DHI (Dizziness Handicap Inventory), IPAQ (International Physical Activity Questionnaire), VH (Vestibular Hypofunction).

analyses will be conducted by the Ergo CarMedisoft S.S, Belgium Ref. USM001 V1.0 system and calibration will be performed before each test following manufacturer instructions. Breath-by-breath data will be constantly measured during the test and averaged every 60 s. Achievement of VO_{2peak} criteria will be assumed when two or more of the following items will be obtained: 1) achieving >85 % of age-predicted maximum heart rate (HR); 2) perceived maximum fatigue (>18 on the Borg scale); 3) peak respiratory exchange ratio ≥1.10; 4) omission of increment of oxygen uptake and/or HR with increases in work rate [31]. Perceived fatigue will be reported (scale 6–20) at the end of each minute/stage. Blood pressure will be assessed every 2 min. Measurements of the first and second VT (VT1 and VT2) will be carried out by the V-slope and ventilatory equivalents standardized methods [31]. After achieving the peak effort, participants will remain stationary on the bike for 5 min in recovery with an electrocardiogram and BP monitoring. Absolute and relative indications for finishing the exercise test will be considered [32]. Three different exercise intensity ranges will be determined by the identification of the two VTs: R1, light to moderate with HR values below VT1; R2, moderate to vigorous with HR values between VT1 and VT2; and R3, vigorous to severe with HR values higher

than the ones associated with the VT2 [31].

2.4. Study intervention

Both EX and AC groups will have all antivertiginous drugs withdrawn and will perform the same assessments before and after the intervention period. The AC group will perform only home vestibular rehabilitation exercises that are usually prescribed in consultation with this type of patient, especially focused on complex visual and postural environments.

Participants in the EX group will train for two non-consecutive days per week for eight weeks under the supervision of exercise specialists (sports physical educators). All sessions will start and finish with BP measurements, and participants' physical effort will be monitored by HR monitors (Polar Electro, Kempele, Finland) and the rate of perceived exertion using the original Borg scale [6–20]. Each session (Appendix A) will include a standardized 15-min warm-up with joint mobility exercises and gait technique and a 5-min cooldown with basic stretching exercises and controlled breathing. The central part of each training session will consist of: 1) a low-volume (less than 10 min at R3) aerobic HIIT program on the bicycle (15 min of total volume), plus 5min of retrowalking on the treadmill at R1-R2, and 2) a timed (45/20 seg) circuit training with nine balance and resistance exercises including postural control and integration of the main muscle groups and basic motor patterns, including four "core" exercises at the end. During the first four weeks of the circuit training, the speed of execution will be slow (*i.e.,* 3–4 s into the concentric and eccentric phases) and with little load to ensure the technique and breathing learning. During the second four weeks, an increase in the speed (*i.e.,* 2–3 s) into the concentric phase of execution will be encouraged with an increase also in the load, allowing each exercise to be performed for 45 s at a time (Appendix A). The training load in the circuit training will be adjusted by a rating of the perceived exertion scale based on "repetitions in reserve" [33,34].

The intensity on the bike will be individually tailored to each participant's HR at R2 or R3, adjusting the power of the bike to achieve the planned target HR. The protocol of HIIT will consist of a 3–5 min warm-up, plus five series of 30 s at R3 followed by 60 s at R2, gradually increased to eight series in the last four weeks, finishing with a 2–5 min cool-down period at R2.

The exercise specialist will record all the exercise sessions, reporting the HR and Borg scale values of every interval. The importance of achieving the target of moderate and high intensity will be emphasized. A criterion for completing the study was set at 100 %. Thus, all participants in the EX group will perform 16 sessions; if a session is missed (a maximum of two will be allowed), these will be added to the end of the eight-week program, maintaining the two sessions per week. Some strategies will be used to achieve adherence, such as individualized attention while exercising and telephone calls following missed sessions. A minimum of 85 % exercise program compliance will be required for the EX participants to be included in the final statistical analyses.

At the end of the intervention, all participants will receive physical activity recommendations for the following six months. Participants will have no further supervised intervention or attention from any of the research staff. Participants will also receive HR data for their current moderate and high exercise intensity domains to enable them to self-monitor.

2.5. Sample size estimation

To analyze the effects on the balance after the intervention and to achieve a power of 80 % to detect differences in the counterfactual of the null hypothesis H_0: the difference in means is equal to the Superiority limit, through a one-sided T-Student Test (of Superiority) for two independent samples, taking into account that: the significance level is 5 %, assuming that the superiority limit is 2 units in the main variable MDGI, the expected value for the control treatment is 3 units, the mean of intervention group is 5.8, the standard deviation of both groups is 1.2 units and the ratio of experimental units in the reference group to the total is 50 %, it will be necessary to include 29 participants in each group (total 58). Considering that the expected dropout rate is 10 %, it would be crucial to recruit 33 participants in each group, so a total of 66 patients would need to be included in the study.

The sample size calculation was performed using the "Ene" 3.0 program based on the main study variable "MDGI", according to previously published studies [35].

2.6. Statistical analysis

To determine the baseline status of the participants, a descriptive analysis will be carried out in which qualitative variables will be expressed as frequency and percentage, and for quantitative variables, the mean and standard deviation will be given. In the case of not following a normal distribution, the median and interquartile range will be given.

To evaluate the effects on balance, as well as on the quality of life and psychological well-being, the T-student test for related samples will be carried out, and in the case of not meeting normality criteria, its non-parametric analog Wilcoxon. This test will also be performed for the secondary objectives to analyze the change after the intervention.

A covariate analysis (ANCOVA) will be performed to evaluate the change after the intervention taking into account the two different groups EX and AC groups (*i.e.,* independent variable), where it will be considered the dependent variable (*i.e.,* the variable of interest after the intervention) and the covariate variable (*i.e.,* the pre-intervention same variable). The magnitude of the differences will be assessed using 95 % confidence intervals and Hedges'g effect sizes [36].

To evaluate the association between changes in balance and the rest of the variables analyzed, multiple linear regression analyses will be performed. The accuracy of each regression will be evaluated using the standard error of estimate and the 95 % confidence intervals of the slope.

3. Discussion

This study describes the protocol of a controlled, randomized, prospective, single-blinded, two-arm, parallel intervention study for adults ≥18 years old comprehended on the EXERVEST Study.

One of the aims of otoneurology is to try to achieve new strategies that improve clinical conditions in patients. In this sense, the present randomized controlled trial aspires to investigate whether the implementation of individualized multicomponent exercise intervention as an adjuvant program will ameliorate the prognosis of patients with UVH and BVH by enhancing their functionality.

Previous studies have shown that VR is effective in improving patients' balance and, is a safe and effective proposal for UVH and BVH patients [3]. However, a previous study has shown that just 65 % of the participants responded to the therapy [37]. Alternative ways of approaching the condition, such as a multicomponent exercise program combining strength, balance, and low-volume HIIT exercises, could offer a complementary way of improving balance, postural control, and fitness. Nevertheless, no research has been performed in this sense. Therefore, in the present protocol study, it was hypothesized that the positive effects of a supervised multicomponent exercise program on functionality will be related to improved balance stability and quality of life in people diagnosed with UVH and BVH.

In conclusion, future results of the present investigation will help to better understand the potential need for an adjuvant multicomponent exercise program for improving the well-being of people with UVH and BVH.

Ethics approval and consent to participate

The Ethics Committee of Investigation of Alava University Hospital has approved this protocol (January 19, 2023, Certificate No. 2021-095).

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CRediT authorship contribution statement

All authors critically reviewed and approved the final version and agreed with all aspects of the work ensuring integrity and accuracy. CRediT roles: Conceptualization (AL, MTE, SMM), Data curation (MRR, AL, JPL, MTE, SMM), Formal analysis (MRR, AL, JPL, MTE, SMM), Funding acquisition (AL, MSS), Investigation (MRR, AL, JPL, MTE, IAI, IGT, SMM), Methodology (MRR, ASL, JPL, MTE, IAI, SMM), Project administration (AL, SMM), Resources (AL, MTE, SMM), Supervision (MRR, AL, JPL, MTE, IAI, SMM). Roles/writing-original draft (MRR, JPL, SMM). Writing-review & editing (MRR, AL, MTE, IGT, SMM).

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors have not used any AI or AI-assisted technologies.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2023.101213.

References

[1] P.F. Smith, C.L. Darlington, Personality changes in patients with vestibular dysfunction, Front. Hum. Neurosci. 7 (2013), https://doi.org/10.3389/fnhum.2013.00678.

[2] E. Grill, M. Heuberger, R. Strobl, M. Saglam, R. Holle, B. Linkohr, K. Ladwig, A. Peters, E. Schneider, K. Jahn, N. Lehnen, Prevalence, determinants, and consequences of vestibular hypofunction. Results from the KORA-FF4 survey, Front. Neurol. 9 (2018), https://doi.org/10.3389/fneur.2018.01076.

[3] S. Hillier, M. McDonnell, Is vestibular rehab effective in improving dizziness and function after unilateral peripheral vestibular hypofunction? an abridged version of a cochrane review, Eur. J. Phys. Rehabil. Med. 52 (4) (2016) 541–556.

[4] T.C. Hain, M. Cherchi, D.A. Yacovino, Bilateral vestibular loss, Semin. Neurol. 33 (3) (2013) 195–203, https://doi.org/10.1055/s-0033-1354597.

[5] C.D. Hall, S.J. Herdman, S.L. Whitney, S.P. Cass, R.A. Clendaniel, T.D. Fife, J. M. Furman, T.S.D. Getchius, J.A. Goebel, N.T. Shepard, S.N. Woodhouse, Vestibular rehabilitation for peripheral vestibular hypofunction, J. Neurol. Phys. Ther. 40 (2) (2016) 124–155, https://doi.org/10.1097/npt.0000000000000120.

[6] M.E. Tinetti, C.S. Williams, T.M. Gill, Health, functional, and psychological outcomes among older persons with chronic dizziness, J. Am. Geriatr. Soc. 48 (4) (2000) 417–421, https://doi.org/10.1111/j.1532-5415.2000.tb04700.x.

[7] H. Morimoto, Y. Asai, E.G. Johnson, Y. Koide, J. Niki, S. Sakai, M. Nakayama, K. Kabaya, A. Fukui, Y. Mizutani, T. Mizutani, Y. Ueki, J. Mizutani, T. Ueki, I. Wada, Objective measures of physical activity in patients with chronic unilateral vestibular hypofunction, and its relationship to handicap, anxiety and postural stability, Auris Nasus Larynx 46 (1) (2019) 70–77, https://doi.org/10.1016/j.anl.2018.06.010.

[8] B. Kundakci, A. Sultana, A.J. Taylor, M.A. Alshehri, The effectiveness of exercise-based vestibular rehabilitation in adult patients with chronic dizziness: a systematic review, F1000Res 7 (2018), https://doi.org/10.12688/f1000research.14089.1.

[9] C.D. Hall, S.J. Herdman, S.L. Whitney, E.R. Anson, W.J. Carender, C.W. Hoppes, S. P. Cass, J.B. Christy, H.S. Cohen, T.D. Fife, J.M. Furman, N.T. Shepard, R. A. Clendaniel, J.D. Dishman, J.A. Goebel, D. Meldrum, C. Ryan, R.L. Wallace, N. J. Woodward, Vestibular rehabilitation for peripheral vestibular hypofunction: an updated clinical practice guideline from the academy of neurologic physical therapy of the american physical therapy association, J. Neurol. Phys. Ther. 46 (2) (2022) 118–177, https://doi.org/10.1097/NPT.0000000000000382.

[10] D.E. Krebs, K.M. Gill-Body, P.O. Riley, S.W. Parker, Double-blind, placebo-controlled trial of rehabilitation for bilateral vestibular hypofunction: preliminary report, Otolaryngol. Head Neck Surg. 109 (4) (1993) 735–741, https://doi.org/10.1177/019459989310900417.

[11] S.J. Herdman, Role of vestibular adaptation in vestibular rehabilitation, Otoryngol. Head. Neck 119 (1) (1998) 49–54, https://doi.org/10.1016/s0194-5998(98)70195-0.

[12] D.E. Krebs, K.M. Gill-Body, S.W. Parker, J.V. Ramirez, M. Wernick-Robinson, Vestibular rehabilitation: useful but not universally so, Otolaryngol. Head Neck Surg. 128 (2) (2003) 240–250, https://doi.org/10.1067/mhn.2003.72.

[13] F.C. Bull, S.S. Al-Ansari, S. Biddle, K. Borodulin, M.P. Buman, G. Cardon, C. Carty, J. Chaput, S. Chastin, R. Chou, P.C. Dempsey, L. Dipietro, U. Ekelund, J. Firth, C. M. Friedenreich, L. Garcia, M. Gichu, R. Jago, P.T. Katzmarzyk, E. Lambert, M. Leitzmann, K. Milton, F.B. Ortega, C. Ranasinghe, E. Stamatakis, A. Tiedemann, R.P. Troiano, H.P. Van Der Ploeg, V. Wari, J.F. Willumsen, World health organization, Guidelines on physical activity and sedentary behaviour, Br. J. Sports Med. 54 (24) (2020) 1451–1462, https://doi.org/10.1136/bjsports-2020-102955, 2020.

[14] M. Buchheit, P.B. Laursen, High-intensity interval training, solutions to the programming puzzle, Sports Med. 43 (10) (2013) 927–954, https://doi.org/10.1007/s40279-013-0066-5.

[15] R.N. Sultana, A. Sabag, S.E. Keating, N.A. Johnson, The effect of low-volume high-intensity interval training on body composition and cardiorespiratory fitness: a systematic review and meta-analysis, Sports Med. 49 (11) (2019) 1687–1721, https://doi.org/10.1007/s40279-019-01167-w.

[16] A. Sabag, J.P. Little, N.A. Johnson, Low-volume high-intensity interval training for cardiometabolic health, J. Physiol. 600 (5) (2022) 1013–1026, https://doi.org/10.1113/JP281210.

[17] D. Wen, T. Utesch, J. Wu, S. Robertson, J. Liu, G. Hu, H. Chen, Effects of different protocols of high intensity interval training for VO_2max improvements in adults: a meta-analysis of randomised controlled trials, J. Sci. Med. Sport 22 (8) (2019) 941–947, https://doi.org/10.1016/j.jsams.2019.01.013.

[18] H.G. MacDougall, K.P. Weber, L.A. McGarvie, G.M. Halmagyi, I. Curthoys, The video head impulse test: diagnostic accuracy in peripheral vestibulopathy, Neurol. 73 (14) (2009) 1134–1141, https://doi.org/10.1212/WNL.0b013e3181bacf85.

[19] M. Alfarghal, M.A. Algarni, S.K. Sinha, A. Nagarajan, VOR gain of lateral semicircular canal using video head impulse test in acute unilateral vestibular hypofunction: a systematic review, Front. Neurol. 13 (948462) (2022), https://doi.org/10.3389/fneur.2022.948462.

[20] J.E. Visser, M.G. Carpenter, H. van der Kooij, B.R. Bloem, The clinical utility of posturography, Clin. Neurophysiol. 119 (11) (2008) 2424–2436, https://doi.org/10.1016/j.clinph.2008.07.220.

[21] M.B. Badke, J.A. Miedaner, C.R. Grove, T.A. Shea, G.M. Pyle, Effects of vestibular and balance rehabilitation on sensory organization and dizziness handicap, Ann. Otol. Rhinol. Laryngol. 114 (1) (2005) 48–54, https://doi.org/10.1177/000348940511400109.

[22] A. Shumway-Cook, C.S. Taylor, P.N. Matsuda, M.T. Studer, B.K. Whetten, Expanding the scoring system for the dynamic gait index, Phys. Ther. 93 (11) (2013) 1493–1506, https://doi.org/10.2522/ptj.20130035.

[23] E.A. Phelan, J.E. Mahoney, J.C. Voit, J.A. Stevens, Assessment and management of fall risk in primary care settings Med, Clin. North Am. 99 (2) (2015) 281–293, https://doi.org/10.1016/j.mcna.2014.11.004.

[24] K. Norton, N. Whittingham, L. Carter, D. Kerr, C. Gore, M. Marfell-Jones, Measurement techniques in anthropometry, Anthropometrica 1 (1996) 25–75.

[25] C.L. Craig, A.L. Marshall, M. Sjöström, A.E. Bauman, M.L. Booth, B.E. Ainsworth, M. Pratt, U. Ekelund, A. Yngve, J.F. Sallis, International physical activity questionnaire: 12-country reliability and validity, Med. Sci. Sports Exerc. 35 (8) (2003) 1381–1395, https://doi.org/10.1249/01.MSS.0000078924.61453.FB.

[26] D.S. Ward, K.R. Evenson, A. Vaughn, A.B. Rodgers, R.P. Troiano, Accelerometer use in physical activity: best practices and research recommendations, Med. Sci. Sports Exerc. 37 (11) (2005) 582, https://doi.org/10.1249/01.mss.0000185292.71933.91.

[27] G.P. Jacobson, C.W. Newman, The development of the dizziness handicap inventory, Arch. Otolaryngol. Head Neck Surg. 116 (4) (1990) 424–427, https://doi.org/10.1001/archotol.1990.01870040046011.

[28] A.T. Beck, R.A. Steer, G.K. Brown, Beck Depression Inventory, Harcourt Brace Jovanovich, New York, 1987.

[29] A.T. Beck, N. Epstein, G. Brown, R. Steer, Beck anxiety inventory, J. Consult. Clin. Psychol. (1993).

[30] G. Mancia, R. Fagard, K. Narkiewicz, J. Redon, A. Zanchetti, M. Böhm, T. Christiaens, R. Cifkova, G. De Backer, A. Dominiczak, ESH/ESC guidelines for

the management of arterial hypertension, Arter. Hypertens. 17 (2) (2013) 69–168, https://doi.org/10.1097/01.hjh.0000431740.32696.cc, 2013.

[31] A. Mezzani, L.F. Hamm, A.M. Jones, P.E. McBride, T. Moholdt, J.A. Stone, A. Urhausen, M.A. Williams, Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the european association for cardiovascular prevention and rehabilitation, the american association of cardiovascular and pulmonary rehabilitation and the canadian association of cardiac rehabilitation, Eur. J. Prev. Cardiol. 20 (3) (2013) 442–467, https://doi.org/10.1177/2047487312460484.

[32] M.F. Piepoli, U. Corrà, P.G. Agostoni, R. Belardinelli, A. Cohen-Solal, R. Hambrecht, L. Vanhees, Statement on cardiopulmonary exercise testing in chronic heart failure due to left ventricular dysfunction: recommendations for performance and interpretation part II: how to perform cardiopulmonary exercise testing in chronic heart failure, Eur. J. Cardiac. Rehabil. Exerc. Physiol. 13 (3) (2006) 300–311, https://doi.org/10.1097/01.hjr.0000209812.05573.04.

[33] M.C. Zourdos, A. Klemp, C. Dolan, J.M. Quiles, K.A. Schau, E. Jo, E. Helms, B. Esgro, S. Duncan, S. Garcia Merino, R. Blanco, Novel resistance training-specific rating of perceived exertion scale measuring repetitions in reserve, J. Strength Cond. Res. 30 (1) (2016) 267–275, https://doi.org/10.1519/JSC.0000000000001049.

[34] E.R. Helms, J. Cronin, A. Storey, M.C. Zourdos, Application of the repetitions in reserve-based rating of perceived exertion scale for resistance training, Strength Condit. J. 38 (4) (2016) 42–49, https://doi.org/10.1519/SSC.0000000000000218.

[35] S.A. Arnold, A.M. Stewart, H.M. Moor, R.C. Karl, J.C. Reneker, The effectiveness of vestibular rehabilitation interventions in treating unilateral peripheral vestibular disorders: a systematic review, Physiother. Res. Int. 22 (3) (2017), https://doi.org/10.1002/pri.1635.

[36] L.V. Hedges, I. Olkin, Statistical Methods for Meta-Analysis, Academic Press (INC), London (UK), 1985, p. 369.

[37] D.E. Krebs, K.M. Gill-Body, S.W. Parker, J.V. Ramirez, M. Wernick-Robinson, Vestibular rehabilitation: useful but not universally so, Otolaryngol. Head Neck Surg. 128 (2) (2003) 240–250, https://doi.org/10.1067/mhn.2003.72.