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Master's Degree in Physical Activity and Sports Sciences

Master´s Degree Final Project

Supervised exercise as an adjuvant program for people with unilateral chronic vestibular hypofunction: EXERVEST Study protocol and preliminary baseline results

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Master´s Degree in Physical Activity and Sport Sciences

Supervised exercise as an adjuvant program for people with unilateral chronic vestibular hypofunction: EXERVEST Study protocol and preliminary baseline results

Master's Thesis for the Master's Degree in Physical Activity and Sport Sciences.

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TITLE: Supervised exercise as an adjuvant program for people with unilateral chronic vestibular hypofunction: EXERVEST Study protocol and preliminary baseline results.

ABSTRACT

Introduction: Unilateral peripheral vestibular dysfunction (UPVD) often complains of dizziness, gaze and balance disturbances. There is a lack of evidence on exercise intervention in UPVD patients.

Objectives: 1) To present the study protocol with the goal to investigate the effect of an 8-week supervised exercise concurrent program (*i.e.,* aerobic and resistance exercises) in people suffering from UPVD in comparison with a control group doing conventional vestibular rehabilitation at home. 2) To describe a preliminary sample providing characterization data related to body composition, cardiorespiratory fitness, balance and perception of health-related quality of life data.

Methods: This longitudinal, controlled, randomized, prospective, single-blinded, two-arm, parallel intervention study will include 146 adults (18-65 years old) with chronic unilateral vestibular hypofunction. Participants will be randomly assigned to an exercise intervention group (concurrent program) or an attention crontrol group (AC). Participants will be assessed at baseline, after a 2-month intervention period, and 6-month follow-up. The primary variable will be balance, measured by posturography and Dynamic Gait Index test. Secondary outcome variables will include 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), blood pressure monitoring, and cardiorespiratory fitness (peak cardiopulmonary exercise test).

Results: Participants in the EXERVEST study showed 1) body composition values outside the ranges considered optimal (overweight and 29.9% of fat body mass), moderate cardiorespiratory fitness level (26.5±6.63 $mL \cdot kg^{-1} \cdot min^{-1}$) and optimal BP values (<120/80mmHg) and, 2) common dizziness, moderate anxiety level and mild depression.

Conclusion: The need for research in this area is clear and this will be an innovative study that will test physical exercise as an adjuvant program to improve the prognosis of these patients.

KEY WORDS: Exercise design, vestibular dysfunction, balance, health-related quality of life.

ABBREVIATIONS:

ABPM (Ambulatory Blood Pressure Monitoring)
AC (Attention Control group)
BAI (Beck Anxiety Inventory)
BDI-2 (Beck Depression Inventory)
BMI (Body Mass Index)
BP (Blood Pressure)
CPET (Cardiopulmonary Exercise Test)
DBP (Diastolic Blood Pressure)
DGI (Dynamic Gait Index)
DHI (Dizziness Handicap Inventory)
EX (Exercise group)
FBM (Fat Body Mass)
F (Female)
FFM (Fat Free Mass)
FITT principle (Frecuency, Intensity, Time, Type)
HIIT (High-Intensity Interval Training)
HR (Heart Rate)
IPAQ (International Physical Activity Questionnaire)
M (Male)
MET (Metabolic Equivalent of Task)
SBP (Systolic Blood Pressure)
SOT (Sensory Organization Test)
TBW (Total Body Water)
UPVD (Unilateral Peripheral Vestibular Dysfunction)
VD (Vestibular dysfunction)
vHIT (Video Head Impulse Test)
VR (Vestibular Rehabilitation)
VT (Ventilatory Threshold)
WHR (Waist to Hip Ratio)

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INTRODUCTION

The vestibular system is a complex neural network that provides information on head movements and body position. It aims to maintain control of vision as well as balance and it is organized into two different functional units: the vestibulo-ocular system (responsible for visual stability during head movements) and the vestibulospinal system (responsible for postural control). According to neurophysiology, vestibulo-ocular involvement is manifested by dizziness/vertigo and visual instability, while vestibulospinal dysfunction causes imbalance (1).

More than 95 million adults in Europe and the USA suffering from vestibular dysfunction (VD) often complain of dizziness, and gaze and balance disturbances (2). Moreover, the cause of this dysfunction can be both related to a disease or trauma. Some examples of these conditions include Ménière´s Disease and perilymphatic fistula, which can be also caused by a surgical intervention such as unilateral labyrinthectomy (3). Unilateral vestibular pathology may also be manifested itself acutely and symptoms will spontaneously disappear within weeks, even though, about 30% of patients may have persistent dizziness, imbalance, and poor trunk control (4). This condition is related to an increased risk of falls and it is known that the public costs of fall-related injuries in adults are substantial. The 2020 annual expenditure of the U.S. healthcare system on this issue was around 30 billion dollars (5). Vestibular rehabilitation (VR) is an accepted program that pretends to fix balance impairment caused by unilateral peripheral vestibular dysfunction (UPVD). The main exercises of VR consist of postural and gaze stabilization (6). These exercises can be adaptive (*i.e.,* aiming at long-term changes in the neural response to cephalic movements to reduce symptoms by normalizing gaze and postural stability), substitution (*i.e.,* using other visual strategies such as slow tracking or central preprogramming of eye movements), or habituation (*i.e.,* aiming at reducing vestibular symptoms by repeated exposure to the stimulus with the objective of reducing the response to the stimulus) (6). The performance of vestibular habituation exercises using virtual reality has also been studied (7). Significant beneficial results have been found with all types of exercises, being advisable to combine several of them (8). Furthermore, an alternative therapy, such as Tai Chi, has recently gained popularity because of its implication for body control (9).

The question is, could an intervention with exercise improve the symptoms of these patients and ultimately their health-related quality of life? It should be noted that the World Health Organization (WHO) states that 18–64-year-old adult people must perform intense aerobic physical activity for at least 75 to 150 minutes throughout the week and should also perform moderate to more intense muscle-strengthening activities that exercise all major muscle groups on two or more days per week. Even so, these patients often avoid activities that require head movements due to fear of a loss of balance and subsequent fall, leading to a decrease in their physical activity level. Physical inactivity is known to be one of the most important risk factors in numerous diseases, particularly cardiovascular ones (10). Thus, exercise is not only effective in improving these patients´ comorbidities, but it seems to be an important factor for recovering from vestibular injuries (11). Body control or stability is one of the main difficulties these patients have. Therefore, balance training using unstable surfaces is highly recommended in VR to stimulate the somatosensorial input and replace impaired vestibular function (1,12). In this sense, standing body balancing improves control of the center of mass, and recovery of normal postural strategies. Further, endurance training and gait technique exercises have also proven strong evidence of improving the quality of life of UPVD patients (1). Thence, High-Intensity Interval Training (HIIT), is nowadays one of the most efficient manners of improving cardiorespiratory fitness and metabolic function and, successively, people´s health-related quality of life (13). In this sense, several studies have found HIIT to be more effective than moderate-intensity continuous aerobic exercise training in improving cardiac and vascular functions, aerobic capacity, post-exercise heart rate recovery, and psychological states in other pathologies (14,15). Supervised exercise is, therefore, among the potentially beneficial adjuvant programs in this population (16), although comparatively little studied with other pathologies. In addition, in vestibular hypofunction, there is insufficient evidence on specific interventions in specific clinical situations, the optimal amount of exercise, and the duration of programs (17,18).

As stated above, previous studies have shown that VR is an effective manner of decreasing UPVD symptoms, however, no research has been performed on a supervised exercise program, according to FITT principle (Frequency, Intensity, Time, Type). In light of the above, the EXERVEST study has been designed to investigate the effect of an 8-week supervised EXERcise concurrent program (*i.e.*. aerobic and strength exercises in the same

session) in people suffering from unilateral peripheral VESTibular hypofunction in comparison with a control group doing conventional VR at home.

We hypothesize that supervised concurrent exercise as an adjuvant program to conventional rehabilitative treatment will improve balance and quality of life in people diagnosed with chronic unilateral vestibular hypofunction. Hence, the main objectives of this randomized controlled trial will be to analyze 1) the effects of a concurrent exercise program with resistance, balance, and aerobic exercises on balance in people with a diagnosis of unilateral vestibular hypofunction, compared to a control group, and 2) the effect at 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 according to the etiology that caused the vestibular hypofunction and the time elapsed after the establishment of vestibular hypofunction, (3) to analyze the effect on body composition, cardiorespiratory fitness, blood pressure, physical activity level, sedentary behavior, and sleep quality, and (4) to evaluate the association between changes in balance and the rest of the analyzed variables.

MATERIAL AND METHODS

Study design

EXERVEST is a controlled, randomized, prospective, single-blinded (staff of the otorhinolaryngology department of the hospital), two-arm, parallel intervention study, 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 (November 02, 2021, Certificate No. 2019-095). 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 8 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 was performed by a technician from Bioaraba Research Institute (http://aleatorizacion.bioaraba.org/) using the technique of stratified randomization (1:1) by etiology and age. The participants were randomized to one of the two groups of intervention: 1) exercise + conventional rehabilitation treatment (EX group) and conventional rehabilitation treatment (Attention control group, AC). The flow diagram of the study can be seen in Figure 1.

Participants and selection criteria

The sample will include 146 adults (18-65 years old) with chronic unilateral vestibular hypofunction attending the Otoneurology Department of the local hospital.

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

Participants may 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 may withdraw participants from the study for the following reasons, among others:

- Failure of the participant to comply with procedures and recommendations, including procedures related to the administration of study medication.
- Voluntary withdrawal.
- 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.
- 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.

- Injury to the participant 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 should be assessed again.

Measurements

Assessments used in the protocol will be evaluated before (T0), after an 8-week intervention period (T1), and a 6-month follow-up period (T2). The study protocol procedure is outlined in Figure 1. Participants from the two groups will be evaluated at the same time.

The primary variable will be the equilibrium (balance), measured by posturography and the Dynamic gait index test. Secondary outcome variables will include 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 SPIRIT figure showing the time points for assessments and intervention is apportioned in Figure 2.

Anthropometry and body composition

Anthropometry measurements were taken following the guidelines from the International Society for the Advancement of Kinanthropometry (19), and included the stature (SECA 213), total body mass (SECA 869), Body Mass Index (BMI) calculated as [total body mass (kg)/stature (m^2)], and waist and hip circumferences (SECA 200) to calculate waist/hip ratio (WHR). In addition, fat-free mass, fat mass, and total body water were assessed with bioelectrical impedance analysis (Tanita, BF 350 and Tanita, BC-418 MA).

Clinical variables

Degree and type of vestibular dysfunction.

Participants were measured by the video Head Impulse Test (vHIT) (ICS Impulse USB, Natus hearing and balance, EEUU) to determine their degree and type of VD. This test collects computerized vestibulo-ocular reflex, measuring the speed of head movement and the ocular response. Two parameters were 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) (20).

Instability, balance, and risk of falls.

On the one hand, the participant's instability was assessed by a dynamic posturography (dynamic SPS system, Synapsys, France) (21). The sensory organization test (SOT) was 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 from 0 to 100 the degree of dependence on visual information, which indicates pathology, but adequate compensation at a central level. The first three conditions are 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 (22).

On the other hand, the balance and risk of falls were measured by the Dynamic Gait Index (DGI). It is composed of eight exercises to assess the technique and capacity to overcome obstacles, each scored from 0 (severe impairment) to 3 (highest level of functionality). The maximum score is 24 points and a score less than 19 is predictive of fall risk (23).

Lifestyle and health-related quality of life

Physical activity and sedentary behavior were 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 (24); and 2) a 3-axis accelerometer (ActiGraph wGT3X-BT, Pensacola, FL, USA) worn on the non-dominant wrist for a whole week by the participants as proposed in the practice guidelines for research (25). Each participant was given oral instructions on how to wear the accelerometer and how to complete the diary log. On the eighth day after the accelerometers were distributed, both accelerometers and diaries were collected. All participants answered the Dizziness Handicap Inventory (DHI) questionnaire for the assessment of health-related

quality of life (26). 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, 36–52 moderate, while a score over 54 points severe quality of life worsening.

Psychological evaluation protocols included the Beck Depression Inventory (BDI) (27) and Beck Anxiety Inventory (BAI) (28). 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 0-13 indicate minimal depression, 14-19 mild depression, 20-28 moderate depression; and 29-63 severe depression. For BAI, scores between 10–16 indicate mild anxiety, 17–to 29 moderate anxiety, and scores above 30 represent severe anxiety.

Resting cardiovascular measurements

A 12-lead electrocardiogram was performed at rest with the wireless device of the Ergo CarMedisoft S.S, Belgium Ref. USM001 V1.0 system and the data were analyzed by a blind specialist. The assessment of the blood pressure was carried out in line with the guidelines set by the ESH/ESC (29). Ambulatory blood pressure monitoring (ABPM) was conducted for 24 hours using the ABPM 7100 (Welch Allyn, New York City, NY, USA). The device measured blood pressure (BP) at 30-minute intervals during the daytime, and at 60-minute intervals during the nighttime. Values will be registered from the recorder as mean values of systolic and diastolic BP of both periods.

Cardiorespiratory fitness

A peak, symptom-limited cardiopulmonary exercise test performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands) was used to determine peak oxygen uptake (VO_{2peak}) and ventilatory thresholds (VT). The protocol started at approximately 70 rpm and 40 watts, with gradual increments of 10 watts every minute to exhaustion. Continuous electrocardiogram monitoring was conducted throughout each test. During the test, participants were encouraged by the exercise specialist in the

laboratory. Expired gas analysis was conducted by the Ergo CarMedisoft S.S, Belgium Ref. USM001 V1.0 system and calibration was performed before each test session. Data of every breath were measured constantly during the test and averaged every 60 seconds. Achievement of VO_{2peak} criteria was assumed when two or more of the following items were 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 ≥ 1,1; (4) omission of increment of VO_2 and/or HR with increases in work rate (30). Perceived fatigue will be reported (scale 6-20) at the end of each minute/stage. Blood pressure will be assessed every two minutes. Measurements of the VT 1 and 2 (VT1 and VT2) were carried out by the V-slope and ventilatory equivalents standardized methods (30). After achieving the peak effort, participants remained stationary on the bike for five minutes in recovery with electrocardiogram and BP monitoring. Absolute and relative indications for finishing the exercise test will be considered (31). Three different exercise intensity ranges will be determined by the identification of the two VT: R1, light to moderate with HR values below VT1; R2, moderate to vigorous with HR values between VT1 and VT2; and R3, high to severe with HR values higher than VT2 (30).

Exercise intervention program

Both EX and AC groups will have all antivertiginous drugs withdrawn. The AC group will perform only home vestibular rehabilitation exercises that are usually prescribed in consultation to this type of patient, performing the same assessments as the intervention group in all phases of the study.

Participants in the EX group will train for two non-consecutive days per week for eight weeks under the supervision of exercise specialists and sports physical educators, (See more details in Appendix 2). All sessions will start and finish with BP measurements, and exercise intensity will be monitored by HR monitors (Polar Electro, Kempele, Finland) and through the rate of perceived exertion using the original Borg scale (6-20). Each session will include a 10min warm-up with joint mobility exercises and gait technique and a 10 min cooldown with basic stretching exercises and controlled breathing. The main part of each training session will consist of: 1) 8-10 balance and strength exercises with postural control and integration of the main muscle groups and motor patterns, 2) low-volume aerobic HIIT on

the bicycle (15 min). The intensity will be individually tailored to each participant's HR at moderate (R2) or vigorous intensities (R3), adjusting the power and speed on the bike to achieve the planned target HR. The protocol of HIIT will consist of 5-min warm-up, plus five series of 30 seconds at R3 followed by 60 seconds at R2, gradually increased to eight series, finishing with 2-5 min cool-down period at R2; and 3) five minutes of retro walking on the treadmill at low-to-moderate intensity 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 performed 16 sessions; if a session was missed (a maximum of two were allowed), these were added on to the end of the 8-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.

At the end of the intervention, participants will receive physical activity recommendations for the following six months. Participants had 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.

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).

To evaluate the association between changes in balance and the rest of the variables analyzed, multiple linear regression analyses will be performed.

Sample size

To answer the main objective of analyzing an improvement of the effects on balance in people with a diagnosis of unilateral vestibular hypofunction, a superiority design will be carried out. Taking into account that the significance level is 5% and the power 80% and assuming that the superiority limit is 9.75 units, the mean of the reference group is 14.39 units, the mean of the experimental group is 24.69 units and the standard deviation of both groups is 1.76 units, it will be necessary to include 65 pairs of experimental units in the study. Taking into account that the expected dropout rate is 10%, it would be necessary to recruit 73 pairs of experimental units in the study, a total of 146 participants.

The sample size calculation was performed using “ene” 3.0 program based on the main study variable "Dynamic gait index", according to previously published studies (7).

RESULTS

The previous sample determination of the EXERVEST study was estimated to be 146 participants to detect an effect of the intervention. However, taking into account that we are in the early phase of the study, preliminary data will be presented to describe the sample. Thus, seven people were recruited from the otoneurology services in the local hospital. However, one person declined to participate. Therefore, six participants diagnosed with VD performed an exhaustive assessment.

Characteristics of the studied population are shown in Table 2. Related to body composition, EXERVEST participants showed upper optimal values of body mass index (*i.e.,* BMI>25 kg/m^2 considered overweight) and fat body mass (*i.e.,* FBM=29.93% considered obesity)

which are contemplated as cardiovascular risk factors (Us Department of Health and Human Services, 2013). Further, 33% of participants informed currently smoking cigarettes.

However, the group showed optimal BP values (*i.e.,* systolic blood pressure<120 mmHg, diastolic blood pressure<80 mmHg) (32).

Exercise function values are shown in Table 3. The average time, distance, and peak workload performed in the cardiopulmonary exercise test were 13±4.52 min, 2.47±1.17 km, and 146.67±49.46 watts, respectively. Regarding cardiorespiratory fitness, EXERVEST participants showed a medium level regarding MET_{peak} (7.63±1.85) (33), and were classified in the 60th percentile (VO_{2peak} =26.5±6.63 $mL \cdot kg^{-1} \cdot min^{-1}$) (34).

Balance assessment through DGI scores ranged from 20 to 24, out of a possible 24 (Table 4). The subjective perception of vertigo among the study participants was acquired using the DHI. Dizziness was common and results showed a severe handicap (i.e., >54 points) (26). A moderate anxiety level (i.e., 17-29 points) (28) and mild depression (i.e., 14-19 points) (27) were shown after evaluating the mental health through BAI and BDI-2 questionnaires, respectively.

DISCUSSION

In the present preliminary characterization, analysis of the body composition, resting cardiovascular values, exercise function, balance and perception of health-related quality of life in people with UPVD (i.e., EXERVEST sample) is shown. The main findings of the study were that the participants in the EXERVEST study showed 1) body composition values outside the ranges considered optimal, moderate cardiorespiratory fitness level, and optimal BP values and, 2) common dizziness, moderate anxiety level, and mild depression.

It is necessary to note that activities requiring continuous head movements and changes in position could contribute to inaccurate vestibular responses (35). Patients with UPVD often avoid discomfort by reducing these kinds of activities due to common dizziness (Table 3), leading to a lack of exercise or physical activity periods. As stated above, it is known that physical inactivity is one of the most important cardiovascular risk factors (10), which could

be a direct consequence caused by the condition (35). In light of the above, the participants showed (Table 1) overweight (>25kg/m^2), obesity (fat body mass = 29.93%), and close to high metabolic risk based on WHR values (>0.86 in women and >0.95 in men) (36); and they also proved a moderate cardiorespiratory fitness (Table 2), which is considered a healthy key parameter. Moreover, the aforementioned could lead to a sedentary lifestyle which could, indeed, affect psychological well-being regarding depression and anxiety values (37). Therefore, coordinated interventions to minimize cardiovascular risk factors (38) and improve psychological well-being should be targeted, and a controlled exercise program is among the potentially beneficial adjuvant programs in these areas (37,38).

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

Previous studies have shown that VR is effective in improving patients´ balance and, a safe and effective proposal for UPVD patients (3). However, a previous study has shown that just 65% of the participants responded to the therapy (39). Alternative ways of approaching the condition, such as an exercise concurrent program combining strength, balance, and low volume and high-intensity aerobic 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 concurrent exercise program on functionality will be related to balance stability and quality of life in people diagnosed with UPVD.

In conclusion, the preliminary results of the present investigation help to better understand the potential need for an adjuvant concurrent exercise program for improving the well-being of people with UPVD.

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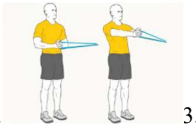
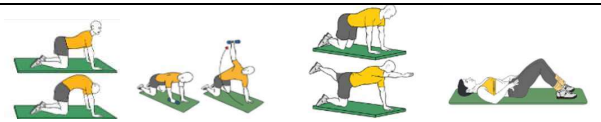
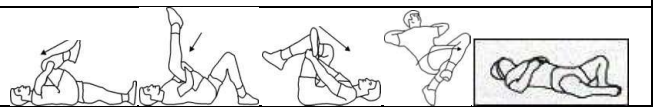
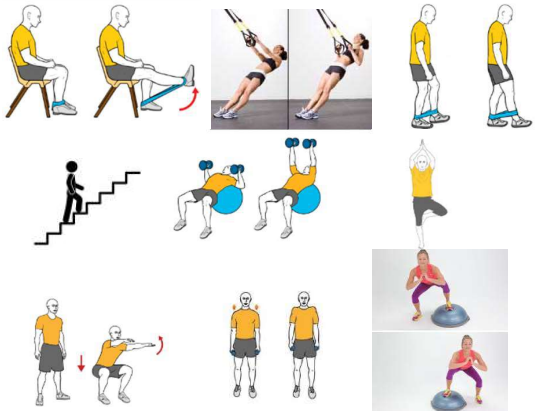
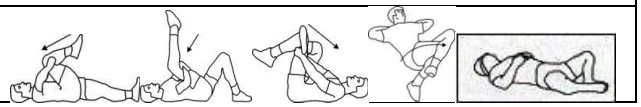
Appendixes

Appendix 1

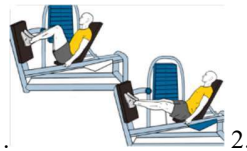
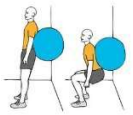
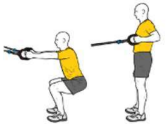
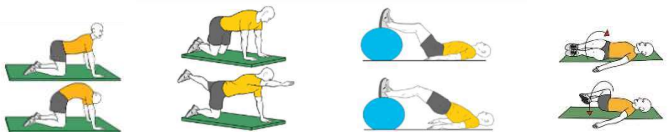
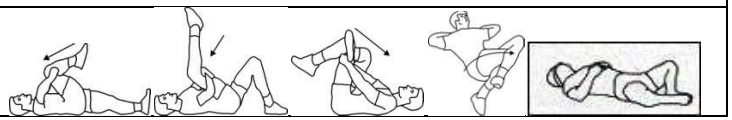
Session 1, month 1.

SESIÓN 1-MES 1		
CALENTAMIENTO 15min	Movilidad articular estático: de arriba abajo. Cuidado con el cuello y los movimientos hacia atrás. 	Ejercicios de técnica de marcha: Andar de puntas, talones, talón punta, rodillas arriba, talones atrás, alternar rodillas arriba y talones atrás, hacer también unilateral. Incluir brazos adelante y hacia atrás mientras se mueven.
PARTE PRINCIPAL-AERÓBICO BICI+CINTA	Bici HIIT (12min)	Retrowalking (2-5min)
15min PARTE PRINCIPAL-FUERZA 45”-ejercicio 15” cambio	CIRCUITO FUERZA Velocidad de ejecución: lenta Poca carga. Aprendizaje 1. Prensa horizontal 2. Press Palof (echar aire en la extensión) 3. Caminar sobre una línea recta con brazos en pecho. 4. Squat sobre silla con mini band debajo de las rodillas 5. Remo mancuernas (bisagra cadera) 6. Equilibrio sobre BOSU 7. Step alternando pies de frente-se baja primero con el que se ha subido. Meter mancuernas 8. Press banca máquina 9. Equilibrio-con ambas piernas	1.  2.  3.  4.  5.  6.  7.  8.  9. 
ESCUELA DE ESPALDA 10min	1) Gato-camello. 2) Elevación lateral. 3) Lumbares cruzados-echar aire en la extensión con palma de la mano mirando hacia arriba. 4) Hipopresivo-respiración	
VUELTA A LA CALMA 5min	Estiramientos finales-10-15” en cada posición	

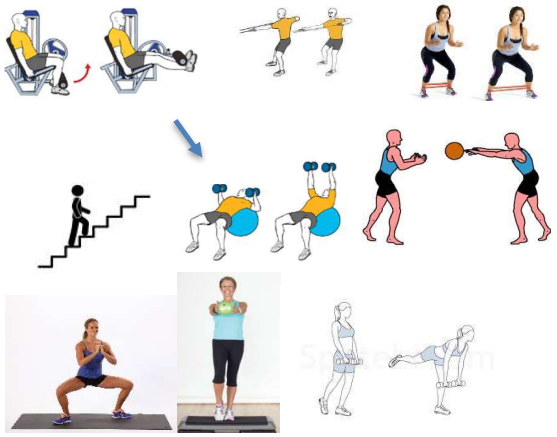
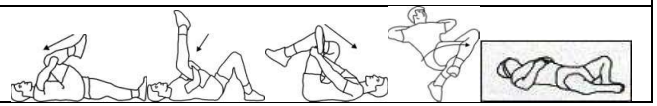
Session 2, month 1.

SESIÓN 2-MES 1		
CALENTAMIENTO 15min	Movilidad articular estático: de arriba abajo. Cuidado con el cuello y los movimientos hacia atrás. 	Ejercicios de técnica de marcha: Andar de puntas, talones, talón punta, rodillas arriba, talones atrás, alternar rodillas arriba y talones atrás, hacer también unilateral. Incluir brazos adelante y hacia atrás mientras se mueven.
PARTE PRINCIPAL-AERÓBICO BICI+CINTA	Bici HIIT (12min)	Retrowalking (2-5min)
15min PARTE PRINCIPAL-FUERZA 45”-ejercicio 15” cambio	CIRCUITO FUERZA Velocidad de ejecución: lenta Poca carga. Aprendizaje 1. Extensión de rodilla con banda elástica 2. Remo con TRX 3. Caminar con mini-band en tobillos-pasos largos. 4. Escaleras 5. Pectoral con mancuernas (agarre neutro) sobre fitball-caderas arriba. 6. Equilibrio: postura del árbol 7. Media sentadilla elevando brazos 8. Encogimiento de hombros con mancuernas 9. Step lateral sobre bosu	
ESCUELA DE ESPALDA 10 min	1. Dead bug 2. Puente de glúteos 3. Crunch abdominal con ligera elevación de la parte superior de la espalda con control respiratorio (meter tripa) 4. Lumbares con elevación unilateral	
VUELTA A LA CALMA	Estiramientos sentados-10-15” en cada posición	

Session 1, month 2.

SESIÓN 1-MES 2		
CALENTAMIENTO 15min	Movilidad articular estático: de arriba abajo. Cuidado con el cuello y los movimientos hacia atrás. 	Ejercicios de técnica de marcha: Andar de puntas, talones, talón punta, rodillas arriba, talones atrás, alternar rodillas arriba y talones atrás, hacer también unilateral. Incluir brazos adelante y hacia atrás mientras se mueven.
PARTE PRINCIPAL-AERÓBICO BICI+CINTA	Bici HIIT (12min)	Retrowalking (2-5min)
15min PARTE PRINCIPAL-FUERZA 45''-ejercicio 15'' cambio	CIRCUITO FUERZA Velocidad de ejecución: MEDIA. Incrementar carga Respiración: echar aire y contraer abdominal en la fase concéntrica 1. Prensa horizontal 2. Press Palof (echar aire en la extensión) sobre BOSU UP 3. Caminar sobre una línea recta con brazos en pecho. 4. Medio Squat con fitball en espalda (echar aire al subir contrayendo abdominal). 5. Remo mancuernas (bisagra cadera) 6. Medio squat sobre BOSU. Si controla hacer pases con balón de 1kg. 7. Subir y bajar escaleras 8. Press banca máquina 9. Coordinación pies (adelante-atrás sobre una línea). 1) der+izq. 2) Izq+der. Meter velocidad si lo hace bien y no se marea.	1.  2.  3.  4.  5.  6.  7.  8.  9. 
ESCUELA DE ESPALDA 10min	1) Gato-camello. 2) Lumbares cruzados-echar aire en la extensión con palma de la mano mirando hacia arriba. 3) Puente sobre fitball-contrae periné 4) Rotación caderas en prono	
VUELTA A LA CALMA 5min	Estiramientos finales-10-15'' en cada posición	

Session 2, month 2.

SESIÓN 2-MES 2		
CALENTAMIENTO 15min	Movilidad articular estático: de arriba abajo. Cuidado con el cuello y los movimientos hacia atrás. 	Ejercicios de técnica de marcha: Andar de puntas, talones, talón punta, rodillas arriba, talones atrás, alternar rodillas arriba y talones atrás, hacer también unilateral. Incluir brazos adelante y hacia atrás mientras se mueven.
PARTE PRINCIPAL-AERÓBICO BICI+CINTA	Bici HIIT (12min)	Retrowalking (2-5min)
15min PARTE PRINCIPAL-FUERZA 45”-ejercicio 15” cambio	CIRCUITO FUERZA Velocidad de ejecución: MEDIA. Incrementar carga Respiración: echar aire y contraer abdominal en la fase concéntrica 1. Leg extension en máquina 2. Remo alterno con gomas. 3. Caminar lateral (rodillas flex, caderas atrás) con mini-band en tobillos. 4. Escaleras con mancuernas en manos. 5. Pectoral con mancuernas (agarre neutro) sobre fitball-caderas arriba. Descender y subir caderas al ritmo de flexión y extensión de los brazos. Contracción suelo pélvico y abdominal en la extensión. 6. Pasar balón de 1-2kg 7. Media sentadilla abierta sin carga o con carga elevando brazos. 8. STEP con B de 1-2kg. 1. Subir y bajar con los brazos adelante con el Balón. 2. Después de subir girar y pasar el Balón al entrenador que estará a un lado 9. Single dead lift con mancuernas-MUYDESPACIO!	
ESCUELA DE ESPALDA 10 min	1. Roll out con fitball 2. Dead bug con fitball 3. Abductor isométrico con balón en rodillas, con control respiratorio (meter tripa) 4. Lumbares con elevación unilateral	
VUELTA A LA CALMA	Estiramientos sentados-10-15” en cada posición	

Appendix 2

Figure 1. *Exervest study procedure.*

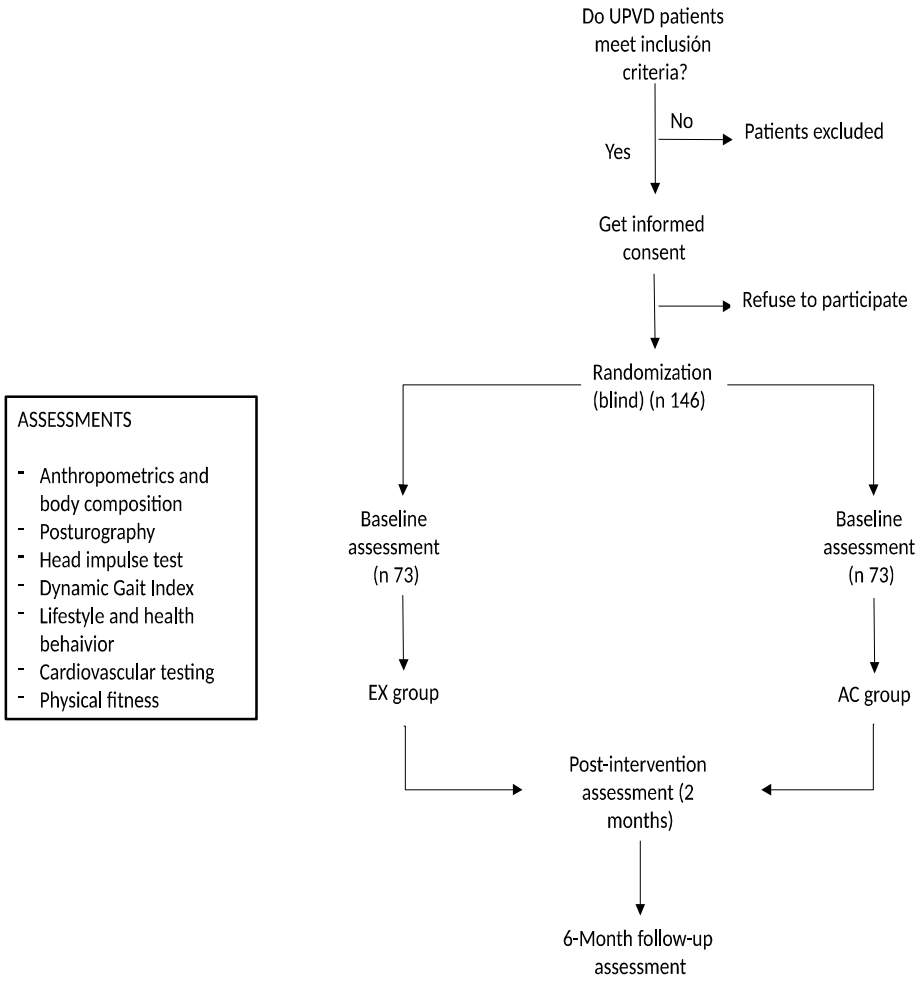


Figure 2. *SPIRIT figure showing an overview of the assessment schedule at baseline and follow-up in the EXERVEST study.*

Activity/Assessment	Study period			
	Pre-study	Baseline	Intervention (8 weeks)	Follow-up
TIMEPOINT	T-1	T0	T1	T2
Eligibility screen	X			
Informed consent	X			
Clinical and physical examination	X			
Randomisation		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 VD and instability: Posturography, Head Impulse Test, Dynamic Gait Index		X	X	X
Lifestyle and health behavior: IPAQ, DHI, BAI, BDI, Accelerometry.		X	X	X
Cardiovascular rest measures		X	X	X
Cardiorespitory fitness		X	X	X

IPAQ (International Physical Activity Questionnaire), DHI (Dizziness Handicap Inventory), BAI (Beck´s Anxiety Inventory), BDI (Beck´s Depression Inventory), CPET (Cardiopulmonary Exercise Test)

Table 1. *Inclusion and exclusión criteria for the EXERVEST study*

Inclusion criteria

- Patient with unilateral vestibular hypofunction.
- More than 6 months since the onset of vestibular hypofunction (chronic instability).
- Age between 18-65 years old.
- No previous rehabilitation treatment for vestibular hypofunction 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 (vHIT); anemia, blood disorders, chronic thrombotic disorders or hypercoagulant 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.
- Have plans to be out of town for more than two weeks.

Table 2. *Characteristics of the studied population.*

Variables	EXERVEST n=6
Age (yr old)	52.67 ± 6.71
Gender (M/F) (%)	50/50
Height (cm)	170 ± 0.075
Body mass (kg)	78.02 ± 17.72
BMI (kg/m^2)	26.79 ± 5.05
WHR	0.86 ± 0.1
FFM (%)	70.07 ± 7.34
TBW (%)	51.31 ± 5.39
FBM (%)	29.93 ± 7.34
Mean SBP (mmHg)	114 ± 10
Mean DBP (mmHg)	77 ± 11
Mean HR (bpm)	69 ± 8
Cigarrette smoking (%)	33.33

M, male; F, female; BMI, body mass index; WHR, waist to hip ratio; FFM, fat-free mass; TBW, total body water; FBM, fat body mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.

Table 3. *Participants´ exercise function.*

Variables	EXERVEST n=6
Workload$_{peak}$ (W)	146.67 ± 49.46
Time (min)	13 ± 4.52
Distance (km)	2.47 ± 1.17
HR$_{peak}$ (bpm)	164 ± 14
VO$_{2peak}$ (L•min^{-1})	2.04 ± 0.47
VO$_{2peak}$ (mL•kg^{-1}•min^{-1})	26.5 ± 6.63
MET$_{peak}$	7.63 ± 1.85
RER$_{peak}$	1.15 ± 0.08
HR$_{rec1}$ (bpm)	138.17 ± 17.21
HR$_{rec3}$ (bpm)	107.17 ± 19.86
VT$_1$ (mL•kg^{-1}•min^{-1})	16.33 ± 2.94
VT$_2$ (mL•kg^{-1}•min^{-1})	23 ± 5.66

$HR_{peak,}$ peak heart rate; VO_{2peak}, peak oxygen uptake; $MET_{peak,}$ peak metabolic equivalent of task; $RER_{peak,}$ peak respiratory exchange ratio; $HR_{rec1,}$ heart rate values in the first minute of recovery after the test; $HR_{rec3,}$ heart rate values in the third minute of recovery after the test; $VT_{1,}$ first ventilatory threshold; $VT_{2,}$ second ventilatory threshold

Table 4. *Dizziness, balance, and mood questionnaires*

Variables	EXERVEST n=6
DHI	55.67 ± 25.09
DGI	22.17 ± 1.94
BDI-2	14.67 ± 7.66
BAI	22.33 ± 11.003

DHI, Dizziness Handicap Inventory; DGI, Dynamic Gait Index; BDI-2, Beck Depression Inventory; BAI, Beck Anxiety Inventory