



UNIVERSIDADE DA CORUÑA

Grupo de Investigación en Gerontología y Geriatria

## Study Protocol and Statistical Analysis Plan

Protocol Official Title: **Low-volume Cycling Training Improves Body Composition and Functionality in Older People With Multimorbidity: a randomized controlled trial**

ClinicalTrials.gov ID: [Not yet assigned]

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## INTRODUCTION

Aging is a risk factor for most chronic diseases, and the presence of more than two diseases (i.e., multimorbidity), which is frequent in almost two out of three older adults, has been related to an increased risk of disability and frailty, a decrease in quality of life, and mortality (Pedersen, 2019). Physical activity (PA) acts as a nonpharmacological intervention and regular physical activity (rPA) reduces rates of all-cause mortality, compresses morbidity, decreases healthcare costs, and has relatively minimal adverse effects compared to drugs (Fiuza-Luces et al., 2013).

It has been estimated that 27.5% of the world's population in 2016 did not meet the recommendations established for the member states of the World Health Organization (WHO) for health-enhancing physical activity. Furthermore, recent studies showed that moderate-intensity physical activity may be sufficient for reducing the risk of all-cause dementia and that some of the protective benefits of physical activity for older adults (Cunningham et al., 2020). It seems indispensable to study adequate doses of exercise for older people who often have low levels of physical activity and fitness, who spend a large amount of time sitting down, and whose multimorbidity keeps them away from exercising.

## OBJECTIVES

To study the effects of perception-regulated low-volume and low- to moderate intensity training on body composition, hemodynamic parameters, and functional performance in older adults with multimorbidity.

## MATERIAL AND METHODS

### Study design

This longitudinal and prospective study conducted between September and December 2019, is a 2 x 2 randomized controlled trial using a two-group design (exercise vs. control) and two repeated measures (pre- vs. postintervention). This study is performed following the CONSORT (CONsolidated Standards of Reporting Trials) 2010 guideline.

### Study setting and participants

Participants are recruited between September and October 2019 at the Gerontological Complex La Milagrosa (A Coruña, Spain), consisting of a daycare center and a nursing home.

Inclusion criteria: (a) men and women aged 65 and older, (b) users of a care setting—daycare patients or nursing home residents, and (c) a score < 5 in the Global Deterioration Scale (GDS; Reisberg et al., 1982), from no cognitive decline to moderate cognitive decline.

Exclusion criteria: (a) physical limitations or musculoskeletal injuries that could affect cycling training performance; physical exercise contraindicated by the physiotherapist and verified by the medical doctor according to the medical register of each participant; (b) heart failure with a functional class according to the New York Heart Association (NYHA) Classification of NYHA III and IV; (c) the presence of acute pain that does not allow exercise training; (d) recent acute



myocardial infarction (in last 6 months) or unstable angina; (e) uncontrolled hypotension; (f) uncontrolled arterial hypertension (>180/100 mmHg); (g) active cancer treatment with chemotherapy; (h) patients with an active pacemaker and/or uncontrolled block; (i) diabetes mellitus with acute decompensation or uncontrolled hypoglycemia; or (j) any other circumstance that precludes individuals from completing the training intervention.

24 participants will be recruited and randomly placed into two groups: the exercise group (EG, n=12) and the control group (CG, n=12). A stratified permuted block randomization is employed that accounted for the GDS score, sex, and type of institutionalization. A nurse and a medical doctor enrolled and assigned participants to intervention.

## Intervention

### Cycloergometers

The Gerontological Complex La Milagrosa features a kinesiotherapy room equipped with three MOTomed®muvi cycle ergometers (Fig. 1) adapted for older people. These cycle ergometers have the ability, through electric motors, to provide resistance to oppose cycling and, on the other hand, to passively move the limbs of the trainees. This movement system allows even subjects with loss of functional ability to mobilize (bipedestation or walking) to perform the activity from their wheelchair or geriatric chair.

Through the machines, the subjects can simultaneously activate more than 80% of the muscles of the body, because the device allows the execution of the activity, both for the upper and lower limbs. The MOTomed®muvi allows you to control through your records the parameters: distance (Km), speed (m/s), duration (min), resistance (load), caloric consumption (Kcal), work done (J), and symmetry members' contralateral (%) (Fig. 2).



Figure 1



Figure 2. MOTomed®muvi' Screen

### Familiarization

Participants familiarized themselves with the activities over 2 days of 4 to 16 minutes of simultaneous upper and lower limb cycling at a comfortable pace, progressing until volitional



stop. Older adults cycled on a recumbent motorized cycle (MOTomed® Muvi Movement Therapy Trainer; Reck-Technik GmbH & Co., Betzenweiler, Germany). The MOTomed Muvi has a display where velocity (m/s) and resistance (kg) can be observed when cycling; thus, within the familiarization session, researchers annotated the velocities employed for the participants cycling 2 minutes with 1 kg and encouraged them to maintain this cadence when the load was increased at a rate of 2 kg each 2-minute stage. The trial was terminated when the participant volitionally stopped exercise owing to fatigue or discomfort. Furthermore, the trial was finished when the investigator determined that the participant could not maintain the designated pedaling rate for more than 10 consecutive seconds at the current load.

Before they began cycling, participants were anchored to the perception scale using a combination of exercise and memory procedures. This procedure required the participant to cognitively establish a perceived intensity of effort that is consonant with that depicted visually by a cyclist figure at the bottom (i.e., low anchor, rating 0) and top (i.e., high anchor, rating 10) of the hill, as presented in the OMNI-RPE scale illustrations [40]. The OMNI-RPE scale was visible at all times of the progressively increased resistance cycling exercise, and participants indicated a number before starting cycling and in the last 15 seconds of each stage. The familiarization period was conceived to train participants to anchor a score on the OMNI-RPE against a spectrum of intensities, defined by resistance applied, ensuring that they stop voluntarily at least once due to an inability to maintain the cadence set or a symptom-related alert (i.e., leg tightness/pain, dizziness, chest tightness/pain) that prevented them from exercising safely.

## Intervention

The exercise group is requested to accomplish 18 sessions on the MOTomed Muvi, a low volume (i.e., 20 minutes per session, 3 days per week) and low-to-moderate intensity combining upper and lower limb recumbent cycling training for six weeks at an intensity guided by the perception of effort.

The interventions are divided into three stages, 10 minutes of activity, 5 minutes of rest, and again 10 minutes of activity. The exercise performed consists of raising the resistance (load) adapted to each subject, starting with a resistance of 5KJ, increasing from 5KJ by 5KJ to a maximum of 20KJ. The speed of exercise is set subjectively, i.e. each patient manages and maintains the speed with which they feel most comfortable so that they can end the total time of each training session. In any case, and to prevent the cycle ergometer from passively boosting the upper or lower limbs, a basal (minimum) speed of 15 rpm is set. So, participants are informed and encouraged to increase their speed of movement above the minimum threshold. Besides, and to maintain a minimum control of rotations per minute and the machine presenting an isopotential mechanism (automatic adjustment of power according to speed and resistance) states that patients should not exceed a speed of 30rpm.

Therefore, a cycling cadence is fixed between 25 and 30 rpm for all sessions since that cadence is comfortable for every participant. Researchers adjust the resistance on the motorized cycle to increase the external load until it reached the level required to reach the intensity of effort programmed by the OMNI-RPE (Guidetti et al., 2011). The six weeks are programmed in the form of two intensity- differentiated training phases of three weeks. In the first training phase (i.e., the first three weeks), participants are requested to cycle simultaneously with the upper and



lower limbs at an intensity equivalent to a perception of 3 (i.e., easy to somewhat moderate) on the OMNI-RPE (0-10).

Control of adverse events was measured through the assessment and monitoring of vital signs before, during (within the first 10 minutes), and after the intervention sessions. Vital signs [heart rate (per minute), systolic and diastolic blood pressure (in millimeters of mercury, mm Hg), and oxygen saturation (in percentage)] were monitored by a nurse and a medical doctor using mobile finger pulse oximeters.

Throughout the training, evaluators are responsible for postural control and patient symmetry parameters controlled through the cycle ergometer screen.

The body posture of the participants in the chair in front of the machine is controlled considering the measurements of the appropriate joint angles in the knee, through a rule of ergometry. Two types of chairs are used for the performance of the activity, one conventional chair, and a geriatric chair in case the patient needs it to move.

For sitting, conventional geriatric chairs are used, seeking to respect the angles of the knee joint corresponding to a 152° extension, a 110° flexion, and a Range of Movement (ROM) of 42°. For the geriatric armchair, the values are extension 144°, flexion 105°, and ROM 39°.

Finally, it is established as a final criterion to consider the participant to complete at least 80% of the scheduled sessions (14 out of 18 sessions).

Participants (experimental and control group) are evaluated to examine the changes in body composition, functional performance, and resting cardiovascular state. Furthermore, participants are monitored physiologically during each session (heart rate and blood pressure) to control any possible adverse effects.

## Measures

Pre- and post-intervention assessments are made on all subjects of the sample (control and experimental group). Pre-intervention data were collected one week before the start of training, while post-intervention data were recorded at the end, after six weeks of intervention.

### Socio-demographic variables

Age (years) and gender.

### Body composition evaluation



Bioimpedance analysis (Inbody 270): body weight (kg), height (cm), muscle mass (MM), fat mass (FM), and FM percentage. Waist circumference (WC, cm) is taken at end-tidal using a measuring tape to the nearest 0.1 cm, midway between the lowest rib and the iliac crest, which corresponded with the level of the umbilicus. Body mass index (BMI) is established by the Quetelet index:  $BMI (kg/m^2) = mass (kg) / height (m)^2$ .

Figure 3. InBody 270



### Hemodynamic parameter evaluation

The baseline hemodynamic state is characterized by storing the mean of the three lowest values for thirty seconds of heart rate (HRrest, mm Hg) and oxygen saturation with a finger pulse oximeter; blood pressure by the auscultator method using a properly calibrated mercury column sphygmomanometer flexible cuff of the appropriate size and a stethoscope; three systolic (SBPrest) and diastolic blood pressure (DBPrest) measurements are recorded at 1-minute intervals. Mean blood pressure (MBPrest) is calculated as follows:

$$MBP = DBP + 1/3 (SBP - DBP).$$

### Functional evaluation

a) Frailty. Assessed by Fried et al. (2001), based on the presence or absence of 5 specific and phenotypic components (1) unintentional weight loss: at least 4.5 kg in the past year; (2) self-reported exhaustion, identified by 2 questions from the modified 10-item Center for Epidemiological Studies-Depression scale; (3) weakness: grip strength in the lowest 20% at baseline, adjusted for sex and body mass index; (4) slow walking speed: the slowest 20% at baseline, based on time to walk 4.6 m, adjusting for sex and standing height; and (5) low physical activity: the lowest 20% at baseline, based on a weighted score of kilocalories expended per week.

b) The Performance-Oriented Mobility Assessment (i.e., POMA; Tinetti, 1986), which measures balance (i.e., POMA-B) and gait performance (i.e., POMA-G) and the total score (i.e., POMA-T).

c) The Short Physical Performance Battery test (i.e., SPPB; Guralnik et al., 1994) to evaluate the time spent to complete three balance tasks (i.e., SPPB-B), walk 4 meters at a comfortable speed (i.e., SPPB-G), and sit-to-stand 5 times from a chair (i.e., SPPB- ChS).

d) Chair Sit-and-Reach Test (CSR; Jones et al., 1998) to measure lower body flexibility.

### **Ethics**

All subjects are informed in advance about the study to obtain written informed consent to participate in the study, either directly or through their legal representatives. The present study was carried out following the process approved by the Autonomic Research Ethics of Galicia Committee, Spain (code 2018/010), and in agreement with the Declaration of Helsinki.

### **Data management and statistical analysis**

The data of the participants are coded/pseudo-anonymized to ensure confidentiality and users' privacy for research use. Identifiable information is coded with artificial identifiers. The documentation to re-identify the participants will be only available to a medical doctor that collaborates with the research group, ensuring privacy during all data exploitation and dissemination (conferences, Ph.D. thesis, and scientific articles).

Data analysis will be made with the statistical programs SPSS, RStudio software package (Version 1.3.1093) and JAMOVI (The jamovi project, 2020, Version 1.2).

Data will be presented as the median and interquartile range for ordinal variables and the estimated marginal mean  $\pm$  standard deviation (SD) for continuous variables. The effect of the intervention will be analyzed employing nparLD (robust rank-based analysis of longitudinal data in factorial experiments) from the RStudio software package for nonparametric variables. Changes within and between groups will be analyzed by employing mixed models for repeated measures designs with the module GAMLj, which uses the R formulation of random effects as implemented by the lme4 R package in Jamovi software. The mixed models are a modern class of statistical models that extend regular regression models by including random effects parameters to account for dependencies among related data. We have chosen mixed models analysis as we expect a within-subject dependency in the variables measured before and after the intervention. Compared to traditional analyses that ignore these dependencies, mixed models provide more accurate (and generalizable) estimates of the effects, improved statistical power, and non-inflated Type I errors.

#### Duration of the project

	2019					2020	2021
	Jan-Aug	Sept	Oct	Nov	Dec	Jan-Dec	Jan-Dec
1. Project preparation and methodology							
2. Recruitment							
3. Baseline assessment							
4. Intervention (6 weeks per user)							
5. Post-intervention assessment							
6. Data analysis							
7. Dissemination							

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