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Multicomponent versus aerobic exercise intervention: Effects on hemodynamic, physical fitness and quality of life in adult and elderly cardiovascular disease patients: A randomized controlled study

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ABSTRACT

Objective: Cardiovascular diseases (CVDs) remain a leading cause of mortality globally, emphasizing the need for effective preventive measures. This study aimed to investigate the effects of a multicomponent compared to an aerobic training program on the hemodynamic parameters, physical fitness, psychophysical health status and quality of life (QoL) of adults and elderly with stabilized CVDs.

Methods: Thirty-three subjects (19M and 14F; age 69.5 \pm 4.9 years; BMI 27.34 \pm 4.95 kg/m2) suffering from CVDs voluntarily participated in this 10-week randomized controlled study and were allocated into three groups: multicomponent training group (MTG; 6M, 6F; cardiorespiratory, resistance, flexibility and breathing exercises; 60′, 2d⋅wk-1), aerobic training group (ATG; 7M, 5F; aerobic-only training; 60′, 2d⋅wk-1) or a wait-list control group (CG; 6M, 3F; no PA). Hemodynamic parameters were assessed through resting hearth rate (RHR) and peripheralsystolic and diastolic blood pressure (P-SBP/P-DBP). Physical fitness was assessed via a 30" chair stand test (30CST), timed up and go (TUG) test, handgrip strength (HGS) test, and 2' step test (TMST). The health status, QoL and enjoyment were evaluated with short form-12 (SF-12), world health organization quality of life-bref (WHOQoL-bref) and physical activity enjoyment scale (PACES), respectively.

Results: After the intervention, MTG showed significant improvements in hemodynamic parameters (95 % CI, RHR: 2.76 to 9.07; P-SBP: 3.28 to 13.71; P-DBP: 3.56 to 8.94; p *<* 0.001), physical fitness (95 % CI, 30CST: 4.42 to − 1.90; TUG: 0.56 to 1.58; TMST: 35.24 to − 18.58; Dominant HGS: 4.00 to − 1.65; Undominant HGS: 2.87 to − 0.79, p *<* 0.001) and enjoyment (PACES: 15.18 to − 5.48, p *<* 0.001) compared to CG; ATG showed significant improvement in hemodynamic parameters (95 % CI, RHR: 1.76 to 8.07; P-SBP: 3.19 to 13.63; P-DBP: 4.47 to 9.85, p *<* 0.001), physical fitness (95 % CI, 30CST: 2.59 to − 0.07; TUG: 0.03 to 1.05; Dominant HGS: 2.42 to − 0.07, p *<* 0.05; TMST: 36.08 to − 19.41, p *<* 0.001) and enjoyment (PACES: 14.68 to − 4.98, p *<* 0.001) compared to CG. No significant changes were observed in QoL and SF-12 (p *>* 0.05).

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Significant differences between MTG and ATG were only found in physical fitness variables (95 % CI, 30CST: 3.21 to − 0.45, p *<* 0.01; Dominant HGS: 0.00 to 3.00, p *<* 0.05).

Conclusions: Findings showed significant improvements in hemodynamic parameters and physical fitness suggesting the effectiveness of the multicomponent exercise program, similar to aerobiconly training, and greater efficacy for lower limb strength and dominant hand grip strength in adults and elderly with stabilized CVDs. Both exercise groups showed similar levels of enjoyment.

1. Introduction

Cardiovascular diseases (CVDs) continue to pose a significant global health challenge, contributing substantially to morbidity and mortality rates. The prevalence of CVDs is consistently increasing, exerting a profound impact on individuals' physical well-being and quality of life (QoL) [[1](#page-11-0),[2](#page-11-0)]. Effective management of CVDs requires multifaceted interventions addressing both the physiological and psychosocial dimensions of the disease [[3](#page-11-0)].

Risk factors such as obesity, high blood pressure, hypercholesterolemia, ageing, and physical inactivity can predispose individuals to CVDs [\[4](#page-11-0)–6]. Physical activity has emerged as a pivotal therapeutic strategy in the management and prevention of CVDs, contributing to enhanced cardiovascular function, physical fitness, and overall QoL [\[7\]](#page-11-0). Furthermore, physical activity has been demonstrated to improve cardiovascular fitness, mitigate the risk of cardiovascular events, and improve various health outcomes in individuals with CVDs, irrespective of weight loss [8–[11](#page-11-0)].

CVDs encompass a range of conditions that affect the heart and blood vessels, including the most common hypertension, valvular heart disease, aortic valve disease, atrial fibrillation, and previous myocardial infarction. These conditions represent significant health challenges, often requiring a combination of medical treatments and lifestyle adjustments to manage effectively.

Hypertension is a prevalent yet often silent condition that can lead to severe complications if left untreated. Effective management involves lifestyle modifications such as adopting a heart-healthy diet, engaging in regular physical activity, maintaining a healthy weight, reducing alcohol and caffeine intake, quitting smoking, and managing stress, along with pharmacological treatment. These changes not only help control blood pressure but also contribute to overall cardiovascular health. Valvular heart disease, which includes dysfunctions such as stenosis or regurgitation of heart valves, presents with symptoms like shortness of breath, fatigue, and palpitations. Lifestyle management plays a crucial role in mitigating symptoms and preventing disease progression. Regular exercise, a balanced diet, smoking cessation, and weight management are essential components of care, alongside medical treatments and potential surgical interventions [[12\]](#page-11-0). Aortic valve disease, involving conditions like aortic stenosis and regurgitation, can gradually lead to heart failure if unmanaged. While medications and surgical options are pivotal, lifestyle modifications are equally important. Patients are encouraged to maintain a physically active lifestyle, follow dietary recommendations, and avoid smoking, which collectively improve heart function and delay disease progression [\[13](#page-11-0)]. Also, atrial fibrillation, characterized by an irregular heartbeat, increases the risk of stroke and other complications. Managing atrial fibrillation effectively requires a combination of medications and lifestyle changes. Adopting a heart-healthy diet, engaging in regular physical activity, and avoiding excessive alcohol and caffeine intake are key strategies. Additionally, smoking cessation is critical in reducing the overall cardiovascular risk [[14\]](#page-11-0). Finally, for individuals with a history of myocardial infarction, lifestyle management is vital in preventing recurrent heart attacks and promoting recovery. Cardiac rehabilitation programs, which include supervised exercise, nutritional counselling, and stress management, are integral to comprehensive care. Emphasizing a heart-healthy diet, regular physical activity, smoking cessation, and weight management can significantly enhance quality of life and reduce the risk of further cardiovascular events [\[15](#page-11-0)–17].

Exercise training, particularly aerobic and resistance exercises, has garnered attention as a non-pharmacological approach to managing CVDs. Research consistently indicates that aerobic training enhances exercise tolerance, reduces resting heart rate (RHR), and improves vascular function in individuals with CVDs $[18–21]$ $[18–21]$. Moreover, aerobic exercise positively influences lipid profiles, glucose metabolism, and body composition, thereby contributing to the overall management of CVD risk factors [\[22](#page-12-0),[23\]](#page-12-0). Resistance training has been shown to improve muscle function, skeletal muscle mass, and insulin sensitivity, potentially leading to improved daily physical activities and reduced frailty, thereby supporting cardiovascular health [\[24](#page-12-0)–26]. Additionally, it may positively impact blood pressure regulation and endothelial function [[5](#page-11-0)[,27](#page-12-0)]. While aerobic exercise has long been championed for its cardiovascular benefits, recent research underscores the significance of strength training in mitigating CVDs risk factors and improving overall cardiovascular health [\[28](#page-12-0)]. Strength training, which can be included within so called resistance training, can improve muscular strength and endurance by exerting muscles against external resistance. This form of exercise has been associated with numerous cardiovascular benefits, including improved heart function, enhanced vascular health, and favorable modulation of traditional cardiovascular risk factors such as hypertension, dyslipidemia, and insulin resistance [[29,30\]](#page-12-0). The underlying mechanisms by which strength training exerts its cardiovascular benefits are multifaceted. Physiologically, it enhances muscle mass and strength, which in turn improves glucose metabolism and insulin sensitivity, both critical factors in the management of type 2 diabetes and metabolic syndrome, conditions frequently comorbid with CVDs. Furthermore, strength training promotes favorable changes in body composition, reducing visceral fat, a key player in the development of atherosclerosis. The hemodynamic adaptations to resistance training, including reductions in resting blood pressure and improvements in arterial stiffness, further contribute to cardiovascular health [[31\]](#page-12-0). Beyond its direct physiological effects, strength training also positively influences psychological well-being, reducing stress and anxiety levels, which are known contributors to cardiovascular risk [[32\]](#page-12-0). Similarly, balance training can improve autonomic regulation, muscle strength, and coordination, contributing to better heart rate variability, functional capacity, and reduced fall risk. These

improvements can enhance overall cardiovascular health and patient outcomes [\[33,34](#page-12-0)]. While exercise is generally beneficial, careful consideration of individualized exercise prescriptions is essential in individuals with CVDs. Close medical supervision, appropriate exercise intensity, and gradual progression are crucial to ensure safety and optimize outcomes. Pre-existing health conditions, medication regimens, and individual fitness levels should be considered when designing exercise programs.

The compromised blood flow and oxygen delivery associated with CVDs can affect the structural integrity and functional capacity of muscles, tendons, and ligaments supporting joint flexibility. Reduced oxygen supply may lead to tissue fibrosis, collagen crosslinking, and increased muscle stiffness, all contributing to limited joint flexibility and range of motion (ROM) [\[35](#page-12-0)]. Flexibility training can enhance joint and muscle range of motion, potentially improving functional capacity and quality of life for CVD patients. Flexibility training positively impacts the underlying mechanisms of CVDs, such as reducing arterial stiffness, improving endothelial function, and modulating autonomic balance. These physiological changes can enhance vascular health and lower cardiovascular risk [\[36](#page-12-0)]. Additionally, flexibility exercises are low impact, making them suitable for CVD patients who might struggle with more intense activities. Furthermore, chronic inflammation characteristic of CVDs can promote joint inflammation, further compromising flexibility [\[35](#page-12-0)]. Stretching exercises have been shown to reduce arterial stiffness and improve endothelial function [[35,](#page-12-0)37–[39\]](#page-12-0).

The multifaceted nature of CVDs warrants a holistic approach to exercise prescription. Multicomponent training (MCT) protocols target multiple aspects of physical fitness, addressing not only cardiovascular endurance but also muscular strength, flexibility, and balance [\[40](#page-12-0)]. These components collectively contribute to enhanced functional capacity, reduced risk of falls, and improved QoL [[40\]](#page-12-0). MCT program has been proposed as a possible physical exercise program design, recently [\[41](#page-12-0)]. Because it can incorporate various exercise modalities (such as aerobic, resistance, flexibility, and balance) into a single exercise session or routine, this type of exercise is appealing reducing the need for lengthy sessions while enhancing a variety of physical abilities and skills [[41\]](#page-12-0). This MCT feature is crucial since CVDs patients tend to shy away from time-consuming physical exercise regimens, which may contribute to this population's low treatment adherence [\[42](#page-12-0)]. Few research have been done to far on how MCT affect older adults with CVDs [\[43](#page-12-0)]. It is important to note, for example, that De Moraes et al.'s findings [\[43](#page-12-0)] indicate that the reduction in response to the physical stimulus is inversely correlated with blood pressure levels prior to the start of the MCT. This suggests that volunteers with uncontrolled high blood pressure may exhibit greater drops in blood pressure values than those with controlled blood pressure. MCT appears to offer the most comprehensive benefits for CVDs patients. Preliminary studies have shown that this protocol can significantly reduce peripheral and central blood pressure, increase cardiorespiratory fitness, improve muscle strength, and enhance lean body mass [\[44](#page-12-0)]. It also leads to improvements in aerobic capacity, functional capacity, and QoL [[45\]](#page-12-0). Moreover, MCT has demonstrated favorable effects on both physiological parameters, such as muscle strength, and biochemical markers, including lipid profiles and inflammation status [[46\]](#page-12-0). Regular participation in MCT programs has been associated with increased oxygen transportation system capacity and physical working capacity in chronic heart disease patients [\[47](#page-12-0)].

However, the holistic impact of integrating these exercise modes into a unified multicomponent training protocol in CVDs field remains poorly explored. The effects of integrating multiple exercise modalities into an MCT for CVDs remain poorly understood. It is yet unclear whether this protocol can be more effective and safer than an aerobic training-only protocol in improving physiological and psychological parameters in subjects with stabilized CVDs. It has been demonstrated that regular physical activity enhances overall health in middle-aged, inactive individuals. Finding the most efficient and least time-consuming exercise training is crucial because most individuals do not have much time or willingness for it [[48\]](#page-12-0). Furthermore, many studies on multicomponent exercise training lack well-controlled randomized trials or do not include an aerobic-only group [\[49](#page-12-0)] or a real non-treatment control group, which instead receives a lifestyle education sessions and diet information before beginning [[44\]](#page-12-0). As a result, it's unclear if the benefits of multicomponent exercise stem from the individual additive benefits of each aerobic and resistance exercise or from the extra exercise duration.

Therefore, this study aimed to investigate the effects of a MCT versus an aerobic-only training program on the hemodynamic parameters, physical fitness, psychophysical health status and QoL of adults and elderly with stabilized CVDs. Also, we aimed to assess the enjoyment of different training protocols. It was hypothesized that the MCT group would experience greater improvements in hemodynamic parameters, cardiovascular fitness, muscular strength, flexibility, psychophysical health status and overall QoL compared to the aerobic training and control group. The MCT, as an integrated and varied protocol should, in addition, increase enjoyment of the program contributing to the most favorable outcomes.

2. Materials & methods

2.1. Participants and study design

This study used a randomized controlled study design conducted over 10-week period in a non-clinical setting, to compare two experimental groups and a waitlist control group at the pre- and post-intervention on all measured dependent variables. Eligible patients are randomly assigned to one of the three groups: Multicomponent training group (MTG), Aerobic training group (ATG) or no exercise wait-list control group (CG).

A computer-generated random number sequence, using an online Random Allocation Software ([randomizer.org\)](http://randomizer.org), was used to allocate participants to either the MTG, ATG or CG. Block randomization with varying block sizes was employed to ensure balanced group sizes. The allocation sequence was generated by an independent statistician not involved in participant recruitment or intervention delivery.

Participant enrollment was conducted by trained research assistants who screened potential participants, obtained informed consent, and collected baseline data. These assistants were blinded to the allocation sequence.

After completing enrollment and baseline assessments, participants were assigned to interventions using sequentially numbered, opaque, sealed envelopes containing group assignments. A research coordinator not involved in direct participant care or data collection opened the envelopes and communicated assignments to the intervention team. This process-maintained allocation concealment and reduced the risk of selection bias.

The intervention team, responsible for delivering the exercise protocols, was necessarily aware of group assignments but was instructed not to disclose this information to other study personnel or participants when possible.

This study did not involve human individuals from a clinical or therapeutic point of view. The procedures followed were in accordance with the ethical standards of the Helsinki Declaration and approved by the Ethics Committee of Bari University (protocol code 0030611|28/03/23).

Participants were recruited through the volunteer organization "Amici di Cuore" based in Bari (Italy) and a preliminary medical examination was performed before the start of the study (November 2023). The participants were diagnosed by board-certified cardiologists with extensive experience in cardiovascular medicine. Each cardiologist holds an MD degree with specialization in

Fig. 1. Study flow diagram.

cardiology and has over 10 years of clinical practice, including diagnosing and managing various cardiovascular conditions. Their qualifications and experience ensure the accuracy and reliability of the diagnoses provided for the study. After consent from the corresponding cardiologist, participants were considered eligible based on the following inclusion criteria: age between 45 and 80 years, absence of serious medical conditions (unstable coronary heart disease, decompensated heart failure, severe pulmonary hypertension) or acute onset that would prevent safe participation in physical activity according to American College of Sports Medicine (ACSM), American Heart Association (AHA) and European Society of Cardiology (ESC) guidelines [50–[53](#page-12-0)]; presence of stabilized CVDs; sedentary lifestyle, subjects who have not followed the WHO guidelines for aerobic and resistance exercise in the last 3 months [\[54](#page-13-0)]. Additionally, participants were excluded based on the following criteria: smoking; anticipated absence of more than one week during the intervention period; lack of sports suitability confirmed by a cardiologist; presence of joint pain, dizziness, chest pain or angina during physical exercise; high peripheric blood pressure: PBP ≥160/100.

An a priori power analysis [[55\]](#page-13-0) with an assumed type I error of 0.05 and a type II error rate of 0.20 (80 % statistical power) has calculated that 10 participants per group would be sufficient to observe moderate "Time x Group" interaction effects. However, thirty-three participants (19 males and 14 females, 69.5 ± 4.9 years) among those that have been contacted (n = 39; 21 males, 18 females) met all the above-mentioned eligibility criteria. The participants were allocated into three groups: MTG ($n = 12$, 6 males and 6 females) who underwent progressive multicomponent training (60 min, 2d⋅wk-1), ATG (n = 12, 7 males and 5 females) who underwent progressive aerobic-only training (60 min, 2d⋅wk-1) or a wait-list CG (n = 9, 6 males and 3 females) who did not engage in any structured physical activity during the intervention period. Among the CVDs diagnosed are included: hypertension (ICD-11, BA00.0) $(n = 24)$, valvular heart disease (ICD-11, BA60) $(n = 2)$, aortic valve disease (ICD-11, BA62) $(n = 2)$, atrial fibrillation (ICD-11, BA81.0) $(n = 1)$ and previous myocardial infarction (ICD-11, BA41) $(n = 4)$. All participants were advised to maintain all their prescribed medications during the intervention, although we do not have assessed the medical treatment compliance rate. None of the participants followed a specific food plan. The study was carried out between the months of November 2023 and January 2024. All participants completed the study, no drop-out or adverse effects were observed. Adherence rate for the MTG was 92.92 %, for the ATG was 91.25 %. [Fig. 1](#page-3-0) shows the eligibility assessment of the participants.

2.2. Testing procedures

Data were collected and recorded at week 1 (Baseline) and after week 10 (Post-test), in the same place, in a climate-controlled (22–23 ◦C) room with relative air humidity of 40–60 % always in the morning to minimize circadian cycle effects. First, the anthropometric measurements were collected. Body height (in cm to the nearest 0.1 cm) was measured using a SECA® stadiometer, and body mass (in kg to the nearest 0.1 kg) was measured using a SECA® digital scale (0–200 kg, accuracy of 0.1 kg). The subjects were barefooted and wore light clothing during the measurements. Body mass index (BMI) was calculated as body weight (kg) divided by the square of body height (m2).

Second, resting heart rate (RHR) and peripheral blood pressure (systolic blood pressure: P-SBP; diastolic blood pressure: P-DBP) were measured, by medical staff, using the Sphygmocor XCEL (AtCor Medical, Itasca, IL, USA) automated oscillometric device. After a 5-min rest, a blood pressure cuff was applied to the participant's left arm, positioned over the brachial artery, while they were seated. The device took three consecutive measurements of brachial pressure, with a 2-min break between each reading. The average of the measurements taken was adopted.

Finally, the following measures were collected: (1) Physical Fitness: 30-s chair stand (30CST) test, Timed Up and Go (TUG) Test, Handgrip Strength (HGS) test and 2-Minute Step Test (TMST); (2) Psychological: Short Form Survey (SF-12), World Health Organization Quality of Life – Bref (WHOQoL-BREF) and Physical Activity Enjoyment Scale (PACES). In order to prevent the previous test from influencing the result of the next one, 5 min of rest was guaranteed between one motor test and the next. Psychological tests were administered under the supervision of a psychologist from the team two consecutively days before the motor tests, to avoid possible interferences. All participants were trained in a sporting club (Angiulli Gymnastics Club, Bari, Italy). One week before the pre-test, two familiarization sessions were held. Initial and final test measurements were made at the same time of day and under the same experimental and treatment conditions. All measurements were performed and supervised by the same Adapted Physical Activity (APA) specialists, professional who focuses on modifying and adapting physical activities, exercises, and sports to meet the needs of individuals with disabilities, chronic conditions, or other special needs.

2.2.1. 30-S chair stand (30CST) test

This test is one of the most important functional evaluation clinical tests because it measures lower body strength and relates it to the most demanding daily life activities (e.g., climbing stairs, getting out of a chair or bathtub or rising from a horizontal position) [[56\]](#page-13-0). It is also able to assess functional fitness levels and the fatigue effect caused by the number of sit-to-stand repetitions (ICC = 0.95). It consists of standing up and sitting down from a chair as many times as possible (n) within 30 s. A standard chair (with a seat height of 42 cm) without armrests was used. Initially, the participants were seated on the chair with their back in an upright position. They were instructed to look straight forward and to rise after the "1, 2, 3, go" command at their preferred speed with their arms folded across their chest [[57\]](#page-13-0).

2.2.2. Timed up and go (TUG) test

This test is the one most used to assess the mobility of subjects. It assesses several aspects related to mobility such as static/dynamic balance and gait speed, along with lower limb strength. TUG results are predictors of several outcomes (i.e., falls, frailty, QoL and difficulty in performing daily activities) [58–[61\]](#page-13-0). Furthermore, it appears to be the best test of physical function in the prediction of cardiovascular disease in older adults $[62]$ $[62]$ and the reliability of the test was found to be very high (ICC = 0.90) [[63\]](#page-13-0). Subjects wear their regular footwear and can use a walking aid if needed (no one used it). Begin by having the patient sit back in a standard chair (height of 42 cm) with armrests and identify a line 3 m on the floor. Subjects were instructed to stand up from the chair, at the signal, and walk towards the line, at a self-selected speed, turn, walk towards the chair, and sit down again. At the go signal, timing starts and ends (s) when the subject sits back down [\[64](#page-13-0)].

2.2.3. Handgrip strenght (HGS) test

The handgrip strength test is a practical and validated instrument for assessing the maximum voluntary strength of the extrinsic and intrinsic muscles of the hand. Its results are an indicator of clinical conditions such as sarcopenia and correlate with general muscle strength (ICC dominant $= 0.97$; ICC undominant $= 0.98$). It may be a predictor of the incidence of chronic diseases, independence in daily life and nutritional status [[65\]](#page-13-0). Grip strength was measured with a mechanic Smedley hand dynamometer (GIMA, Milan, Italy). The participants were positioned sitting in a straight-backed chair with feet on the floor, shoulder adducted with 0◦ flexion, elbow flexed to 90◦ and forearm in a neutral position; participants were instructed to hold the dynamometer and squeeze it as hard as possible for 5 s. The measurement was performed three times with an interval of 30 s between measurements and 60 s before evaluating the other hand. The mean of the two measurements, expressed in kilograms (Kg), was used for the analysis.

2.2.4. 2-Minute Step Test (TMST)

The TMST aims to assess subjective aerobic capacity, a fundamental component of physical fitness (ICC = 0.90) [[66\]](#page-13-0). Subjects standing near a wall measured the height of the iliac crest and the patella and placed a marker on the wall halfway between the two. At the starting signal, the subjects began stepping in place by raising their knees to the height of the mark on the wall, as many times as possible during the 2 min. The number of times the right knee reaches the mark represents the test score (n).

2.2.5. Short Form Survey (SF-12)

The SF-12 is a shortened version questionnaire of SF-36, consisting of 12 items assessing physical (PCS-12) and mental (MCS-12) health [\[67](#page-13-0),[68\]](#page-13-0). Designed as a general measure of health it can be used with the general population (Cronbach's $\alpha = 0.91$). It comprises eight domains such as physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. PCS and MCS were computed using the scores of 12 questions ranging from 0 to 100, where zero indicates the lowest level of health and 100 indicates the highest level of health.

2.2.6. World health organization quality of life - bref (WHOQoL-BREF)

The WHOQoL-BREF is a questionnaire, developed as a short version of the WHOQOL-100, available in multiple languages and in this study, the Italian version was used to assess the quality of life [\[69](#page-13-0)]. This self-administered questionnaire presents 26 items concerning the perception of individual health and well-being over the past two weeks. Scored in four domains: Domain 1: Physical health (Cronbach's $\alpha = 0.80$), Domain 2: Psychological well-being (Cronbach's $\alpha = 0.75$), Domain 3: Social relations (Cronbach's $\alpha = 0.75$) 0.65) and Domain 4: Environment health (Cronbach's $\alpha = 0.73$) with all facet items scored as part of their hypothesized domain [[70\]](#page-13-0). Zero points represent the worst possible state of health, while 100 points represent the best possible state of health with regard to the respective domain.

2.2.7. Physical ACtivity enjoyment scale (PACES)

The Physical Activity Enjoyment Scale (PACES) is a questionnaire utilized to evaluate an individual's subjective enjoyment of physical activity [[71,72\]](#page-13-0). Comprising 16 items rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), the PACES includes nine positively framed items (e.g., "it energizes me") and seven negatively framed items (e.g., "it's boring") (with a Cronbach's alpha ranging from 0.78 to 0.89) [[73\]](#page-13-0). This tool evaluates multiple aspects of enjoyment, such as positive affect, psychological engagement, and overall satisfaction with the activity [\[74,75](#page-13-0)]. Widely employed in research, the PACES aids in comprehending individuals' perceptions and attitudes toward physical activity, shedding light on motivational factors influencing exercise behavior. The PACES is typically administered to participants after each session.

2.3. Exercise intervention

Before starting the training session, blood pressure and resting heart rate were measured. For patient safety, the exercise session was only performed if P-SBP was between 110 and 180 mmHg and/or P-DBP between 50 and 100 mmHg and, also, resting heart rate between 50 and 100 bpm. Sessions were performed within two small groups. These groups were closely supervised by APA specialists. To monitor and adjust the training intensity (internal load) as the sessions progressed, the Borg Rating of Perceived Exertion (RPE) scale $(6-20)$ [\[76](#page-13-0)] was employed at the end of each set of aerobic and resistance exercises, to adjust the load in Borg = 13 to 15 points [\[51](#page-13-0)], considering that the higher the number chosen, the more intense the exercise session was. The participants were prior familiarized with the scale.

The 10-week study period followed the initial data collection, with the MTG and ATG performing an intervention program consisting of twice-per-week (Monday and Wednesday) exercise sessions lasting 60 min each, usually performed from 3:30 p.m. to 4:30 p. m. Every single exercise session included an initial phase of muscle activation through a 10-min warm-up (brisk walk) to increase heart rate, improve muscle blood flow, and prepare the main joints for the subsequent work phase, a 40-min main exercise period and a 10 min cooldown period (breathing and stretching exercises).

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2.3.1. Multicomponent training

During the main exercise period, cardiorespiratory training consisted of progressive aerobic exercises: controlled and rhythmic jumping jacks, step-ups on a sturdy platform (such as a low step or a stable surface), standing knee raises (alternating legs), brisk side steps or lateral leg raises. The exercises were performed at an intensity ensuring that the perceived exertion (RPE) stayed between 13 and 15 points on the Borg Scale (6–20). Finally, conclude with 3 min of light walking to facilitate recovery for the next phase of training. The main goal of this phase was to maintain a consistent exercise duration of \sim 15 min while gradually intensifying the exercise stimuli.

Flexibility training consisted of specific exercises (thoracic extensions, cat to cows, overhead reach with stick and hips active internal rotation) targeting the main joint, performed maximally (1–3 sets) but avoiding pain. Duration was gradually increased from 30 to 60 s per repetition, repeating one to three times, before the threshold of pain. Participants were provided with rest intervals of 30–60 s between sets and exercises.

Resistance training consisted of exercises targeting various muscle groups: quadriceps (seated leg extension with anklet weight/half squat with chair), biceps brachii (unilateral curl with dumbbell), shoulder (shoulder press with dumbbell), triceps brachii (French press with dumbbell), pectoralis major (dumbbell chest press/dumbbell flyes), latissimus dorsi (dumbbell rows). The resistance training program adhered to the principle of gradually progressive load. Initially, participants performed a set of 10–15 repetitions, which progressed to three sets of 10–15 repetitions. Adjustments to the load were made to ensure that the perceived exertion (RPE) stayed between 13 and 15 points on the Borg Scale (6–20). Throughout the protocol, participants were provided with rest intervals of 60–120 s between sets and exercises to promote recovery. To prevent premature muscle fatigue, the exercises were carried out using an alternating training method based on muscle groups (upper muscle exercises were performed on Monday, and lower muscle exercises were performed on Wednesday). To avoid breath holding and any compromise in circulatory the significance of correct breathing was underscored.

The Cool down period consisted of breathing and stretching exercises. Stretching was performed maximally on all major muscle groups (1–3 sets per muscle group) avoiding joint pain. Duration was gradual from 10 to 30 s per stretch, repeating one to three times for a total of 60 s per stretch.

2.3.2. Aerobic training

During the main exercise period, lasting 40 min, aerobic training consisted of 25 min of progressive aerobic exercises: controlled and rhythmic jumping jacks, step-ups on a sturdy platform (such as a low step or a stable surface), standing knee raises (alternating legs), brisk side steps or lateral leg raises. Followed by 15 min of walking. The exercises were performed at an intensity ensuring that the perceived exertion (RPE) stayed between 13 and 15 points on the Borg Scale (6–20). Progression over the weeks will be given by maintaining the intensity in this range. The main goal of this phase was to maintain a consistent exercise duration while gradually intensifying the exercise.

The Cool down period consisted of breathing and stretching exercises. Stretching was performed maximally on all major muscle groups (1–3 sets per muscle group) avoiding joint pain. Duration was gradual from 10 to 30 s per stretch, repeating one to three times for a total of 60 s per stretch.

2.3.3. Statistical analysis

All statistical analyses were conducted using the JASP software v. 0.17.2.1 [[77\]](#page-13-0). The Shapiro–Wilk test was used to test the normality of all variables. Levene's test was used to check the homogeneity of variances between groups. One-way ANOVA was used to compare at pre-test the anthropometric characteristics and all outcome measures between the three groups and to compare their pre-post differences. For a non-normal distribution of the dependent variables, the non-parametric Kruskal-Wallis's test was performed. In case of statistical significance, Tukey-Kramer (parametric) or Steel-Dwass (non-parametric) post hoc tests were performed.

A two-way ANOVA (group (Multicomponent/Aerobic/control) \times time (pre/post-intervention)) with repeated measures was conducted to examine the effects of the intervention on all dependent variables. When 'Time x Group' interactions reached the level of significance, group-specific post hoc tests (i.e., Tukey's test) were conducted to identify the significant comparisons.

Eta squared (η2) for the non-parametric Steel-Dwass post hoc test and partial eta squared (η2p) for the two-way ANOVA were used to estimate the magnitude of the difference within each group and interpreted using the following criteria: small (η2p *<* 0.06), medium (0.06 ≤ η2p *<* 0.14), and large (η2p ≥ 0.14) effect size (ES). The ES for Tukey-Kramer post hoc pairwise comparisons was determined by Cohen's d, calculated as post-training mean minus pre-training mean divided by pooled SD before and after training and interpreted as small (0.20 \le d \lt 0.50), moderate (0.50 \le d \lt 0.79) and large (d \ge 0.80) ES [\[78](#page-13-0)].

Note: data are expressed as mean (**±**SD). Abbreviations: BMI, Body Mass Index.

The statistical significance was set a priori at $p < 0.05$.

3. Results

All the MTG and ATG participants completed the intervention, and no adverse effects were detected over the ten weeks. [Table 1](#page-6-0) shows the descriptive data of the study participants.

No statistically significant difference was found between the groups at pre-test about age, anthropometric characteristics, and all outcome measures ($p > 0.05$).

3.1. Hemodynamic parameters

A two-way ANOVA with repeated measures found significant 'Time x Group' interaction effects in: RHR (F = 11.323, p *<* 0.001, η2p = 0.43, large ES), P-SBP (F = 8.072, p = 0.002, η2p = 0.35, large ES), P-DBP (F = 20.521, p *<* 0.001, η2p = 0.57, large ES).

In the MTG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for RHR (95 % CI, 2.76 to 9.07) (t = 5.977, p *<* 0.001, d = 1.02, large ES), P-SBP (95 % CI, 3.28 to 13.71) (t = 5.194, p *<* 0.001, d = 0.88, large ES), P-DBP (95 % CI, 3.56 to 8.94) (t = 7.410, $p < 0.001$, d = 1.12, large ES).

In the ATG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for RHR (95 % CI, 1.76 to 8.07) (t = 4.967, p *<* 0.001, d = 0.85, large ES), P-SBP (95 % CI, 3.19 to 13.63) (t = 5.143, p *<* 0.001, d = 0.87, large ES), P-DBP (95 % CI, 4.47 to 9.85) (t = 8.496, p < 0.001, d = 1.28, large ES). No significant changes were found in the CG (p > 0.05).

3.2. Physical fitness parameters

A two-way ANOVA with repeated measures found significant 'Time x Group' interaction effects in 30CST (F = 27.749, p *<* 0.001, η2p = 0.64, large ES), TUG (F = 16.158, p *<* 0.001, η2p = 0.51, large ES), TMST (F = 39.255, p *<* 0.001, η2p = 0.72, large ES), (D)HGS (F = 12.121, p *<* 0.001, η2p = 0.44, large ES), (U)HGS (F = 11.479, p *<* 0.001, η2p = 0.43, large ES);

In the MTG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for 30CST (95 % CI, − 4.42 to − 1.90) (t = − 8.005, p *<* 0.01, d = 1.59, large ES), TUG (95 % CI, 0.56 to 1.58) (t = 6.705, p *<* 0.001, d = 0.73, moderate ES), TMST (95 % CI, − 35.24 to − 18.58) (t = − 10.303, p *<* 0.001, d = 2.20, large ES), (D)HGS (95 % CI, − 4.00 to − 1.65) (t = − 7.695, p *<* 0.001, d = − 0.37, small ES), (U)HGS (95 % CI, − 2.87 to − 0.79) (t = − 5.602, p *<* 0.001, d = − 0.22, small ES).

In the ATG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for 30CST (95 % CI, − 2.59 to − 0.07) (t = − 3.371, p *<* 0.05, d = 0.67, moderate ES), TUG (95 % CI, 0.03 to 1.05) (t = 3.423, p *<* 0.05, d = 0.37, small ES), TMST (95 % CI, − 36.08 to − 19.41) (t = − 10.622, p *<* 0.001, d = 2.27, large ES), (D)HGS (95 % CI, − 2.42 to − 0.07) (t = − 3.395, p *<* 0.05, $d = -0.16$, small ES). No significant changes were found in the CG ($p > 0.05$).

3.3. Psychological parameters

A two-way ANOVA with repeated measures found significant 'Time x Group' interaction effects only in the PACES score ($F =$ 13.949, p *<* 0.001, η2p = 0.48, large ES). No significant interaction was observed in the QoL and both components of SF-12 (p *>* 0.05).

In the MTG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for PACES (95 % CI, -15.18 to -5.48) (t = -6.798 , p < 0.001, d = 1.61, large ES).

In the ATG, the post-hoc analyses revealed a significant improvement in the score from pre-to post-intervention for PACES (95 % CI, − 14.68 to − 4.98) (t = − 6.469, p *<* 0.001, d = 1.53, large ES). No significant changes were found in the CG (p *>* 0.05).

3.4. Multicomponent versus aerobic exercise intervention

A comparison between the pre- and post-intervention differences of the groups was performed to evaluate the most effective training method.

For variables with a normal distribution, a one-way ANOVA was performed to compare the pre-post differences between the three groups. For 30CST, a significant difference was found between the groups (F = 27.749, p *<* 0.001, η2 = 0.649, large ES) and the Tukey-Kramer post-hoc test revealed a significant difference between MTG and ATG (95 % CI, − 3.21 to − 0.45) (t = − 3.277, p *<* 0.01, d = 1.34, large ES).

For variables with a non-normal distribution, the non-parametric Kruskal-Wallis's test was performed to compare the pre-post differences between the three groups. For (D)HGS, a significant difference was found between the groups (H = 15.344, p *<* 0.001, η2 = 0.48, large ES) and the Steel-Dwass post-hoc test revealed a significant difference between MTG and ATG (95 % CI, 0.00 to 3.00) $(Z = 2.427, p < 0.05, \eta2 = 0.08, \text{ moderate ES}).$

No significant differences were found between MTG and ATG for all other dependent variables (p *>* 0.05).

Pre- and post-intervention outcomes for all the variables considered and the statistical analysis results are shown in [Table 2.](#page-8-0)

4. Discussion

This study primarily aimed to investigate the effects of a multicomponent versus an aerobic-only exercise program on the

Table 2 Changes after 10 weeks for all the dependent variables.

Notes. Data are expressed as mean (**±**SD). Psychological variables are shown in scores. Abbreviations: HR, Heart Rate; P-SBP, peripheral systolic blood pressure; 30CST, 30″ Chair Stand Test; TUG, Timed Up and Go Test, (D)HGS, Dominant Hand Grip strength, (U)HGS, Undominant Hand Grip Strength, TMST, 2 min Step Test; SF12 (PCS-12), Short Form-12 (Physical Component Score-12); SF12 (MCS-12), Short Form-12 (Mental Component Score-12); WHOQoL, World Health Organization quality of Life; PACES, Physical Activity Enjoyment Scale.

^a Statistically significant difference within groups from pre-to post-intervention (Tukey-Kramer test, $p < 0.05$).

b Statistically significant difference between the Multicomponent and Aerobic group (Tukey-Kramer/Steel-Dwass test, *p <* 0.05).

hemodynamic parameters, physical fitness, psychophysical health status and QoL of adults and elderly with stabilized CVDs. Our findings suggests that multicomponent training could be as effective as aerobic training alone and even more effective in improving lower limb strength and dominant handgrip strength. Specifically, MCT revealed significant improvements in peripheral blood pressure (P-SBP and P-DBP) supporting the previously reported results of other combined training protocols in hypertensive subjects [\[5,](#page-11-0)[79](#page-13-0)]. Whereas, Schroeder et al. [[44\]](#page-12-0) observed a reduction in P-DBP, but not in P-SBP, after 8 weeks of combined exercise training in previously sedentary adults with elevated blood pressure/hypertension and overweight/obese. The authors point to the short duration of the intervention as a possible cause of this contradiction. Many works observe a reduction in blood pressure after interventions lasting at least 12 weeks [\[31](#page-12-0)[,80](#page-13-0)]. Our results showed that a 10-week MCT protocol may be sufficient to improve blood pressure in adults and the elderly with stabilized CVDs. Similarly, aerobic-only training led to a significant reduction of P-SBP and P-DBP values. Those results are in line with the extensive literature on aerobic training and blood pressure reduction that estimates a reduction, for every 30 min/week of aerobic activity, of about 1.78 mmHg for SBP and about 1.23 mmHg for DBP [\[81](#page-13-0)]. The observed reduction in blood pressure values may have several underlying physiological mechanisms, for example improving endothelial function by increasing the bioavailability of nitric oxide, which promotes vasodilation and reduces vascular resistance, leading to lower blood pressure. Moreover, both protocols could have reduced sympathetic nervous system activity and increases parasympathetic activity, together with improved baroreceptor sensitivity enhancing the body's ability to regulate blood pressure, resulting in lower blood pressure [\[49](#page-12-0)]. Both in the MTG and ATG, we found a significant reduction, in RHR that appears to be inversely correlated with life expectancy and positively correlated with cardiovascular and all causes of mortality [\[82\]](#page-13-0). These results are in line with previous studies of healthy older adults [[21](#page-12-0)] or those with medical conditions [\[83](#page-13-0)]. It's known that regular aerobic and resistance exercise strengthens the heart muscle, allowing it to pump more efficiently with fewer beats per minute, also improves autonomic regulation by increasing parasympathetic (vagal) tone and reducing sympathetic activity, which lowers resting heart rate [\[21](#page-12-0)].

Furthermore, the results of our research work showed improvements in lower body strength among both MTG and ATG participants. Loss of muscle mass and strength was associated with increased arterial stiffness and subsequent higher blood pressure [\[84](#page-13-0),[85\]](#page-13-0). Specifically, the improvement noted in lower limb strength could be also important in decreasing the risk of falls and muscle injuries and better performance in daily activities, in adults and the elderly [\[86](#page-13-0)]; these results are in line with previous research, where after combined training was observed improvement in strength, especially of lower limb, in hypertensive patients [\[24](#page-12-0)] or subjects at risk of cardiovascular events [\[87\]](#page-13-0). Moreover, we observed a significant difference between the two training protocols in the 30CST, which highlights the greater effectiveness, for the same duration and frequency, of the MCT protocol. This suggests that, despite being administered at the same conditions, the MCT protocol yields superior improvements in lower body strength. These results are particularly relevant as enhanced performance in the 30CST reflects better functional capabilities, such as reduced risk of falls and muscle injuries, and improved performance in daily activities among adults and elderly.MCT, which includes resistance exercises, can stimulate muscle hypertrophy and neuromuscular adaptations, leading to increased lower limb strength. Paired with, similar to aerobic training-only, improved recruitment and synchronization of muscle fibers, which contribute to enhancing strength. We also observed increase in lower limb strength, although less than the MCT, in the aerobic training-only. In this regard, it should be considered that aerobic exercises require the continuous use of large muscle groups, particularly in the lower limbs; this repeated use leads to increased recruitment of muscle fibers [\[88](#page-13-0)]. It can also lead to hypertrophy, at some extent, of slow-twitch muscle fibers, especially in non-training subjects, contributing to improvements in muscular strength and endurance. Added to this is the ability to stimulate the production of new mitochondria in muscle cells (mitochondrial biogenesis) [\[89](#page-14-0)], promote angiogenesis, the formation of new capillaries in muscle tissue [\[90](#page-14-0)], and improve the synchronization of motor units during aerobic activity, which can lead to more effective and powerful muscle contractions. While not directly increasing maximal strength, these aspects allow muscles to do more work over time, which can lead to increased strength as a side effect [[91\]](#page-14-0).

Reduced functional mobility has been associated with the occurrence of future cardiovascular and all causes of mortality [[62\]](#page-13-0). The TUG is the validated test most used to assess physical mobility, gait speed and balance, used as a predictor of falls and evaluation of dynamic balance, specifically in older adults and the elderly [[92,93\]](#page-14-0). Furthermore, the TUG test has been associated with future cardiovascular mortality in women and subjects without obesity, diabetes, or cigarette smoking [\[62](#page-13-0)]. A recent meta-analysis showed that multicomponent training could be an optimal strategy to improve functional mobility, even more efficient than strength training only, in older adults [\[37](#page-12-0)]. Similarly, our results showed a significant decrease in time in the TUG test in the MTG. Also, aerobic training revealed a significant improvement in the TUG test, in line with previous work exploring the effects of aerobic activity on the elderly [\[94](#page-14-0)]. The mechanisms of action behind these improvements can be attributed to increased muscle mass and strength, particularly in the lower limbs. This improvement in strength helps people stand up from sitting more efficiently and walk with greater stability. Improved cardiovascular health, resulting in better oxygen delivery to muscles during exercise, also contributes to improved endurance during the walking component of the TUG test. Finally, improved joint range of motion makes it easier to perform the sitting-to-standing and turning movements, improving functional mobility and reducing risk of fall [\[95](#page-14-0)]. The improvement seen in the aerobic training-only group can be explained similarly to the improvements observed in the 30CST.

Similar to what has been observed in other studies [[9](#page-11-0)], our study found statistically significant pre to post changes in handgrip strength values in the MTG and ATG compared to CG. This is despite the shorter duration and frequency of our protocol (2d⋅wk-1 for 10 weeks), compared with previous studies [[9](#page-11-0)[,96](#page-14-0)] (3d⋅wk-1 for 12 weeks). However, it should be noted that a meta-analysis aiming to evaluate the actual transfer effect of different types of exercise on handgrip strength showed only small effects, in healthy older adults [\[97](#page-14-0)]. Moreover, we observed a significant difference between multicomponent and aerobic training, in the (D)HGS value showing greater effectiveness of the multicomponent training protocol than aerobic training alone. The resistance exercises included in the MCT likely increased grip strength by improving muscle and tendon strength in the hands and forearms, along with increased recruitment and synchronization of motor units [\[98](#page-14-0)].

As expected, in the ATG, we observed a significant improvement in aerobic capacity which is important for individuals with CVDs contributing to better disease management. Similarly, and with no significant differences between the two training modalities, the same improvements were also found in the MTG. This finding supports previous research [\[5,9,](#page-11-0)[99\]](#page-14-0), which highlights the effectiveness of combined training in improving cardiovascular function in this population. Specifically, considering that aerobic training is the most common exercise for aerobic capacity and cardiovascular improvements [[100,101\]](#page-14-0), a good portion of these previous work's training volume was composed of aerobic training, from 25 [[5](#page-11-0)] to 45 [[9](#page-11-0)] or 50 min [\[99](#page-14-0)]. In our protocol, the time of each component of the main exercise period was roughly equally distributed $(-15')$ and despite the shorter duration of the aerobic component, compared to previous studies, our work showed similar results.

Although several studies have reported that aerobic and combined training can improve psychophysiological well-being [[102,103\]](#page-14-0) and, despite improvements in parameters related to physical performance found in our study, the QoL and health status outcomes, contrary to what we expected, shown no significant changes in both MTG and ATG. However, should be noted that many studies observing improvement in QoL and perceived health status have been conducted over a longer time frame than the one we used, up to eight months in some cases $[102]$. Therefore, our shorter intervention time frame may not have been sufficient for participants to fully integrate their physical improvements into their daily lives and subsequently perceive enhancements in their overall QoL. This suggests a potential time lag between physiological adaptations and perceived well-being, highlighting the complex relationship between physical fitness and QoL. Another consideration is the baseline QoL and health status of our participants. Initial scores were relatively high, so there might have been limited room for improvement, resulting in a ceiling effect.

Enjoyment plays a dual role as both a predictor and an outcome of participation in physical activity. The anticipated enjoyment derived from physical activities can bolster exercise intentions, while the mere anticipation of positive emotions is indicative of both the initiation and perpetuation of physical activity [\[74\]](#page-13-0). The positive affective experiences during and after exercise can reinforce behavior, creating a feedback loop that promotes regular engagement in physical activity. This aligns with the hedonic theory of motivation, which posits that individuals are more likely to repeat activities they find pleasurable [\[104,105](#page-14-0)]. Our observation of high enjoyment levels, correlating with high adherence rates, suggests that designing exercise interventions that prioritize participant enjoyment could be a key strategy for improving long-term adherence to physical activity programs, particularly in populations with CVDs who may face additional barriers to exercise. The comparable enjoyment levels between multicomponent and aerobic training-only indicate that both types of training can provide satisfying experiences for participants. This is particularly noteworthy as it suggests that the additional components in the multicomponent training did not detract from the overall enjoyment of the exercise experience.

5. Strenghts and limitations

To the best of our knowledge, this is the first study aiming to assess and compare the effects of a multicomponent versus an aerobiconly training program on the hemodynamic parameters, physical fitness, psychophysical health status, QoL and enjoyment of adults and elderly with stabilized CVDs. This study offers new insights into the comparative effectiveness of MCT versus aerobic-only training in individuals with stabilized CVDs, addressing a gap in existing literature. The research could lay a foundation for future studies, encouraging further exploration into multifaceted exercise regimens and their impacts on these populations. The findings can inform subsequent research, promoting a deeper understanding of how different exercise modalities contribute to cardiovascular health. Furthermore, the study could provide clinicians with evidence-based guidance on incorporating MCT or aerobic training-only, according to specific need, into standard care protocols for patients with stabilized CVDs. Clinicians can use these insights to develop more personalized and effective treatment plans, optimizing patient outcomes and enhancing the overall management of CVDs. Finally, for patients, the study underscores the importance of engaging in comprehensive exercise programs that integrate various modalities. By understanding the multifaceted benefits, patients could be empowered to take an active role in their health management, fostering motivation and sustained engagement in physical activity.

However, this study has some limitations that should be considered. The lack of strict dietary and clinical control may, to some extent, account for a bias in the interpretation of the results obtained, although the randomization of the groups and having the aim of comparing two training methodologies and not simply observing the effects of exercise mitigated this bias. The relatively small sample size might limit the broader applicability of the results. Without long-term follow-up evaluation, it cannot be determined how sustainable the observed improvements are over time. It's also important to note that this study did not investigate the influence of nutrition, which is a significant factor in managing CVDs.

6. Conclusions

The findings showed that, likewise aerobic training, a 10-week multicomponent exercise protocol is effective in improving hemodynamic parameters and physical fitness in adults and elderly with stabilized CVDs, without adverse effects. Furthermore, the study highlighted the enjoyability of this training intervention, which can promote adherence. Notably, the multicomponent exercise protocol appeared more efficient than aerobic training alone in improving parameters related to lower limb strength and dominant hand grip strength.

However, although both exercise interventions led to significant physical and physiological improvements, QoL and perceived health status were not improved suggesting that these factors may take longer to reach the statistical significance. Further randomized controlled trials with a larger sample size are needed to strengthen these findings.

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Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Bari University (protocol code 0030611|28/03/23).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Luca Poli: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Gianpiero Greco:** Writing – review & editing, Writing – original draft, Validation, Methodology, Data curation, Conceptualization. **Stefania Cataldi:** Resources, Methodology. **Marco Matteo Ciccone:** Visualization, Validation, Formal analysis. **Annamaria De Giosa:** Visualization, Validation, Software, Investigation, Formal analysis. **Francesco Fischetti:** Writing – review & editing, Supervision, Resources.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Gianpiero Greco is Associate Editor of Heliyon. If there are other authors, they 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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