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Effects of a high-intensity progressive-cycle program on quality of life and motor symptomatology in a Parkinson's disease population: a pilot randomized controlled trial.

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Key words: Neurodegenerative, quality of life, Parkinson`s disease, balance, physical activity, endurance.

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Abstract

Introduction: The benefits of aerobic exercise in persons with Parkinson's disease (PD) have been widely studied. Recent studies support the use of high-intensity aerobic exercise to improve oxidative stress values and functional performance in PD patients.

Objective: To ascertain whether high-intensity aerobic training with lower extremity cycle ergometers and balance training can improve motor symptoms and quality of life in a PD population of Hoehn &Yahr (H&Y) disability score 1-3.

Setting: Rehabilitation centers in secondary care.

Design: A pilot randomized controlled trial.

Participants: A total of 14 outpatients participated in the 8-week study.

Interventions: They were comprised of a control group (n=7) that followed a balance protocol and an experimental group (n=7) that performed high-intensity (70% heart rate reserve) aerobic workout using an lower extremity cycle ergometer and a balance protocol once a week.

Main Outcome Measures: The primary outcome measures included the 8-Foot Up and Go test, 6-minute walk test, 2-minute step test, Parkinson Disease Questionnaire-39 (PDQ39), Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Tinetti test.

Results: Significant improvements in the PDQ39 ($F_{1.23}$= 3.102; sig=0.036), the MDS-UPDRS III ($F_{1.23}$= 4.723; sig=0.033) and total ($F_{1.23}$=4.117; sig=0.047) were observed in the experimental group as against the control group.

Conclusion: After taking into account the number of subjects in each group, the results suggest that the PD population can withstand high-intensity aerobic workouts with an lower extremity cycle ergometer. This exercise is a beneficial therapy for them because it reduces motor symptoms of the disease and furthermore increases and improves patient's quality of life.

Key words: Neurodegenerative, quality of life, Parkinson`s disease, balance, physical activity, endurance.

Introducition

Parkinson's Disease (PD) is a progressive, neurodegenerative disorder of unknown aetiology and has no known curative treatment to date. It is caused by the degeneration of neurons in the brain, particularly the dopaminergic neurons, where loss is greater than 80%.[1] The most characteristic symptom of PD is bradykinesia, in which patients have an impaired ability to perform complex voluntary body movements.[2] There is currently no fully tested drug therapy that can modify or slow progression of the disease. Patients lose postural stability as the disease progresses and moreover present motor disorders, difficulty in carrying out daily living activities and frequent falls. Although some motor disorders such as tremor, can be alleviated with drug therapy, symptom such as postural instability depend on the disease severity (unilateral-bilateral), medication state (on-off) and medication dose (mg/day) of the patient.[3] Postural instability is one of the symptoms that can be improved the most through alternative therapies.[4] Exercise is an integral part of PD management and studies have shown that physical activity can complement drug therapy to slow deterioration of motor functions and prolong functional independence, thereby leading to improved quality of life.[5-9] However, many questions remain with respect to the identification of the most effective exercise for treating PD symptoms.

Several authors have confirmed that aerobic exercises are good to slow down the progression of Parkinson's Disease.[10,11] The next step would be the determination of the "right dose" (intensity and volumen) of aerobic exercise for PD. Recent studies have presented findings related to high-intensity training and PD.[12,13] One of the reasons for focussing on this type of training is its neuroprotective effects observed in animal models and its stimulation of neurogenesis,[14,15] but evidence of such physical activity benefits in PD patients is limited.[12,16] Schenkman et al.[12] conducted a study with 128 PD patients aged 40-80 years. Non-medicated PD patients, with less than 5-year diagnosis, were subject to four days/week high-intensity workouts for six months. At the end of this intervention protocol, results showed that high-intensity exercise was safe, delayed worsening of disease symptoms, improved muscular strength, reduced stiffness, tremors and slowness, and furthermore improved gait and balance. Another of the benefits of high intensity work in patients with PD is to increase endogenous antioxidant protection and decrease the production of reactive oxygen and nitrogen species. Oxidative stress seems to be involved in the pathogenesis of Parkinson's disease.[17,18]

Impaired balance is one of the cardinal signs of Parkinson's disease (PD). People with Parkinson's disease experience balance impairment to a larger extent than the general population of older adults and the majority of those who fall, do so recurrently. [19] Aerobic exercise showed immediate beneficial effects in improving balance and reducing falls in PD Patients. [20, 21] Li et al, [22] Duncan & Earhart [23] and Earhart et al [24] indicated that aerobic exercise decreased alterations to balance, improved functional capacity and led to a reduction in the number of falls in mild to moderate Parkinson´s patients.

Patients with PD can participate in aerobic exercise in different ways.[20] Treadmill training, dancing, walkways, cycle ergometers and cross training machines are the most common [20,21] but so far, nobody has used lower extremity cycle ergometers for high intensity aerobic workouts. At present, the effects that high-intensity resistance training can have on specific PD characteristics such as motor symptoms are unknown.

The hypothesis of this research indicates that high intensity aerobic training undertaken with the lower extremity cycle ergometer, and also balance training, improve the motor symptoms and quality of life in PD patients. Therefore, the objective of this research was to determine whether high intensity aerobic training in conjunction with balance training improves the motor symptoms and quality of life of Parkinson's disease patients in the early or middle stages of the illness.

Methods

Study design

This is a single-blind randomized controlled trial.

Participants

The study was performed on outpatients from the Parkinson's Association of XXX on an initial sample of twenty-four persons that contained both sexes (22 males and 2 females). A sample of 14 patients fitted into 2 intervention groups was finally recruited (a control group: 6 males and 1 female; and an experimental group: 6 males and 1 female) after discarding patients' incompatibilities related to time-tables, travel, operations, diseases and motor symptoms unrelated to PD (eg.: hip prosthesis). These patients fulfilled the following inclusion criteria: diagnosed with PD, Hoehn & Yahr score of 1-3; no history or evidence of dementia or any other neurological impairment/cardiovascular diseases that may affect the high-intensity endurance workout.

The lead researcher performed trial randomization after conclusion of initial assessment. A total of 14 PD patients met the inclusión criteria: 12 males and 2 females. These were randomly allocated on a 1:1 ratio, either to the experimental group or the control group. Sample randomization was performed using the statistical program SPSS IBM (version 22), following the sequence: data>select cases>random sample of cases>exactly men and 7 cases from the first 14 cases. The variables taken under consideration were age, gender, Hoehn and yahr scale.

All participants gave their written informed consent prior to participation in the study. The study was approved by the Ethics Committee of the XXXXXX (XXXXXXXX) and complies with the Declaration of Helsinki on ethical principles for medical research involving human subjects. The design of the study was registered on the ClinicalTrials. gov database with code: NCT03882398.

Fig 1. Flow Diagram of Patient Participation in the Study.

Interventions

The experimental group (EG) participated in a once a week physical exercise program for 8 weeks. The session consisted of balance training followed by aerobic endurance training with a lower extremity cycle ergometer (Oxycycle III, active & passive. MSD Europe). At the beginning of the program, each session lasted 25 minutes and progressed to 35 minutes, in the last two weeks. The control group (CG) only performed routine balance exercises once a week (10 min). Both groups also practiced one hour of Tai Chi twice a week.

The balance exercises were performed for a total duration of 10 minutes prior to training with the lower extremity cycle ergometer. After finishing the balance exercises, the experimental group began training with the lower extremity cycle ergometer (see table 1). The aerobic workout was high intensity,[25] at 70% of heart rate reserve (HRR). The Karvonen formula[26] was used to calculate HRR. Heart rate was used to control intensity during the aerobic session and was monitored using *Polar Heart Rate Monitors (PolarElectro, Inc., PortWashington, NY).* Patients were seated in an armchair (seat height 45.5 cm) when exercising with the lower extremity cycle ergometer. Both resistance and duration progression are shown in table 1. Only patients with ≥80% attendance at sessions were considered for analysis.[6] The intervention program was supervised by health professionals (a physiotherapist and an exercise therapist). Evaluations were carried out by the research group XXXXXX (XXXXXXXX); an independent group of professionals that supervised the program. The Tai Chi program, which lasted 45 minutes, focussed on the 24 posture classical Yang style.[27] Staff from XXXXX supervised the program. The association has been implementing this activity for more than 5 years.

Table 1. Description of the programs followed by the Control Group (CG) and the Experimental Group (EG).

Outcome measures

Patients' information was collected 15 days prior to start of the program and 15 days after completion. The following batteries and questionnaires were used:

AD-HOC Record Sheet

The AD HOC sheet records information on variables like age, weight, height, academic level, stage of disease, year of diagnosis, surgical intervention, personal history related to illnesses or surgeries, number of years patient has been in the Association and activities performed therein.

MDS-UPDRS (Unified Parkinson's Disease Rating Scale)

The MDS-UPDRS scale[28] is used to measure the severity of PD, where lower values indicate better patient condition. The scale is highly reliable[29] and the Cronbach alpha scores in its different parts are =0.79-0.93.

PDQ-39 (Parkinson's Disease Quality of Life Questionnaire)

This is a specific questionnaire that assesses the quality of life,[30] **where a lower score means patient has a better quality of life.** The Spanish version of the questionnaire[25] presents satisfactory reliability, with a Cronbach alpha score of between 0.63 (social support dimension) and 0.94 (mobility dimensión).

Senior Fitness Test (SFT)

This is a battery of 7 tests created by Rikli & Jones that assesses the different variables in elderly persons, and has been validated for PD by Cancela et al.[31]

2-Minute Step test: Subject stands next to the wall and counts number of full steps completed in 2 minutes, raising each knee to a point midway between the patella (kneecap) and iliac crest (top hip bone). Counts are made once per cycle (from right to left).

6-Minute Walk: Subject walks as many laps as possible around a set course in 6 minutes. The course has a dimension of 20 yards (18.8 meters) x 5 yards (4.57 meters). There is a cone at each end of the circuit and a line at every 5 yards (4.57 meters).

8-Foot Up-and-Go: Number of seconds required to get up from a seated position, walk 8 feet (2.44 m) to the cone, turn, and return to seated position. The cone is located 2.44 meters from the chair. Subject takes the test 2 times and the average of the two is then calculated.

Tinetti test

The objective of the Tinetti test is to assess and evaluate aspects and possible alterations of gait and balance in a population of elderly persons.[32] The test has two parts: nine balance items and six gait items. In 2012, this test scale was validated for the Spanish language with high reliability,[32] at a Cronbach alpha score of 0.95.

Statistical analysis

The non-parametric variables were described using percentages (%), while the parametric ones were described using the mean and standard deviation. Data normality and variance homogeneity were analyzed using the Shapiro-Wilk and the Levene tests, respectively. The paired Student's t-test was used for intragroup comparison, and the Wilcoxon test, whenever appropriate. The variance analysis (MANCOVA two-way; moment*program) was used for intergroup comparison, where the covariate was the stage of the disease. Effectiveness of each program was calculated via effect size[33] (ES: Cohen's d) and % improvement. ES values were classified as trivial (0.20≤ES<0.50), moderate (0.50≤ES<0.80), and large (ES≥0.80). The degree of correlation between dynamic balance and aerobic endurance was tested through the Pearson's correlation coefficient. The statistical package SPSS® version 26.0 for MAC (IBM Corporation, Armonk, NY, USA) was used for all analyses, and the accepted significance level for this study was p≤0.05.

Results

The effect of the progressive-cycle program followed by patients over 8 weeks is described below. The study sample's adherence to the program points to the viability of using this workout intensity, for programs aimed at aerobic resistance in a Parkinsonian population. Participants showed 100% tolerance during program implementation at the scheduled heart rate. Fourteen patients were randomly assigned to the two groups (CG and EG). After applying the adherence criteria, the CG was composed of 5 patients. There were more males than females and their average age was 68.33 years. They presented Class 1 obesity (BMI: 30.0 to 34.9) and 58.34% have schooling. The demographic characteristics of the sample are shown in table 2. No significant differences were observed between groups.

Table 2. Baseline characteristics of subjects (Mean±SD; %).

Table 3 shows the inter- and intra-group analysis of the variables quality of life and motor symptoms. The program carried out by the experimental group produced better results than the one carried out by the control group for PDQ39 ($F_{1.23}$= 3.102; p=0.036), MDS-UPDRS III Motor ($F_{1.23}$ = 4.723; p = 0.033), MDS-UPDRS Total ($F_{1.23}$ = 4.117; p= 0.047) and 2-Minute Step ($F_{1.23}$ = 3.369; p = 0.041). Results for effect size show a moderate ES for the PDQ39 (EG, d=0.719) and MDS-UPDRS III Motor (EG, d=0.708), but a high ES for MDS-UPDRS Total (EG, d=0.867) and the 2-Minute Step (EG, d=0.804). No differences between groups were observed in the balance test or in the 6-Minute Walk test.

Table 3. Differential effects of the quality of life, motor symptoms and progressive cycle programs.

Figure 2 shows the relationship between the 8-Foot Up-and-Go (dynamic balance), the 6-Minute Walk and the 2-Minute Step (aerobic endurance) tests for the EG. Even though the intervention led to improvements in the aerobic endurance tests, their relationship with the dynamic balance test presents varying degrees of association (2-Minute Step, R^2= 0.158; 6-Minute Walk, R^2= 0.803), such association being higher in post-intervention (2-Minute Step, R^2= 0.263; 6-Minute Walk, R^2= 0.941).

Discussion

The objective of this randomised controlled study was to ascertain the effects of a high-intensity aerobic workout with a lower extremity cycle ergometer, on motor symptoms and quality of life, of PD patients. Our results showed that after 8 weeks of intervention, symptoms significantly improved in the EG, in terms of quality of life, motor symptoms and general symptomatology of PD patients.

The quality of life of PD patients improved by 44.62% in the EG and 26.98 in the CG. We believe that these improvements were due to high-intensity physical exercise, as this reduces the symptoms of the disease (rigidity, akinesia, bradykinesia, tremor, ...), allowing the patient to carry out their normal daily activities independently and without the bodily discomfort of the disease. These results are in line with other studies that use high-intensity workouts such as high-intensity eccentric resistance training [34] or high-intensity multicomponent agility programs. [35]

Motor symptoms (MDS-UPDRS III) improvement of 40.80% and 24.72% was observed in the EG and CG, respectively, and of 42.44% and 33.39% in the MDS-UPDRS Total score. These results show that the prescription of high-intensity, controlled frequency exercises, in conjunction with balance exercises, improves the motor and non-motor symptoms impacting on the health status of PD patients. This means greater independence in their day to day lives and a better quality of life.[37,36,38] The improvements achieved in this study are higher than those obtained in previous studies.[37-39] Perhaps these improvements are due to the fact that the lower extremity cycle ergometer allowed us an adequate individualization of the high intensity program for each patient, even if the ACSM recommendations were not complied with. In future research, it would be useful to study whether the improvements obtained in this study are maintained by continuing with the individualization of high intensity training and applying the ACSM recommendations for aerobic work.

In terms of aerobic parameters, significant differences were observed between the groups, where the EG fared better in the 2-Minute Step test. The possible explanation could be that the 2-Minute Step test requires a cyclical movement and sizeable balance, because the person spends most of the time in single leg stance, while the 6-Minute Walk involves decision-making, changing direction and a greater demand in terms of motor control. PD patients may find it easier to perform cyclical movements and hence may be able to directly improve conditional aspects rather than cognitive ones. Arcolin, et al[38] reported gait improvements in PD patients after doing high-intensity aerobic workout on a cycle ergometer. Training with lower extremity cycle ergometers involves cyclical movements and hence can be a good method for PD patients to perform high-intensity, safe, aerobic workouts. The lower extremity cycle ergometer permits gradual changes in exercise intensity, in line with the patient's exercise capacity. Therefore, the level of exercise can be easily quantified and the risk of falls minimised. PD is a progressive disease that requires patients to constantly exercise, in order to maintain achievements obtained through intensive training.[40] The lower extremity cycle ergometer can be used safely, and moreover, its cost, weight, and minimum space requirement means that it can be used at home by such patients.

The Senior Fitness Test is a battery of tests widely used for the elderly population and patients with Parkinson's disease.[31] It includes the two tests that evaluate aerobic endurance, namely; the 2-Minute Step and the 6-Minute Walk. These tests when applied to a PD population show a correlation with dynamic balance, however, their behaviour differs, i.e., there is a strong correlation in the 6-Minute Walk but low correlation in the 2-Minute Step. An in-depth study is needed to ascertain whether the 2-Minute Step improves aerobic endurance in PD patients.

No significant balance improvements were observed between the CG and the EG. Even though both groups improved, the percentages were higher in the EG. The absence of significant balance differences could possibly be due to inadequate intervention duration for adjusting the neuromotor patterns. It may also be due to both groups practising Tai chi, since there are several studies that relate the practice of Tai chi with improved balance.[41,42] Arcolin et al[38] observed improvements in balance after performing an intervention with a cycle ergometer, and suggest that balance improvement is achieved due to the need for active stabilisation of the trunk. This aspect needs to be checked using a lower extremity cycle ergometer.

Study limitations

There are several limitations to this study. The most noteworthy one being the small sample size which is because the study wanted to include elderly persons with a mild-to-moderate PD stage but without cardiovascular disorders. Moreover, intervention was only possible once a week per patient; hence little adaptation could be acquired at the physical level. The duration of intervention should be prolonged to verify any cognitive adaptations attributed to PD patients by high-intensity aerobic workouts. Since both groups practiced Tai chi, its effect on high-intensity aerobic training could likewise not be established. There was no follow-up period foreseen in the study and hence residual effects of the program could not be analysed.

Conclusions

After considering the sample size used, we would suggest that high-intensity exercise combined with balance workouts do help in improving quality of life in PD patients. However, there are not many studies published and more research into this is needed to correct some limitations of this work.

Clinical messages

- The use of cycle ergometers with PD patients is feasible and appropriate.
- High-intensity aerobic training with cycle ergometers improves the symptoms and quality of life in PD patients.
- Aerobic training carried out at 70% of heart rate reserve (HRR) and during rate 8-week improves the functional capacity of PD patients.

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Table 1 . Description of the programs followed by the Control Group (CG) and the Experimental Group (EG).

Control Group	Experimental Group
Tai Chi (Twice a week)	
Warm-up (5-10 minutes)	
Classical Yang style (45 minutes) 24 forms Weight shifting Awareness of body alignment Multisegmental movement coordination	
Cool-down (10-5 minutes)	
Balance program (One a week)	
Balance program (10 minutes)	*Balance program (10 minutes)*
Balance on bosu ball and ball drills Coordination in rings with single leg stance and ball drills Straight line walk with head up Straight line walk and hip flexion, knee flexion and head up	Balance on bosu ball and ball drills Coordination in rings with single leg stance and ball drills Straight line walk with head up Straight line walk and hip flexion, knee flexion and head up
(Duration: 10 minutes. Sets: 2 minutes per exercise. Rest: 30 seconds between exercises)	(Duration: 10 minutes. Sets: 2 minutes per exercise. Rest: 30 seconds between exercises)

Progressive-cycle program (15-25 minutes)

Warming up

Pedalling with 0 resistance (2 minutes)

Main Part*

Week 1-2 : 3x2 minutes

Week 3-4 : 4x2 minutes

Week 5-6 : 5x2 minutes

Week 7-8 : 6x2 minutes

Return to resting stage

Pedalling with 0 resistance (1 minute)

(*Pedalling with resistance set at 3-4. Rest: 2 minutes between sets or 120 beats/minute. One more set added every two weeks and workout intensity maintained at 70% of heart rate reserve-HRR)

Rejuvenation Research

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Table 2. Baseline characteristics of subjects.

		Total Group (n=12)		Experimental Group (n=7)		Control Group (n=5)	
		Mean	SD	Mean	SD	Mean	SD
Age (y)		68.33	4.40	67.71	4.61	69.20	4.44
BMI (m/ Kg^2)		29.21	4.36	28.27	4.45	30.53	4.34
H&Y disability score		2.25	0.62	2.29	0.76	2.20	0.45
UPDRS.Total (score)		40.75	24.61	38.71	24.51	43.60	27.33
PDQ39.Total (score)		15.14	10.57	14.79	12.13	15.64	9.29
Sex (Female)		25.00%		14.28%		40.00%	
Academic Level	No schooling	41.66%		42.85%		40.00%	
	Primary Education	16.67%		-		40.00%	
	High School	25.00%		28.57%		20.00%	
	Vocational Training	16.67%		28.57%		-	

The results are presented as the means and (SD).

Table 3 . Differential effects of the quality of life, motor symptoms and progressive cycle programs.

Measures	Group	Pre-intervention		Post-intervention		95% CI (mean difference)	Improvement (%)	Effect Size	Manova Moment x Program
		Mean	SD	Mean	SD				
Quality of Life									
PDQ39.Total (score)	EG	14.79	12.13	8.19	4.85*	-1,23 to 4.09	44.62%	d=0.719 r=0.338	$F_{1,23}$= 3.102; sig=0.036
	CG	15.64	9.29	11.42	7.95	-1,25 to 0.45	26.98%	d=0.477 r=0.227	
Motor symptoms									
UPDRS-III Motor	EG	19.29	13.79	11.43	7.02*	-1,95 to 17.66	40.80%	d=0.708 r=0.330	$F_{1,23}$= 4.723; sig=0.033
	CG	17.80	12.45	13.40	9.81	-3,48 to 12.28	24.72%	d=0.389 r=0.187	
UPDRS Total	EG	38.71	24.50	22.28	10.59*	-2,43 to 35.29	42.44%	d= 0.867	$F_{1,23}$=4.117;

								r=0.388	sig=0.047
	CG	43.60	27.32	28.80	20.01	-1,86 to 31.46	33.94%	d=0.607 r=0.288	
Tinetti Balance	EG	15.57	1.13	16.18	0.87	-2,56 to 11.21	3.91%	d=-0.604 r=0.277	$F_{1,23}$=0.238; sig=0.631
	CG	15.60	0.89	15.67	1.09	-2,31 to 10.09	0.44%	d=-0.070 r=0.029	
6-Minute Walk (m)	EG	457.87	122.32	480.15	144.02	-55,94 to 11.38	4.86%	d=-0.157 r=0.077	$F_{1,23}$=0.126; sig=0.726
	CG	439.35	53.29	450.77	66.10	-168,20 to 65.37	2.60%	d=-0.193 r=0.092	
2-Minute Step (n)	EG	65.85	19.36	84.57	26.55*	-42,01 to 4.58	28.42%	d=-0.804 r=0.374	$F_{1,23}$=3.369; sig=0.041
	CG	72.80	13.25	74.40	13.92	-3,48 to 0.28	2.19%	d=-0.113 r=0.047	

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8-Foot Up-and-Go (s)	EG	8.59	1.50	9.35	1.94	-2,05 to 0.52	8.84%	d=-0.427 r=0.209	$F_{1,23}$=0.025; sig=0.974
	CG	8.47	4.05	9.15	4.70	-2,35 to 0.98	8.02%	d=-0.153 r=0.073	

Obs. d: Cohen's coeficient; Manova: stage of the disease was used as a covariate for analysis; r: Pearson´s correlation coefficient; *: sig< 0.05, pre-post intervention.

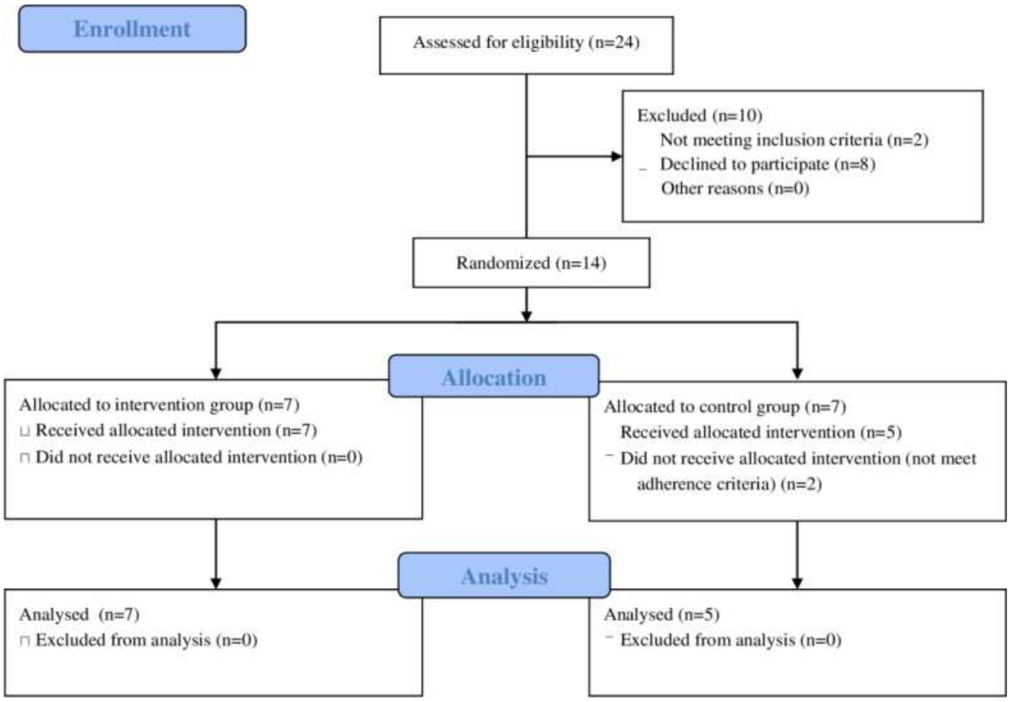

Figure 1. Flow Diagram of Patient Participation in the Study.

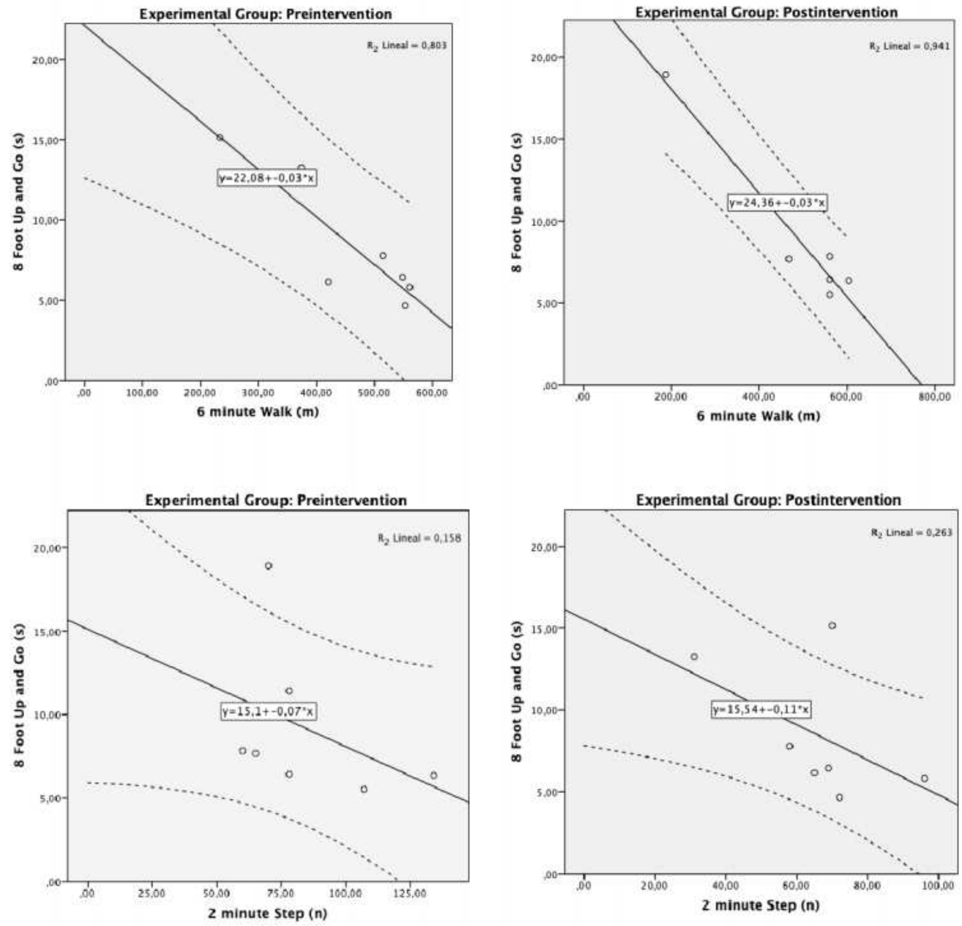

Figure 2. The correlation analysis between the dynamic balance and aerobic endurance tests.