



**UNIVERSIDADE FEDERAL DA BAHIA
FACULDADE DE MEDICINA DA BAHIA
PROGRAMA DE PÓS-GRADUAÇÃO EM
CIÊNCIAS DA SAÚDE**



COMPARAÇÃO DOS EFEITOS DO *EXERGAMING*, TREINO FUNCIONAL E BICICLETA ESTACIONÁRIA SOBRE OS ASPECTOS MULTIDIMENSIONAIS DA DOENÇA DE PARKINSON: UM ENSAIO CLÍNICO RANDOMIZADO

Karen Valadares Trippo

Professor-orientador: Jamary Oliveira Filho

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METADADOS

I. RESUMO

COMPARAÇÃO DOS EFEITOS DO *EXERGAMING*, TREINO FUNCIONAL E BICICLETA ESTACIONÁRIA SOBRE OS ASPECTOS MULTIDIMENSIONAIS DA DOENÇA DE PARKINSON: UM ENSAIO CLÍNICO RANDOMIZADO. Introdução: A Fisioterapia é clinicamente recomendada no tratamento das desordens motoras e não motoras que contribuem para o aumento do risco de quedas e piora da qualidade de vida em pacientes com doença de Parkinson, entretanto não há um consenso sobre a intervenção mais adequada. Por se tratar de uma desordem neurodegenerativa multifacetada, o tratamento deve contemplar seu aspecto multidimensional. Objetivos: Analisar os efeitos do *Exergaming*, do Treino Funcional e da Bicicleta Estacionária sobre o aspecto multidimensional (motor: quedas, *balance* e mobilidade funcional; cognitivo: função executiva; e emocional: qualidade de vida) da doença de Parkinson. O primeiro objetivo específico foi determinar os preditores de queda e qualidade de vida de idosos com doença de Parkinson num período de seguimento de seis meses. O segundo foi comparar os efeitos das três modalidades de exercício físico sobre o número de quedas e proporção de caídores únicos e recorrentes de idosos com doença de Parkinson, considerando um período de seis meses pré-tratamento e o seguimento de seis meses após o tratamento. E o terceiro foi comparar os efeitos das três modalidades de exercício físico sobre o *balance*, mobilidade funcional, função executiva e domínios de qualidade de vida de idosos com doença de Parkinson. Desenho do estudo: Ensaio Clínico Randomizado, cego, longitudinal e prospectivo (PROBE). Material e Métodos: Participaram do estudo 79 idosos (≥ 60 anos) com Doença de Parkinson Idiopática (Hoehn&Yahr modificado 2, 2.5 ou 3) randomizados em três grupos: G1-Treino Funcional (n=27), G2-Bicicleta Estacionária (n=27) e G3-*Exergaming* com XBOX₃₆₀ e sensor *Kinect*TM (n=25). O desfecho queda foi avaliado por um diário de quedas e contato telefônico de um avaliador cego durante um *follow-up* de seis meses. Os preditores de queda e qualidade de vida (Euroqol-5D) foram determinados utilizando as regressões de Cox e Linear, respectivamente. Apenas as variáveis com uma associação significativa ($p < 0,05$) nas análises univariadas de ambas as regressões foram incluídas nos respectivos modelos multivariados ajustados para o grupo tratamento. Para a comparação dos efeitos das modalidades de exercícios pré e pós-intervenção, avaliamos os desfechos secundários: *balance* (*Balance Evaluation Systems Test* - BESTest), função executiva (Bateria de Avaliação Frontal - BAF), mobilidade funcional (*Timed Up and Go Test* - TUG) e domínios da qualidade de vida (*Parkinson Disease Questionnaire-39*-PDQ39). As variáveis quantitativas foram expressas como mediana e intervalo interquartil e as categóricas foram expressas como proporção. Foram utilizados os testes de

Sinais Wilcoxon para comparações intragrupo e o Kruskal-Wallis para comparar os resultados intergrupos das variáveis contínuas. Para as variáveis categóricas utilizamos o teste de Sinais de Wilcoxon e o exato de Fisher para comparações intragrupo e intergrupos, respectivamente. O nível de significância foi de 5%. Resultados: No artigo 1, o desfecho queda ocorreu em 19 (24%) pacientes, com uma taxa de queda no G1 de 5,12 quedas/100 pacientes-mês, G2=5,48 e G3=4,26 (Mantel-Cox log-rank test $p=0.910$). Preditores de queda: duração da doença (HR=1,16 por ano, 95% CI=1,03-1,29) e força muscular em membros inferiores (melhora no Teste de Sentar e Levantar, HR=1,14 por segundo, 95% CI=1,01-1,28), independentemente das mensurações iniciais do *balance*. Preditores de qualidade de vida: gravidade da doença (efeito=-0,01 ponto na Euroqol-5D por ponto acrescido na *Unified Parkinson's Disease Rating Scale*; 95% CI -0,01 a -0,002) e performance de marcha (efeito=-0,03 ponto na Euroqol-5D por segundo acrescido no TUGcognitivo; 95% CI -0,05 a -0,01). No artigo 2, G2 e G3 reduziram significativamente a proporção de caídores para 26% (22% caídores únicos e 4% recorrentes; $p=0,008$) e 20% (12% caídores únicos e 8% recorrentes; $p=0,021$), respectivamente, no seguimento de 6 meses. O G2 também reduziu significativamente o número de quedas em 60% ($p=0,005$) durante o *follow-up*. Melhora no *balance* e na função executiva foram demonstradas no G1 e G3. O G3 melhorou significativamente os domínios estigma e atividade de vida diária. Conclusões: Os três exercícios não diferiram na proporção de caídores, no número e taxa de quedas, e na qualidade de vida num período de seguimento de seis meses. Entretanto, nas análises intragrupos, os grupos Bicicleta Estacionária e *Exergaming* reduziram a proporção de caídores no período do *follow-up*, sendo que o grupo Bicicleta também reduziu o número de quedas. Quedas foram associadas à maior duração da doença e à melhora da força de membros inferiores com manutenção dos valores basais do *balance*. Melhor qualidade de vida foi associada à menor gravidade da doença e melhor *performance* da marcha. Não houve diferença entre os grupos com relação aos desfechos secundários. Entretanto, o grupo *Exergaming* mostrou efeitos mais amplos, com resultados positivos na melhora do *balance*, da função executiva, da mobilidade funcional e dos domínios estigma e atividade de vida diária da qualidade de vida. *Exergaming* possui características de uma terapia multissensorial e multidimensional para prevenir quedas em idosos com doença de Parkinson.

Palavras chave: 1. Doença de Parkinson; 2. Idoso; 3. Terapia por Exposição à Realidade Virtual; 4. Equilíbrio Postural; 5. Quedas.

II. ABSTRACT

COMPARISON OF THE EFFECTS OF EXERGAMING, FUNCTIONAL TRAINING AND STATIONARY BICYCLE ON THE MULTIDIMENSIONAL ASPECT OF PARKINSON'S DISEASE: A RANDOMIZED CLINICAL TRIAL. Introduction: Physical therapy is clinically recommended in the treatment of motor and non-motor disorders in patients with Parkinson's disease that contribute to the increased risk of falls and worse quality of life; however there is no consensus on the most appropriate intervention. Because it is a multifaceted neurodegenerative disorder, treatment should address its multidimensional aspect. Objectives: To analyze the effects of Exergaming, Functional Training and Stationary Bicycle on the multidimensional aspect (motor: falls, balance and functional mobility; cognitive: executive function; and emotional: quality of life) of Parkinson's disease. The first specific objective was to determine the predictors of fall and quality of life of elderly with Parkinson's disease over a six-month follow-up period. The second was to compare the effects of the three physical exercise modalities on the number of falls and proportion of recurrent fallers of elderly with Parkinson's disease, considering a six-month pre-treatment period and six-month follow-up. And the third was to compare the effects of the three physical exercise modalities on balance, functional mobility, executive function and quality of life domains of elderly with PD. Study design: Randomized, blinded, longitudinal and prospective clinical trial (PROBE). Material and Methods: Seventy-nine elderly (≥ 60 years) with Idiopathic Parkinson's disease (modified Hoehn & Yahr 2, 2.5 or 3) were randomized into three groups: G1- Functional Training (n = 27), G2- Stationary Bicycle (n = 27) and G3-Exergaming with XBOX₃₆₀ and Kinect sensor (n = 25). The fall outcome was assessed by a fall diary and a blind assessor's telephone contact during a six-month follow-up. Predictors of fall and quality of life (Euroqol-5D) were determined using Cox and Linear regressions, respectively. Only variables with a significant association ($p < 0.05$) in the univariate analyzes of both regressions were included in the respective multivariate models adjusted for the treatment group. To compare the effects of pre- and post-intervention exercise modalities, we assessed the secondary outcomes: balance (Balance Evaluation Systems Test - BESTest), executive function (Front Assessment Battery - FAB), functional mobility (Timed Up and Go Test -TUG) and quality of life domains (Parkinson Disease Questionnaire-39 - PDQ39). Quantitative variables were expressed as median and interquartile range and categorical variables were expressed as proportion. Wilcoxon Sign test were used for intragroup comparisons and Kruskal-Wallis to compare intergroup results of continuous variables. For categorical variables we used the Wilcoxon Signs test and Fisher's exact test for intragroup and outcome occurred in 19 (24%) patients, with a G1 fall rate of 5.12 falls/100 patient-months,

intergroup comparisons, respectively. The level of significance was 5%. Results: In article 1, fall G2=5.48 and G3=4.26. Predictors of fall: disease duration (HR=1.16/year, 95% CI=1.03-1.29) and lower limb muscle strength (improvement in Sit to Stand Test, HR=1.14/second 95% CI=1.01-1.28), regardless of initial balance measurements. Quality of life predictors: disease severity (effect=-0.01 point on Euroqol-5D per point increase in Unified Parkinson's Disease Rating Scale; 95% CI -0.01 to -0.002) and gait performance (effect = - 0.03 points at Euroqol-5D per second increase in cognitiveTUG; 95% CI -0.05 to -0.01). In article 2, G2 and G3 significantly reduced the proportion of fallers to 26% (22% single fallers and 4% recurrent fallers, p=0.008) and 20% (12% single fallers and 8% recurrent fallers, p=0.021), respectively, during follow-up. G2 significantly reduced by 60% the number of falls (p=0.005) in follow-up. Improvements in balance and executive function have been demonstrated in G1 and G3. G3 significantly improved the domains stigma and activity of daily living. Conclusions: The three exercises did not differ in the proportion of fallers, the number and rate of falls, and the quality of life over a six month follow-up period. However, in intragroup analyzes, the Stationary Bicycle and Exergaming groups reduced the proportion of fallers in the follow-up period, and the Bicycle group also reduced the number of falls. Falls were associated with longer disease duration and improved lower limb strength with maintenance of baseline balance values. Better quality of life was associated with lower disease severity and better gait performance. There was no difference between groups regarding secondary outcomes. However, the Exergaming group showed more general effects by improving balance, executive function, functional mobility, and the stigma and daily life activity domains of quality of life. Exergaming has the characteristics of a multisensory and multidimensional therapy to prevent falls in elderly with Parkinson's disease.

Keywords: 1. Parkinson's disease; 2. Elderly; 3. Virtual Reality Exposure Therapy; 4. Postural Balance; 5.Fall

III. PRINCIPAIS RESULTADOS

Artigo 1

Table 2: Characteristics of 79 participants with PD before treatment with Functional, Bicycle or Exergame in a reference movement disorders center. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	G1-Functional (n=27)	G2-Bike (n = 27)	G3-Exergame (n =25)	P
	Median (IQR) or n (%)	Median (IQR) or n (%)	Median (IQR) or n (%)	
Female sex	8 (29.6)	12 (44.4)	12 (48.0)	0.346
Age (years)	70.0 (66.0-75.0)	67.0 (64.0-72.0)	67.0 (65.5-70.5)	0.156
Weight (Kg)	69.5 (62.0-73.0)	66.5 (58.0-73.5)	68.5 (54.0-79.1)	0.746
Height (m)	1.62 (1.53-1.65)	1.63 (1.55-1.69)	1.61 (1.54-1.68)	0.754
BMI (Kg/m ²)	26.4 (22.8-29.3)	24.6 (21.6-26.8)	27.2 (20.6-29.3)	0.246
AbnC (cm)	96.0 (89.0-103.0)	91.0 (83.0-98.0)	98.0 (88.5-105.0)	0.386
Education (years)	8.0 (5.0-11.0)	8.0 (5.0-11.0)	8.0 (4.5-11.0)	0.665
Disease D. (years)	5,5 (3.0-8.5)	6.0 (4.0-8.0)	5.0 (4.0-9.0)	0.748
MMSE	27.0 (24.8-28.0)	27.0 (25.0-29.0)	27.0 (23.0-29.0)	0.778
UPDRS	27.0 (19.0-41.0)	25.0 (18.0-40.0)	33.0 (19.0-44.0)	0.845
Hoehn & Yahr	2.5 (2.5-3.0)	2.5 (2.0-3.0)	2.5 (2.0-2.5)	0.459
Fall History*	11 (40.7)	14 (51.9)	14 (56.0)	0.518
Number of Falls**	0.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-1.5)	0.731
Freezing	15 (55.6)	21 (77.8)	13 (52,0)	0.101
Motor Fluctuation	12 (44.4)	12 (48.0)	12 (48.0)	0.957
Dyskinesias	7 (25.9)	11 (40.7)	4 (16.0)	0.130
Fear of falling	17 (63.0)	16 (59.3)	14 (56.0)	0.877
Hyperkyphosis	13 (48.1)	19 (70.4)	16 (64.0)	0.229
Depression	14 (51.9)	12 (44.4)	15 (60.0)	0.532
BESTest	86.5 (74.0-94.5)	86.0 (79.0-93.0)	86.0 (76.5-95.0)	0.935
SRT (s)	15.0 (10.3-19.1)	14.0 (11.6-16.7)	15.3 (11.4-17.5)	0.479
TUG (s)	9.7 (7.8-11.0)	8.8 (8.0-11.0)	10.2 (8.2-10.8)	0.753

* Individual with one or more falls in the prior six months (pretraining).

** Number of falls in the prior six months (pretraining).

Kg: kilogram; m: meters; cm: centimeters; s: seconds; BMI: Body Mass Index; UPDRS: Scale Unified Parkinson's Disease Rating; AbnC: Abdominal circumference; Disease D.: Disease duration; MMSE: Mini-Mental State Examination; IQR: interquartile range; SRT: Sitting-rising test; BESTest: Postural Balance test; TUG: Timed Up and Go test.

Table 3. Treatment group and baseline clinical factors associated with the occurrence of the first fall during the 6-month follow-up period of 79 individuals with Parkinson's Disease, Salvador, Bahia, Brazil, December / 2015 to March / 2018.

Variable	Unadjusted	
	HR (Hazard Ratio) CI (95%)	p*
Treatment		
Functional	0.96 (0.34-2.73)	0.910
Bike	1 (reference category)	
Exergame	0.79 (0.25-2.49)	
Age (years)	1.03 (0.94-1.13)	0.567
Sex Female	1.19 (0.48-2.92)	0.700
Education (years)	1.02 (0.90-1.15)	0.759
Weight pretraining (Kg)	1.00 (0.96-1.04)	0.847
BMI pretraining (Kg/m²)	0.96 (0.85-1.08)	0.483
AbnC pretraining (cm)	1.00 (0.97-1.04)	0.821
UPDRS	1.02 (0.99-1.05)	0.184
Hoehn Yahr	1.70 (0.51-5.68)	0.386
Disease duration (years)	1.13 (1.04-1.23)	0.005
MMSE	1.14 (0.93-1.41)	0.217
Fear of falling pretraining^a	4.19 (1.22-14.40)	0.010
Fall history pretraining**	3.20 (1.15-8.90)	0.015
Number of falls pretraining	1.36 (1.16-1.60)	<0.001
Hyperkyphosis pretraining	0.51 (0.21-1.27)	0.127
Depression pretraining	0.89 (0.36-2.18)	0.783
Dyskinesias	2.32 (0.94-5.71)	0.052
Freezing	1.06 (0.42-2.70)	0.897
Motor Fluctuation	0.69 (0.27-1.76)	0.419

*Log Rank test for categorical variables, and Cox for quantitative variables

^aPDQ39

** Individual with one or more falls in the prior six months.

HR: Hazard Ratio; CI: Confidence Interval; Kg: kilogram; m: meters; cm: centimeters; BMI: Body Mass Index; AbnC: Abdominal circumference; UPDRS: Scale Unified Parkinson's Disease Rating; MMSE: Mini-Mental State Examination.

Table 4. Clinical assessment scales before and after treatment period relative to the hazard ratio (HR) of falls, adjusted by the treatment group, during the six-month follow-up period of 79 individuals with Parkinson's disease, Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	Adjusted by the treatment group	p
	HR (CI 95%)	
6MWT pretraining (m)	1.00 (1.00–1.01)	0.908
6MWT (post-pretraining) (m)	1.00 (0.99-1.01)	0.961
10MWT pretraining (s)	0.25 (0.06-1.10)	0.066
10MWT (pre-posttraining) (s)	5.99 (0.61-59.14)	0.125
SRT pretraining (s)	1.04 (0.98-1.11)	0.179
SRT (pre-posttraining) (s)	1.13 (1.03-1.24)	0.011
BESTest pretraining	0.95 (0.91-0.99)	0.026
BESTest (post-pretraining)	0.98 (0.89-1.07)	0.584
TUG pretraining (s)	1.00 (0.78-1.27)	0.965
TUG (pre-posttraining) (s)	1.31 (0.94-1.82)	0.107
cTUG pretraining (s)	1.01 (0.88-1.17)	0.892
cTUG (pre-posttraining) (s)	1.14 (0.91-1.42)	0.259
FAB pretraining	1.03 (0.88-1.20)	0.712
FAB (post-pretraining)	0.93 (0.75-1.15)	0.477
GDS15 pretraining	0.92 (0.78-1.08)	0.301
GDS15 (post-pretraining)	1.08 (0.83-1.40)	0.590
WHODAS 2.0 pretraining	1.00 (0.98-1.02)	0.810
WHODAS 2.0 (post-pretraining)	0.99 (0.95-1.03)	0.567
PDQ39 pretraining	1.01 (0.98-1.04)	0.563
PDQ39 (pre-posttraining)	1.00 (0.95-1.06)	0.970
PDQ39 Mobility pretraining	1.00 (0.99-1.02)	0.740
PDQ39 Mobility (pre-posttraining)	1.00 (0.97-1.04)	0.838
PDQ39 ADL pretraining	1.01 (0.99-1.03)	0.329
PDQ39 ADL (pre-posttraining)	1.00 (0.97-1.04)	0.879
PDQ39 Emotional Well-being pretraining	1.00 (0.98-1.02)	0.947
PDQ39 Emotional Well-being (pre-posttraining)	0.99 (0.97-1.02)	0.651
PDQ39 Stigma pretraining	1.01 (0.99-1.03)	0.553
PDQ39 Stigma (pre-posttraining)	1.00 (0.96-1.03)	0.820
PDQ39 Social Support pretraining	1.00 (0.97-1.03)	0.904
PDQ39 Social Support (pre-posttraining)	1.02 (0.96-1.08)	0.501
PDQ39 Cognition pretraining	1.00 (0.98-1.03)	0.749
PDQ39 Cognition (pre-posttraining)	1.01 (0.98-1.03)	0.648
PDQ39 Communication pretraining	1.01 (0.99-1.03)	0.384
PDQ39 Communication (pre-posttraining)	1.02 (0.98-1.05)	0.389
PDQ39 Bodily Discomfort pretraining	1.00 (0.98-1.02)	0.866
PDQ39 Bodily Discomfort (pre-posttraining)	0.99 (0.96-1.02)	0.338

HR: Hazard Ratio; CI: Confidence Interval; m: meters; s: seconds; 6MWT: 6-minute walk test; 10MWT: 10-meters walk test; SRT: Sitting-rising test; BESTest: Postural Balance test; TUG: Timed Up and Go test; cTUG: cognitive TUG; FAB: Frontal Assessment Battery; GDS15: 15 item Geriatric Depression Scale; WHODAS 2.0: World Health Organization Disability Assessment Schedule 2.0; PDQ39: Parkinson Disease Questionnaire-39; ADL: Activities of Daily Living.

Table 5. Final Cox multivariate regression model, with Hazard Ratio (HR) and 95% Confidence Interval (CI) for time to first fall and variables assessed in 79 individuals with Parkinson's disease during the six-month follow-up period , Salvador, Bahia, Brazil, December /2015 to March /2018.

Variable	HR	CI 95%	p
Treatment			
Functional	0.68	0.14-3.40	0.637
Bike	1	Ref.	-
Exergame	1.05	0.25-4.42	0.943
Fear of falling pretraining ^a	2.08	0.39-11.14	0.394
Fall history pretraining *	0.63	0.12-3.46	0.599
Disease duration (years)	1.16	1.03-1.29	0.011
SRT (pre-posttraining) (s)	1.14	1.01-1.28	0.036
BESTest pretraining	0.97	0.90-1.05	0.404
Number of falls pretraining	1,22	0.91-1.64	0.181

^aPDQ39

* Individual with one or more falls in the prior six months.

s: seconds; 10MWT: 10-meters walk test; SRT: Sitting-rising test; BESTest: Postural Balance test; Ref.: Reference category.

Table 6. Variables associated with quality of life (EQ5D) during the six-month follow-up period of 79 patients with Parkinson's disease, Salvador, Bahia, Brazil, December / 2015 to March / 2018.

Variable	Unadjusted	p	Adjusted	p
	Effect (CI 95%)		Effect (CI 95%)	
Treatment				
Functional	-0.17 (-0.36 a 0.02)	0.076		
Exergame	0.07 (-0.12 a 0.27)	0.473		
Bicycle	0	-		
Sex Female	-0.20 (-0.37 a 0.04)	0.018		
Age (years)	-0.01 (-0,02 a 0.01)	0.638		
Education (years)	0.03 (0.01 a 0.05)	0.009	0.02 (-0.01 a 0.03)	0.073
Height (m)	1.38 (0.45 a 2.31)	0.004	0.74 (-0.01 a 1.49)	0.054
Weight pretraining (Kg)	0.01 (-0.01 a 0.01)	0.222		
Weight (pre-posttraining) (Kg)	-0.01 (-0.04 a 0.03)	0.848		
BMI pretraining (Kg/m²)	0.01 (-0.01 a 0.02)	0.778		
BMI (pre-posttraining) (Kg/m²)	-0.01 (-0.10 a 0.07)	0.726		
AbnC pretraining (cm)	0.01 (-0.01 a 0.01)	0.604		
AbnC (pre-posttraining) (cm)	0.02 (-0.01 a 0.03)	0.084		
UPDRS	-0.01 (-0.02 a 0.01)	0.004	-0.01 (-0.01 a -0.002)	0.011
Hoehn Yahr	-0.18 (-0.40 a 0.04)	0.098		
Disease duration (years)	-0.01 (-0.03 a 0.02)	0.731		
MMSE	0.02 (-0.01 a 0.05)	0.116		
Fear of falling pretraining^a	-0.23 (-0.40 a - 0.07)	0.005		
Fall history pretraining *	-0.06 (-0.23 a 0.11)	0.487		
Hyperkyphosis pretraining	0.12 (-0.06 a 0.29)	0.189		
Freezing	-0.02 (-0.19 a 0.16)	0.864		
Dyskinesias	-0.11 (-0.29 a 0.08)	0.252		
Motor Fluctuation	-0.01 (-0.18 a 0.16)	0.938		
6MWT pretraining (m)	0.01 (0.00 a 0.01)	0.013		
6MWT (post-pretraining) (m)	0,000 (-0,002 a 0,002)	0,967		
10MWT pretraining (s)	0.30 (0.02 a 0.59)	0.039		
10MWT (pre-posttraining) (s)	-0.09 (-0.43 a 0,26)	0.618		
SRT pretraining (s)	-0.01 (-0.03 a 0.01)	0.209		
SRT (pre-posttraining) (s)	-0.01 (-0.03 a 0.01)	0.130		
BESTest pretraining	0.01 (0.01 a 0.02)	0.020		
BESTest (post-pretraining)	-0.01 (-0.02 a 0.01)	0.491		
TUG pretraining (s)	-0.03 (-0.08 a 0.01)	0.129		
TUG (pre-posttraining) (s)	-0.01 (-0.05 a 0,05)	0.978		
cTUG pretraining (s)	-0.03 (-0.06 a -0.01)	0.016	-0.03 (-0.05 a -0.01)	0.008
cTUG (pre-posttraining) (s)	-0.03 (-0.06 a -0.01)	0.039		
FAB pretraining	0.03 (-0.01 a 0.05)	0.069		
FAB (post-pretraining)	-0.02 (-0.05 a 0.01)	0.190		
WHODAS 2.0 pretraining	-0.01 (-0.02 a -0.01)	<0.001		
WHODAS 2.0 (post-pretraining)	-0.01 (-0.01 a 0.01)	0.482		
GDS15 pretraining	-0.03 (-0.05 a -0.01)	0.038		
GDS15 (post-pretraining)	-0.02 (-0.06 a 0.02)	0.261		

^aPDQ39 - Parkinson Disease Questionnaire-39

* Individual with one or more falls in the prior six months.

HR: Hazard Ratio; CI: Confidence Interval; Kg: kilogram; m: meters; cm: centimeters; m: meters; s: seconds; BMI: Body Mass Index; AbnC: Abdominal circumference; UPDRS: Scale Unified

Parkinson's Disease Rating; MMSE: Mini-Mental State Examination; 6MWT: 6-minute walk test; 10MWT: 10-meters walk test; SRT: Sitting-rising test; BESTest: Postural Balance test; TUG: Timed Up and Go test; cTUG: cognitive TUG; FAB: Frontal Assessment Battery; WHODAS 2.0: World Health Organization Disability Assessment Schedule 2.0; GDS15: 15 item Geriatric Depression Scale.

Figure 1

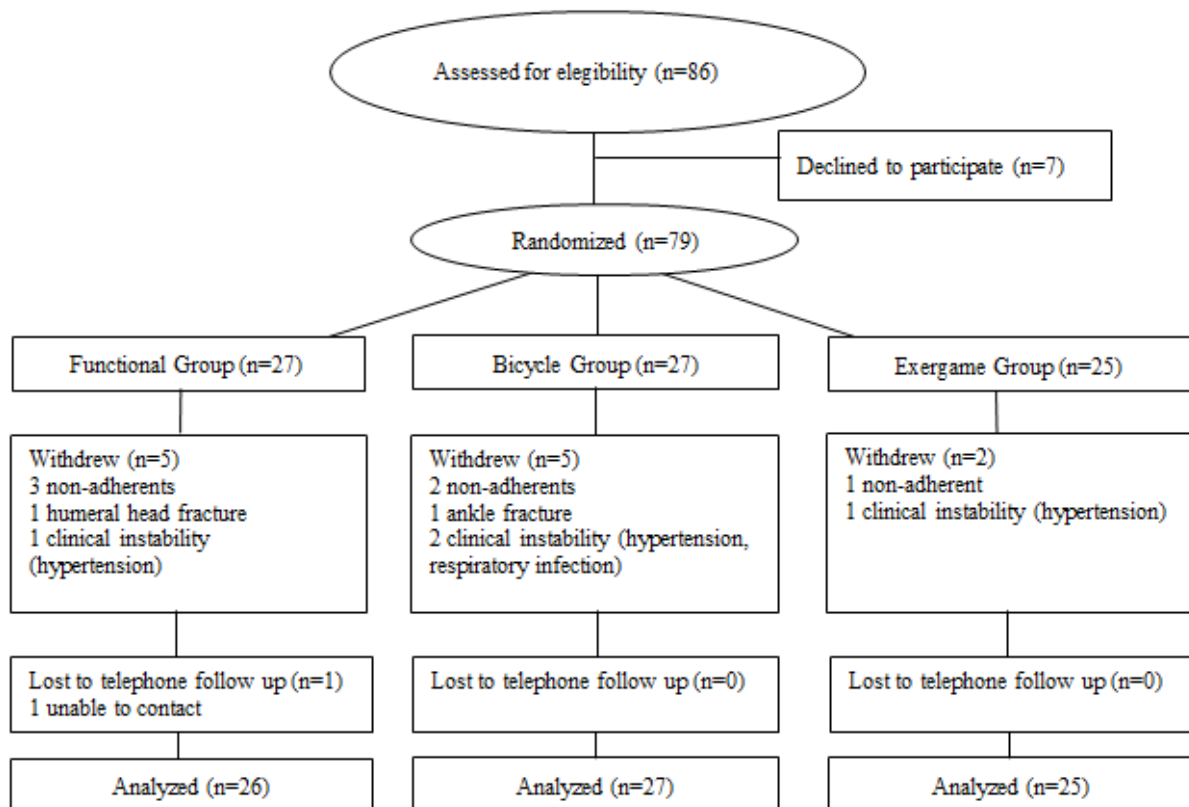


Figure 1. Flow diagram of the progress through the phases of a parallel randomized trial of three intervention groups. Salvador, Bahia, Brazil, December/2015 to March/2018.

Figure 2

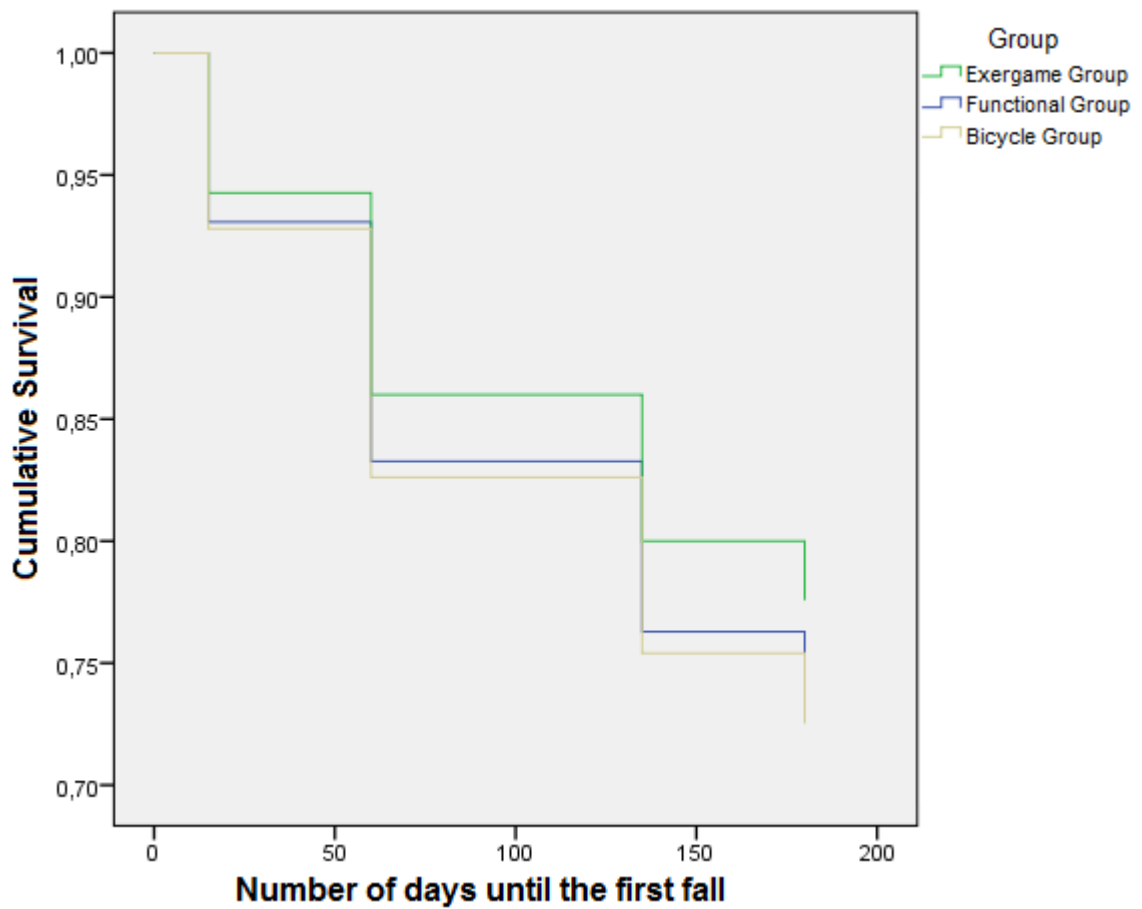


Figure 2. Kaplan-Meier survival function graph showing number of days until the first fall (evaluations on day 0, 15, 60, 135 and 180) of 79 individuals with Parkinson's Disease, treated with Functional training, Bicycle or Exergame, Salvador, Bahia, Brazil, December/2015 to March/2018.

Artigo 2

Table 2: Characteristics of 79 participants with PD before treatment with Functional, Bicycle or Exergaming in a reference movement disorders center. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	G1-Functional (n=27)	G2-Bicycle (n = 27)	G3-Exergaming (n =25)	p
	Median (IQR) or n (%)	Median (IQR) or n (%)	Median (IQR) or n (%)	
Female sex	8 (29.6)	12 (44.4)	12 (48.0)	0.346
Age (years)	70.0 (66.0-75.0)	67.0 (64.0-72.0)	67.0 (65.5-70.5)	0.156
Weight (Kg)	69.5 (62.0-73.0)	66.5 (58.0-73.5)	68.5 (54.0-79.1)	0.746
Height (m)	1.62 (1.53-1.65)	1.63 (1.55-1.69)	1.61 (1.54-1.68)	0.754
BMI (Kg/m ²)	26.4 (22.8-29.3)	24.6 (21.6-26.8)	27.2 (20.6-29.3)	0.246
AbnC (cm)	96.0 (89.0-103.0)	91.0 (83.0-98.0)	98.0 (88.5-105.0)	0.386
Education (years)	8.0 (5.0-11.0)	8.0 (5.0-11.0)	8.0 (4.5-11.0)	0.665
Disease D. (years)	5,5 (3.0-8.5)	6.0 (4.0-8.0)	5.0 (4.0-9.0)	0.748
MMSE	27.0 (24.8-28.0)	27.0 (25.0-29.0)	27.0 (23.0-29.0)	0.778
UPDRS	27.0 (19.0-41.0)	25.0 (18.0-40.0)	33.0 (19.0-44.0)	0.845
Hoehn & Yahr	2.5 (2.5-3.0)	2.5 (2.0-3.0)	2.5 (2.0-2.5)	0.459
Fall History*	11 (40.7)	14 (51.9)	14 (56.0)	0.518
Number of Falls**	0.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-1.5)	0.731
Freezing	15 (55.6)	21 (77.8)	13 (52,0)	0.101
Motor Fluctuation	12 (44.4)	12 (48.0)	12 (48.0)	0.957
Dyskinesias	7 (25.9)	11 (40.7)	4 (16.0)	0.130

* Individual with one or more falls in the prior six months (pretraining).

** Number of falls in the prior six months (pretraining).

IQR: interquartile range; n: number; Kg: kilogram; m: meters; cm: centimeters; s: seconds; BMI: Body Mass Index; UPDRS: Unified Parkinson's Disease Rating Scale; AbnC: Abdominal Circumference; Disease D.: Disease duration; MMSE: Mini-Mental State Examination.

Table 3. Characteristics of 79 participants with PD (intention to treat) treated with Functional, Bicycle or Exergaming in a reference movement disorders center, considering single fallers, recurrent fallers, and non-fallers during the 6-months follow-up period. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	Single Fallers*	Recurrent Fallers** (n=8)	Non-Fallers (n=60)	p
	(n=11)			
	Median (IQR) or n (%)	Median (IQR) or n (%)	Median (IQR) or n (%)	
Treatment				
Functional	2 (18.2)	5 (62.5)	20 (33.3)	0.253
Bicycle	6 (54.5)	1 (12.5)	20 (33.3)	
Exergaming	3 (27.3)	2 (25.5)	20 (33.3)	
Sex				
Female	7 (63.6)	2 (25.0)	23 (38.3)	0.187
Male	4 (36.4)	6 (75.0)	37 (61.7)	
Age (years)	70.0 (66.0-72.0)	69.0 (65.5-74.0)	67.0 (65.0-72.8)	0.702
Education (years)	5.0 (5.0-15.0)	11.0 (7.3-11.0)	8.0 (5.0-11.0)	0.503
Weight pretraining (Kg)	66.5(54.5-74.5)	69.0 (59.9-83.1)	68.5 (58.1-74.5)	0.803
BMI pretraining (Kg/m ²)	26.6 (20.3-28.3)	24.6 (20.1-29.3)	25.5 (22.3-29.1)	0.818
AbnC pretraining (cm)	94.5 (90.0-101.0)	95.3 (85.5-111.0)	94.5 (83.8-102.5)	0.862
UPDRS	34.0 (23.0-43.0)	35.5 (22.3-45.5)	27.0 (18.0-39.8)	0.326
Hoehn & Yahr	2.5 (2.0-2.5)	3.0 (2.3-3.0)	2.5 (2.0-3.0)	0.179
Disease D. (years)	4.0 (3.0-8.0)	13.0 (11.5-17.5)	5.0 (4.0-6.8)	0.001
MMSE	27.0 (27.0-28.0)	27.0 (24.5-28.0)	27.0 (24.0-29.0)	0.395
Fear of falling pretraining***	9 (81.8)	7 (87.5)	31 (51.7)	0.029
History of fall****	8 (72.7)	6 (75.5)	25 (41.7)	0.047
Number of falls pretraining	1.0 (0.0-2.0)	2.5 (0.5-7.3)	0.0 (0.0-1.0)	0.005
Hyperkyphosis pretraining	6 (54.5)	3 (37.5)	39 (65.0)	0.302
Depression pretraining	4 (36.4)	5 (62.5)	32 (53.3)	0.475
Dyskinesias	5 (45.5)	4 (50.0)	13 (21.7)	0.106
Freezing	7 (63.6)	5 (62.5)	37 (61.7)	0.992
Motor Fluctuation	3 (27.3)	4 (50.0)	29 (48.3)	0.406

* Individuals with one fall.

** Individuals with two or more falls.

*** Item 9 – PDQ39

**** Individuals with one or more fall in the prior six months (pretraining).

BMI: Body Mass Index; UPDRS: Scale Unified Parkinson's Disease Rating; AbnC: umbilical-level Abdominal Circumference; Disease D.: Parkinson's Disease duration; MMSE: Mini-Mental State Examination; IQR: interquartile range.

Table 4. Comparison between Functional, Bicycle and Exergaming groups of Initial (six months prior to the treatment) and Final (6-month follow-up period) results for number of falls and proportion of falls category (non-faller, single faller, and recurrent faller) of 79 older adults with PD (intention to treat) in a reference movement disorders center. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variables	Functional (n = 27)		Bicycle (n = 27)		Exergaming (n = 25)		p*
	I. Median (IQR) or n (%)	p	I. Median (IQR) or n (%)	p	I. Median (IQR) or n (%)	p	
	F. Median (IQR) or n (%)		F. Median (IQR) or n (%)		F. Median (IQR) or n (%)		
Number of Falls	0.0 (0.0-1.0) 0.0 (0.0-1.0)	0.282	1.0 (0.0-1.0) 0.0 (0.0-1.0)	0.005	1.0 (0.0-1.5) 0.0 (0.0-0.0)	0.073	0.814
Falls Category		0.248		0.008		0.021	0.253
Non-faller	16 (59.3) 20 (74.1)		13 (48.1) 20 (74.1)		11 (44.0) 20 (80.0)		
S. Faller (=1)	5 (18.5) 2 (7.4)		9 (33.3) 6 (22.2)		8 (32.0) 3 (12.0)		
R. Faller (≥2)	6 (22.2) 5 (18.5)		5 (18.5) 1 (3.7)		6 (24.0) 2 (8.0)		

*Comparison between groups of final results.

n: number, I: Initial, F: Final, IQR: Interquartile Range, S: Single, R: Recurrent.

Table 5. Pretraining (Pre) and Posttraining (Post) results for PB test (BESTest), Timed Up and Go test (TUG), Frontal Assessment Battery (FAB) and QOL domains questionnaire (PDQ39) applied in 67 older adults with PD in a reference movement disorders center. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	G1-Functional (n = 22)		p	G2-Bicycle (n = 22)		p	G3-Exergaming (n = 23)		p
	Pre Median (IQR)	Post Median (IQR)		Pre Median (IQR)	Post Median (IQR)		Pre Median(IQR)	Post Median (IQR)	
BESTest	86.5 (74.0-94.5)	93.0 (79.3-97.3)	0.007	87.5 (79.8-95.0)	90.5 (83.8-96.5)	0.100	86.0 (77.0-93.0)	92.0 (82.0-98.0)	<0.001
TUG	9.8 (7.6-11.1)	8.7 (6.8-10.7)	0.108	8.7 (7.8-11.1)	7.8 (7.2-9.8)	0.008	10.2 (8.6-10.9)	9.0 (7.1-10.4)	0.011
FAB	13.0 (10.0-15.0)	15.0 (12.8-16.3)	0.016	14.5 (11.8-17.0)	15.5 (12.3-17.0)	0.830	15.0 (13.0-16.0)	16.0 (15.0-17.0)	0.007
PDQ39 mobility	38.8 (19.4-65.0)	26.3 (17.5-48.1)	0.014	36.3 (10.0-47.5)	18.8 (10.0-35.0)	0.007	37.5 (10.0-55.0)	25.0 (10.0-40.0)	0.001
PDQ39 ADL	22.9 (15.7-45.8)	22.9 (15.7-38.6)	0.333	25.0 (12.5-51.1)	18.8 (08.3-37.5)	0.050	33.3 (08.3-54.2)	29.2 (00.0-41.7)	0.002
PDQ39 emotional well-being	31.3 (12.5-46.9)	22.9 (12.5-46.9)	0.663	14.6 (11.5-33.3)	16.7 (08.3-34.4)	0.940	29.2 (12.5-45.8)	16.7 (04.2-41.7)	0.076
PDQ39 stigma	06.3 (00.0-32.9)	12.5 (00.0-31.3)	0.824	12.5 (00.0-26.6)	06.3 (00.0-26.6)	0.522	18.8 (06.3-37.5)	06.3 (00.0-37.5)	0.049
PDQ39 social support	00.0 (00.0-16.7)	04.2 (00.0-16.7)	0.291	08.3 (00.0-16.7)	00.0 (00.0-16.7)	0.653	00.0 (00.0-16.7)	00.0 (00.0-16.7)	0.395
PDQ39 cognition	25.0 (12.5-39.1)	25.0 (11.0-43.8)	0.575	25.0 (17.2-43.8)	31.3 (17.2-39.1)	0.415	25.0 (12.5-43.8)	18.8 (06.3-31.3)	0.205
PDQ39 communication	20.9 (08.3-41.7)	16.7 (00.0-41.7)	0.150	20.9 (06.2-33.3)	20.9 (00.0-33.3)	0.638	16.7 (00.0-25.5)	08.3 (00.0-16.7)	0.130
PDQ39 bodily discomfort	25.0 (16.7-52.1)	37.5 (08.3-54.2)	0.686	33.3 (16.7-52.1)	33.3 (16.7-52.1)	0.703	25.0 (08.3-41.7)	25.0 (08.3-33.3)	0.972

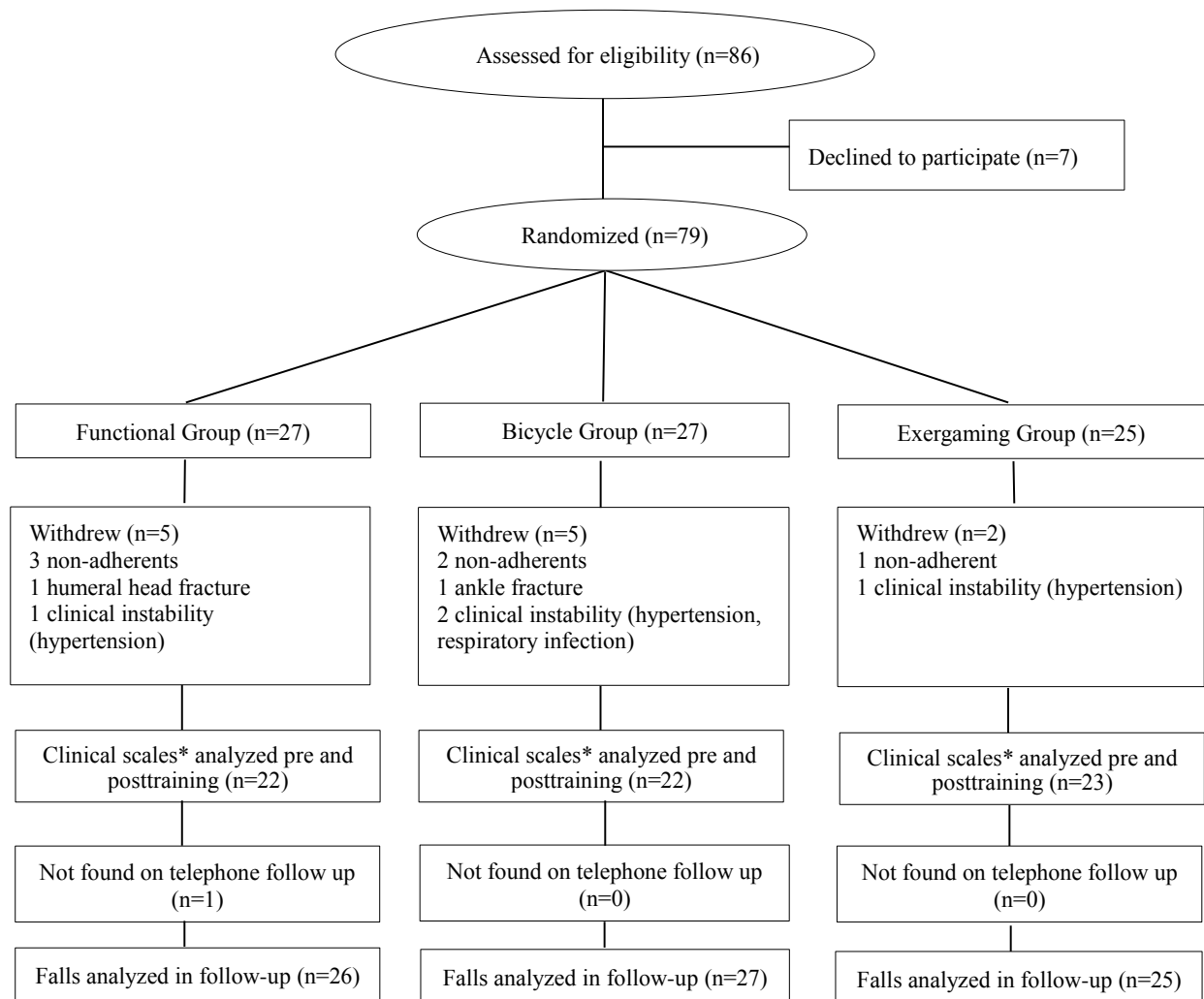
Pre: Pretraining, Post: Posttraining, IQR: Interquartile Range, BESTest: PB test, TUG: Timed Up and Go test, FAB: Frontal Assessment Battery, QOL: quality of life, PDQ39: Parkinson's Disease Questionnaire-39, ADL: Activities of Daily Living.

Table 6. Comparison between Functional, Bicycle and Exergaming groups based on the scores changes (median of the differences between the pretraining and posttraining) in relation to quantitative variables (BESTest, TUG, FAB and PDQ39 domains) applied in 67 older adults with PD in a reference movement disorders center. Salvador, Bahia, Brazil, December/2015 to March/2018.

Variable	G1-Functional Median (IQR)	G2-Bicycle Median (IQR)	G3-Exergaming Median (IQR)	p
BESTest	3.5 (-1.3 to 6.0)	2.5 (-0.5 to 8.5)	4.0 (1.0 to 7.0)	0.694
TUG	0.9 (-0.1 to 1.5)	0.7 (0.5 to 1.6)	1.0 (-0.1 to 1.7)	0.877
FAB	1.0 (-0.3 to 3.3)	0.0 (-2.3 to 3.0)	2.0 (0.0 to 3.0)	0.202
PDQ39 mobility	7.5 (-3.1 to 18.1)	8.8 (-1.3 to 16.3)	5.0 (0.0 to 17.5)	0.970
PDQ39 ADL	2.1 (-5.3 to 16.6)	6.3 (-4.2 to 18.8)	8.3 (0.0 to 16.6)	0.478
PDQ39 emotional well-being	0.0 (-8.3 to 9.4)	0.0 (-20.8 to 13.6)	8.3 (-4.2 to 20.8)	0.400
PDQ39 stigma	0.0 (-12.5 to 12.5)	0.0 (0.0 to 1.6)	6.3 (0.0 to 12.5)	0.133
PDQ39 social support	0.0 (-10.5 to 2.1)	0.0 (-8.3 to 2.1)	0.0 (0.0 to 0.0)	0.479
PDQ39 cognition	3.1 (-12.5 to 14.1)	-0.1 (-25.0 to 6.3)	6.2 (-6.2 to 18.7)	0.391
PDQ39 communication	0.0 (-2.1 to 16.7)	0.0 (-8.3 to 8.3)	0.0 (0.0 to 16.7)	0.680
PDQ39 bodily discomfort	0.0 (-16.6 to 10.5)	0.0 (-16.6 to 8.3)	0.0 (-8.4 to 16.6)	0.951

BESTest: PB test, TUG: Timed Up and Go test, FAB: Frontal Assessment Battery, PDQ39: Parkinson's Disease Questionnaire-39, ADL: Activities of Daily Living, IQR: Interquartile Range.

Figure 1



* Clinical scales: Postural Balance test (BESTest), Parkinson's Disease Questionnaire-39, Timed Up and Go Test (TUG), and Frontal Assessment Battery (FAB).

Figure 1. Flow diagram progress through the phases of a parallel randomized trial of three intervention groups (Functional, Bicycle and Exergaming). Salvador, Bahia, Brazil, December/2015 to March/2018.