



## Effects of Two Different Exercise Training Programs Periodization on Anthropometric and Functional Parameters in People Living with HIV: A Randomized Clinical Trial

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### ABSTRACT

*International Journal of Exercise Science* 15(3): 733-746, 2022. The purpose of this study was to investigate the effects of two different exercise training programs periodization on anthropometric and functional parameters in people living with HIV (PLHIV). This was a randomized clinical trial that involved participants ( $n = 31$ ) living with HIV aged over 18 years and undergoing antiretroviral therapy which were randomized to periodized exercise training (PET;  $n = 13$ ), non-periodized exercise training (NPET;  $n = 13$ ), or control group (CON;  $n = 15$ ). The PET and NPET groups performed 12 weeks of combined training while the CON group maintained the usual activities. Before and after 12 weeks of intervention were measured body composition and perimeters, muscle strength, Short Physical Performance Battery (SPPB) and Timed Up and Go (TUG) test time. Results: The PET and NPET groups increased fat-free mass ( $p < 0,001$ ), right ( $p < 0,001$ ) and left thigh perimeter ( $p < 0,001$ ), muscle strength ( $p < 0,001$ ), handgrip force ( $p < 0,001$ ), and reduced the fat mass ( $p < 0,001$ ), neck perimeter ( $p < 0,001$ ), chair stand ( $p < 0,001$ ), and time-up and go test time ( $p < 0,001$ ) compared to CON. Furthermore, PET was significantly different to increase right thigh and muscle strength ( $p < 0,05$ ) compared to NPET. Conclusion: Both exercise training periodization protocols were effective to improve body composition and functional outcomes; however, seems that PET presents better results compare to NPET in PLHIV.

KEY WORDS: Timed up and go, muscle strength, body composition

### INTRODUCTION

People living with HIV (PLHIV) have increased life expectancy after antiretroviral therapy (ART) development; however, there is increasing evidence that this population is experiencing a fan of premature aging and age-related comorbidities such as sarcopenia, impaired physical function, increased visceral adiposity (3, 12, 13, 20). Furthermore, previous studies reported that PLHIV does not perform the recommended amount of physical exercise which contributes to

the development of metabolic disorders, higher risk of cardiovascular disease, and all-cause mortality. Thus, interventions should be encouraged to counterbalance this scenario.

It is well established that physical exercise training is an important non-pharmacological intervention for PLHIV and can minimize and/or revert the morphophysiological changes provided by ART. Despite the American College of Sports Medicine recommends physical exercise to improve various health parameters few guidelines can establish the best strategy for the treatment of PLHIV (9, 27). Some evidence shows that combined resistance and aerobic training increase strength and muscle mass, improve body composition and physical performance in functional tests (19, 28). However, the continuous stimuli are given in non-periodized exercise training (NPET) can cause long-term plateaus and stagnation (4). Thus, advanced strategies are needed to promote additional strength gains as training progress (15).

Periodization is a strategy widely used in the sports context which involves the manipulation of acute training variables (load, sets, and repetitions) in order to optimize strength gains and prevent the onset of overtraining syndrome. The main objective of training periodization is to promote continuous adaptations to the neuromuscular system and, thus, avoid the training plateaus. Linear and nonlinear periodization models are more frequently used over the last few decades. In the first, changes in exercise volume and load occur within the mesocycles. On the other hand, in nonlinear periodization models, changes in exercise volume and load are handled with reduced periodicity (daily, weekly). Regardless of the periodization model used, there is always an advantage of its use in relation to NPET for muscle strength gains (4, 6, 7, 26, 35). Several studies have been carried out to investigate the effect of periodization in the clinical setting in patients with the chronic obstructive pulmonary disease (8), coronary artery disease (22) and obesity (8, 22, 30). Likewise, Zanetti et al (37) investigated the effect of periodized combined exercise training and proved to be an effective and safe strategy in PLHIV.

A previous study of our laboratory demonstrated that either periodized exercise training (PET) and NPET improved maximal strength, aerobic capacity, and lymphocyte TCD4<sup>+</sup> compared to the control group and the PET significantly increased these variables compared to NPET, evidencing an additional effect of periodization (29). However, the additional effect of periodization on health outcomes remains uncertain. Thus, the present study aimed to evaluate the effects of PET and NPET on muscle strength, functional capacity, body composition, and anthropometric profile in PLHIV.

## **METHODS**

### *Participants*

This is the second analysis of a previous randomized clinical trial that involved PLHIV between January 2018 and February 2019 (29). The sample size was calculated by the software G\*Power using effect size = 0.51 and power = 0.80. The volunteers were identified by alphanumeric code and were allocated in simple randomization (1:1:1) using the Research Randomizer tool to allocate participants into three groups: control (CG), PET and NPET.

The present study included participants from both sexes, aged between 18 and 60 years, diagnosed with HIV infection and are undergoing ART for at least 1 year, with CD4+ count  $\geq 300$  cells  $\text{mm}^{-3}$  and undetectable viral load and were sedentary or did not practice systemic exercise in the at last six months. The exclusion criteria were the presence of hypertension, uncontrolled and unmedicated diabetes, opportunistic diseases, neuropathies, liver disease, and osteoarticular disorders. All participants were informed about the aims and procedures of this study and those who agreed to participate signed the informed consent term. The research was carried out fully in accordance with ethical standards of International Journal of Exercise Science (18).

#### *Protocol*

Before and after the 12-week intervention all participants underwent assessments on anthropometric measurements, body composition, muscle strength, and functional capacity. The procedures were performed by the same evaluator. Data from sex, age, ethnicity, and smoking were collected using a structured questionnaire. The level of physical activity was determined by the International Physical Activity Questionnaire (IPAQ) (14). Data on time from diagnosis of HIV infection, time on ART use, CD4+, CD8+ cell count, and other diseases were obtained from the participant's medical records.

All participants were weighed and measured with light clothing and barefoot. Body mass (BM) was measured using a digital platform type anthropometric scale, with a capacity of up to 150 kg and height was assessed by a stadiometer coupled to the balance. The body mass index (BMI) was determined using the formula  $\text{BMI} = \text{body mass (kg)} / \text{height (m}^2\text{)}$  (25). The circumferences were measured at neck, chest, waist, hip, medial thigh, and leg by a single evaluator using an inextensible millimeter tape. The waist-hip ratio (WHR) was determined using the equation  $\text{WHR} = \text{waist circumference} / \text{hip circumference}$  (25). The fat-free mass (FFM) and fat mass (FM) were estimated using four-pole bioimpedance analysis, following the manufacturer's collection instructions (Byodynamics® 310e, USA). The muscle strength was determined by the one-repetition maximum test (1RM) as previously reported (29). All volunteers performed from three to five attempts and the maximum load adopted was determined when the volunteer performed only a complete repetition of the exercise.

For short physical performance battery (SPPB), Participants performed a warm-up of 5 minutes on a treadmill. After warming up, the balance test was performed in three parts: 1) position with the feet together; 2) standing position with one foot partially forward; 3) standing position with one foot forward. The participant should maintain balance for 10 seconds in each position. The gait speed of 3m and 4m was determined in two attempts using the shortest time to cover 3 and 4 meters marked on the ground at the usual speed, with 1m for the acceleration phase and 1m for the deceleration phase. The sit-and-stand test was determined by the time required to perform 5 Complete repetitions in the shortest possible time on a 42 cm chair. The SPPB features three tests with a maximum score of 4 points each, totaling 12 points (32).

For Timed Up and Go (TUG) participants were encouraged to get up from a chair (42 cm), walk a distance of 3 meters and return to the chair and sit back in the shortest possible time without running (23). Handgrip strength was assessed using a dynamometer (Hydraulic Hand Dynamometer Model SH5001, Korea). The individual should wield the dynamometer at a 90° angle to the elbow and perform maximum force for 3 seconds. Three attempts were made on the dominant and non-dominant limbs, with 1-minute rest between attempts. The average value of the 3 attempts of each member was adopted (25).

The PET and NPET groups performed 12 weeks of supervised physical training, 3 times a week on non-consecutive days (Table 1). The resistance exercises chosen were squats, bench press, leg press, lat pull-down, hamstring curl, triceps pulley, and seated calf. After the end of the resistance exercises, the aerobic exercise on the treadmill was performed.

The intensity adjustment and target zone of proposed repetitions were performed weekly. On Friday both protocols performed 10 repetitions in the first and second series at 90-second intervals. In the last series, the participant was encouraged to perform as many repetitions as possible, and based on the number of repetitions performed, the load was adjusted for the next training session. For each repetition performed above 10, there was an increase of 1 kg for lower limbs. For the upper limbs, there was an increase of 1 kg for each repetition above 12 (21).

The intensity of aerobic training in both groups was based on the maximum heart rate (HR) obtained from a submaximal test. The training HR (tHR) was calculated by the reserve HR formula ( $tHR = \% \text{ training} \times \text{heart rate reserve} + \text{HR at rest}$ ) and was followed by a cardiac monitor.

On the first day of the week, the PET group performed 3 sets of 4 to 6 repetitions with 90% of 1RM and 180-second intervals between sets. Soon after, the high-intensity interval aerobic training was performed. It consisted of 7 sets of 30 seconds and speed corresponding to 90% of tHR and 60 seconds of passive recovery.

On the second day, 3 sets of 15 to 20 repetitions were performed with 50% of 1RM with an interval of 60 seconds between sets. After that, intermittent aerobic training was performed. It consisted of 5 sets of 120 seconds at 75% tHR and 60 seconds of active recovery at 45-50% tHR.

On the last day, 3 sets of 8 to 12 repetitions were performed with 70% of 1RM with an interval of 90 seconds between sets. After continuous aerobic training of 20 minutes at 70% of tHR was performed.

The NPET followed the recommendations of the ACSM (15). The resistance training consisted of 3 sets of 8 to 12 repetitions with 70% of 1RM with a 90-second interval between sets. Soon after, continuous aerobic training of 20 minutes at 70% of tHR was performed.

**Table 1.** Periodized and non-periodized exercise training program.

Exercises	PET			NPET
	Monday <sup>a*</sup>	Wednesday <sup>b**</sup>	Friday <sup>c***</sup>	Mon/Wed/Fri
Squat	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Bench press	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Leg press 45°	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Lat pull-down	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Hamstring curl	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Triceps pulley	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Seated calf	3 x 4- 6	3 x 15 - 20	3 x 8 - 12	3 x 8 - 12
Aerobic	7 x 30 s: 1 min <sup>d</sup>	5 x 2 min: 1 min <sup>e</sup>	20 min	20 min
Intensity	90% tHR	75% tHR: 45% tHR	70% tHR	70% tHR

PLHIV: people living with HIV; \* 90% of 1RM; \*\* 50% of 1RM; \*\*\* 70% of 1RM; Recovery Interval (RI) a, b, c between series; aRI = 180 seconds; bRI = 60 seconds; cRI = 90 seconds; d = passive recovery; and e = active recovery; tHR = training heart rate.

### Statistical Analysis

Data normality was verified by the Shapiro-Wilk test. Levene's test was applied to analyze the homogeneity of variances between the groups. Group baseline differences were assessed by one-way analysis of variance (ANOVA).  $\Delta$  (post - pre) values were calculated and covariance analysis (ANCOVA) was used with Bonferroni post hoc test using preintervention values as a covariate. Values are expressed as mean  $\pm$  standard deviation, 95% confidence interval (CI) [lower limit; upper limit], and statistical significance was set when  $p < 0.05$  for all analyses. Data were processed using the Statistical Package for Social Sciences 20.0 software (SPSS, USA).

## RESULTS

Initially, 85 volunteers were recruited and 51 PLHIV were considered eligible for the study. At random, the participants were allocated to the PET ( $n = 17$ ), NPET ( $n = 17$ ) and CG ( $n = 17$ ) groups. During the 12 weeks of intervention, there were 10 cases (19.6%) of dropouts/abandonment of which five reported health problems, two for personal reasons, two for surgery reasons, and one for family reasons. Thus, the study ended with 41 volunteers, as shown in Figure 1.

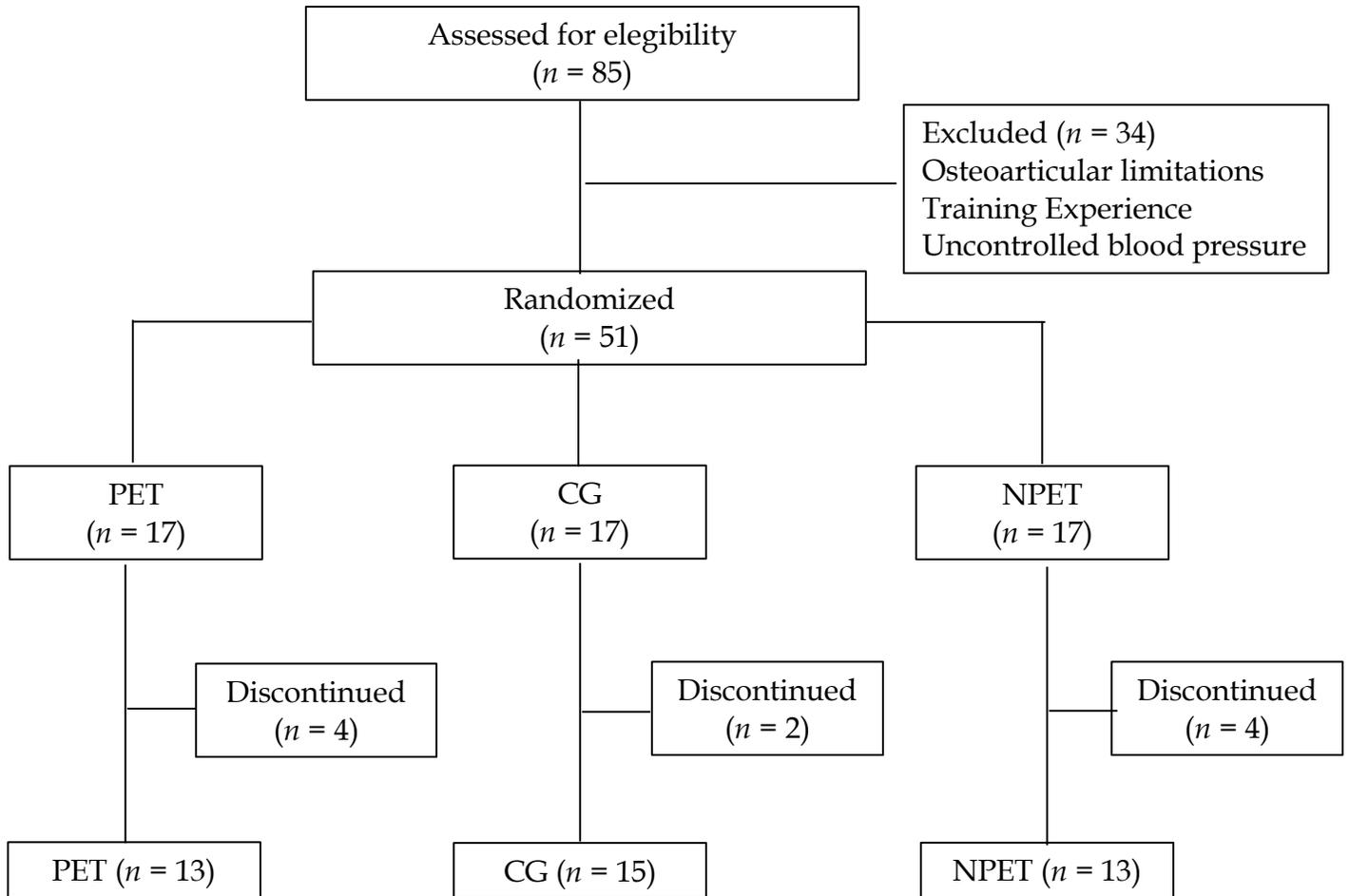


Figure 1. Flowchart of included volunteers.

The demographic data, disease status, anthropometric measurements, body composition, strength, and functional capacity are presented in Table 2. There was no significant difference between groups for variables at baseline ( $p > 0.05$ ).

Table 2. Demographic characteristics, disease status, anthropometric measurements, body composition, strength, and basic functional capacity for PET, NPER and CON groups.

Variables	PET (n = 13)	NPET (n = 13)	CG (n = 15)	p-value
Sex, M/F (n)	8/5	5/8	7/8	0.510
Age, years (mean ± sd)	38.76 ± 13.86	40.00 ± 12.18	39.80 ± 9.97	0.961
Smoker (n)	5	3	6	
Ethnic/Racial self-identification				
White	10	9	7	
Mixed* (n)	2	2	5	
Black	1	2	3	

ARV regimen				
BIOVIR+EFV (n)		1		
TDF+3TC+DTV (n)	2			
ABC+3TC+DTV (n)		1		
3TC+TDF+EFV (n)	4	5	6	
3TC+TDF+DTV (n)	1	1		
TDF+3TC+RAL (n)		1		
DRV+RTV+3TC (n)			1	
ATV+3TC+RTV (n)			1	
BIOVIR+ATV+RTV (n)		1		
TDF+3TC+ATV (n)	1	1	3	
DRV+ETV+DTV (n)		2		
TDF+3TC+DRV+RTV (n)	2		1	
ATV+RTV+AZT+3TC (n)	1			
TDF+3TC+ATV+RTV (n)	2		2	
3TC+TDF+DTV+DRV+RTV (n)			1	
Length of infection, years (mean ± SD)	11.76 ± 9.30	9.38 ± 7.05	13.40 ± 8.25	0.445
Length of ART, years (mean ± SD)	9.53 ± 8.74	9.07 ± 6.96	11.20 ± 6.62	0.729
Medical treatment				
Hypotensive (n)	4	3	4	
Hypoglycemic drugs (n)		2		
Beta-blockers (%)		1	1	
Body composition				
FFM, kg (mean ± SD)	59.42 ± 14.21	49.90 ± 9.06	49.29 ± 10.99	0.051
FM, kg (mean ± SD)	19.13 ± 8.80	18.14 ± 9.54	17.38 ± 9.02	0.880
Profile anthropometric				
BM, kg (mean ± SD)	78.35 ± 19.31	67.99 ± 12.98	66.68 ± 14.49	0.124
Height, cm (mean ± SD)	1.69 ± 0.11	1.63 ± 0.11	1.61 ± 0.12	0.202
BMI, kg/m <sup>2</sup> (mean ± SD)	27.17 ± 5.23	25.53 ± 5.37	25.50 ± 4.75	0.461
Perimeters				
Neck, cm (mean ± SD)	36.96 ± 3.18	35.03 ± 1.94	35.06 ± 2.84	0.126
Chest, cm (mean ± SD)	102.15 ± 10.49	95.84 ± 10.76	95.83 ± 10.11	0.211
Waist, cm (mean ± SD)	93.92 ± 12.15	86.76 ± 11.43	85.90 ± 10.89	0.152
Hip, cm (mean ± SD)	101.88 ± 13.94	94.80 ± 10.62	95.37 ± 10.57	0.240
Thigh R, cm (mean ± SD)	55.30 ± 8.54	54.07 ± 7.25	52.73 ± 6.86	0.669
Thigh L, cm (mean ± SD)	55.23 ± 8.66	53.84 ± 7.61	52.23 ± 6.64	0.587
Leg R, cm (mean ± SD)	37.46 ± 4.96	35.46 ± 3.35	35.50 ± 3.56	0.348
Leg L, cm (mean ± SD)	37.50 ± 4.98	35.80 ± 3.41	35.56 ± 3.59	0.409
Muscle strength				
Squat, kg (mean ± SD)	63.30 ± 27.46	51.69 ± 31.95	47.46 ± 28.68	0.356
Handgrip				
Right hand, kg (mean ± SD)	35.30 ± 11.58	28.46 ± 9.21	30.80 ± 9.78	0.234
Left hand, kg (mean ± SD)	31.92 ± 10.57	27.84 ± 8.64	28.13 ± 8.55	0.457

SPPB				
Balance (s)	-	-	-	
Gait speed test 3m, m/s (mean ± SD)	1.32 ± 0.26	1.41 ± 0.32	1.27 ± 0.25	0.393
Gait speed test, m/s (mean ± SD)	1.36 ± 0.31	1.46 ± 0.26	1.34 ± 0.25	0.521
Chair stand test, s (mean ± SD)	9.70 ± 2.32	9.39 ± 2.68	10.24 ± 2.54	0.673
SPPB, score (mean ± SD)	11.61 ± 0.76	11.69 ± 0.85	11.26 ± 1.53	0.570
TUG				
Time, s (mean ± SD)	6.51 ± 1.00	7.29 ± 0.93	6.91 ± 0.82	0.108

M: male, F: female; ART = antiretroviral therapy; PET = periodized exercise training; NPET = non-periodized exercise training; CON = control group; EFV: efavirenz; TDV: tenofovir; 3TC: lamivudine; DTV: dolutegravir; ADR: raltegravir; DRV: darunavir; RTV: ritonavir; ATV: atazanavir; ETV: etavirin; AZT: zidovudine; BM = body mass; BMI: body mass index; FFM: fat-free mass; FM: fat mass; R: right; L: left; SPPB: short physical performance battery; TUG: timed up and go; \* Mixed ("pardo" in official Portuguese)

The effects of PET and NPET after 12 weeks on anthropometric profile, body composition, muscle strength, and functional capacity are present in Table 3.

The PET and NPET groups increased FFM ( $p = 0.016$ ;  $p = 0.043$ ) and reduced FM ( $p = 0.001$ ;  $p = 0.028$ ), respectively, compared to CG.

The PET and NPET groups reduced neck circumference ( $p = 0.002$ ;  $p = 0.042$ , respectively). Only PET group reduced waist circumference compared to CG ( $p = 0.002$ ). Furthermore, PET and NPET groups increased right thigh ( $p = 0.001$ ;  $p = 0.005$ ) and left thigh ( $p = 0.001$ ;  $p = 0.004$ ) circumference, respectively, compared to CG. PET group was significantly different from NPET to increase right thigh ( $p = 0.034$ ).

The PET and NPET groups showed significant increases in lower limb muscle strength in the squat exercise compared to the CG ( $p = 0.001$ ;  $p = 0.001$ ), respectively. In addition, the PET group showed higher gains compared to the NPET group ( $p = 0.004$ ). There was a significant increase in hand grip strength in PET and NPET groups for the right side ( $p = 0.001$ ;  $p = 0.043$ ) and left side ( $p = 0.001$ ;  $p = 0.003$ ) compared to the CG, respectively.

The PET group showed a significant increase in gait speed of 3m compared to CON ( $p = 0.005$ ) with a difference of this variable compared to the NPET group ( $p = 0.018$ ). The PET and NPET groups showed reductions in sitting and rising time compared to the CON ( $p = 0.001$ ;  $p = 0.001$ ), respectively. In addition, the PET group showed a significant difference compared to the NPET group ( $p = 0.017$ ). Finally, the PET group showed significant changes in the final SPPB score compared to the CG ( $p = 0.030$ ).

**Table 3.** Effects of PET and NPET after 12 weeks on anthropometric profile, body composition, muscle strength, and functional capacity.

Variables	PET ( <i>n</i> = 13) Δ ± SD [CI]	NPET ( <i>n</i> = 13) Δ ± SD [CI]	CG ( <i>n</i> = 15) Δ ± SD [CI]	ETA <sup>2</sup>	Power
<b>Body composition</b>					
FFM (kg)	2.00 ± 2.58 [0.44; 3.57] *	1.44 ± 0.85 [0.92; 1.96] *	- 0.06 ± 0.28 [- 0.22; 0.08]	0.22	0.81
FM (kg)	- 1.66 ± 1.22 [- 2.40; -0.93] *	- 1.09 ± 1.41 [- 1.94; - 0.23] *	0.03 ± 0.35 [- 0.16; 0.22]	0.32	0.96
<b>Perimeter (mm)</b>					
Neck	- 0.69 ± 0.69 [- 1.11; 0.27] *	- 0.46 ± 0.51 [- 0.77; -0.14] *	0.06 ± 0.37 [- 0.13; 0.27]	0.29	0.92
Chest	0.03 ± 2.74 [- 1.6; 1.70]	- 1.30 ± 8.60 [- 6.50; 3.89]	0.06 ± 0.45 [- 0.18; 0.32]	0.01	0.08
Waist	- 3.15 ± 3.43 [- 5.23; - 1.07] *	- 1.00 ± 1.88 [- 2.13; 0.13]	0.43 ± 0.53 [0.13; 0.72]	0.27	0.90
Hip	0.38 ± 3.34 [- 1.63; 2.40]	0.46 ± 1.80 [-0.63; 1.55]	0.06 ± 0.51 [- 0.22; 0.34]	0.01	0.09
Thigh R	2.84 ± 1.86 [1.71; 3.97] * §	1.53 ± 1.10 [0.86; 2.20] *	- 0.06 ± 0.17 [- 0.16; 0.03]	0.50	1.00
Thigh L	2.88 ± 1.85 [1.76; 4.00] *	1.69 ± 1.47 [0.79; 2.58] *	- 0.06 ± 0.25 [- 0.20; 0.07]	0.48	1.00
Leg R	0.34 ± 0.85 [- 0.16; 0.86]	0.50 ± 0.73 [0.05; 0.94]	-	0.11	0.44
Leg L	0.38 ± 1.02 [- 0.23; 1.00]	0.46 ± 0.72 [0.02; 0.89]	-	0.08	0.35
<b>Muscle strength</b>					
Squat (kg)	57.92 ± 22.15 [44.53 - 71.30] * §	34.61 ± 19.65 [22.73 - 46.49] *	- 0.80 ± 7.97 [- 1.89 - 0.29]	0.68	1.00
<b>Handgrip</b>					
Right hand (kg)	4.46 ± 3.57 [2.30; 6.62] *	2.46 ± 3.25 [0.49; 4.42] *	- 0.33 ± 0.61 [- 0.67; 0.00]	0.39	0.99
Left hand (kg)	4.38 ± 3.59 [2.21; 6.55] *	3.07 ± 2.72 [1.43; 4.72] *	- 0.20 ± 0.56 [- 0.51; 0.11]	0.45	0.99
<b>SPPB</b>					
Balance (s)	-	-	-		
Gait speed 3m (m/s)	0.18 ± 0.19 [0.06; 0.30] §	0.00 ± 0.17 [- 0.09; 0.11]	- 0.00 ± 0.03 [- 0.02; 0.01]	0.26	0.89
Gait speed 4m (m/s)	0.12 ± 0.28 [- 0.05; 0.29]	0.02 ± 0.16 [- 0.07; 0.12]	- 0.02 ± 0.06 [- 0.06; 0.00]	0.11	0.45
Chair stand (s)	- 3.86 ± 2.14 [- 5.16; - 2.57] * §	- 2.34 ± 1.80 [- 3.43; - 1.25] *	0.20 ± 0.22 [0.08; 0.32]	0.71	1.00
SPPB (score)	0.38 ± 0.76 [- 0.07; 0.84] *	0.23 ± 0.59 [- 0.13; 0.59]	-	0.17	0.67
<b>TUG (s)</b>					
Time	- 0.89 ± 0.66 [- 1.29; - 0.49] *	-1.15 ± 0.87 [- 1.68; - 0.61] *	0.29 ± 0.56 [- 0.02; 0.60]	0.53	1.00

PET = periodized exercise training; NPET = non-periodized exercise training; CON = control group; FFM: fat-free mass; FM: fat mass; R: right; L: left; SPPB: short physical performance battery; TUG: timed up and go. \* Difference between the control; § Difference between protocols

## DISCUSSION

The study aimed to investigate the effects of PET and NPET on muscle strength, functional capacity, body composition, and anthropometric profile in PLHIV. The results show that both protocols enhance these variables, however, the PET showed better results in increasing muscle strength and reduce the waist circumference (WC), time in the chair stand test, and gait speed test 3 meters compared to NPET.

In the present study, both training protocols were effective in increasing FFM and reducing FM. These findings are clinically relevant as the number of people aging with HIV is increasing, with negative implications on lean mass with advanced age, which is associated with accelerated progression of HIV infection and morbidity and mortality in this population (28). In addition, PLHIV presents a high prevalence and risk of sarcopenia (5, 20). Our previous study using the combined training protocol showed results in line with the present study in ameliorating body composition in PVHIV (37). Thus, an exercise training program should be an integral part of PLHIV care in combating morphophysiological changes caused by infection and the use of ART. Has been reported that PLHIV presents lower muscle strength compared to non-HIV people. The present study found a significant increase in muscle strength (squat and handgrip) in the PET and NPET groups, in agreement with previous studies that showed increases in muscle strength after exercise training programs (16, 19, 36). In addition, the current study corroborates previous studies that showed greater gains in muscle strength in the PET group compared to NPET, demonstrating that both the manipulation of volume and intensity variables and the high load presented in this protocol (90% 1RM) seem to be vital to promote additional strength gains (4, 6, 31, 35). It is noteworthy that our intervention lasted 12 weeks, as were two of the other studies mentioned above (36, 4). The others lasted 24 weeks (16) and a meta-analysis included 6–24 week intervention studies (19). Study length has been associated with larger improvements in maximal strength, although a majority of the studies in this scenario are less than 16 weeks in duration (35). Thus, PET can be prescribed to optimize muscle strength gains in PLHIV, since this variable is independently associated with all-cause mortality (10, 33). It is common that PLHIV under ART present with morphological alterations such as lower limb fat reduction and trunk fat accumulation. In the present study, a reduction in WC was observed only in the PET group compared to the NPET. Changes in WC have been reported in previous studies after an exercise training program, promoting positive changes in body composition in PLHIV (16, 37).

Although Zanetti's study reported periodization as an effective strategy for anthropometric changes in PLHIV, it did not highlight the superiority of this strategy compared to NPET<sup>18</sup>. The study by Bhagwat et al, 2017 showed that WC is a reliable and affordable measure for assessing visceral adipose tissue in PLHIV (1). Considering that WC is a predictor of CVD, PET may be prescribed for PLHIV to control such parameters in the short term (12 weeks), as approximately 70% of PLHIV under ART had abdominal lipohypertrophy. (17). In addition, total trunk and limb fat gain remain faster in PLHIV compared to long-term non-HIV people, impairing physical function in this population (11). Thus, WC can be a practical and easily accessible

measure included in outpatient care, helping to monitor and manage patients with abdominal obesity to reduce the risk of CVD in this population.

HIV infection and poor physical performance (SPPB  $\leq 10$ ) are independently associated with increased mortality. In addition, poorly performing PLHIV have a six-fold increased risk of mortality when compared to non-HIV people with high physical performance (SPPB  $\geq 10$ ) (12). In the present study, by evaluating the SPPB domains separately, the PET group was more efficient in the CST ( $p = 0.017$ ) and GST3M ( $p = 0.018$ ) compared to the NPET. It has been reported that increases in walking speed of 0.10 m/s have been shown to represent substantial changes, and increases of 0.5 in the final SPPB score to clinical changes (2). Whereas PLHIV has a faster decline in gait speed (24) and takes a longer time to perform the CST in SPPB compared to non-HIV people ( $p = 0.047$ ) (37), the results of the present study demonstrated that the speed of 3m and 4m gait were increased in 0.18 m/s and 0.12 m/s, respectively, resulting in  $0.38 \pm 0.76$  in the final SPPB score compared to the CON ( $p = 0.030$ ). Thus, PET seems to be a more efficient strategy for increasing functional capacity in PLHIV, reducing all-cause mortality and over the next 5 years (12).

It is known that in the first weeks of training there is a substantial increase in muscle strength due to several factors, such as musculotendinous stiffness, motor unit recruitment, coding rate, motor unit synchronization, and neuromuscular inhibition (4). It has been shown that high-intensity training can mitigate the symptoms of fatigue, insomnia, pain, sadness, and anxiety experienced by PLHIV (34). However, training always performed at high intensity can generate accumulated fatigue throughout the week and enhance the immunology window by the "J" curve. (7). Thus, variation in stimuli plays a critical role to prevent stagnation. Since there is still no cure for HIV and ART treatment should be maintained, periodization of training is an interesting strategy in the treatment of PLHIV due to significant improvements in strength, functional capacity, and anthropometric profile, in addition to the varied stimuli that may contribute to increasing practice adherence in this population. Thus, the present study suggests that PET is a strategy that should be used at the clinical level in order to optimize adaptations of PLHIV training.

The strengths of the present study include its rigorous RCT methodology (treatment allocation, randomization, adequate sample size to achieve power, and blinding) and low dropout rate. On the other hand, the study's small sample size may have affected the statistical power of our analyses. Additionally, the present study did not control the participants' diet and could, to some extent, influence the results. However, all participants were instructed to maintain their usual diet throughout the intervention period. Furthermore, based on the data presented, the use of PET may be a more efficient strategy than NPET for the treatment of PLHIV. Future studies should be designed with a longer duration of intervention ( $> 12$  weeks) in order to confirm the data presented here. Another future direction would be to recruit resistance-trained PLHIV for experimentation ( $> 6$  months) in order to observe the effects of periodization on muscle strength and other variables. In addition, future studies may benefit from more sensitive methods for body composition analysis (MRI, DEXA, CT).

We conclude that both exercise training periodization were effective to improve body composition and functional outcomes however it seems that PET presents better results compared to NPET in PLHIV. These results should be interpreted with caution once all volunteers were clinical stable and using ART.

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