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Original Research

Effect of a 12-Week Mixed Training on Body Quality in People Living with HIV: Does Age and HIV Duration Matter?

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Abstract

BACKGROUND: The impact of HIV duration on exercise adaptations has not yet been studied. Moreover, the age at which subjects living with HIV are the most responsive to exercise is not clear.
AIMS: Investigate the effect of a mixed exercise training program on physical performance changes in individuals living with HIV and explore if age or HIV duration influence these adaptations in men.
METHODS: In this feasibility study, participants followed a 12-week mixed exercise training program, three times/week, 45 min/session. Physical performance including functional capacities (normal 4-m walking test, 6min walking test), grip strength (hand dynamometer), muscle power, body composition (android and gynoid fat masses, appendicular lean mass) were evaluated pre- and post-intervention. Subgroup analysis according to the median age of the participants (age<50yrs vs. age≥50yrs) and median HIV duration (HIV<20yrs vs. HIV≥20yrs) were performed in men.
RESULTS: A total of 27 participants (age: 54.5±6.8yrs, men: 85%; HIV duration: 19.3±7.6yrs) were included. At the end of the intervention, significant increases compared to baseline were seen in grip strength (p=0.017), leg power (p<0.001), normal walking speed (p<0.001) and 6-min walking distance (p=0.003). Following the intervention, parameters improved similarly in both age groups. However improvement was greater in those with HIV>20yrs than those with a shorter infection duration, with change (%) on total (p<0.001), android (p=0.02), and gynoid (p=0.05) fat masses as well as appendicular lean mass index (p=0.03).
CONCLUSION: Mixed exercise training seems to be an effective intervention to improve physical performance in individuals living with HIV. In addition, this study suggests that neither age nor HIV duration has influence on the effect of mixed training in this population.

Key words: HIV, mixed training, body composition, muscle strength, physical capacities, body composition, older adults.

Introduction

The concept of "successful aging" includes the ability to maintain functional status and independence despite accruing disease burden (1). However, the normal aging process is associated with an increase in fat mass (FM) and a decrease in lean body mass (LBM) and bone mineral density (BMD), leading to a decline in muscle function and functional capacity (2).

Human immunodeficiency virus (HIV) infection seems to accelerate the health-related consequences of aging and perhaps the aging process itself (3). Geriatric syndromes are more prevalent among persons living with HIV, even in middle age, and these conditions are associated with functional decline (4). The prevalence of frailty and associated deaths are higher among persons living with HIV (5). Guaraldi et al. observed that frailty prevalence presented a 3-fold increase among older people (75 years and older) living with HIV, compared to people living without HIV (6). Therefore, functional and physical complications of aging were identified as a priority area in HIV (7).

Osteoporosis is also common in chronic HIV infection. Persons living with HIV have several risk factors for low BMD and fracture, both traditional (tobacco use, alcohol abuse, hypogonadism, exposure to trauma and low body mass index (BMI)) and HIV-related (antiretroviral therapy, chronic inflammation and comorbidities) (8). HIV also reduces muscle mass, strength and function (i.e., leads to sarcopenia) (9). A recent cross-sectional study reports that the prevalence of sarcopenia was 12% among people living with HIV aged 50 years or older and that sarcopenic subjects had more fragility vertebral fractures and a tendency towards a higher frequency of multiple vertebral fractures when compared with non-sarcopenic subjects (44.4% vs. 16.2%, p = 0.066). Finally, the proportion of overweight and obese persons with HIV has increased since the introduction of antiretroviral therapy (10). HIV and antiretroviral therapy may contribute to fat gain in treated HIV infection, particularly the development of visceral adiposity (11). As HIV accelerates the physical aging process, identifying specific interventions to counteract these phenomena is important.

It is well known that physical activity, whether it be a lifelong habit or as an intervention, is important to counter the harmful effects of aging (12, 13). Growing evidence suggests that mixed training (i.e. aerobic training combined with resistance training) induces promising results in various populations. Specific to the population living with HIV, a systematic review including 7 individuals studies concluded that combined aerobic and resistance training improves

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physical health (14). Effectively, all strength, cardiovascular, and flexibility outcome measures associated with these interventions demonstrated a significant improvement ($p \leq .05$) in the intervention group as compared to control group participants (15-21). The duration of the interventions ranged between 6 weeks (17) and 6 months (19, 20) while the number of participants varied from 25 (16) and 198 (21). The majority of these studies included both men and women while Dudgeon et al. included only men (17) and Dolan et al. focused only on women (15).

However, more work is needed: First, the impact of HIV and more specifically HIV duration (biological aging) on exercise adaptations has not yet been studied. Second, the age at which HIV-positive subjects are the most responsive to exercise is not clear. This is important to increase physical function and therefore quality of life in individuals with HIV through exercise intervention. Thus, this sub-study explore the potential effects of a 12-week mixed training program (high Intensity Interval training (HIIT) + power training (PT)) on physical performance among middle-aged adults with HIV. This study also aimed to explore if the exercise adaptations in HIV are related to chronological age or duration of HIV infection.

Methods

Study Design

A single arm feasibility interventional study was conducted within an ongoing larger multiple RCT project described elsewhere (22). In the present feasibility study, participants agreed to participate in the exercise arm. The Consolidated Standards of Reporting Trials (CONSORT) guidelines for pilot and feasibility studies were followed (23). The ethics approval was obtained from the McGill University Health Centre (MUHC) and from the research ethics review committee at the Université du Québec à Montréal (UQAM). All participants gave written informed consent.

Participants

Eligibility Criteria

The eligibility criteria have been described previously (22, 24). To be included, participants had 1) to be HIV+ for at least 1 year; 2) to be aged ≥35 years; 3) to be mostly sedentary (moderate level of PA of 30 min duration less than twice a week); 4) to have limitations in performing vigorous activities, walking a kilometer, or climbing stairs and; 5) to communicate adequately in either French or English. Participants were excluded if 1) they had exercise contraindication for exercise from cardiovascular or musculoskeletal co-morbidity as determined by the medical history or by Physical Activities Readiness Questionnaire (PAR-Q) (25).

Groups

Out of those deemed eligible, 64 participants showed interest in the exercise program. Forty-one participants went through baseline evaluation and 32 took part in the exercise program. To answer the main objective of this study, all participants who completed the intervention were included (per-protocol analysis; n=27). Participants needed to complete 80% or more of their training sessions to be included in the analysis. The 5 dropouts were due to change in availability (n=1); sickness (n=3) and an ankle fracture unrelated to the intervention (n=1).

To explore the secondary objectives, only men (n=23/27; 85%) were included to avoid sex bias and divided a-posteriori according to the median age and the median HIV duration, as follows:

- Age group: <50 yrs old (n= 11) vs ≥50yrs old (n= 12)
- HIV duration: <20 yrs (n= 9) vs ≥20yrs (n= 14)

Intervention

We conducted a 12-week mixed exercise intervention, including aerobic (HIIT) and resistance (power) exercises delivered 3 times per week on non-consecutive days (45 minutes per session). All sessions were supervised by the same trained professionals (i.e. kinesiologist or physiotherapist) at UQAM facilities to ensure safety, adherence and adequate supervision (e.g. monitoring, weight load, intensity, etc.). Training was conducted in a group setting, including 4-5 participants in each session. Participants received an honorarium of $103 to offset transportation costs and time spent in the evaluation.

The HIIT was performed using elliptical device, to reduce lower extremity joint impact, lasting 21 minutes (26) including a 3-minut warm-up and cool down (60% to 65% of maximum heart rate (MHR)). The interval program lasted around 15 min with 15 s bursts of exercise at an intensity of 80-85% of MHR (Borg' scale > 17) followed by 1 min and 30 s of active recovery.

Power training for major muscle groups (hamstrings, pectorals, quadriceps and latissimus dorsi) at tempo: 1–0–2–0 (i.e. 1-s concentric, 0-s isometric, 2-s eccentric) was carried out with weight machines and lasted 24 minutes, included 2 sets of 12 repetitions. The resistance was set at 80% of the one-repetition maximum (1RM).

Measures

Socio-demographic characteristics of the participants were obtained from the main study (22). In addition, the following physical measurements were administered at baseline and after the 12-week intervention:

Body composition

Dual-energy X-ray absorptiometry (DXA; GE Prodigy Lunar) was used to measure lean body masses [LBM (kg); total, arms, legs and appendicular (arm + leg)], fat masses [FM (%): total, android and gynoid] and BMD [(g/cm^3): total, hip and spine] (27). In addition, appendicular muscle mass index was expressed using the following and validated equation usually used to assess sarcopenia in community-dwelling older adults: appendicular lean mass (kg)/ height (m^2) (28).

Peripheral quantitative computed Tomography (pQCT)

Peripheral Quantitative Computed Tomography (pQCT) scan of the right leg was obtained using the Stratec XCT3000 (STRATEC Medizintechnik GmbH) at the 33% distance of the femur, measured from the lateral epicondyle to the greater trochanter. Soft tissue and bone area and density were defined according to the following tissue thresholds: 200.0000 (i.e. Separates bone from soft-tissue. Pixels ≥ the threshold are considered soft-tissue), 550.0000 and 690.0000. Bone (cortical and trabecular aeras, bone marrow density, cortical density, total bone density, bone torsion strength, bone compressive strength and bone strength index), muscular (lean muscle area) and adipose tissue (total, subcutaneous and intramuscular adipose tissue area) thresholds were defined based on parameters of a previous study (31) and results were all provided automatically in the ImageJ analysis output.

Muscle function

Muscle strength and power are considered to be main predictors of functional capacity decline and loss of mobility and autonomy (2, 32). Grip Strength: Maximum voluntary upper limb muscle strength was measured using Jamar dynamometer, as described elsewhere (27, 33). Lower limb muscle power: It was measured with Nottingham Leg Extensor Power rig (43) using the protocol described by our team in a recent publication (27).

Physical capacities

Six-Minute Walk Test (6MWT): walking endurance was determined using the 6MWT. The American Thoracic Society guidelines were followed (31).

Walking speed: Normal (i.e. walking at comfortable speed) gait speed was measured using instrumented walkaway system (GAITRite®) (38). The time taken (in seconds) to complete the 4 meters was measured (27).

Statistical analysis

Baseline characteristics were summarized using descriptive statistics. Continuous variables were presented as mean ± standard deviation. Categorical variables were reported as frequencies and percentages. Data distributions were tested using the Kolmogorov test. In accordance to the main objective, effects on physical capacities (6MWT and walking speed), body composition and muscle function following the 12-week intervention (pre vs. post) were estimated using a paired t-test. To meet secondary objectives, subgroup analysis were performed in men. First, subjects were divided a-posteriori in 2 groups according to their median HIV duration (0: <20yrs vs. 1:≥ 20yrs). Then, subjects were divided a-posteriori in 2 groups according to their median age (i.e. 50 years old). Independent t-tests or Fisher tests were used to compare the baseline characteristics between these groups. Paired t-tests were used to compare the intervention effect within group. All statistical analyses were performed using SPSS 25.0 (Chicago, IL, USA) and Statistica 10. A p-value ≤ 0.05 was considered statistically significant.

Results

Participants (n=27) who completed the intervention were 54.5 ± 6.86 years old, were mostly men (85%) and had been living with HIV on for 19.3 ± 7.62 years. Baseline characteristics of the population are presented in Table 1.

Table 1. Baseline characteristics of the population (n=27)

Characteristics	Mean ± SD or N (%)
Age (years)	54.4 ± 6.86
Gender : men / women	23 (85.0%) / 4 (15.0%)
Employment status	
Employed	7 (25.9%)
Unemployed	10 (37.0%)
Disability/Retired/Other	10 (37.0%)
Years since HIV diagnosis	19.3 ± 7.62
Current smoker : Yes / No	5 (18.5%) / 21 (80.7%)

Effects of the intervention on physical performance and body composition & quality

At the end of the 12-week intervention, the following physical parameters had improved significantly compared to baseline: grip strength (kg, PRE: 37.2±67.9 vs. POST: 37.9±8.8, p=0.017), leg power (W, PRE: 204±84 vs. POST: 240±88, p<0.001), walking speed (m/s, PRE: 1.29±0.29 vs. POST: 1.57±0.22, p<0.001), and distance traveled during the 6-min walking test (m, PRE: 613±57.5 vs. POST: 632±55.2, p=0.003) (Table 2). However, no improvement in body composition or quality has been observed (p>0.05 for all the parameters) during the intervention (Table 2).

Effects of the intervention on physical performance and body composition & quality according to the age of the participants

The 23 men with HIV who completed this interventional study were divided in 2 groups according to their median age (i.e. 50 yrs): group <50yrs: n=11, 48.5±3.9 years and group ≥50 yrs: n=12, 59.8±5.4 years. At baseline, both groups were

Table 2. Effects of a 12-week mixed training program on functional capacities in people living with HIV (n=27)

Characteristics	PRE	POST	p-value	Delta change (%)
Physical parameters				
BMI (kg/m²)	25.7 ± 4.1	25.7 ± 3.8	0.76	0.05 ± 0.89
Normal walking speed (m/s)	1.29 ± 0.29	1.57 ± 0.22	<0.0001	0.27± 0.28
Grip strength (kg)	37.2 ± 7.9	37.9 ± 8.2	0.017	0.69 ± 1.41
Leg Power (W)	204 ± 84	240 ± 88	<0.0001	36.3 ± 42.3
6MWT (m)	613 ± 57	632 ± 55	0.003	19.0 ± 19.5
Body composition				
Total FM (%)	24.5 ± 11.2	23.9 ± 11.1	0.08	0.57 ± 1.67
Android FM (%)	33.5 ± 12.6	33.1 ± 12.5	0.24	0.42 ± 2.32
Gynoid FM (%)	26.8 ± 13.7	26.7 ± 13.6	0.92	0.10 ± 2.32
LBM (kg)	52.8 ± 7.3	53.4 ± 7.5	0.25	0.62 ± 1.47
AMMi (km/m²)	8.76 ± 1.12	8.79 ± 1.11	0.43	0.004 ± 0.029
Total aeral BMD (g/cm³)	1.18 ± 0.12	1.18 ± 0.11	0.43	0.004 ± 0.029
Hip BMD (g/cm³)	1.08 ± 0.17	1.09 ± 0.17	0.65	0.005 ± 0.031
Spine BMD (g/cm³)	1.09 ± 0.19	1.08 ± 0.19	0.65	0.008 ± 0.05
Peripheral quantitative computed tomography				
Lean muscle area (%)	139 ± 23	141 ± 29	0.53	5.42 ± -0.54
Total Fat Area (%)	34.9 ± 24.5	32.4 ± 23.2	0.17	2.49 ± 9.29
Total subcutaneous fat area (%)	4.38 ± 3.37	3.66 ± 2.79	0.14	1.82 ± 1.35
Intra muscular (%)	139.5 ± 22.9	141.4 ± 29.4	0.53	5.42 ± -0.54
Cortical area (mm²)	435.5 ± 46.6	429.7 ± 54.8	0.43	30.8 ± 36.5
Trabecular area (mm²)	601.9 ± 86.1	601.1 ± 83.7	0.83	9.18 ± 56.5
Bone marrow density (mg/cm³)	31.1 ± 7.83	29.8 ± 8.28	0.51	1.19 ± 9.18
Cortical density (mg/cm³)	1102.7 ± 35.9	1104.4 ± 33.6	0.49	-1.70 ± 12.3
Total volumetric BMD (mg/cm³)	788.7 ± 75.5	805.8 ± 61.2	0.16	-17.1 ± 60.3
Bone torsion strength (mm⁴)	55795± 13440	55209±13777	0.34	585.9 ± 3054
Bone compressive strength (mm²)	2896.6 ±569.0	2916.9±570.6	0.65	29.1 ± 346.9
Bone strength index (g²/cm⁴)	4.04 ± 0.77	3.96 ± 0.79	0.53	0.08 ±0.63

Legend : Data are presented as means ± SD. p≤0.05: significant. Intra-group differences between pre and post intervention assessed using paired t-test. Delta change = % of change between POST and PRE (POST-PRE / PRE)*100)); BMI= Body Mass Index ; 6MWT= 6 Minute Walking Test ; FM= Fat Mass ; LBM= Lean Body Mass ; AMMi= Appendiular Muscle Mass Index ; BMD= Bone Mineral Density.

comparable excepted for age (by design, p<0.0001) and grip strength (0: 40.8±8.77 vs. 1: 38.5±4.91, p=0.008).

Among participants aged <50 years old, we observed, at the end of the intervention, a significant increase in normal walking speed (p<0.001), leg power (p=0.03), 6MWT (p=0.03) and total lean body mass (p=0.03). Among participants aged ≥ 50 years old, we observed a significant increase in normal walking speed (p<0.001), grip strength (p=0.003) as well as a significant decrease in android fat mass (p=0.007) (Table 3). No significant differences between groups were observed with regard to the evolution of the outcomes following the intervention (Table 3).

Effects of the intervention on physical performance and body composition & quality according to HIV duration

Twenty-three men completed the exercise intervention and were divided a-posteriori in 2 groups according to their median HIV duration (group <20yrs: n=9; HIV duration: 12.2±4.7yrs) vs. group ≥ 20yrs: n=14; HIV duration: 24.7±6.3yrs). Surprisingly, even if no difference in chronological age was observed (<20yrs: 51.6±6.4yrs vs. ≥20yrs: 54.9±5.3yrs), the HIV<20 yrs group had significantly lower grip strength (Kg, <20yrs: 34.4±6.9 vs. ≥20yrs: 41.1±8.1, p=0.039) and leg power (W, (<20yrs: 169±65 vs. >20yrs: 239±93, p=0.04) but also higher appendicular FM (%, <20yrs: 53±19 vs. >20yrs: 35±22, p=0.038) and gynoid FM (%, <20yrs: 34±10 vs. ≥20yrs: 22±14, p=0.035) than HIV≥20 group at baseline.

Table 3. Effects of a 12-week mixed training program on physical performance and body composition & quality in men living with HIV, according to their age (n=23)

	<50 yrs group (n=11)				**≥ 50 yrs group (n=12)**				
				Physical parameters					
Variables	**PRE**	**POST**	**Delta change (%)**	**p-value intra-group**	**PRE**	**POST**	**Delta change (%)**	**p-value**	**p-value inter-group**
BMI (kg/m^2)	25.8 ± 4.42	25.9 ± 4.03	0.85 ± 3.40	0.58	24.9 ± 4.30	24.9 ± 4.06	0.10 ± 4.06	0.91	0.64
Normal walking speed (m/s)	1.22 ± 0.32	2.54 ± 0.32	41.7 ± 54.3	<0.001	1.36 ± 0.25	2.63 ± 0.28	41.8 ± 54.2	<0.001	0.12
Grip strength (kg)	40.8 ± 8.77	41.9 ± 9.19	2.76 ± 6.38	0.25	38.5 ± 4.91	40.42 ±5.21	5.04 ± 4.67	0.003	0.81
Leg Power (kg)	241 ± 87.8	278.1 ± 95.3	22.5 ± 25.2	0.03	200.4 ± 69.7	219.9 ±66.4	18.4 ± 29.7	0.32	0.87
6MWT (m)	634.9 ± 50.2	658.4 ± 57.2	3.73 ± 4.75	0.03	620.8 ± 50.5	629.8 ± 41.7	1.65 ± 4.92	0.15	0.85
				Body composition					
Total FM (%)	23.2 ± 8.9	22.5 ± 8.37	1.54 ± 5.53	0.22	19.9 ± 9.85	19.0 ± 8.71	1.48 ± 11.7	0.09	0.21
Android FM (%)	32.6 ± 10.7	36.3 ±8.01	0.36 ± 8.04	0.35	29.5 ± 13.3	27.5 ± 19.5	0.27 ± 19.5	0.007	0.45
Gynoid FM (%)	26.8 ± 10.1	26.3± 9.71	1.91 ± 6.29	0.45	19.8 ± 11.1	19.4 ± 9.74	1.56 ± 13.5	0.65	0.30
LBM (kg)	53.6± 8.83	54.5 ±6.13	1.61 ± 1.65	0.03	55.9 ± 6.01	56.5 ± 5.86	1.18 ± 3.43	0.31	0.22
AMMI (kg/m^2)	8.83 ± 0.75	8.76 ±0.67	1.39 ± 2.26	0.14	9.32 ± 0.95	9.44 ± 0.84	0.08 ± 3.94	0.99	0.30
Total aeral BMD (g/cm^3)	1.15 ± 0.09	1.15 ± 0.09	0.59 ± 1.62	0.35	1.22 ± 0.13	1.21 ± 0.13	0.35 ± 2.84	0.62	0.12
Hip BMD (g/cm^3)	0.91 ± 0.12	0.91 ± 0.13	0.64 ± 3.54	0.55	1.05 ± 0.17	1.08 ± 0.18	3.21 ± 5.64	0.09	0.28
Spine BMD (g/cm^3)	1.04 ± 0.16	1.04 ± 0.16	0.11 ± 4.09	0.99	1.16 ± 0.20	1.14 ± 0.23	1.37 ± 4.85	0.45	0.41
				Peripheral quantitative computed tomography					
Lean muscle area (cm^2)	137.6 ± 17.7	142.9 ±26.7	8.59 ± 31.9	0.35	141.2 ± 2701	146.7 ± 33.9	0.79 ± 10.6	0.26	0.15
Total Fat Area (cm^2)	57.5 ± 29.6	52.9 ± 27.2	7.92 ± 37.6	0.17	39.8 ± 25.6	37.5 ± 25.6	8.46 ± 21	0.36	0.65
Total subcutaneous fat area (cm^2)	43.3 ±26.3	39.9 ± 24.4	13.5 ± 32.4	0.33	27.8 ± 21.4	26.1 ± 20.9	5.49 ± 13.3	0.50	0.22
Intra muscular fat area (cm^2)	4.61 ± 3.57	3.88 ± 1.98	8.54 ± 80.9	0.44	4.18 ± 3.36	3.48 ± 3.40	8.54 ± 80.9	0.31	0.38
Intra muscular (%)	141.9 ± 19.1	142.9 ± 26.7	7.91 ± 37.6	0.85	145.4 ± 28.8	146.8 ± 33.9	8.46 ± 21.1	0.76	0.12
Cortical area (mm^2)	437.3 ± 51.6	426.9 ± 53.5	11.2 ± 29.7	0.13	446.4 ± 43.3	443.1 ± 59.7	11.2 ± 29.7	0.83	0.24
Trabecular area (mm^2)	610.4 ± 83.4	611.2 ± 85.6	8.96 ± 30.3	0.88	618.4 ± 88.2	615.6 ± 81.3	8.96 ± 30.3	0.51	0.06
Bone marrow density (mg/cm^3)	30.8 ± 6.49	27.5 ± 6.37	15.4 ± 9.79	31.1 ± 10.2	15.4 ± 37.7	0.70	0.80		
Cortical density (mg/cm^3)	1091 ± 31.4	1092 ± 28.9	8.97 ± 30.2	0.74	1112 ± 35.2	11114 ± 34.5	8.97 ± 30.2	0.65	0.05
Total volumetric bone density (mg/cm^3)	762.9 ± 93.3	785.9 ± 70.5	5.52 ± 33.1	0.38	812.8 ± 51.3	827.8 ± 55.8	5.53 ± 33.2	0.22	0.09
Bone torsion strength (mm^4)	2897 ± 436.7	2955 ± 500.6	7.18 ± 31.7	0.46	3052.7 ± 653.9	3038.6 ± 619.4	0.06 ± 7.53	0.85	0.08
Bone compressive strength (mm^2)	57478 ±13231	56369 ±13830	10.3 ± 31.1	0.15	58265 ±13410	57928 ±13733	0.43 ± 6.65	0.78	0.19
Bone strength index (g^2/cm^4)	6092 ±1168	6035 ± 1362	10.9 ± 29.7	0.58	6338.8 ± 1515	6320 ± 1494	0.06 ± 6.44	0.89	0.11

Legend : Data are presented as means ± SD. p≤0.05: significant. Delta change = % of change between POST and PRE (POST-PRE / PRE)*100)). BMI= Body Mass Index ; 6MWT= 6 Minute Walking Test ; FM= Fat Mass ; LBM= Lean Body Mass ; AMMi= Appendiular Muscle Mass Index ; BMD= Bone Mineral Density.

Following the intervention, normal walking speed (p<0.0001), leg power (p=0.02), 6MWT (p=0.05), total fat mass (p=0.03), total lean body mass (p=0.04) improved significantly in the HIV duration <20 years group. Moreover, in this group, we observed an increase in some body quality parameters: cortical bone aera (p<0.0001), trabecular bone aera (p<0.0001), cortical BMD (p=0.015), torsion strength index (p<0.0001), compressive strength index (p<0.0001) and bone strength index (p<0.0001). Following the intervention, the HIV duration ≥20 years group showed a significant improvement in normal walking speed (p<0.0001), grip strength (p=0.04), leg power (p=0.02), but also in the following body quality parameters: trabecular bone aera (p<0.0001), bone marrow density (p=0.12), cortical BMD (p<0.0001), total volumetric BMD (p=0.001), torsion strength index (p<0.0001), compressive strength index (p<0.0001) and bone strength index (p<0.0001) (Table 4).

In addition, HIV <20 yrs group showed a higher decrease in total FM% (p=0.006), android FM (p=0.02), gynoid FM (p=0.05) and a higher improvement in appendicular muscle mass index (p=0.03), compared to the HIV ≥20 yrs group. However, no significant delta change difference between groups was observed for functional capacity or muscle quality (Table 4).

Discussion

This feasibility study suggests that mixed exercise training (i.e. HIIT combined with PT) in middle aged and older adults living with HIV improves functional capacities but not body composition and quality. Moreover, the age of the participants does not seem to influence the adaptations following a 12-week mixed training in men living with HIV. Nevertheless, the results highlight that the changes of body composition (i.e. FM, android FM, gynoid FM and appendicular lean mass) after mixed exercise training seems influenced by HIV duration. This result should be interpreted with caution since the two groups

Table 4. Effects of a 12-week mixed training program on physical performance and body composition & quality in men living with HIV, according to the HIV duration (n=23)

	HIV < 20 yrs group (n=9)				HIV ≥ 20yrs group (n=14)				
Physical parameters									
Variables	**PRE**	**POST**	**Delta change (%)**	**p-value intra-group**	**PRE**	**POST**	**Delta change (%)**	**p-value**	**p-value inter-group**
BMI (kg/m^2)	25.9 ± 3.42	25.8 ± 3.17	0.45 ± 3.02	0.77	25.1 ± 4.85	25.2 ± 4.53	1.38 ± 4.16	0.59	0.42
Normal walking speed (m/s)	1.32 ± 0.35	2.40 ± 0.25	34.6 ± 50.5	<0.0001	1.28 ± 0.26	2.70 ± 0.28	21.2 ± 24.2	<0.0001	0.25
Grip strength (kg)	36.4 ± 6.46	37.8 ± 7.17	5.28 ± 5.82	0.07	41.6 ± 6.69	43.3 ± 6.67	3.75 ± 6.16	0.04	0.62
Leg Power (kg)	185.1 ± 66.0	230.0 ± 7 9.3	32.9 ± 29.1	0.02	242.6 ±81.9	2473.1 ± 85.5	16.5 ± 23.1	0.02	0.52
6MWT(m)	615.4 ± 52.1	634 ± 53.6	4.35 ± 4.34	0.05	635.3 ± 48.5	649.6 ± 49.8	1.89 ± 4.99	0.15	0.77
Body composition									
Total FM (%)	26.7 ± 6.18	25.3 ± 5.69	3.99 ± 4.35	0.03	16.4 ± 9.24	16.1 ± 8.45	3.21 ± 12.4	0.50	0.006
Android FM (%)	37.2 ± 5.86	35.8 ± 6.89	3.24 ± 5.05	0.09	25.0 ± 13.5	24.8 ± 12.5	6.56 ± 21.4	0.75	0.02
Gynoid FM (%)	30.4 ± 8.04	29.1 ± 6.85	1.95 ± 7.32	0.17	15.8 ± 8.48	16.2 ± 8.58	3.97 ± 13.3	0.53	0.05
LBM (kg)	52.4± 5.33	53.6 ± 5.61	1.62 ± 2.16	0.04	57.1 ± 5.79	57.6 ± 5.77	0.62 ± 3.61	0.42	0.21
AMMI (kg/m^2)	8.69 ± 0.68	8.78 ± 0.69	1.14 ± 2.19	0.24	9.49 ± 0.93	9.49 ±0.82	0.67 ± 4.90	0.96	0.03
Total aeral BMD (g/cm^3)	1.20 ± 0.09	1.19 ± 0.09	0.39 ± 2.22	0.22	1.18 ± 0.15	1.18 ± 0.14	0.48 ± 2.70	0.91	0.63
Hip BMD (g/cm^3)	1.00 ± 0.15	1.03 ± 0.16	1.89 ± 5.14	0.17	0.97 ± 0.19	0.99 ± 0.20	0.36 ± 2.34	0.31	0.24
Spine BMD (g/cm^3)	1.11 ± 0.16	1.12 ± 0.18	0.095 ± 4.30	0.43	1.10 ± 0.23	1.07 ± 0.22	1.59 ± 4.87	0.16	0.61
Peripheral quantitative computed tomography									
Lean muscle area (cm^2)	129.6 ± 15.1	135.6 ± 22.3	3.36 ±31.1	0.09	145.1 ± 25.1	144.7 ±3.1	0.98 ± 11.1	0.94	0.55
Total Fat Area (cm^2)	60.3 ± 25.1	58.3 ±26.5	12.5 ± 28.8	0.42	40.7 ± 28.3	36.6 ± 24.5	5.44 ± 17.9	0.15	0.09
Total subcutaneous fat area (cm^2)	45.9 ± 21.9	45.0 ± 22.6	11.1 ± 29.5	0.63	28.5 ± 24.3	25.1 ± 20.9	1.85 ± 29.3	0.27	0.33
Intra muscular fat area (cm^2)	4.96 ± 2.73	4.09 ±3.37	24.8 ± 60.2	0.24	4.04 ± 3.73	3.41 ±2.51	21.1 ± 88.8	0.42	0.26
Intra muscular (%)	134.6 ±16.9	139.7 ±24.3	8.19 ±34.9	0.13	149.1 ±26.8	148.1 ±33.6	0.81 ±12.2	0.84	0.35
Cortical area (mm^2)	436 ± 56.2	433.9 ± 63.6	11.7 ±33.3	<0.0001	445.8 ± 41.5	436.9 ± 54.1	1.83 ± 9.79	0.06	0.26
Trabecular area (mm^2)	591.6 ± 99.25	591.2 ±92	11.02 ± 33.5	<0.0001	628.1 ± 74.7	626.4 ± 74.9	0.21 ± 2.67	<0.0001	0.33
Bone marrow density (mg/cm^3)	27.9 ± 8.99	29.3 ± 8.85	4.36 ± 67.3	0.69	33.7 ± 7.35	29.6 ± 8.95	11.7±21.1	0.012	0.31
Cortical density (mg/cm^3)	1107.9 ± 21.8	1109.7 ± 28.5	10.9 ± 33.5	0.015	1100.7 ± 40.5	1102.1 ± 36.4	0.15 ±0.97	<0.0001	0.30
Total volumetric bone density (mg/cm^3)	793.9 ±73.4	822.3 ± 56.6	7.34 ± 36.3	0.47	787.9 ± 79.8	801.1 ± 70	2.03 ± 6.63	0.001	0.45
Bone torsion strength (mm4)	2822.3 ±703.2	2863.7 ±672.7	9.45 ±34.5	<0.0001	3073.7 ± 461.3	3079.3 ± 488.9	0.51 ± 8.56	<0.0001	0.45
Bone compressive strength (mm^2)	55066 ±15924	54616±15981.3	11.8 ± 33.2	<0.0001	59531 ±11340	58708 ±12205	1.41 ±6.69	<0.0001	0.24
Bone strength index (g^2/cm^4)	5956.6 ±1715.2	5952.9 ±1713.6	11.2 ± 33.8	<0.0001	6381.2 ±1121.7	6327.5 ±1254.7	2.09 ±16.4	<0.0001	0.26

Legend : Data are presented as means ± SD. p≤0.05: significant. Delta change = % of change between POST and PRE (POST-PRE / PRE)*100)). BMI= Body Mass Index ; 6MWT= 6 Minute Walking Test ; FM= Fat Mass ; LBM= Lean Body Mass ; AMMi= Appendiular Muscle Mass Index ; BMD= Bone Mineral Density.

were not compared at baseline. Effectively, we could expect a greater improvement in people who were more deconditioned at the beginning of the intervention.

Although there are a limited number of investigations assessing the effects of exercise on physical performance and body composition/quality among individuals with HIV, our results are consistent with the current literature with regard to the anticipated adaptations one would expect to observe within the general population (i.e. free from disease). Indeed, a recent narrative review concluded that exercise is efficient to improve aerobic capacity, muscle strength and body composition in people living with HIV (39). More specifically, O'Brien et al. also concluded that performing progressive resistance exercise or a combination of resistance and aerobic exercises at least three times per week for at least six weeks is safe and can lead to improvements in cardiorespiratory fitness, strength, weight, and body composition for adults with HIV (40). A pilot study highlighted that aerobic exercise training in older men with HIV is safe and effective (41). Indeed, in both the moderate-intensity and high-intensity groups, the authors found significant increases in exercise endurance and walking distance. Our study seems to corroborate these results since we observed a statistically significant improvement in walking distance capacity and grip strength after the intervention. However, our study did not show improvement in body composition. This discrepancy can be explained by variability in types of exercise interventions (i.e. aerobic exercise vs. combined aerobic), level of exercise supervision, types of outcomes reported, and methodological quality. Aerobic interventions in the previous trials varied according to constant versus interval exercise, moderate versus heavy intensity exercise, and combined aerobic and resistive exercise versus aerobic exercise alone (40). Another potential explanation of this lack of improvement is the duration of the intervention (i.e. 12 weeks) which may be too short to observe changes in body composition. Indeed, a recent study highlighted that 24 weeks of exercise reduced total and visceral fat in older adults (50-75 years) living with HIV (42). The age of the population could also explained the discrepancy since some authors have shown that 12-weeks of supervised aerobic exercise training safely decreases, weight, BMI, subcutaneous fat and abdominal girth (central fat) in young adults living with HIV (i.e. 36.6 ± 6.2 years) (43). Thus, the absence of body composition modifications could be explained by the duration of the intervention (probably too short), the protocol of training (type of training or exercises, supervision), the age of our population (older than other studies), and the outcomes reported.

Our feasibility study also suggests that age has no influence on the effect of mixed exercise training (i.e. HIIT combined with PT) in middle-aged men living with HIV. Indeed, exercise may be effective in the subpopulation of men with HIV irrespective of age. Although few studies have directly investigated the influence of age on the benefits of physical activity among people living with HIV, individual studies have shown the positive results of such an intervention in middle aged people. For example, high-intensity aerobic exercise in men with HIV (i.e. 54 years old on average) increases endurance and ambulatory function (41). A meta-analysis including participants with HIV (i.e. age ranged between 30 to 49 years old) also concluded that aerobic exercise or mixed training (i.e. aerobic exercise + resistive exercise) induces improvements in cardiorespiratory fitness, strength, body composition and quality of life (40). Therefore, being HIV positive does not affect the response to a physical exercise intervention. Nevertheless, according to Oursler et al. age-associated comorbidity affects physical function in persons living with HIV, and may modify the effect of aging and accelerate the aging process (44). Among individuals diagnosed with HIV, a challenge is therefore presented by the morbidity normally associated with aging. Therefore, it would be interesting to compare old and very old patients to check the potential effects of an exercise intervention in very old HIV-infected adults.

Finally and more importantly, our study suggests that HIV duration attenuates exercise adaptations in men living with HIV. This is consistent with the systematic review of Gomes-Neto et al. highlighting that the appropriate mode of exercise depend of the stage of the disease (and therefore of the HIV duration) (45). Moreover, Grace et al. supported the importance of prescribing exercise training for HIV+ individuals by considering the specific clinical stages (46). Our hypothesis is that a long-lasting infection may decrease the body's adaptive capacity and therefore reduce the effects of exercise. Effectively, responses and adaptations to exercise training will vary depending on current fitness level or disease status. Asymptomatic individuals generally respond in a manner similar to someone without HIV of the same body size, age, and gender (47). Moreover, there is controversy about whether HIV itself accelerates the aging process (48). In the literature, multiple biological mechanisms for aging could be affected by HIV, such as genetic instability, telomere shortening, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication (49). While the observed changes in inflammation, immunity, physical function (e.g. frailty) and co-morbidity, there is not yet correlation with HIV. So, it is not clear that they are related to accelerating aging. It appears that co-morbidities occur at higher rates in the HIV population for any given age but the rate of co-morbidities does not increase with the length of time a person is infected with HIV (50, 51). However, HIV therapy may be a more important aging factor than HIV duration. Changes in body composition may be exacerbated by long-term use of Antiretroviral therapy (52) and lead to loss of functional capacity.

The main limitation of the present feasibility study is the absence of a control group (i.e. patients living with HIV without exercise training) to establish the efficacy of the intervention. Then, because of the feasibility design, we performed per-protocol analysis in order to test the intervention under optimal conditions. The risk is therefore to have overestimated the effects of our intervention. To confirm our encouraging results, intention-to-treat analysis should be also performed in future studies. Regarding participants, the small sample size (n=27) is another limitation of the study. The sample is therefore probably not representative of the population of HIV-infected adults and the extrapolation of the results requires caution. A selection bias is also possible since only voluntary subjects were included in exercise intervention arm and because only women were included in subgroup analysis. Moreover, groups in sub-analysis differed in pre-intervention, therefore the results should be interpreted with caution. Effectively, we can expect a greater improvement in people who are more deconditioned at the beginning of the intervention. Another limitation is that follow-up is short and many changes in body composition assessed by DEXA scans after 12 weeks cannot be observed. Then, this feasibility study focused on statistically significant changes only. However, from a clinical point of view, it would be important to investigate if these changes are also clinically relevant. To observe clinically meaningfull change, it is important to use appropriate and specific to the training tests but also highly recognizable standard test. Finally, a potential bias is due to the inability to blind participants to the exercise intervention. This may have resulted in a Hawthorne effect, whereby participants might perceive greater benefits associated with exercise based on the expectation that exercise should be linked to positive outcomes.

In conclusion, this feasibility study suggests that mixed exercise training (i.e. HIIT combined with PT) in middle-aged and older adults living with HIV significantly improves their physical function. Therefore, exercise may be effective in adults living with HIV to counteract accelerated-aging induced by HIV. In addition, this study suggests that neither age nor HIV duration has influence on the effect of mixed training in this population. Nevertheless, further mechanistic and epidemiological data will be needed to clarify this result.

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