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Exercise Training Reduces Central Adiposity and Improves Metabolic Indices in HAART-Treated HIV-Positive Subjects in Rwanda: A Randomized Controlled Trial

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ABSTRACT

As HAART becomes more accessible in sub-Saharan Africa, metabolic syndromes, body fat redistribution (BFR), and cardiovascular disease may become more prevalent. We conducted a 6-month, randomized controlled trial to test whether cardiorespiratory exercise training (CET), improves metabolic, body composition and cardiorespiratory fitness parameters in HAART-treated HIV$^+$ African subjects with BFR. Six months of CET reduced waist circumference (-7.13 ± 4.4 cm, $p < 0.0001$), WHR (-0.10 ± 0.1, $p < 0.0001$), sum skinfold thickness (-6.15 ± 8.2 mm, $p < 0.0001$) and % body fat mass (-1.5 ± 3.3, $p < 0.0001$) in HIV$^+$BFR$^+$EXS. Hip circumference was unchanged in non-exercise control groups. CET reduced fasting total cholesterol (-0.03 ± 1.11 mM, $p < 0.05$), triglycerides (-0.22 ± 0.48 mM, $p < 0.05$) and glucose levels (-0.21 ± 0.71 mM, $p < 0.05$) ($p < 0.0001$). HDL-, LDL-cholesterol and HOMA values were unchanged after CET. Interestingly, HIV$^+$ subjects randomized to non-exercising groups experienced increases in fasting plasma glucose levels, whereas HIV seronegative controls did not ($p < 0.001$). Predicted VO_2 peak increased more in the HIV$^+$BFR$^+$EXS than in all other groups (4.7 ± 3.9 ml/kg/min, $p < 0.0001$). Exercise training positively modulated body composition and metabolic profiles, and improved cardiorespiratory fitness in HAART-treated HIV$^+$ Africans. These beneficial adaptations imply that exercise training is a safe, inexpensive, practical, and effective treatment for evolving metabolic and cardiovascular syndromes associated with HIV and HAART exposure in resource-limited sub-Saharan countries, where treatment is improving, morbidity and mortality rates are declining, but where minimal resources are available to manage HIV- and HAART-associated cardiovascular and metabolic syndromes.

INTRODUCTION

BODY COMPOSITION AND METABOLIC ABNORMALITIES associated with body fat redistribution (BFR) (central adiposity and/or peripheral lipoatrophy), glucose and lipid abnormalities, and hypertension[1] have been reported in approximately 20–60%[2,3] of HIV-positive (HIV$^+$) patients receiving highly active antiretroviral therapy (HAART).[4] Although treatment with potent HAART has improved the morbidity rate and well-being of HIV$^+$ patients accessing these therapies,[5] HAART- and HIV-related complications have been associated with increased cardiovascular disease (CVD) and diabetes risks.[6,7] Framingham risk equations suggest increased risk for myocardial infarction[8] and greater than a 20% increase in 10-year CVD risk[9] in HIV$^+$ patients receiving HAART compared to age-matched controls. Therefore HAART-treated HIV-infected patients represent an emerging population with increased risk for CVD and diabetes.

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In developing countries, BFR and metabolic abnormalities have been reported in HAART-treated HIV patients[10] and in HIV-infected Africans receiving first line World Health Organization (WHO)-recommended HAART.[11] As HAART becomes more accessible to HIV-infected people in resource-limited regions of the world,[12,13] and their quality of life improves,[14] the challenge is how to manage HIV- and HAART-related metabolic syndromes. Subsequently, there is a growing concern that CVD and diabetes risks, the main causes of morbidity and mortality in the developed world, may emerge, along with infectious diseases, as significant health concerns in HIV^+ individuals in sub-Saharan countries.[15]

Cardiorespiratory exercise training (CET) is an established, cost-effective, and efficacious lifestyle modification that improves insulin sensitivity[16] and dyslipidemia[17] and reduces central adiposity or trunk fat,[18] leading to an improved cardiovascular and diabetic risk profile in HIV^+ individuals from Western countries.[19] Consequently, regular CET has been recommended in the guidelines for management of HIV-related dyslipidemia.[20] Several nonrandomized controlled trials of aerobic and resistance exercise studies with small sample sizes and short training durations have reported improvement in lipid and body composition profiles in HIV^+ individuals with BFR in Western countries.[21–27] In resource-limited areas such as sub-Saharan Africa, CET may be a particularly important treatment for BFR and metabolic disorders in HIV^+ individuals taking HAART. Therefore, we conducted a 6-month randomized controlled trial to test whether CET improves metabolic and anthropomorphic parameters and enhances cardiorespiratory fitness in HAART-treated HIV-infected African men and women with BFR in Rwanda.

MATERIALS AND METHODS

Study population

Participants were screened for eligibility from August to December 2005 at the Centre Hospitalier Universitaire de Kigali, Treatment and Research AIDS Centre, and HIV/AIDS clinics of Kimironko, Kicukiro, Bilyogo-Nyiranuma, Kinyinya, and Kacyiru health centers in Rwanda. Eligible HIV-positive volunteers were between 21 and 50 years old and on a stable WHO-recommended HAART regimen for ≥6 months. Participants had moderate to severe BFR, determined by physical examination and subjects' self reporting, and rating changes in fat content using a validated questionnaire.[28] The degree of body fat redistribution was rated as *absent* (score 0), *mild* (noticeable on close inspection, score 1), *moderate* (readily noticeable by the patient and the physician, score 2), or *severe* (readily noticeable to a casual observer, score 3). The overall score was the mean of the scores given by the participant and a score assigned to each participant by a consensus of three clinicians working in the field of HIV/AIDS. The presence and rating of BFR were confirmed in all participants by physical examination, in which 18% of HIV^+ participants who self-reported moderate to severe BFR were excluded due to lack of confirmation from the clinicians. For the purposes of this study, a clinical diagnosis was given to HIV^+ participants with *moderate* (score 2) to severe (score 3) BFR, and an overall mean score of ≥18 on a validated seven-item inventory for the face, neck, arms, breasts, abdomen, buttocks, and legs, with 21 as the highest score. All included HIV^+ participants with BFR had a waist-to-hip ratio (WHR) ≥0.90 in men and 0.85 in women.

Subjects were excluded if they had emotional distress or psychosis, unstable angina, shortness of breath with exercise, a known medical history that would contraindicate exercise training, acute infections, or AIDS-defining opportunistic illnesses. Subjects were also excluded if they were obese [body mass index (BMI) ≥ 32 kg/m^2], had musculoskeletal or neuromuscular disorders, participated in regular exercise (≥3 sessions/week, ≥30 min/session in the previous 4 weeks), were unwilling to exercise continuously for 6 months, or anticipated changes in HAART medications or were currently taking medications that affect lipid and glucose metabolism. Pregnant or breast-feeding women were excluded. Participants were receiving WHO-recommended first line HAART regimens, with 80% receiving stavudine, lamivudine, and nevirapine, a widely used first-line therapy in resource-limited regions of the world. Another 11% received zidovudine, lamivudine, and nevirapine and 5% received zidovudine, lamivudine, and efavirenz. A small percentage of subjects (3%) received stavudine, lamivudine, and efavirenz and only 1% received lamivudine, abacavir, and nevirapine. HAART regimen use was not different among the HIV^+ participant groups.

One hundred and fifty-two HIV^+ participants with moderate to severe BFR were screened and 52 were not eligible; 21 participants did not meet eligibility criteria for central obesity, 16 participants were determined unfit for the exercise program, 11 participants declined to participate, three anticipated changes in HAART medications, and one participant had epilepsy. One hundred HIV^+ participants with moderate to severe BFR were stratified by gender and randomized to either an exercise group ($n = 50$; HIV^+BFR^+EXS) or a nonexercising control group ($n = 50$; HIV^+BFR^+noEXS). For comparative purposes, we also randomly recruited age, gender, and BMI-matched HIV-infected participants on stable HAART for ≥6 months, without BFR changes (as defined above) ($n = 50$; HIV^+noBFR^+ noEXS). Since there are few normative data on cardiorespiratory fitness and metabolic and body composition parameters in HIV-seronegative Rwandan adults, we also randomly recruited age, gender, and BMI-matched HIV-seronegative healthy adults as an additional comparative control group ($n = 50$; HIV-ve^+noEXS). After obtaining ethical permission from the National Research Ethics Committee (Rwanda), written informed consent was obtained from all volunteers before participation.

Metabolic and anthropometrics

After an overnight fast, a venous blood sample was obtained and serum was isolated and analyzed for total cholesterol, high-density lipoprotein cholesterol (HDL cholesterol), triglycerides (TG), and glucose and insulin levels (Humalyzer 3000; Abbott Laboratories, Abbott Park, IL). The $CD4^+$ count was quantified by flow cytometry using monoclonal antibodies (Simultest CD4, Beckon Dickinson). Low-density lipoprotein cholesterol (LDL cholesterol) was calculated from total cholesterol, HDL cholesterol, and TG using the Friedewald formula.[29]

Height, weight, and hip and waist circumferences were measured while the participant was standing, wearing light clothing

and no shoes. Height and weight were measured to the nearest 0.1 kg and 0.1 cm, respectively. Waist and hip circumferences were assessed by two well-trained research associates. For reproducibility and to minimize interobserver variability, associates were trained on proper anatomic placement of the tape measure, and their measurements were cross-validated on a number of participants until the variability between duplicate measures among associates was minimal. Waist circumference was measured using a cloth tape measure at the narrowest circumference, halfway between the lowest ribs and iliac crests. Hip circumference was measured at the level of the anterior superior iliac spine, where this could be palpated, or at the broadest circumference below the waist. Two measurements were taken; if they differed by >2 cm, a third measurement was taken and the mean of the closest two measurements was used to calculate waist-to-hip ratio (WHR). Mid-triceps, mid-biceps, suprailiac, and subscapular skinfolds were measured using Lange skinfold callipers. For reproducibility, an experienced trained investigator (E.M.) located and measured all skinfolds in triplicate. Measurements were read to the nearest 0.2 mm and averaged for each skinfold site. The sum of four total skinfold measures was used to calculate percentage body fat (% BFM) and lean body mass (% LBM) using equations and formulas[30,31] validated in a black population.[32] All measurements were obtained at baseline and after 6 months of observation, placebo, or exercise intervention.

Exercise training protocol

HIV+BFR+EXS participated in a 6-month, supervised exercise training program (3 sessions/week, 1.5 h/session, alternating days) at Amahoro Fitness Club located in downtown Kigali. All participants were instructed on a progressive exercise program consisting of stretching exercises and 15 min of brisk walking followed by 45–60 min of jogging, running, stair climbing, low back and abdominal stabilization, and strengthening exercises. Participants were instructed to perform primarily jogging and running exercises with a goal of achieving at least 45% age-predicted maximal heart rate (HR) in the first 3 weeks, 60% age-predicted maximal HR in the next 6 weeks, and 75% age-predicted maximal HR by the end of the intervention. Heart rate was approximately assessed in one-third of participants in each training session with all participants age-predicted maximal HR assessed at least every week. This ensured that the exercise stimulus was adequate to elicit cardiorespiratory and musculoskeletal system adaptations. Each exercise training session ended with 15 min of cool down and stretching exercises. Participants' attendance at each session was recorded and noncompliance was defined as 50% missed training sessions. Cardiorespiratory fitness was assessed at baseline and 6 months later using the 20-m multistage shuttle run test (20mMST)[33] to predict maximum oxygen consumption (VO_2 peak; ml/kg/min). During the 20mMST, participants ran continuously in an indoor fitness stadium on a flat hard synthetic surface between two points separated by 20 m at a pace that was incremented by 0.14 m/sec each minute or level. The required running pace was indicated by verbal cues and prerecorded audio signals that sounded when each 20-m "lap" should have been completed (much like a metronome). The inability to maintain the required pace for a particular increment was documented (level and number of 20-m laps completed) and

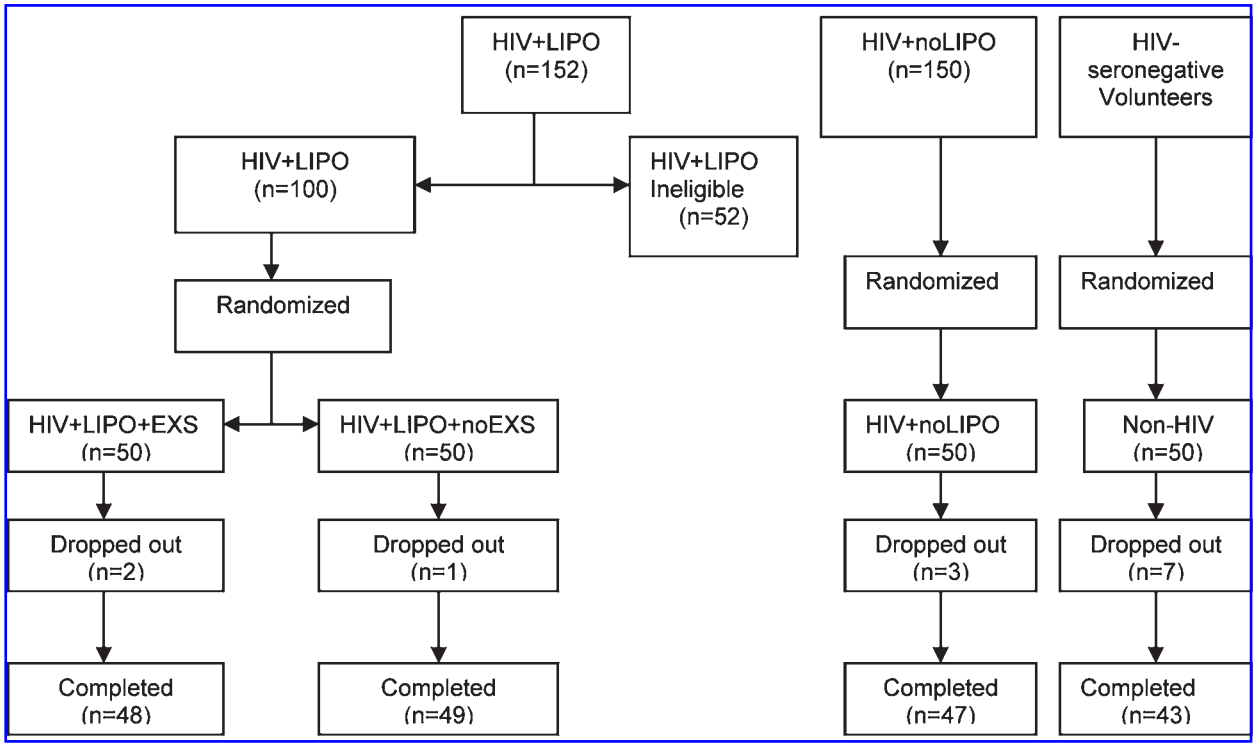

FIG. 1. Flow of participants through the trial; 21 did not meet the criteria for central obesity, 11 were determined unfit to exercise, 11 declined to participate, three anticipated changes in HAART regimens, and one had a neurological disorder.

represents the participants' maximal effort, which is proportional to VO_2 peak. The 20mMST assessment tool for cardiorespiratory fitness and exercise capacity has been validated in health and fitness settings.[34] Each participant's cardiorespiratory fitness was assessed individually during the 20mMST to minimize possible sources of error. Heart rate and blood pressure were taken immediately before and after the exercise test, and perceived exertion was evaluated with the Borg Rating of Perceived Exertion Scale (Borg RPE).

Three HIV^+BFR^+EXS participants did not complete the CET program: two dropped out, one died following surgery, and another one changed jobs to a distant location. One HIV^+BFR^+noEXS participant was lost to follow-up and three HIV^+noBFR$^+$noEXS subjects dropped out; one declined further participation and two started to obtain medications and social support from a rural nongovernmental organization. Seven HIV-ve$^+$noEXS participants declined further participation due to lack of time, interest, family issues, or personal travel arrangements. Compliance with the exercise program was 82.2%. Figure 1 represents a flow diagram of study subjects.

Statistical analyses

Based on previous studies,[22–24] we estimated that a sample of 37 individuals in each group would have a power of 90% to detect a 10% difference in triglycerides and total cholesterols for $\alpha = 0.05$. Assuming a drop-out of 20% per group, at least 44 participants would be required per group. Since all subject groups were ≥44 per group after the intervention, the primary efficacy analyses were based on data from participants who completed the study at a 6-month period.

Between-group comparisons of the changes in the outcome variables were performed using analyses of covariance (ANCOVA). Analyses of covariance with the 6 month change as the dependent variable (absolute change from baseline), the treatment group as the independent variable, and baseline values as the covariates, were used to determine whether there were between-group differences at 6 months after adjusting for the initial baseline values. As part of the ANCOVA, statistical contrasts were used to make pairwise comparisons across groups. All analyses were performed using SAS software, version 9.1.3 of the SAS System for Linux (SAS Institute Inc.,

Table 1. Baseline Characteristics, Body Composition, and Metabolic Data[a]

	HIV^+BFR^+noE XS	*HIV^+BFR^+EXS*	p
Age (years)	37.5 ± 6.9	37.8 ± 5.5	0.807
Number (% females)	50 (60)	50 (60)	—
CD4 cell count (cells/μl)	348 ± 162	353 ± 168	0.882
Height (m)	1.63 ± 0.1	1.64 ± 0.1	0.898
Weight (kg)	64.8 ± 5.7	65.6 ± 10.4	0.891
HAART duration (weeks)	62.7 ± 27.6	71.4 ± 36.7	0.671
BFR score$_{(7\text{-item})}$	18.7 ± 2.3	19.3 ± 2.1	0.882'
Body composition			
Body mass index (kg/m^2)	24.4 ± 2.7	24.0 ± 3.1	0.406
Waist (cm)	92.3 ± 6.9	91.0 ± 8.4	0.341
Hip (cm)	93.7 ± 6.8	92.3 ± 7.6	0.183
Waist-to-hip ratio	0.98 ± 0.0	0.99 ± 0.1	0.796
Skinfold (mm)			
Triceps	14.4 ± 3.4	14.4 ± 3.9	0.979
Biceps	10.8 ± 2.4	10.7 ± 72.9	0.848
Subscapular	18.7 ± 4.9	18.6 ± 5.2	0.884
Suprailiac	18.8 ± 5.1	18.7 ± 5.5	0.915
Total skinfolds	62.7 ± 12.9	62.3 ± 15.0	0.888
Body fat mass (%)	29.3 ± 4.3	29.4 ± 6.2	0.928
Metabolic			
Total cholesterol (mmol/liter)	3.89 (1.04)	3.78 (0.93)	0.499
HDL cholesterol (mmol/liter)	1.27 (0.15)	1.28 (0.19)	0.684
LDL cholesterol (mmol/liter)	2.16 (0.77)	2.10 (0.74)	0.659
Triglyceride (mmol/liter)	1.34 (0.36)	1.33 (0.39)	0.941
Glucose (mmol/liter)	4.95 (0.74)	4.76 (0.76)	0.191
Insulin (ρmol/liter)	59 (28)	67 (29)	0.131
HOMA	1.87 (0.13)	2.04 (0.14)	0.196

[a]Data expressed as mean ± SD or median (interquartile range); BFR score$_{(7\text{-item})}$, 7-item body fat redistribution score; $HOMA_{IR}$, homeostasis model assessment of insulin resistance.

Cary, NC). All statistical tests were two-tailed, and significance was accepted at a p-value = 0.05. Data are presented in tables as arithmetic mean ± SD, or median (interquartile range), and in figures as mean ± SE, unless stated otherwise.

RESULTS

Cardiovascular outcomes

At baseline, participants with BFR randomized to the exercise or nonexercise group were well matched for age, CD4 cell count, body fat redistribution score, gender, body composition, and metabolic variables (Table 1). HIV-seronegative controls had lower diastolic blood pressure at the start of the 20mMST than HIV$^+$noBFR$^+$noEXS subjects ($p < 0.05$). At 6 months, HIV$^+$BFR$^+$EXS achieved a significantly higher HR and RPE at the end of the 20mMST ($p < 0.001$) than other subject groups. Likewise, predicted VO_2 peak during the 20mMST increased more in the HIV$^+$BFR$^+$EXS group (4.7 ± 0.56 ml/kg/min, $p < 0.0001$) than in all other groups (Fig. 2). Following CET, the mean changes in CD4 cell count for HIV$^+$BFR$^+$EXS (19 ± 91 cells/μl) were not significantly different from that of HIV-infected subjects with BFR in the HIV$^+$BFR$^+$noEXS (34 ± 128 cells/μl) ($p = 0.547$) or HIV$^+$noBFR$^+$noEXS subjects (77 ± 160 cells/μl) ($p = 0.079$).

Body composition outcomes

After 6 months of CET, BMI, waist circumference (−7.13 ± 4.4) (Fig. 3) and WHR declined more in HIV$^+$BFR$^+$EXS, while it remained unchanged or increased in the other groups (Table 2). Hip circumference was unchanged after 6 months in all groups; therefore the decline in waist-to-hip ratio in HIV$^+$BFR$^+$EXS was attributed to the decline in waist circumference. In fact, waist circumference increased 1.84 ± 9.2 cm in HIV$^+$noBFR$^+$noEXS subjects. We also observed a decline in WHR in HIV$^+$BFR$^+$noEXS participants compared to HIV-ve$^+$noEXS participants (0.00 ± 0.1 versus 0.01 ± 0.1; $p < 0.05$). After the CET, waist circumference in the exercise group was not different from that of HIV-seronegative subjects (Table 2). The BFR mean score significantly declined more in HIV$^+$BFR$^+$EXS than HIV$^+$BFR$^+$noEXS, while the BFR mean score significantly increased in HIV$^+$noBFR$^+$noEXS (Table 2). Subscapular (−1.9 ± 3.2 mm), suprailiac (−2.13 ± 3.5 mm), and sum skinfold thicknesses (−6.15 ± 8.2 mm) (Fig. 3) declined more in HIV$^+$BFR$^+$EXS than in all other groups ($p < 0.0001$). HIV$^+$BFR$^+$EXS experienced a significant decrease in % BFM (−1.5 ± 3.3, $p < 0.001$) and a significant increase in % LBM (1.5 ± 3.1, $p < 0.0001$) compared to all other groups (Table 2).

Metabolic outcomes

At baseline, total cholesterol was significantly greater in HIV$^+$BFR$^+$EXS and HIV$^+$BFR$^+$noEXS than HIV$^+$noBFR$^+$noEXS and HIV-ve$^+$noEXS (Table 3). Following CET, total cholesterol levels declined more in the HIV$^+$BFR$^+$EXS group than the HIV$^+$BFR$^+$noEXS group ($p < 0.05$). HIV-ve$^+$noEXS showed significantly lower mean changes in total cholesterol than HIV$^+$BFR$^+$EXS ($p < 0.0003$). There were no significant changes in HDL cholesterol, LDL cholesterol, and HOMA values, but insulin levels declined more in the HIV$^+$BFR$^+$EXS than in the HIV$^+$BFR$^+$noEXS group (Table 3). Subjects in the exercise group demonstrated a significant decrease in fasting plasma glucose than HIV$^+$ subjects with BFR in the nonexercise group [−0.21 (0.71) versus 0.39 (1.25), $p < 0.0001$] and HIV$^+$noBFR$^+$noEXS subjects ($p = 0.002$) (Fig. 3). Interestingly, HIV-infected subjects with BFR- and HIV-infected subjects with no BFR in the nonexercise groups had a significant

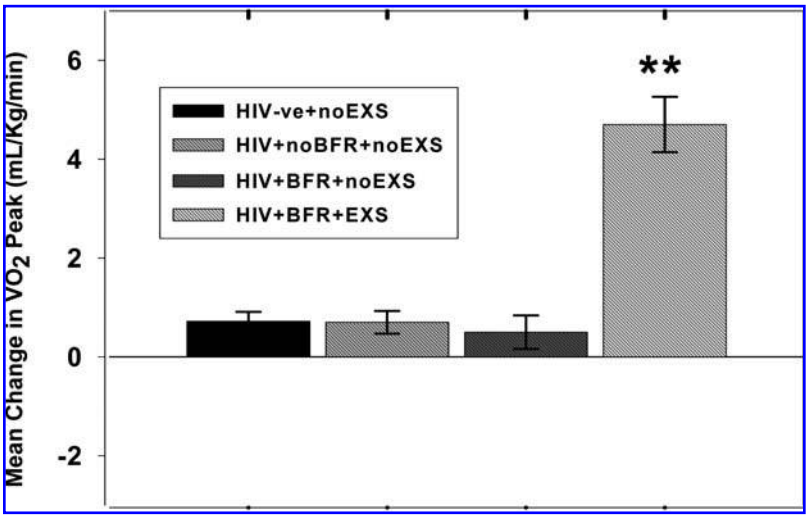

FIG. 2. Mean change in VO_2 peak predicted from a 20-m multistage shuttle run test. **$p < 0.0001$ versus HIV$^+$BFR$^+$EXS group; BFR, body fat distribution; VO_2 peak max, maximum total body oxygen consumption; HIV-ve$^+$noEXS, HIV-seronegative controls; HIV$^+$noBFR$^+$noEXS, nonexercise HIV$^+$ subjects with no BFR; HIV$^+$BFR$^+$noEXS, nonexercise HIV$^+$ subjects with BFR; HIV$^+$BFR$^+$EXS, HIV$^+$ subjects with BFR in the exercise group.

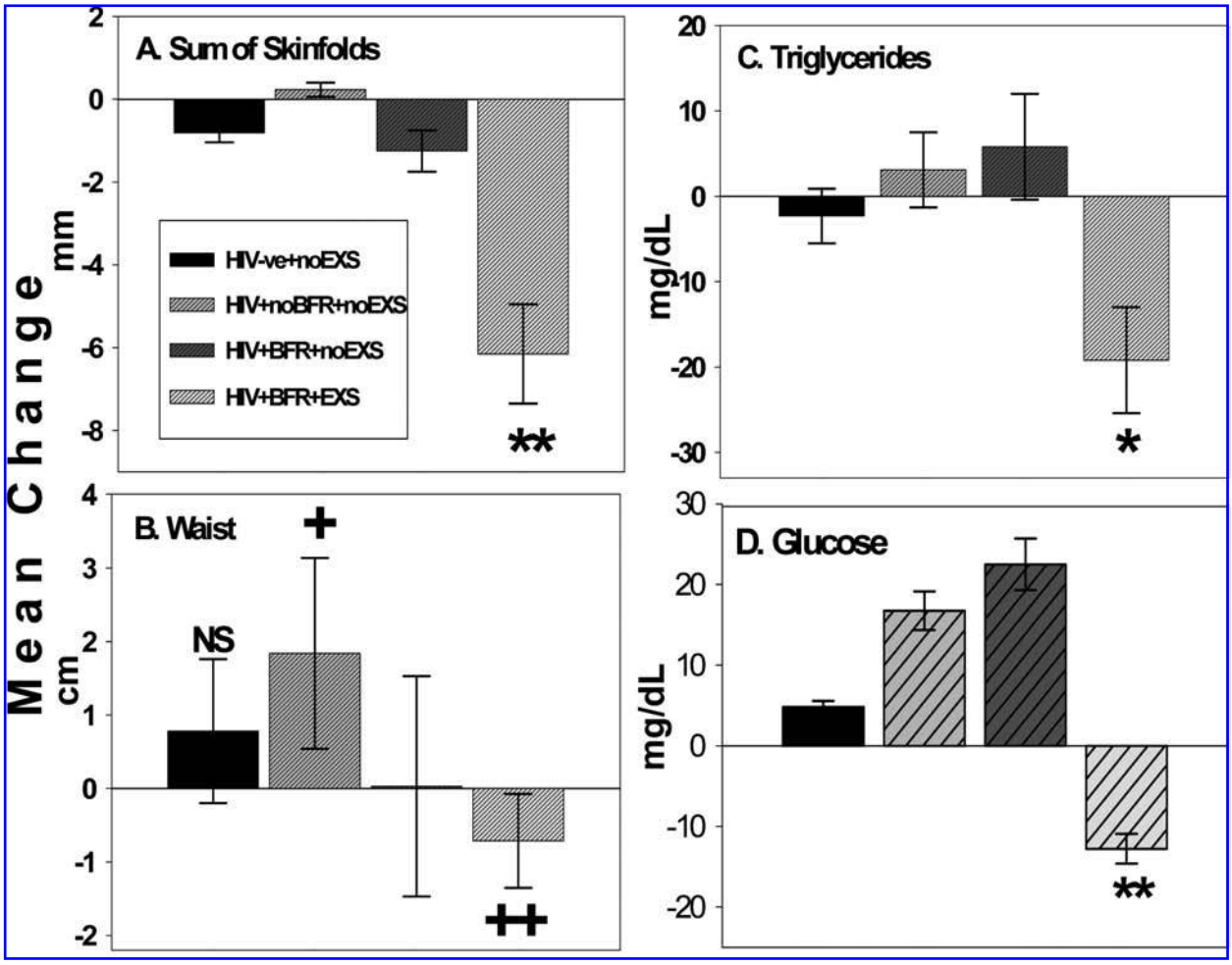

FIG. 3. Mean changes in sum skinfolds, waist circumference, triglycerides, and fasting glucose in 6 months. $*p < 0.05$, $**p < 0.0001$ versus all subject groups; $^{+}p = 0.004$ versus the $HIV^{+}BFR^{+}EXS$ group; $^{++}p < 0.0001$ versus the $HIV^{+}BFR^{+}noEXS$ group; NS, $p = 0.359$ versus the $HIV^{+}BFR^{+}EXS$ group.

increase in fasting plasma glucose, whereas HIV-seronegative subjects did not. Also the serum TG level declined more in $HIV^{+}BFR^{+}EXS$ than in $HIV^{+}BFR^{+}noEXS$ and was not changed in other subject groups (Time 3, Fig. 3).

DISCUSSION

Our findings indicate that CET positively modulates body composition, decreasing waist circumference, waist-to-hip ratio, and percentage body fat mass in WHO-recommended HAART-treated HIV^{+} African subjects with BFR in Rwanda. Exercise training further modulates a decline in total serum cholesterol, TG, and glucose, and also improves cardiorespiratory fitness. To our knowledge, this is the first study to demonstrate that CET is safe, practical, and effective at reducing central adiposity and cardiovascular risk factors and improving cardiovascular fitness in HAART-treated HIV^{+} sub-Saharan Africans with body fat alterations. Previous studies on the effects of CET on metabolic and anthropomorphic abnormalities in HAART-treated HIV^{+} patients were limited by small sample sizes, were disproportionate with respect to gender, and were not largely controlled.[21–25] We believe our findings are particularly important due to increasing access to HAART in sub-Saharan countries and the potential for increased CVD and diabetes risks for HIV^{+} patients starting HAART.

HIV-infected participants with BFR who exercised showed a significant improvement in body composition, particularly resulting in a considerable reduction in waist circumference and WHR and an increase in lean body mass. Exercise training did not significantly affect hip circumference, but reduced waist circumference, which accounted for the decline in WHR. Both waist circumference and WHR are simple and inexpensive measurements used in normal populations to assess central adiposity, and are good predictors of CVD and diabetes risks.[35]

Elevated WHR in HAART-treated HIV-infected individuals is mainly due to a gradual increase in waist circumference rather than to changes in hip circumference.[36] Our findings further showed that sedentary HAART-treated HIV^{+} African participants had an increase in waist circumference over time in comparison to age-, gender-, and BMI-matched HIV-seronegative participants. Others have reported a gradual increase in waist

Table 2. Changes in Body Composition from Baseline to 6 Months in Study Population[a]

	HIV-ve$^+$noEXS (n = *43, 63% females*)		*HIV$^+$noBFR$^+$noEXS* (n = *47, 62% females*)		*HIV$^+$BFR$^+$noEXS* (n = *49, 61% females*)		*HIV$^+$BFR$^+$EXS* (n = *48, 63% females*)	
	Baseline	Δ *at 6 Months*	*Baseline*	Δ *at 6 months*	*Baseline*	Δ *at 6 months*	*Baseline*	Δ *at 6 months*
Body composition								
Body mass index (kg/m^2)	24.2 ± 2.4	0.02 ± 0.2	25.8 ± 2.8	0.14 ± 0.6	24.4 ± 2.7	0.06 ± 0.6	24.0 ± 3.1	−0.53 ± 1.2**,‡
Waist circumference (cm)	83.1 ± 4.6	0.78 ± 6.5	85.0 ± 7.0	1.84 ± 9.2*	92.3 ± 6.9	0.03 ± 10.7	91.0 ± 8.4	−7.13 ± 4.4**,‡
Hip circumference (cm)	98.9 ± 4.6	0.14 ± 0.4	100.3 ± 4.3	0.05 ± 0.5	93.7 ± 6.8	0.22 ± 0.7	92.3 ± 7.6	1.13 ± 5.4
Waist-to-hip ratio	0.84 ± 0.1	0.01 ± 0.1*	0.85 ± 0.1	0.02 ± 0.12	0.98 ± 0.0	0.00 ± 0.1	0.99 ± 0.1	−0.10 ± 0.1**
BFR score(7-item)	7.1 ± 3.44	−0.12 ± 0.2	8.4 ± 3.1	1.51 ± 2.3†	18.7 ± 2.3	0.51 ± 1.3	19.3 ± 2.1	−4.7 ± 0.9**,‡
Skinfold (mm)								
Triceps	14.3 ± 3.8	−0.19 ± 0.5	14.9 ± 3.7	0.09 ± 0.5	14.4 ± 3.4	−0.20 ± 0.7	14.4 ± 3.9	−1.42 ± 2.1**
Biceps	10.6 ± 2.4	0.00 ± 0.0	11.3 ± 2.6	0.17 ± 0.6	10.8 ± 2.4	−0.06 ± 0.3	10.7 ± 2.9	−0.63 ± 1.6*
Subscapular	19.7 ± 4.9	−0.33 ± 0.9	17.7 ± 3.9	−0.06 ± 0.4	18.7 ± 4.9	−0.55 ± 1.7	18.6 ± 5.2	−1.9 ± 3.2**,‡
Suprailiac	19.5 ± 4.7	−0.30 ± 0.9	16.5 ± 2.9	0.04 ± 0.4	18.8 ± 5.1	−0.43 ± 1.4	18.7 ± 5.5	−2.1 ± 3.5**,‡
Sum skinfolds	64.1 ± 12.9	−0.81 ± 1.5	60.4 ± 9.8	0.23 ± 1.2	62.7 ± 12.9	−1.25 ± 3.5	62.3 ± 15.0	−6.15 ± 8.2**,‡
Body fat mass (%)	29.5 ± 4.5	−0.18 ± 0.6	29.1 ± 5.0	−0.14 ± 0.9	29.3 ± 4.3	−0.16 ± 0.7	29.4 ± 6.2	−1.5 ± 3.3**,‡

[a]Data expressed as mean ± SD; *$p < 0.05$, **$p < 0.0001$ versus HIV$^+$ subjects with BFR; †$p < 0.05$, ††$p < 0.0001$ versus HIV$^+$ exercise group; ‡$p < 0.0001$ versus HIV$^+$ subjects with no B FR and HIV-seronegative subjects; BFR score$_{(7\text{-item})}$, 7-tem body fat redistribution score.

Table 3. Changes in Metabolic Profile from Baseline to 6 Months in Study Population[a]

	HIV-ve$^+$noEXS (n = *43, 63% females*)		*HIV$^+$noBFR$^+$noEXS* (n = *47, 62% females*)		*HIV$^+$BFR$^+$noEXS* (n = *49, 61% females*)		*HIV$^+$BFR$^+$EXS* (n = *48, 63% females*)	
Metabolic	*Baseline*	Δ *at 6 months*	*Baseline*	Δ *at 6 months*	*Baseline*	Δ *at 6 months*	*Baseline*	Δ *at 6 months*
Total cholesterol (mmol/liter)	3.00 (0.49)	0.04 (0.41)†	3.15 (0.50)	0.17 (0.63)	3.89 (1.05)‡‡	0.066 (1.28)	3.78 (0.93)‡‡	−0.03 (1.11)*
HDL cholesterol (mmol/liter)	1.29 (0.16)	0.01 (0.14)	1.28 (0.17)	0.06 (0.23)	1.27 (0.15)	0.07 (0.14)	1.28 (0.19)	0.03 (0.21)
LDL cholesterrol (mmol/liter)	2.17 (0.70)	0.01 (0.71)	2.09 (0.74)	−0.01 (0.91)	2.16 (0.77)	0.19 (0.98)	2.10 (0.74)	0.14 (0.89)
Triglycerides (mmol/liter)	1.20 (0.25)	−0.03 (0.24)	1.20 (0.23)	0.03 (0.34)	1.34 (0.36)‡	0.07 (0.49)	1.33 (0.39)‡	−0.22 (0.48)*,‡
Glucose (mmol/liter)	4.44 (0.49)	0.04 (0.27)‡‡	4.63 (0.74)	0.23 (0.93)	4.95 (0.74)	0.39 (1.25)	4.76 (0.76)	−0.21 (0.71)**,‡
Insulin (ρmol/liter)	45 (19)	1 (19)	54 (3.1)	1 (21)	59 (28)	3 (23)	67 (29)	−1 (18)*
HOMA$_{IR}$	1.28 (0.06)	0.0 (0.0)	1.60 (0.10)	0.0 (0.1)	1.87 (0.13)	0.0 (0.2)	2.04 (0.14)	0.0 (0.1)

[a]Data expressed as mean ± SD; *$p < 0.95$, **$p < 0.0001$ versus HIV$^+$BFR$^+$noEXS; ‡$p < 0.05$, ‡‡$p < 0.0001$ versus HIV$^+$noBFR$^+$noEXS and HIV-ve$^+$noEXS; †$p < 0.0001$ versus HIV$^+$noBFR$^+$noEXS; ††$p < 0.0001$ versus HIV$^+$BFR$^+$noEXS and HIV$^+$noBFR$^+$noEXS; HOMA$_{IR}$, homeostasis model assessment of insulin resistance.

circumference in HIV$^+$ patients with body fat redistribution.[36] The cause and existence of this HIV- and HAART-associated central adiposity are under debate.[37] Our findings suggest that waist girth increased over 6 months in HIV-infected African subjects treated with HAART, and that it is preventable with 6 months of aerobic exercise training. Further, the current study supports other studies that found a relationship between reductions in waist circumference and WHR and increases in lean body mass and reductions in body fat mass in subjects who participated in CET.[22,23]

Exercise training induced alterations in central adiposity and glucose and lipid parameters in the current study, and this translates to reduced cardiovascular disease risk in HAART-treated HIV-infected Africans, as seen in HIV-seronegative populations.[38] Exercise training reduces fat mass and increases fat-free mass in other HIV$^+$ cohorts;[21–24] our findings support this notion and further indicate that CET attenuates fasting serum glucose and TG and improves cardiorespiratory fitness in HAART-treated HIV$^+$ African men and women with body fat alterations. Thus, TG may reduce CVD morbidity and mortality rates and improve insulin sensitivity in HAART-treated HIV$^+$ African men and women[39] through its reduction of central adiposity, a strong predictor of insulin resistance in HIV$^+$ patients.[40]

In the current study, exercise training improved the cardiorespiratory fitness of HIV$^+$ African men and women with body fat alterations. At baseline, we did not observe differences in exercise capacity between HIV$^+$ African subjects with or without body fat changes; however, when combined as one group, all HIV-infected subjects had lower baseline VO_2max (ml/kg/min) compared to HIV-seronegative African control subjects. Cardiorespiratory fitness improved 19% in HIV-infected African subjects who exercised for 6 months, but did not achieve the value of the healthy, normal HIV-seronegative African controls in the current study. Lower cardiorespiratory fitness has been reported in HIV-infected subjects irrespective of HAART use,[41] but improves with exercise training.[25,42,43] This may further indicate inadequate aerobic capacity in HIV$^+$ people, possibly due to the effects of HIV disease or HAART on tissue oxygen extraction and utilization. Low cardiorespiratory fitness has been associated with elevated cardiovascular disease morbidity and mortality, as a result central obesity and other risk factors in non-HIV-positive populations.[44]

The current study is limited by lack of more objective fat quantification methods, such as dual energy X-ray absorptiometry (DEXA) or magnetic resonance imaging (MRI) and computed tomography (CT) scans. Although expensive for large sample sizes, the use of MRI and/or CT scans would reveal the direct effects of exercise on visceral and subcutaneous fat content. Anthropometric measurements have proven sensitive and useful in assessing body composition changes in HIV-infected people.[36] Further randomized controlled studies evaluating the effects of exercise training using modern body composition assessment tools are warranted, particularly in subjects whose metabolic variables indicate greater cardiovascular disease risk.

In summary, our findings provide evidence that exercise training is safe, practical, and efficacious in reducing central adiposity and CVD risk parameters and improving cardiovascular fitness in HAART-treated HIV-infected Africans with body fat alterations. The beneficial effects of exercise training are particularly important in sub-Saharan populations, where the accessibility to HIV treatment is improving, but where minimal resources and medications (antihypertensives, antidiabetics, antihyperlipidemics) are available to manage HIV- and HAART-associated metabolic syndromes that threaten to increase CVD risk.

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