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ORIGINAL ARTICLE

The influence of HIV on body composition and its relationship with physical function in mid-life women: a cross-sectional study from Zimbabwe

Mícheál Ó Breasail[a,b], Jakub Mesinovic[a,c], Tafadzwa Madanhire[d,e], Cynthia Kahari[d,e], Peter R. Ebeling[a], Victoria Simms[d,e], Rashida A. Ferrand[d,f], Kate A. Ward[g,h] and Celia L. Gregson[d,i]

[a]Department of Medicine, School of Clinical Sciences, Faculty of Medicine, Monash Medical Centre, Nursing and Health Sciences, Monash University, Clayton, VIC, Australia; [b]Population Health Sciences, Bristol Medical School, Bristol, UK; [c]Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, VIC, Australia; [d]The Health Research Unit Zimbabwe, Biomedical Research and Training Institute, Harare, Zimbabwe; [e]Department of Infectious Disease Epidemiology, Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK; [f]Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK; [g]MRC Lifecourse Epidemiology Centre, Human Development and Health, University of Southampton, Southampton, UK; [h]MRC Unit, The Gambia @ London School of Hygiene and Tropical Medicine, Banjul, The Gambia; [i]Global Musculoskeletal Research Group, Musculoskeletal Research Unit, Bristol Medical School, University of Bristol, Bristol, UK

ABSTRACT

Objective: Menopause-related changes in body composition and physical function are unclear in Southern Africa, particularly in the context of a generalized HIV epidemic with high antiretroviral therapy (ART) coverage.

Method: A total of 263 Zimbabwean women (53% women living with HIV [WLH]) aged 40–60 years provided data on menopause, ART use, anthropometry, body composition (appendicular lean mass [ALM], muscle area, fat mass), handgrip strength (HGS) and gait speed. Linear regression determined relationships between body composition and physical function, unadjusted and age–menopause-adjusted, stratified by HIV status. Univariate logistic regression investigated associations between body composition and self-reported falls.

Results: WLH (96% ART established) were a median (interquartile range) 10.4 (6.4–14.5) years since diagnosis, with lower weight, body mass index, ALM, fat mass and HGS than women living without HIV (WLWOH). With menopause transition, WLH lost weight, ALM, gynoid mass and muscle area (all p-trend <0.05); however, WLWOH did not. Both WLH and WLWOH lost HGS (p-trend <0.05). ALM was positively associated with HGS in all women. In WLH, greater percentage body fat, particularly gynoid fat, was associated with increased odds of falls (1.69 [1.00–2.89], $p=0.049$ and 1.72 [1.08–2.75], $p=0.023$, respectively).

Conclusion: Women living with HIV were more likely to experience adverse changes in body composition through menopause; fat mass gains were associated with risk of falls.

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Menopause; Africa; body composition; physical function; HIV

Introduction

In mid-life women, changes in body composition, particularly the accumulation of excess abdominal adiposity, are linked to negative health outcomes, including cardiovascular disease, stroke and diabetes [1,2]. While mid-life weight gain varies, one large multi-racial American cohort reported an average increase of 0.7 kg per year [3]. A recent meta-analysis of 201 studies reported primarily age-related increases in weight and most measures of adiposity from mid-life, in addition to menopause-related fat redistribution [4]. Increased adiposity coupled with age-related declines in lean mass [5] is associated with poor physical function and frailty [6,7]. In turn, poor mid-life physical function, as measured by simple indicators such as handgrip strength (HGS) and gait speed, is associated with increased mortality and morbidity in high-income countries [8–11]. However, data from African countries remain scarce [12], and our understanding of the relationships between mid-life body composition and physical function, in addition to their role in future health, remain limited. This is important as the prevalence of overweight and obesity is increasing rapidly across Africa, particularly in urban and urbanizing settings [13–15]. Data are needed given the unique challenges faced by low and middle-income African countries, including the high prevalence of HIV, limited healthcare access and widespread food insecurity, since the relationships observed in high-income countries may not be generalizable to these settings.

CONTACT Mícheál Ó Breasail micheal.obreasail@monash.edu Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Level 5/Block E, Monash Medical Centre, 246 Clayton Road, Clayton, VIC 3168, Australia

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In recent decades, life expectancy in Eastern and Southern Africa has increased due to the success of antiretroviral therapy (ART), which has transformed HIV into a chronic manageable, albeit incurable, condition [16,17]. While more women living with HIV (WLH) now reach menopause [18,19], they may be at greater risk of age-associated non-infectious comorbidities (e.g. osteoporosis and sarcopenia) and syndromes of aging (e.g. frailty) [20–23] than their HIV-negative peers. Both HIV and ART affect body composition and physical function [24–29]; untreated HIV is associated with weight loss reversed following ART initiation [24–26], while data suggest dolutegravir (DTG) is associated with weight gain [30–32]. However, longitudinal data that could elucidate the potential long-term effects on body composition as WLH transition through menopause into old age are lacking. While US data suggest synergistic deleterious effects associated with reduced physical function and HIV infection [28], such data are not generalizable to African populations. Equally, relationships between HIV, ART use and sarcopenia are not well established in the African context, due to the few studies, the absence of population-specific normative data and the use of diagnostic criteria developed for other populations [33–35].

Until well-validated population-specific diagnostic criteria are available for the classification of sarcopenia and related geriatric syndromes, simple objective measures of physical function remain the most pragmatic predictors of health from mid-life into older age. Thus, this secondary analysis sought to describe how body composition influences physical function at mid-life in Zimbabwean women, with an emphasis on the impact of HIV. The aims of this study were to determine differences in body composition and physical function in mid-life Zimbabwean WLH and women living without HIV (WLWOH); the relationship between measures of lean mass (as an estimate of muscle mass) and adiposity on physical function in mid-life Zimbabwean women; and the influence of HIV-specific factors on body composition and physical function.

Methods

Recruitment

The study design has been described previously [36,37]; in brief, between April and December 2020, women aged 40–60 years who were resident in Harare were enrolled in a cross-sectional study, sampled by four age strata (40–44, 45–49, 50–54 and 55–60 years, to span the period of menopausal transition) and HIV status with the aim to recruit 400 women equally split by HIV status. WLH were recruited from Sally Mugabe (formerly known as Harare Central) and Parirenyatwa Hospital HIV clinics, the two main public healthcare hospitals in Harare. WLH were asked to identify two female friends of a similar age, with telephone access, who would potentially also be interested in participating (this approach was necessary to comply with COVID-19 guidelines in place at the time). Women aged between 40 and 60 years resident in Harare who were not acutely unwell and were willing to undergo a HIV test were recruited.

Data collection

Socio-demographic data including highest educational attainment, employment status, lifestyle information (e.g. tobacco smoking/use and alcohol intake) and medical history were captured by questionnaire. Medications were recorded, including ART regimen, menopausal hormone therapy and medicines affecting bone health.

Menopause staging

Women were pragmatically staged for menopause based on final menstrual period as conducting gold-standard Stages of Reproductive Aging Workshop (STRAW+10) staging [38] was unfeasible for the research assistants. Women currently having regular periods were classified as premenopausal, women having irregular periods and/or a period within the previous 12 months were classified as perimenopausal, and women who had had no bleeding for 12 months or more were classified as postmenopausal. Twenty-one women who reported a hysterectomy, 20 of whom also had oophorectomy, were excluded as hysterectomy prevents menopausal staging using menstrual bleeding criteria [38,39] (Supplemental Figure S1). A further 113 women who reported the use of hormonal contraceptives, which precluded them from menopause staging, were also excluded from this secondary analysis (Supplemental Figure S1). No women reported using menopause hormone therapy.

HIV testing

All women recruited without an established HIV diagnosis had a point-of-care HIV antibody test performed using Alere Determine HIV-1/2 (Alere San Diego, Inc., San Diego, CA, USA). If negative, they were enrolled into the HIV-negative group. If positive, after a confirmatory test (Chembio SURE CHECK HIV ½ Assay), they were offered enrollment into the WLH group and referred to local HIV services [40]. Blood samples (4 ml) were collected in ethylenediamine tetraacetic acid (EDTA) tubes, from which HIV viral load testing was performed using the Roche COBAS Ampliprep/COBAS Taqman48.

Anthropometry

Two nurses measured height (centimeters) and weight (kilograms) using a Seca 213 stadiometer and Seca 875 digital scales (Seca Precision for health, Hamburg, Germany), respectively, with the mean of both measurements calculated. Body mass index (kg/m^2) was calculated.

Peripheral quantitative computed tomography muscle scanning

Peripheral quantitative computed tomography (pQCT) scans of the non-dominant lower leg were acquired using an XCT 2000 L (Stratec Medizintechnik, Pforzheim, Germany) as described previously [41]. Briefly, muscle density, a surrogate measure of intramuscular adipose tissue, and muscle

cross-sectional area (CSA) were obtained at 66% of the limb length (Supplemental Figure S2). A voxel size of $0.5 \times 0.5\,mm^2$ and slice thickness of 2 mm were used. The CT scan speed was 30 mm/s. pQCT images were processed using the manufacturer's software (Stratec XCT version 6.2). Muscle CSA was derived via subtraction; that is, bone CSA measured at a threshold of $280\,mg/cm^3$ with contour mode 1 and peel mode 2 (C1P2) was subtracted from bone and muscle CSA measured at a threshold of $40\,mg/cm^3$ C1P2 and muscle smoothing filter F03F05 (Supplemental Figure S2). Muscle density was extracted at $100\,mg/cm^3$ using the F03F05 filter. Scans were qualitatively graded through visual inspection and scans with excessive movement or other artifacts excluded.

Dual-energy X-ray absorptiometry body composition

Dual-energy X-ray absorptiometry (DXA) whole-body scans were performed using a Hologic Discovery A instrument (Hologic Inc., Bedford, MA, USA; Apex Version 13.4.2:3 software; S/N 83145). Body composition outcomes were total lean mass, total fat mass, percentage body fat, android and gynoid fat mass. Appendicular lean mass (ALM) was derived by adding the lean mass of the arms and legs, which was normalized to height to calculate the appendicular lean mass index (ALMI = ALM / height^2). For practical reasons, the head was subtracted from whole-body scan regions. A single trained radiographer performed whole-body scans.

Scanner calibration and inter-operator precision

Both scanners were regularly calibrated using their respective manufacturer's phantom to perform daily quality assessment scans and weekly quality control scans throughout the study. Inter-operator precision was obtained from repeat scans from a subset of women ($n = 30$) with root mean squared coefficients of variation derived: pQCT ($n = 28$), 3.2% and 0.8% for muscle CSA and muscle density, respectively; and DXA ($n = 30$), 1.0% and 1.2% for lean mass and fat mass, respectively [41].

Physical function, frailty and falls

HGS was measured by dynamometer (Jamar Hand Dynamometer, IL, USA) [42] with participants seated in an upright position with their arm supported on the armrest of the chair, wrist in a neutral position and the thumb facing upwards. Participants were instructed to exert maximal force. One practice effort was permitted followed by three test measurements. The outcome measured was force (kilograms) for the highest effort. Gait speed was obtained from standing over a 4-m marked course with the participant starting to walk when prompted. Timing stopped when they crossed the end of the course. Gait speed $<0.8\,ms^{-1}$ was considered as 'slow gait speed' [34]. History of falls and number of falls over the previous 12 months was collected by self-report.

Ethical considerations

The study obtained ethical approval from the Biomedical Research and Training Institute Institutional Review Board (Ref: AP152/2019), the Harare Central Hospital Ethics Committee (Ref: HCHEC 181119/66) and the Medical Research Council of Zimbabwe (Ref: MRCZ/A/2551). Informed written consent was collected from all participants.

Statistical analysis

All statistical analyses were performed using RStudio (2023.06.1 Build 524), R v4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) (https://www.r-project.org/). Descriptive data by HIV status are presented, with continuous data that are normally distributed summarized as the mean (standard deviation [SD]), and when skewed as the median (interquartile range) or for categorical data as the count (*n*) and percentage. Differences in continuous variables by HIV status were investigated with independent sample *t*-tests, whereas Pearson's chi-squared tests were used for categorical variables. These data were further stratified by menopause status, with linear regression used to investigate differences in continuous variables by menopause status (ordinal variable, premenopausal, perimenopausal, postmenopausal, *p*-trend), whereas Pearson's chi-squared tests were used for categorical variables.

Linear regression was used to determine associations between body composition measures (percentage body fat [per 10%], total body fat [kilograms], android fat [kilograms], gynoid fat [kilograms], cross-sectional muscle area (CSMA) [square centimeters], ALM [kilograms]) and physical function outcomes (gait speed [meters per second] and HGS [kilograms]) in both WLH and their HIV-negative peers. Analyses were unadjusted, or age and menopause adjusted.

Univariate logistic regression was used to describe associations between these body composition measures with having fallen in the preceding 12 months. Beta-coefficients were standardized to allow for the expression of the association per 1SD change of each body composition measure, and log-odds were exponentiated to produce odds ratios. Subsequently, the models were repeated with an age adjustment.

The associations between HIV-specific factors with the aforementioned body composition and physical function outcomes in WLH were investigated using linear regression. Factors considered were percentage of life spent on ART (per 5%), unsuppressed viral load (>50 copies/ml) and tenofovir disoproxil fumarate (TDF) or DTG exposure. Further adjustments for age and menopause status were subsequently performed.

Results

Of the 399 women enrolled in the study, 263 (65.9%) were staged for menopause and had DXA body composition data (Supplemental Figure S1). These women were of median (interquartile range) age 51 (47–56) years, and 139 (52.9%) were living with HIV. Overall, there were 32%, 13% and 55% in premenopause, perimenopause and postmenopause,

Table 1. Descriptive characteristics of mid-life Zimbabwean women by HIV status.

Characteristic	*WLWOH*	*WLH*	p-*Value*
Participants (*n*)	124	139	
Age (years)	51.2 (5.7)	50.7 (5.5)	0.500
Menopause status,[a] *n* (%)			
Premenopause	40 (32.6)	45 (32.4)	0.600
Perimenopause	18 (14.5)	15 (10.7)	
Postmenopause	66 (53.2)	79 (56.8)	
Highest level of education, *n* (%)			
None or primary only	25 (20.3)	23 (16.6)	<0.001
Secondary only	69 (55.7)	105 (75.5)	
Training college or university	30 (24.2)	11 (7.9)	
In employment, *n* (%)	77 (62.1)	70 (32.4)	<0.001
Parity, *n* (%)			
Nulliparous (0 children)	2 (1.6)	6 (4.3)	0.200
Low parity (1–3 children)	73 (58.9)	91 (65.5)	
Multiparous (≥4 children)	49 (39.5)	42 (30.2)	
Anthropometry			
Height (m)	1.62 (0.05)	1.61 (0.06)	0.400
Weight (kg)	79.9 (17.0)	70.3 (14.1)	<0.001
BMI (kg/m^2)	30.6 (6.5)	27.1 (5.4)	<0.001
BMI category, *n* (%)			
Underweight (<18.5 kg/m^2)	0 (0)	5 (3.6)	<0.001
Normal (18.5 to <25 kg/m^2)	28 (22.6)	43 (30.9)	
Overweight (25 to <30 kg/m^2)	36 (29.0)	53 (38.1)	
Obese (≥30 kg/m^2)	60 (48.4)	38 (27.3)	
Body composition			
Fat mass (kg)	32.2 (11.4)	26.8 (9.9)	<0.001
Fat mass (%)	41.8 (6.6)	39.4 (7.0)	<0.001
Android fat mass (kg)	2.38 (1.15)	1.98 (0.95)	0.002
Gynoid fat mass (kg)	5.61 (1.77)	4.65 (1.64)	<0.001
ALM (kg)	20.9 (3.3)	18.7 (2.9)	<0.001
ALMI (kg/m^2)	7.97 (1.17)	7.20 (0.99)	<0.001
Muscle density (mg/cm^3)	69.6 (2.1) (*n* = 112)	69.7 (2.5) (*n* = 128)	0.900
Muscle cross-sectional area (cm^2)	59.7 (9.6) (*n* = 110)	56.5 (10.3) (*n* = 127)	0.010
Physical function characteristics			
Hand grip strength	31.5 (6.6)	29.4 (6.6) (*n* = 194)	0.010
Gait speed (m/s)	0.96 (0.24)	0.92 (0.22)	0.400
Gait speed <0.8 m/s, *n* (%)	23 (18.6)	40 (19.4) (*n* = 138)	0.800
Self-reported fall in the last year, *n* (%)	16 (12.9)	19 (13.7)	0.900
HIV			
Years since HIV diagnosis, median (IQR)	–	10.4 (6.4–14.5) (*n* = 139)	
Age at HIV diagnosis, mean (SD)	–	40.9 (6.7) (*n* = 139)	
Taking ART, *n* (%)	–	133 (95.7) (*n* = 139)	
Duration on ART, median (IQR)	–	9.0 (5.0–13.0) (*n* = 133)	
Ever-used TDF, *n* (%)	–	113 (85.0) (*n* = 133)	
Ever-used DTG, *n* (%)	–	52 (39.1) (*n* = 133)	
Viral load <50 copies/ml, *n* (%)	–	112 (80.6) (*n* = 139)	

[a]Menopause stage defined by time since last menstrual period: premenopause, regular menses; perimenopause, irregular menses/amenorrhea ≤12 months; post-menopause, >12 months after last menses.

Hypothesis testing for continuous variables performed using an independent *t*-test (unpaired); Pearson's chi-squared test used for categorical variables. ALM, appendicular lean mass; ALMI, appendicular lean mass index; ART, antiretroviral therapy; BMI, body mass index; DTG, dolutegravir; IQR, interquartile range; SD, standard deviation; TDF, tenofovir disoproxil fumarate; WLWOH, women living without HIV; WLH, women living with HIV.

respectively. Age, height and menopause status did not differ by HIV status (Table 1). In all women, multiparity (i.e. ≥4 children) was common at *n* = 91 (35%), and median parity did not differ between WLH and WLWOH (Table 1). WLWOH were approximately 12% heavier than WLH (Table 1). Underweight (i.e. body mass index <18.5 kg/m^2) was only observed in WLH (*n* = 5, 3.6%), whereas almost 50% of WLWOH were obese compared to 27.3% of WLH (Table 1). The proportion of women who reported falls in the previous year did not differ by HIV status. No women in either group reported the use of menopause hormone therapy.

WLH were a median (interquartile range) 10.4 (6.4–14.5) years since HIV diagnosis, and 95.7% (*n* = 133) were established on ART, for a median duration of 9 (5–13) years. Of those on ART, 85.0% (*n* = 113) and 39.1% (*n* = 52) were taking a regimen containing TDF or DTG, respectively. All women taking DTG had been TDF exposed. Of those established on ART, 84.2% had a viral load <50 copies/ml and only four women on ART had a viral load >1000 copies/ml.

Unadjusted differences in body composition and physical function by HIV and menopause status

When comparing WLH to WLWOH, WLH had lower weight, body mass index, total body and regional fat mass, ALM, ALMI and muscle CSA (Table 1). Differences were not seen in muscle density (Table 1). Muscle strength (measured as HGS) was lower in WLH, although muscle function (measured as gait speed) was similar between WLH and WLOH (Table 1). The proportions of WLH and WLWOH with slow gait speed or self-reported falls in the preceding year were similar (Table 1). When stratified by HIV status and menopausal stage, body composition in WLWOH was broadly similar (Table 2). WLH had lower ALM and muscle CSA, whilst gynoid fat increased

Table 2. Anthropometry, body composition and physical function outcomes of Zimbabwean women at mid-life by HIV and menopause status.

	WLWOH				*WLH*			
Characteristic	*Premenopause*	*Perimenopause*	*Postmenopause*	p-*Value*	*Premenopause*	*Perimenopause*	*Postmenopause*	p-*Value*
Anthropometry	40	18	66		45	15	79	
Height (m)	1.62 (0.06)	1.63 (0.04)	1.61 (0.05)	0.440	1.63 (0.05)	1.59 (0.06)	1.60 (0.06)	0.021
Weight (kg)	78.2 (17.4)	81.6 (12.5)	80.4 (17.8)	0.520	73.5 (13.9)	71.6 (17.4)	68.2 (13.3)	0.043
BMI (kg/m^2)	29.8 (6.6)	30.8 (5.6)	30.9 (6.7)	0.400	27.7 (5.3)	28.2 (6.6)	26.5 (5.3)	0.240
BMI category, *n* (%)								
Underweight (<18.5 kg/m^2)	0 (0)	0 (0)	0 (0)	0.100	1 (2.2)	1 (6.7)	3 (3.8)	0.900
Normal (18.5 to <25 kg/m^2)	9 (22.5)	3 (16.7)	16 (24.2)		12 (22.7)	4 (26.7)	27 (34.1)	
Overweight (25 to <30 kg/m^2)	17 (42.5)	3 (16.7)	16 (24.2)		19 (42.2)	5 (33.3)	29 (36.7)	
Obese (≥30 kg/m^2)	14 (35.0)	12 (66.7)	34 (51.5)		13 (28.9)	5 (33.3)	20 (25.3)	
Body composition								
Whole body fat mass (kg)	30.3 (11.1)	33.2 (9.1)	33.2 (12.1)	0.210	28.2 (9.3)	28.7 (13.5)	25.6 (9.4)	0.150
Whole body fat mass %	40.1 (6.6)	42.3 (6.3)	42.7 (6.7)	0.053	39.9 (6.1)	40.8 (8.2)	38.8 (7.2)	0.400
Android fat mass	2.17 (1.12)	2.42 (1.01)	2.50 (1.19)	0.150	1.99 (0.87)	2.35 (1.30)	1.90 (0.91)	0.620
Gynoid fat mass	5.35 (1.64)	5.71 (1.30)	5.74 (1.96)	0.270	5.08 (1.59)	4.72 (2.17)	4.39 (1.52)	0.025
ALM (kg)	21.0 (3.6)	21.6 (2.1)	20.6 (3.4)	0.550	19.6 (2.8)	18.3 (2.8)	18.2 (2.8)	0.009
ALMI (kg/m^2)	7.99 (1.23)	8.12 (0.99)	7.92 (1.19)	0.770	7.40 (0.98)	7.23 (0.95)	7.08 (1.00)	0.086
Muscle density (mg/cm^3)	70.1 (2.2) (*n* = 35)	70.1 (1.9) (*n* = 15)	69.3 (2.0) (*n* = 62)	0.078	69.5 (2.3) (*n* = 41)	70.3 (2.6)	69.7 (2.6) (*n* = 72)	0.700
Muscle cross-sectional area (cm^2)	61.6 (9.8) (*n* = 34)	63.0(10.4) (*n* = 25)	57.8 (9.1) (*n* = 61)	0.069	60.4 (9.3) (*n* = 40)	57.6 (9.3)	54.1 (10.4)	0.002
Physical function								
Handgrip strength (kg)	33.4 (6.3)	33.7 (7.1)	29.6 (6.1)	0.003	31.5 (7.7) (*n* = 43)	27.9 (5.9)	28.5 (5.9) (*n* = 72)	0.018
Gait Speed (ms^{-1})	0.989 (0.238)	0.959 (0.238)	0.934 (0.233)	0.240	0.916 (0.238)	0.950 (0.302)	0.937 (0.190	0.620
Gait speed <0.8 m/s, *n* (%)	4 (10)	3 (16.7)	16 (24.2)	0.200	11 (24.4)	3 (20.0)	13 (16.5)	0.600
Falls in the last year, *n* (%)	3 (7.5)	1 (5.6)	12 (18.2)	0.200	7 (15.6)	1 (6.7)	11 (13.9)	0.700

Hypothesis testing for continuous variables performed using linear regression with menopause treated as an ordinal variable. Pearson's chi-squared test used for categorical variables. ALM, appendicular lean mass; ALMI, appendicular lean mass index; BMI, body mass index; WLWOH, women living without HIV; WLH, women living with HIV.

through menopause stage. Body composition did not differ across menopausal stage in WLWOH (Table 2). A pattern of lower HGS with increasing menopause stage was seen in both WLH and WLWOH (Table 2).

Associations between body composition, physical function and falls

For each additional 1 kg in ALM, a 0.86 [95% CI: 0.50; 1.22] kg and 0.54 [95% CI: 0.21; 0.86] kg greater HGS was observed in WLH and WLWOH, respectively (Supplemental Table S1). No associations were found between measures of percentage body fat, regional fat mass or muscle CSA with HGS in either WLH or WLWOH (Supplemental Table S1). No relationships were found between any measures of body composition and gait speed (Supplemental Table S1). In WLH, but not in WLWOH, a 1SD higher percentage body fat and gynoid mass were associated with a greater likelihood of having fallen in the preceding 12 months (Supplemental Table S2). Measures of muscle CSA and ALM were not associated with falls (Supplemental Table S2). Adjustment for age did not materially change these relationships.

Associations between HIV-specific factors with body composition and physical function

In univariate analysis in WLH, each 5% of life spent on ART was associated with a 0.71% (−1.39 to −0.03) lower percentage body fat mass and a 0.18 kg (−0.34 to −0.02) lower gynoid fat mass (Figure 1). These associations were weakened after adjustment for age and menopause status (Figure 1). No associations were observed between the percentage of life spent on ART and physical function outcomes (Figure 1). TDF use was associated with greater muscle CSA at 6.44 (1.59–11.30) cm^2, which was robust to further adjustment for age and menopause stage (Supplemental Figure S3). Neither unsuppressed viral load nor DTG use were associated with any body composition or physical function outcomes before or after adjustment for age and menopause (Supplemental Figure S3).

Discussion

This cross-sectional study of mid-life urban-dwelling Zimbabwean women observed that WLH weighed less and

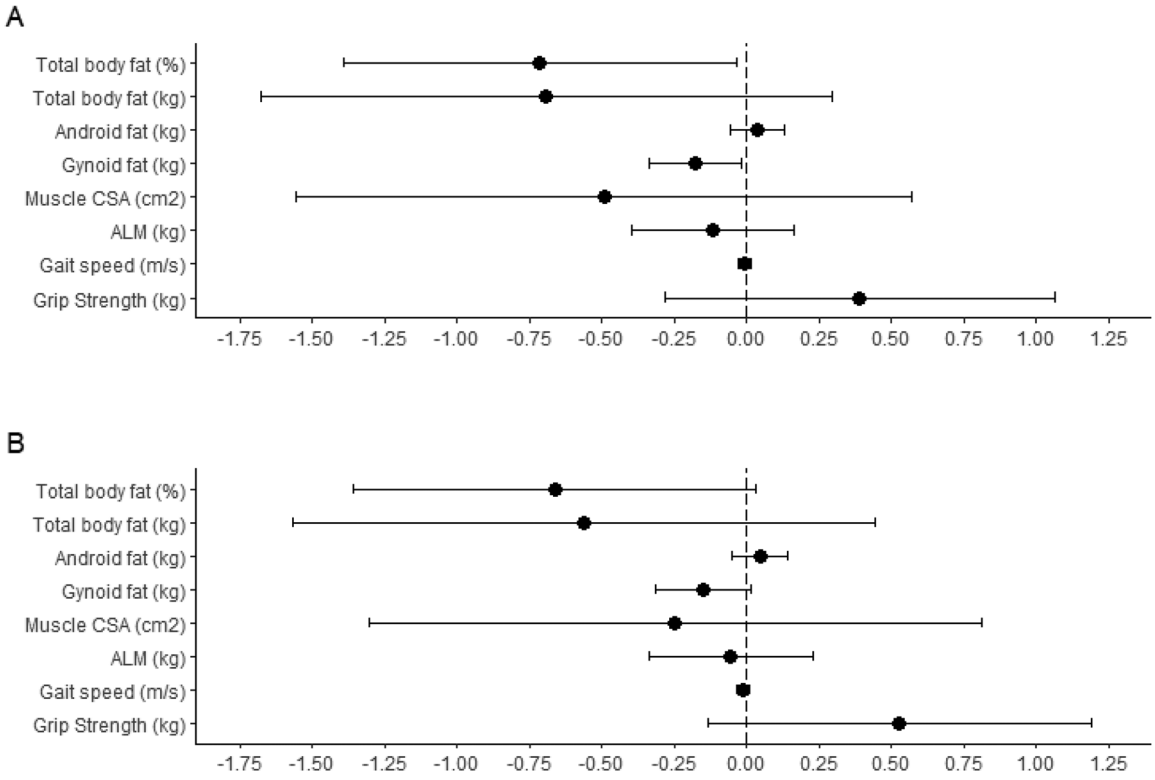

Figure 1. Associations between percentage life spent on ART (per 5%) and body composition and physical function measures in mid-life Zimbabwean women living with HIV: (A) unadjusted; (B) adjusted for age and menopause status. ALM, appendicular lean mass; ART, antiretroviral therapy; CSA, cross-sectional area.

had considerably less lean and fat mass than peers without HIV. Muscle strength (as measured by HGS) was lower in WLH, although muscle function (gait speed) was similar to WLWOH. In WLH, advancing menopause stage was associated with progressively lower measures of ALM, muscle size and gynoid fat mass. In absolute terms, the percentage of body fat was greater with advancing menopause stage in WLWOH but not in WLH. Measures of adiposity, rather than ALM, were consistently associated with more falls in the previous 12 months in WLH only.

Differences in body composition in Zimbabwean mid-life women by HIV status and menopause

The sizeable differences in almost all measures of lean and fat mass between WLWOH and WLH, whereby WLH had consistently lower measures, likely reflects the impact of multiple deleterious factors acting alone or in combination over a long period of time. WLH in this study had lived with HIV for a median of 10 years, over which time low-grade viremia [43], chronic inflammation [44] and higher energy expenditure [45,46] are all plausible contributors to the body composition differences we observe relative to their peers. In high income countries (HICs), menopause transition has been associated with weight gain and increases in adiposity [5,7]. WLWOH had stable lean mass measures across menopause stages, with a suggestion of increasing percentage body fat mass. In WLH, however, although lower ALM and muscle size were apparent, there was little evidence of greater adiposity. Indeed, WLH had lower gynoid fat mass with advancing menopause status. Although obesity was high in both WLH and WLWOH, with high body fat in this context, such relationships may be confounded by previously reported concerns about household food insecurity in this cohort [36]. Relationships between food insecurity and obesity are well established [47,48], and in the African context sources of processed white starch are affordable and energy dense but often of relatively little nutritional value [49].

There are some parallels between our body composition findings with the SWEET study in neighboring South Africa, where there was little change in measures of adiposity by menopause stage along with progressively lower lean mass measures [13]. In the SWEET study, ART-treated WLH had substantially lower absolute fat and lean body composition measures than HIV-negative women, with ART-naïve WLH being more similar to those without HIV [13]. However, comparisons with the present study are difficult as the methods of determining menopause stage were not fully comparable and the SWEET study did not report the length of time women had lived with HIV nor how long they had been taking ART. Our study has a larger, more homogeneous group of WLH (>95% ART use, >80% suppressed viral load) compared with only 55% of WLH ($n = 86$) in the SWEET study being ART-treated. Recently published follow-up data from a subset of women in the SWEET study reported minimal increases in body weight of a mean (SD) 1.7 (7.0) kg in WLH over 5 years, while over the same period women without HIV lost a mean (SD) 0.26 (6.1) kg [50]. Irrespective of HIV status, fat mass increased while lean mass declined, although fat mass gains were greater in WLH [50].

Associations of body composition with physical function and falls

In our sample of Zimbabwean women at mid-life, declines in physical function were evidenced by poorer HGS but not gait speed with advancing menopause stage in both WLWOH and WLH. Controlling for age and menopause status, only ALM was associated with HGS in WLH and WLWOH, whereas gait speed was not associated with body composition in either group. Further exploring relationships between dichotomized outcomes (i.e. falls, slow gait and low HGS) was hampered by a lack of context-specific cut-off values. Pragmatically using international cut-off values, only one woman met the revised European Working Group on Sarcopenia in Older People (EWGSOP2) criteria for low HGS, whereas 34 women had a slow gait speed. While ALM was not associated with self-reported falls in either WLH or WLWOH, a 1SD higher percentage body fat or gynoid mass was associated with an approximately 1.7-fold likelihood of falls in WLH, although a weaker association was seen for total body fat mass. This is interesting given that associations between greater adiposity and falls have been reported in some US populations where the prevalence of overweight and obesity are high [51]. It is plausible that greater gynoid fat mass is indicative of fat infiltration of the proximal lower limb muscles, which may impact mobility.

HIV-specific factors that might influence body composition and physical function at mid-life

This study found that the percentage of life spent on ART was associated with lower percentage body fat and gynoid fat mass, although the magnitude of the effect was diminished by adjustment for age and menopause status. Duration of ART exposure was not associated with lean tissue outcomes. In contrast to other studies, we did not find evidence of a negative association between TDF use and physical function [52]. While muscle size was greater in those with TDF exposure, there was no association with more conventional measures of muscle such as ALM. In our study we did not find any associations between DTG and body composition as described elsewhere in the region [32]; however, associations in our study may be confounded by the fact that all DTG-exposed women had also been exposed to TDF. Broadly speaking, WLH in the present study were relatively homogeneous with high ART adherence (>84%), good viral load suppression and the majority exposed to TDF (>80%). These factors may in part explain why our observations differ from some previously published research, although they may also reflect that data collected in HICs may not be fully generalizable to low and middle income countries (LMICs). This homogeneity likely limited our ability to fully discern the influence of these HIV-related factors on body composition and physical function.

Strengths and limitations

These unique data were captured from an under-represented population, with a matched comparator group. This work complements our previous findings that HIV is associated with more severe menopause-related symptoms [36] and poorer bone health [37]. Our findings have some generalizability to the wider region where the prevalence of chronic ART-controlled HIV remains high. However, the study has limitations; the study design is cross-sectional, so temporal directions of association cannot be established. As described earlier, STRAW +10, the gold standard for menopause staging, was not performed as this was as was unfeasible for the research assistants. Also, because of pandemic-associated lockdown restrictions, participants without HIV had to be identified and recruited through friendships of WLH, potentially introducing selection bias. Falls history was self-reported and subject to recall bias. ART usage data were not sufficient to account for the potential impact of sequential regimes and switching, although it should be noted this is relatively uncommon in this setting, and our findings are more likely related to unknown factors which impact poor HIV control.

Conclusions

In contrast to high-income settings, this study found no clear evidence of menopause-related weight gain or fat accrual in mid-life Zimbabwean women. However, menopause-related declines in lean mass and poorer physical function were evident in both WLH and WLWOH, with WLH having lower absolute values at each stage. ALM was the sole predictor of physical function in all women, with greater adiposity associated with up to a 1.7-fold higher risk of falls in WLH. While this cross-sectional study has highlighted mid-life HIV-related differences in body composition and physical function, further longitudinal studies are needed to establish how these relate to future adverse health outcomes. This could allow for the validation of simple cost-effective physical function measures to predict future adverse events in this underserved population.

Disclosure statement

No potential conflict of interest was reported by the authors.

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ORCID

Mícheál Ó Breasail http://orcid.org/0000-0002-9695-6378
Jakub Mesinovic http://orcid.org/0000-0003-1297-2731
Tafadzwa Madanhire http://orcid.org/0000-0003-2449-0027
Cynthia Kahari http://orcid.org/0000-0002-7289-5152
Peter R. Ebeling http://orcid.org/0000-0002-2921-3742
Victoria Simms http://orcid.org/0000-0002-4897-458X

Rashida A. Ferrand http://orcid.org/0000-0002-7660-9176
Kate A. Ward http://orcid.org/0000-0001-7034-6750
Celia L. Gregson http://orcid.org/0000-0001-6414-0529

Data availability statement

The data used to prepare this manuscript are available from the corresponding author upon reasonable request.

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