Associations between body fat distribution and cardiometabolic risk factors in mixed-ancestry South African women and men

Florence E Davidson, Tandi E Matsha, Rajiv T Erasmus, Andre Pascal Kengne, Julia H Goedecke

Abstract

Objective: To investigate the relationship between body fat distribution and cardiometabolic risk in mixed-ancestry South African (SA) men and women, and to explore the effect of menopausal status on these relationships in women.

Methods: In a cross-sectional study, 207 mixed-ancestry SA women and 46 men underwent measurement of body composition using dual-energy X-ray absorptiometry, blood pressure, oral glucose tolerance, lipid profile and high-sensitivity C-reactive protein determination. The associations between different body fat compartments and associated cardiometabolic risk factors were explored.

Results: Men had less percentage fat mass (%FM) [26.5% (25–75th percentiles: 19.9–32.5) vs 44.0% (39.8–48.6), $p \leq 0.001$], but more central and less peripheral fat (both $p < 0.001$) than women. Post-menopausal women had greater %FM, waist and visceral adipose tissue (VAT), and less gynoid %FM than pre-menopausal women (all $p \leq 0.004$). After adjusting for age and gender, VAT accounted for the greatest variance in insulin resistance ($R^2 = 0.27$), while trunk %FM and leg %FM accounted for the greatest variance in triglyceride ($R^2 = 0.13$) and high-density lipoprotein cholesterol concentrations ($R^2 = 0.14$). The association between fat mass and regional subcutaneous adipose tissue and cardiometabolic risk factors differed by gender and menopausal status.

Conclusion: Central fat was the most significant correlate of cardiometabolic risk and lower body fat was associated with reduced risk. These relationships were influenced by gender and menopausal status.

Department of Medical Imaging and Therapeutic Sciences, Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology, Bellville, Cape Town, South Africa
Florence E Davidson, MTech, davidsonf@cput.ac.za

Department of Biomedical Sciences, Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology/South African Medical Research Council/ Cardiometabolic Health, Bellville, Cape Town, South Africa
Tandi E Matsha, PhD

Division of Chemical Pathology, Faculty of Medicine and Health Sciences, National Health Laboratory Service (NHLS), University of Stellenbosch, Cape Town, South Africa
Rajiv T Erasmus, FMC Path, FC Path, DABCC (Am Board Certified), DHSM

Non-Communicable Diseases Research Unit, South African Medical Research Council, Parow, Cape Town, South Africa
Andre Pascal Kengne, MD, DSCS, PhD
Julia H Goedecke, PhD

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Globally, chronic non-communicable diseases (NCDs) are responsible for more deaths than any other cause, with people from the low- and middle-income countries being disproportionately affected.[1] In 2012, cardiovascular diseases (CVDs) and diabetes accounted for 46.2 and 4% of NCDs-related deaths, respectively.[1] The South African (SA) cause-of-death profile for 2012 shows similar trends.[2] An analysis of pooled population-based studies conducted by the NCD Risk Factor Collaboration Africa working group found that estimates of adiposity and diabetes prevalence in SA were higher than the global average.[3] NCD deaths are attributable to the high prevalence of major risk factors, including obesity, which is driven by lifestyle factors such as poor dietary intake and physical inactivity.[4]

Obesity is a well-known risk factor for CVD and metabolic diseases,[5-7] but body fat distribution appears to be a more significant discriminator of risk than generalised adiposity. The association of body fat with CVD risk differs by fat depot. A meta-analysis of 40 observational studies on the associations of different adipose tissue depots with insulin resistance revealed the strongest correlate of insulin resistance to be visceral adipose tissue (VAT).[8] By contrast, the relationship between abdominal subcutaneous adipose tissue (SAT) and cardiometabolic risk is weaker than VAT, as shown in multi-ethnic studies in men and women.[9,10] However, the accumulation of lower body SAT (gluteofemoral obesity) has shown opposing associations with cardiometabolic risk.[11-13]

Body fat distribution is also gender specific, with women having more SAT and less VAT than men.[14,15] The greater central adiposity, in particular VAT, in men translates to higher insulin resistance,[14] type 2 diabetes[16] and an adverse cardiometabolic risk profile in general. The risk of cardiometabolic disease increases with age,[17] and in women, after menopause,[18] when weight gain and increased central adiposity are common.[19]

Differences also exist in body fat distribution among different ethnic groups.[5,20] International studies have shown that Asian Indians have more total and central fat mass than their Caucasian and black counterparts.[21-23] Black Africans on the other hand have less VAT but more abdominal SAT than Caucasians,[24-27] and greater gluteofemoral fat mass compared to Caucasian women.[27]

In addition to differences in body fat distribution, the association with cardiometabolic risk also differs according to gender, age and ethnicity. For example, African American women were shown to have a weaker association between VAT and blood pressure, triglyceride, high-density lipoprotein cholesterol (HDL-C) and total cholesterol (TC) concentrations than Caucasian women, while African American men displayed a stronger association between VAT, triglyceride and low HDL-C concentrations and the metabolic syndrome (MetS) than their Caucasian counterparts.[28]

While differences in body fat distribution, and associations with cardiometabolic risk between black, Caucasian and Asian women have been described in SA,[24,29,30] no studies have examined the mixed-ancestry population of SA, who present with a high prevalence of the MetS (62%) and type 2 diabetes (28.2%), placing this population at high risk for CVD.[31]

The composition of the mixed-ancestry (collectively referred to as 'Coloured') population of SA is Khoisan (32–43%), Bantu-speaking Africans (20–36%), Europeans (21–28%) and a smaller Asian contribution (9–11%).[32] This population accounts for 8.9% of the South African population and 48.8% of the population of the Western Cape Province. [33] The aims of the study were therefore, for the first time, to investigate the relationship between whole-body fat distribution and cardiometabolic risk factors in mixed-ancestry SA men and women, and to explore the effect of menopausal status on these relationships in women.

Methods

The study sample included all self-described mixed-ancestry volunteers who completed a whole-body dual X-ray absorptiometry (DXA) scan as part of the Cape Town Vascular and Metabolic Health (VMH) study described previously.[34] Inclusion criteria were adults aged 20 years and older. Subjects were excluded if they were pregnant or acutely ill. A total of 46 men and 207 women volunteered for the study.

Ethical approval was obtained from the Ethics Committees of the Cape Peninsula University of Technology and Stellenbosch University (respectively, NHREC: REC-230 408-014, CPUT/HWS-REC 2015/H03 and N14/01/003). All participants signed written informed consent and the study was conducted according to the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Anthropometric measurements were taken and included body weight, height and body mass index (BMI), as described in detail previously.[34] Body composition (fat mass and fat-free mass) was acquired by a suitably trained and experienced radiographer using a Hologic Discovery W DXA whole-body scanner configured with software version 13.4.1 (Hologic, Bedford, MA). Participants were positioned as per the NHANES body composition manual, as advocated by Hangartner.[35]

DXA-derived measures of body composition regions included six standard regions of interest (ROI), namely the whole body; the trunk defined by the lower border of the mandible and including the chest, abdomen and pelvic triangle; the arm ROIs (right and left) defined by a line bisecting the shoulder joint of the right and left arm; and the leg ROIs (right and left) defined by a line bisecting the hip joint aligned with the iliac crest and pubis.[27] For the android fat measurement, the ROI is automatically defined with a caudal limit placed on top of the iliac crests and its height is set to 20% of the distance from the top of the iliac crest to the base of the skull as the cephalic limit.[36] The height of the gynoid ROI is double that of the android ROI with the separation between the two regions equating to 1.5 times the height of the android ROI. VAT and SAT were estimated within this android region.

DXA has proved to be as accurate as a clinical computed tomography scan in the quantification of VAT and SAT in adults.[36] Sub-total body fat % and kg, which excluded the head, was used in the analysis. The head was excluded to reduce the possibility of any artefacts in the head region, and total body adipose tissue classification excludes the head. Regional fat distribution (arms, legs, trunk, android and gynoid) are expressed as a percentage relative to sub-total fat mass (%FM).

Blood pressure was measured according to the World Health Organisation (WHO)[37] guidelines using a semi-automatic digital blood pressure monitor (Omron M6 comfort-preformed cuff BP monitor) on the right arm, in a seated position and at rest for 10 minutes. The lowest of three consecutive readings was taken in the analyses.[34]

After an overnight fast (eight to 14 hours), blood samples were taken to measure levels of glycated haemoglobin (HbA_{1c}), glucose, insulin, lipid profile, and biochemical marker for inflammation, high-sensitivity C-reactive protein (hsCRP). After collection of the fasting blood sample, the subjects without previously diagnosed diabetes underwent an oral glucose tolerance test as per the WHO criteria.[38] Participants drank 75 g of anhydrous glucose in 250–300 ml of water over the course of five minutes,[39] following which blood samples were collected after the two-hour test load. Blood samples were transported daily in an icebox for processing using standard pathology practices.

Biochemical parameters were analysed at an ISO 15189 accredited pathology practice (Pathcare, Reference Laboratory, Cape Town, South Africa) as described elsewhere.[34] Plasma glucose level was measured by the enzymatic hexokinase method (Beckman AU, Beckman Coulter, South Africa). HbA_{1c} level was assessed by high-performance liquid chromatography (Biorad Variant Turbo, BioRad, South Africa). Insulin concentration was measured with the paramagnetic particle chemiluminescence assay (Beckman DXI, Beckman Coulter, South Africa). Levels of HDL-C were measured by enzymatic immuno-inhibition, triglycerides by glycerol phosphate oxidase-peroxidase assays, and low-density lipoprotein cholesterol (LDL-C) by enzymatic selective protection (Beckman AU, Beckman Coulter, South Africa). Analysis of hsCRP was performed on the BNA nephelometer (Dade Behring) by particle-enhanced immunonephelometry with a detection limit of 0.18 mg/l and a measuring range of 0.18–1 150 mg/l.

Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated from fasting glucose and insulin levels.[40] The MetS was quantified using the Joint Interim Statement (JIS) criteria[39] and the WHO glucose tolerance categories were used.

Statistical analysis

Data were analysed using SPSS® version 24 (Armonk, NY: IBM Corp.) and STATA® version 14.2 (STATA corporation, Texas, USA). The participants in the study were a convenient sub-sample of the larger study. The 253 available volunteers who participated in the study provided an 80% power at a 5%

significance level to detect a coefficient of determination (R^2) of 0.042 or greater from the linear regression model comprising three predictors. Categorical variables are presented as frequencies and percentages, while continuous variables are presented as mean ± standard deviation (SD) for normally distributed variables, and median and 25–75th percentiles for skewed variables. Data were tested for normality using the Kolmogorov–Smirnov and Shapiro–Wilk statistic.

The women were also split into two groups based on menopausal age, which was estimated to be 50 years in this population.[41] Group comparisons were made using the Mann–Whitney *U*-test or chi-squared test. Robust regression analyses were used to investigate the associations between body fat distribution and cardiometabolic risk factors (insulin resistance, lipid levels, blood pressure and inflammatory markers), adjusting for age and gender. In addition, we explored the interactions between gender and body composition on cardiometabolic risk factors, adjusting for age, and in women, between menopausal age and body composition.

To investigate whether one body compartment was more closely associated with the risk factor than the other, coefficients of determination were used from robust regressions. We calculated the R^2 for the model with covariates only (age and gender), then the R^2 for models containing covariates and each of the adiposity measures.

Results

In all, 253 participants (18% men and 82% women) were included. The average age of the participants was 55 years, and was similar between men and women ($p = 0.630$). Differences in body composition and body fat distribution between women and men, as well as between pre- and post-menopausal women are presented in Table 1. On average, the women were obese (mean BMI = 32.6 ± 7.2 kg/m^2), whereas the men were overweight (mean BMI = 27.4 ± 6.1 kg/m^2) ($p < 0.001$).

Men had higher fat-free soft tissue mass compared to women, ($p < 0.001$), but body fat mass (kg and %) was significantly higher in the women than men ($p < 0.001$). As a percentage of total fat mass, women had significantly less central fat mass ($p < 0.001$) and greater peripheral fat mass (arm, leg and gynoid fat %, $p \leq 0.003$ for all) than men. VAT area was not different between men and women ($p = 0.474$), but SAT area was higher in women than men ($p < 0.001$).

When examining differences in body composition between the pre- and post-menopausal women, we found that although there were no differences in BMI, more post- than pre-menopausal women were obese (68.9 vs 57.3%), and post-menopausal women had greater fat mass ($p = 0.026$) and %FM ($p < 0.001$) than pre-menopausal women. Although trunk fat mass (%) and android fat mass (%) did not differ between pre- and post-menopausal women (both $p \geq 0.415$), post-menopausal women had greater waist circumference and VAT (both $p \leq 0.004$), and less gynoid %FM ($p = 0.001$) than pre-menopausal women.

Differences in cardiometabolic risk factors between mixed-ancestry men and women and between pre- and post-menopausal women are described in Table 2. While blood pressure, fasting glucose, insulin and lipid levels were not different between men and women (all $p \geq 0.085$), two-hour post-prandial glucose ($p < 0.05$) and HDL-C ($p < 0.001$) concentrations were higher in women than men. The majority of the sample had normal glucose tolerance (NGT) (men 63.1% and women 57.3%). The

Table 1. Comparison of body composition and body fat distribution between mixed-ancestry men and women, and pre- and post-menopausal women

	Men		*Women*		*Men vs women*	*Women*				*Pre- vs post-menopausal women*
Parameters	n	*Total sample*	n	*Total sample*	p-*value*	n	*20–49 years*	n	*≥ 50 years*	p-*value*
Age (years)	46	53.5 (44.8–65.3)	207	55.0 (45.0–63.0)	0.630	75	39.0 (31.0–45.0)	131	61.5 (56.0–67.0)	< 0.001
Anthropometry										
Height (cm)	46	168.0 (163.3–173.6)	206	156.0 (151.5–160.5)	< 0.001	75	157.5 (153.0–160.5)	131	155.0 (151.0–160.5)	0.043
Weight (kg)	46	75.6 (63.6–89.1)	206	78.2 (66.3–90.4)	0.443	75	74.5 (62.1–92.2)	131	79.8 (67.6–90.2)	0.196
BMI (kg/m^2)	46	27.4 ± 6.1	206	32.6 ± 7.2	< 0.001	75	31.4 ± 7.7	131	33.4 ± 6.9	0.083
Waist (cm)	46	96.2 ± 17.5	206	99.3 ± 15.0	0.284	75	95.0 ± 17.1	131	101.9 ± 13.2	0.004
BMI category	46	*%*	207	*% of total sample*	*Pearson chi-squared*	75	*%*	132	*%*	*Pearson chi-squared*
Underweight	2	4.3	3	1.4	< 0.001	2	2.7	1	0.8%	0.010
Normal	14	30.4	29	14.0		18	24	11	8.3	
Overweight	16	34.8	41	19.8		12	16	29	22	
Obese	14	30.5	134	64.7		43	57.3	91	68.9	
DXA-derived body composition and body fat distribution										
Fat-free soft-tissue mass (kg)	46	50.4 (43.8–56.8)	207	38.9 (35.6–44.7)	< 0.001	75	38.9 (34.3–44.7)	132	37.3 (34.2–42.2)	0.243
Body fat (kg)	46	16.4 (12.7–27.8)	207	31.2 (24.4–40.0)	< 0.001	75	30.0 ± 12.5	132	34.1 ± 11.9	0.026
Body fat (%)	46	26.5 (19.9–32.5)	207	44.0 (39.8–48.6)	< 0.001	75	41.5 (35.3–46.8)	132	44.9 (41.4–49.6)	< 0.001
Trunk fat (%FM)	46	57.1 ± 5.2	207	50.7 ± 6.01	< 0.001	75	50.1 ± 6.9	132	51.0 ± 5.4	0.415
Arm fat (%FM)	46	10.7 ± 1.5	207	12.5 ± 1.97	< 0.001	75	12.1 ± 1.8	132	12.7 ± 2.0	0.059
Leg fat (%FM)	46	31.7 (29.0–34.9)	207	36.1 (31.9–40.5)	< 0.001	75	37.5 (32.0–41.5)	132	35.8 (31.5–40.2)	0.180
Android (%FM)	46	10.8 ± 2.0	207	8.9 ± 1.57	< 0.001	75	8.8 ± 1.8	132	9.1 ± 1.4	0.445
Gynoid (%FM)	46	15.6 (14.6–17.2)	207	17.2 (15.4–19.1)	0.003	75	18.1 (16.0–20.7)	132	16.9 (14.9–18.5)	0.001
VAT (cm^2)	46	167.0 (101.2–260.7)	207	180 (135–236)	0.474	75	154.5 (93.2–211.0)	132	197.2 (149.4–244.1)	< 0.001
SAT (cm^2)	46	263.8 ± 143.7	207	451 ± 142	< 0.001	75	432.6 ± 160.6	132	461.0 ± 129.5	0.220

Values presented as means ± standard deviations (SD), median and 25–75th percentiles, or %. BMI (WHO classification), body mass index; WC, waist circumference; FM, fat mass expressed as a percentage relative to sub-total fat mass; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.

Table 2. Comparison of cardiometabolic risk factors between mixed-ancestry men and women, and pre- and post-menopausal women

	Men		*Women*		*Men vs women*	*Women*				*Pre- vs post-menopausal women*
Risk factors	n	*Total sample*	n	*Total sample*	p-*value*	n	*20–49 years*	n	*≥ 50 years*	p-*value*
SBP (mmHg)	46	128.5 ± 22.5	207	127.2 ± 20.6	0.894	75	116.6 ± 19.0	132	133.3 ± 19.1	< 0.001
DBP (mmHg)	46	81.9 ± 12.9	207	82.6 ± 11.6	0.472	75	81.3 ± 12.0	132	83.4 ± 11.4	0.228
Fasting glucose (mmol/l)	46	5.1 (4.6–5.8)	205	5.1 (4.7–6.0)	0.550	74	4.8 (4.5–5.5)	131	5.3 (4.8–6.3)	0.001
2-h glucose (mmol/l)	35	5.8 (4.5–7.5)	170	6.6 (5.5–8.0)	0.017	63	6.3 (5.0–7.1)	107	7.1 (5.7–8.2)	0.010
Fasting insulin (mIU/l)	46	6.7 (3.8–13.2)	205	8.4 (5.6–12.6)	0.085	74	8.5 (5.9–14.6)	131	8.4 (5.3–12.1)	0.362
HOMA-IR	46	1.6 (0.9–3.3)	204	2.1 (1.2–3.6)	0.085	73	2.0 (1.3–4.2)	131	2.1 (1.2–3.5)	0.940
TG (mmol/l)	46	1.5 (1.0–1.9)	205	1.4 (0.1–2.0)	0.665	74	1.2 (0.8–1.8)	131	1.5 (1.1–2.1)	0.008
TC (mmol/l)	46	5.1 ± 1.3	205	5.4 ± 1.2	0.208	74	5.2 ± 1.1	131	5.5 ± 1.1	0.017
LDL-C (mmol/l)	42	3.1 (2.3–3.9)	201	3.2 (2.7–4.1)	0.385	72	3.3 (2.6–4.0)	129	3.2 (2.7–4.1)	0.527
HDL-C (mmol/l)	46	1.1 (0.9–1.3)	205	1.3 (1.1–1.5)	< 0.001	74	1.2 (1.0–1.3)	131	1.3 (1.1–1.5)	< 0.001
hsCRP (mg/l)	39	2.8 (1.6–5.5)	152	3.3 (1.7–5.7)	0.467	58	2.8 (1.3–6.6)	94	3.3 (1.8–5.7)	0.508
Glucose tolerance categories										
NGT, *n*/%	29	63.1	118	57.3		50	66.7	68	51.9	
IGT/IFG, *n*/%	3	6.5	33	16.0		9	12.0	24	18.3	
Diabetes, *n*/%	14	30.4	55	26.7	0.249	16	21.3	39	29.8	0.166

Values presented as means ± standard deviations (SD), median and 25–75th percentiles or %. SBP, systolic blood pressure; DBP, diastolic blood pressure; HOMA-IR, homeostasis model for insulin resistance; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; NGT, normal glucose tolerance; IGT, impaired glucose tolerance; IFG, impaired fasting glucose.

Table 3. Associations between body composition and cardiometabolic risk factors in the whole sample, adjusted for gender and age

Age and gender	*SBP*	*DBP*	*Fasting glucose*	*2-h glucose*	*Fasting insulin*	*HOMA-IR*	*TG*	*TC*	*LDL-C*	*HDL-C*	*hsCRP*
R^2	0.23	0.03	0.07	0.08	0.01	0.02	0.03	0.03	0.01	0.06	0.01
FM (kg)											
β (95% CI)	0.053 (–0.14 to 0.24)	0.142* (0.02 to 0.27)	0.01** (0.00 to 0.01)	0.03**# (0.01 to 0.05)	0.17**# (0.13 to 0.22)	0.04**# (0.03 to 0.05)	0.01** (0.00 to 0.02)	0.01 (–0.00 to 0.02)	0.01 (–0.00 to 0.02)	–0.01** (–0.01to 0.00)	0.09** (0.06 to 0.12)
R^2	0.23	0.04	0.09	0.11	0.20	0.20	0.04	0.04	0.01	0.08	0.13
FM (%)											
β (95% CI)	0.02 (–0.29 to 0.33)	0.26* (0.05 to 0.46)	0.15* (0.00 to 0.02)	0.05** (0.02 to 0.09	0.27** (0.20 to 0.34)	0.06** (0.05 to 0.08)	0.01* (0.00 to 0.03)	0.03** (0.01 to 0.05)	0.02* (0.00 to 0.04)	–0.00 (–0.00 to 0.00	0.16** (0.09 to 0.24)
R^2	0.23	0.05	0.10	0.13	0.21	0.21	0.04	0.05	0.03	0.10	0.13
Trunk fat (%FM)											
β (95% CI)	0.38 (–0.00 to 0.77)	0.54** (0.30 to 0.79)	0.01** (0.00 to 0.03)	0.08** (0.04 to 0.12)	0.26** (0.15 to 0.37)	0.06** (0.03 to 0.08)	0.04**ª (0.30 to 0.06)	0.02 (–0.00 to 0.48)	0.01 (–0.01 to 0.03)	–0.02** (–0.02 to –0.01)	0.11** (0.04 to 0.18)
R^2	0.24	0.10	0.09	0.13	0.10	0.10	0.13	0.04	0.01	0.12	0.06
Arm fat (%FM)											
β (95% CI)	1.19* (0.01 to 2.36)	1.12** (0.34 to 1.90)	0.01 (–0.03 to 0.05)	0.04 (–0.10 to 0.18)	0.40* (0.03 to 0.76)	0.09**# (0.01 to 0.18)	0.04 (–0.10 to 0.09)	–0.00 (–0.08 to 0.08)	0.01 (–0.06 to 0.08)	–0.03** (–0.05 to –0.01)	0.19 (–0.02 to 0.41)
R^2	0.24	0.05	0.07	0.08	0.03	0.03	0.03	0.03	0.01	0.08	0.02
Leg fat (%FM)											
β (95% CI)	–0.43* (–0.79 to –0.08)	–0.56** (–0.79 to –0.34)	–0.01** (–0.03 to –0.00)	–0.06** (–0.10 to –0.03)	–0.25** (–0.36 to –0.15)	–0.06** (–0.08 to –0.03)	–0.04**ª (–0.05 to –0.03)	–0.02 (–0.04 to 0.00)	–0.01 (–0.03 to 0.01)	0.02** (0.01 to 0.02)	–0.11** (–0.17 to –0.05)
R^2	0.24	0.12	0.09	0.13	0.10	0.10	0.13	0.03	0.01	0.14	0.07
Android fat (%FM)											
β (95% CI)	0.46 (–0.91 to 1.82)	1.74** (0.87 to 2.62)	0.08** (0.04 to 0.13)	0.29** (0.14 to 0.42)	1.01** (0.65 to 1.39)	0.24** (0.15 to 0.32)	0.13**ª (0.08 to 0.18)	0.10* (0.01 to 0.19)	0.06 (–0.02 to 1.43)	–0.05** (–0.07 to –0.03)	0.59** (0.35 to 0.82)
R^2	0.23	0.08	0.13	0.14	0.12	0.13	0.10	0.04	0.01	0.11	0.11
Gynoid fat (%FM)											
β (95% CI)	–1.12** (–1.93 to –0.31)	–1.13** (–1.66 to –0.60)	–0.03** (–0.06 to –0.00)	–0.15** (–0.23 to –0.06)	–0.70** (–0.91 to –0.47)	–0.17** (–0.22 to –0.11)	–0.10**ª (–0.13 to –0.07)	–0.04 (–0.09 to 0.02)	–0.01 (–0.06 to 0.04)	0.03** (0.02 to 0.05)	–0.25** (–0.40 to –0.10)
R^2	0.25	0.09	0.09	0.12	0.15	0.15	0.12	0.03	0.01	0.11	0.06
VAT (cm²)											
β (95% CI)	0.02 (–0.01 to 0.05)	0.03** (0.01 to 0.05)	0.00** (0.00 to 0.00)	0.01** (0.00 to 0.01)	0.04** (0.03 to 0.05)	0.01** (0.01 to 0.01)	0.00**ª (0.00 to 0.00)	0.00 (–0.00 to 0.00)	0.00 (–0.00 to 0.00)	–0.00** (–0.00 to –0.00)	0.01** (0.01 to 0.02)
R^2	0.23	0.07	0.12	0.16	0.29	0.27	0.09	0.03	0.01	0.12	0.14
SAT (cm²)											
β (95% CI)	0.01 (–0.01 to 0.02)	0.02** (0.01 to 0.03)	0.00** (0.00 to 0.00)	0.00**# (0.00 to 0.00)	0.01**# (0.01 to 0.02)	0.00**# (0.00 to 0.00)	0.00** (0.00 to 0.00)	0.00* (0.00 to 0.00)	0.00 (–0.00 to 0.00)	–0.00** (–0.00 to –0.00)	0.01** (0.01 to –0.01)
R^2	0.23	0.06	0.11	0.12	0.19	0.20	0.06	0.05	0.02	0.09	0.15

Diabetic participants were excluded from insulin-sensitivity measurements. Beta coefficients, confidence intervals, total R^2 for: %FM, expressed as a percentage of sub-total fat mass (FM). HOMA-IR, homeostasis model for insulin resistance; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.
*$p < 0.05$, **$p < 0.01$, #significant in men, ªsignificant in women

prevalence of diabetes (30.4 and 26.7%) and screen-detected diabetes (8.7 and 9.2%) was similar in men and women, respectively ($p = 0.249$).

Post-menopausal women had higher systolic blood pressure (SBP), fasting glucose ($p < 0.001$), two-hour glucose ($p = 0.01$), triglyceride ($p < 0.01$), TC ($p < 0.05$) and HDL-C ($p < 0.001$) concentrations than pre-menopausal women. The prevalence of impaired glucose tolerance (IGT)/impaired fasting glucose (IFG) and type 2 diabetes was similar in the pre-and post-menopausal women ($p = 0.166$).

Table 3 shows the associations between body fat variables and cardiometabolic risk factors in the whole sample, adjusting for gender and age. In terms of total body fat (kg and %), positive associations were observed for diastolic blood pressure (DBP) ($p < 0.05$), two-hour glucose, fasting insulin, HOMA-IR (all $p < 0.01$) and triglyceride concentrations ($p < 0.05$) as well as hsCRP, and in the case of body fat %, TC ($p < 0.01$) and LDL-C levels ($p < 0.05$).

When examining associations between central fat mass (trunk fat %FM, android %FM, VAT and SAT area) and cardiometabolic risk profile, we found positive associations with DBP, fasting glucose, two-hour glucose, fasting insulin, HOMA-IR, triglyceride and hsCRP concentrations ($p < 0.01$ for all), and negative association with HDL-C levels ($p < 0.01$ for all). When examining the relationships of peripheral fat mass, we found that arm fat mass was positively associated with SBP ($p < 0.05$), DBP ($p < 0.01$), levels of fasting insulin ($p < 0.05$) and HOMA-IR ($p < 0.01$), and negatively associated with HDL-C ($p < 0.01$) levels. By contrast, lower body peripheral fat mass (gynoid %FM and leg %FM) was negatively associated with all CVD risk markers, except for HDL-C, which was positively associated with gynoid and leg %FM ($p < 0.01$).

We then compared the proportion of the variance that age, gender and the different body composition measures explained for each cardiometabolic risk factor. Together with age and gender, VAT area accounted for the greatest variance in fasting insulin (29%) and HOMA-IR (27%) levels, while SAT area accounted for the greatest variance in hs-CRP (15%) concentrations. Trunk %FM and leg %FM contributed equally

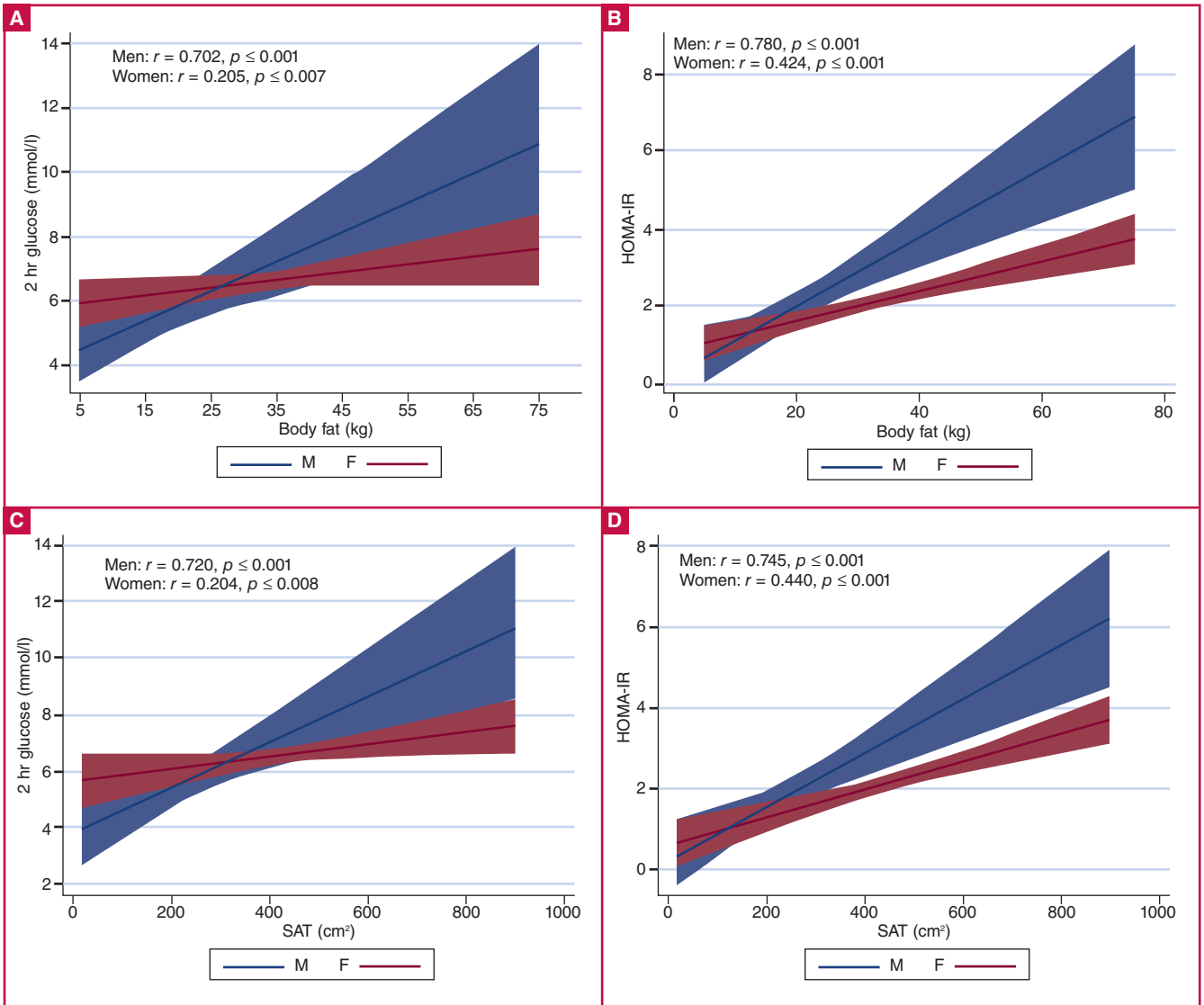

Fig. 1. Gender-specific associations between total body fat and abdominal subcutaneous adipose tissue (SAT) and two-hour glucose (A, C) and insulin resistance, estimated using HOMA-IR (B, D), respectively.

Table 4. Associations between body composition and cardiometabolic risk factors in the pre- and post-menopausal women

Body composition	*SBP*	*DBP*	*Fasting insulin*	*TG*	*TC*	*LDL-C*	*hsCRP*
FM (kg)							
Pre-meno	0.264[a]	0.292[a]	0.629[A]	0.502[A]	0.459[A]	0.394[A]	0.592[A]
Post-meno	–0.092[#]	0.028	0.380[B#]	0.081[#]	–0.120[#]	–0.079[#]	0.198
FM (%)							
Pre-meno	0.198	0.246[a]	0.509[A]	0.357[A]	0.462[A]	0.451[A]	0.528[A]
Post-meno	–0.123[#]	0.006	0.318[B]	0.001	–0.073[#]	–0.053[#]	0.226[b]
Trunk fat (%FM)							
Pre-meno	0.443[A]	0.507[A]	0.562[A]	0.585[A]	0.199	0.128	0.504[A]
Post-meno	–0.002[#]	0.118	0.358[B]	0.525[B]	0.126	0.004	0.067[#]
Arm fat (%FM)							
Pre-meno	0.209	0.283[a]	0.156	0.203	0.190	0.260[a]	0.400[A]
Post-meno	0.131	0.158	0.215[b]	0.076	–0.098	–0.076[#]	–0.023[#]
Gynoid (%FM)							
Pre-meno	–0.449[A]	–0.531[A]	–0.615[A]	–0.591[A]	–0.242[a]	–0.164	–0.679[A]
Post-meno	–0.158	–0.107	–0.388[B]	–0.450[B]	0.023	0.137[#]	0.074[#]
VAT (cm)^2							
Pre-meno	0.415[A]	0.436[A]	0.737[A]	0.635[A]	0.411[A]	0.339[A]	0.597[A]
Post-meno	–0.047[#]	0.037[#]	0.519[B]	0.336[B]	–0.086[#]	–0.098[#]	0.243[b]
SAT (cm)^2							
Pre-meno	0.274[a]	0.334[A]	0.601[A]	0.533[A]	0.430[A]	0.369[A]	0.605[A]
Post-meno	–0.117[#]	0.063	0.387[B]	0.132	–0.059[#]	–0.040[#]	0.231[b]

Values are Spearman's correlation coefficients. %FM, expressed as percentage of sub-total fat mass (FM). SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein.
[a]$p < 0.05$ and [A]$p < 0.01$ for pre-menopausal women; [b]$p < 0.05$ and [B]$p < 0.01$ for post-menopausal women; [#]$p < 0.05$ for age × body composition interaction.

to the greatest variance in triglyceride concentrations (13%). Additionally, leg %FM also accounted for the greatest variance in HDL-C (14%) levels. Body composition did not add to variance in TC and LDL-C concentrations above that of age and gender.

There were gender-specific differences in the associations between body fat distribution and measures of cardiometabolic risk. While fat mass (kg) and abdominal SAT were associated with two-hour glucose (Fig. 1A, C), HOMA-IR (Fig. 1B, D) and fasting insulin levels in both men and women, the association was stronger in men compared to women (all interactions $p \leq 0.027$). Conversely, the associations between serum triglycerides and the distribution of body fat were significant in women, but not in men. Specifically, central adiposity measures (trunk %FM and android %FM) were positively associated with serum triglyceride concentrations (Fig. 2A, B, all interactions $p \leq 0.014$), and peripheral fat mass (leg %FM and gynoid %FM) were negatively associated with serum triglyceride levels (Fig. 2D, E, both interactions $p \leq 0.022$) in women, but not in men. The association between VAT and triglyceride concentrations was stronger in women than men (Fig. 2C, interaction $p = 0.012$).

The associations between body composition and cardiometabolic risk factors in pre-and post-menopausal women are shown in Table 4. For the most part, the association between body fat distribution and cardiometabolic risk did not differ between the pre- and post-menopausal women. Significant interactions were however seen between fat mass (kg), central fat distribution (%FM, trunk %FM, VAT and SAT area) and SBP (all interactions $p \leq 0.042$) and VAT and DBP (interactions $p = 0.030$), such that these were significant in pre-menopausal women but not in post-menopausal women.

Similarly, fat mass (kg), fat mass (%), VAT and SAT were associated with TC (all interactions $p \leq 0.002$) and LDL-C levels (all interactions $p \leq 0.007$) in pre-menopausal women only. Fat mass (kg) was associated with fasting insulin in both pre- and post-menopausal women, but the association was stronger in pre- than post-menopausal women (interaction $p = 0.019$), while fat mass (kg) was associated with triglyceride concentrations in pre-menopausal women only (interaction $p = 0.016$). Peripheral fat (arm %FM and gluteofemoral %FM) was associated with LDL-C (both interaction $p \leq 0.032$) and hsCRP levels (both interactions $p \leq 0.012$) in pre- but not post-menopausal women.

Discussion

This is the first study to investigate the relationship between body composition and cardiometabolic risk profile in mixed-ancestry South Africans. The main findings of the study are that body fat and, in particular central adiposity, were associated with unfavourable cardiometabolic risk profiles, while lower-body peripheral fat was associated with favourable risk profiles. However, the associations between body fat distribution and cardiovascular risk profile differed by gender and menopausal status, such that the associations were stronger in men and pre-menopausal women.

Although the women in our sample had nearly twice as much body fat mass, and had higher obesity rates than the men, the prevalence of cardiometabolic risk factors was similar between genders (apart from two-hour glucose and HDL-C concentrations being higher in women). This may be explained by the fact that despite marked differences in total body fat, VAT area was similar in men and women. Indeed, VAT was the most consistent and significant correlate of cardiometabolic risk (insulin resistance, glucose tolerance, triglyceride and HDL-C concentrations) in this sample. Furthermore, the association between VAT and cardiometabolic risk did not differ by gender.

Similarly, a recent study among Korean men and women showed that DXA-derived VAT was the best correlate of diabetes and pre-diabetes.[42] Likewise, the meta-analysis by Zhang and co-workers[8] supports VAT as the strongest correlate of insulin resistance, followed by total fat mass. The mechanisms linking VAT accumulation to metabolic complications include a higher production of pro-inflammatory cytokines and higher lipolytic activity compared to SAT, with the consequent increase in cytokine and free fatty acid delivery to the hepatic portal system impacting on insulin sensitivity.[5] VAT is also proposed to be a marker of insulin resistance as a consequence of lipotoxicity, in particular an increase in fat deposition in the liver.[5]

In contrast to VAT, women had more abdominal SAT than men.[14,15] Notably, the relationship between both total adiposity and abdominal SAT and insulin resistance was stronger in men than women. These differences may relate to the fact that oestrogens regulate insulin sensitivity and that female adipocytes are more insulin sensitive compared with male adipocytes.[43] Alternatively, the gender-specific relationship between abdominal SAT and insulin resistance could, in part, be explained by the fact that men have greater deep SAT (dSAT) and less superficial SAT (sSAT) than women.[44]

Nazare *et al.* showed that of the two SAT layers, dSAT had a higher association with inflammation and oxidative stress, suggesting that dSAT is an important determinant of the

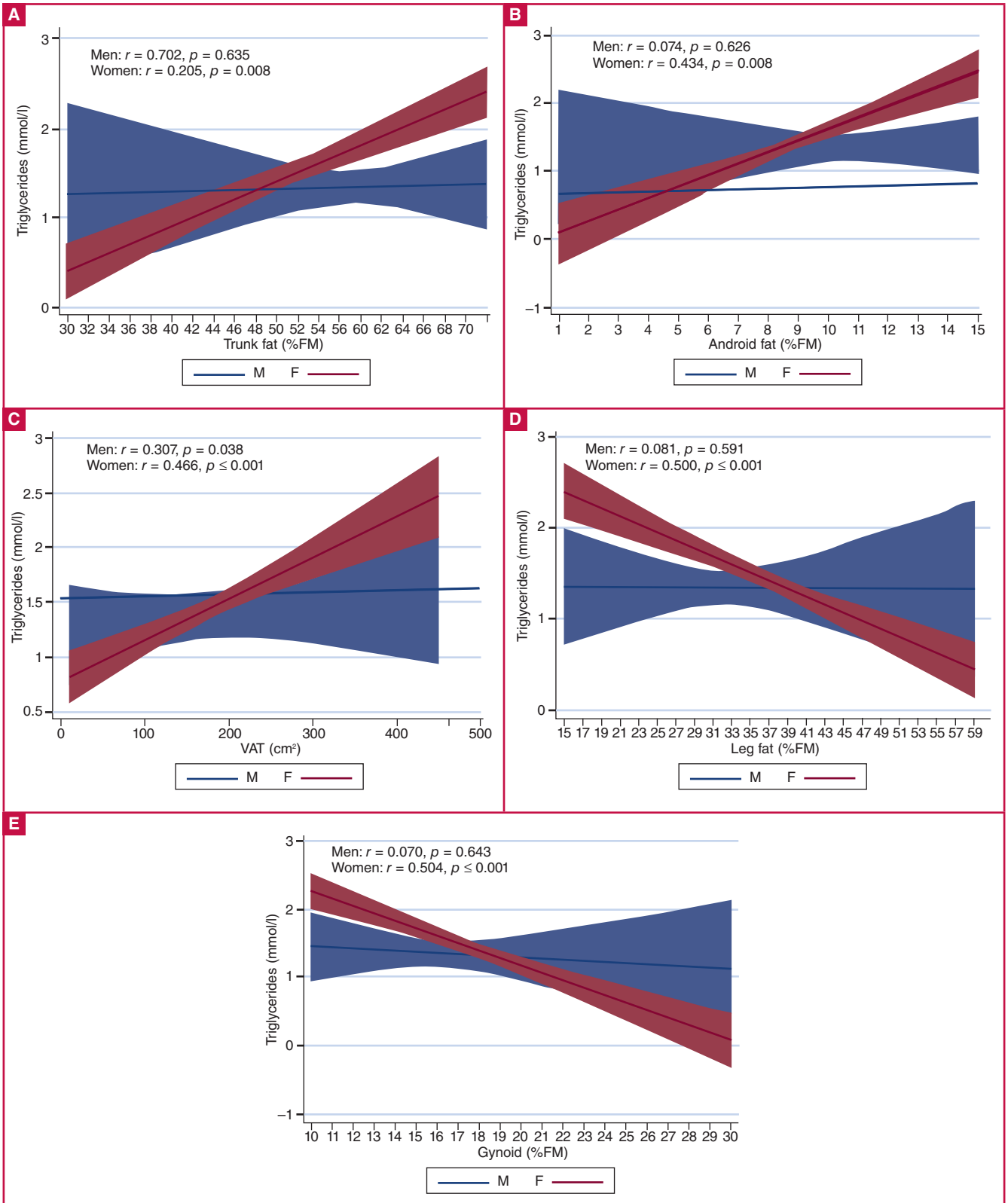

Fig. 2. Gender-specific associations between serum triglyceride concentrations and trunk % fat mass (%FM) (A), android %FM (B), visceral adipose tissue area (VAT) (C), leg %FM (D), and gynoid %FM (E).

MetS.[22] Accordingly, abdominal SAT should be considered as two functionally distinct compartments rather than a single entity.[22] A suggestion for further investigation in this population would be to explore the role of sSAT and dSAT using alternative imaging methods, such as computerised tomography or magnetic resonance imaging, as DXA is unable to differentiate between sSAT and dSAT.

Unlike associations with insulin sensitivity, the associations

between measures of body fat distribution (VAT, android, gynoid and leg %FM) and triglyceride concentrations were more pronounced in women than men. This finding is supported by the results of the Framingham Heart study,[45] where the relationship between VAT in particular and triglyceride concentrations was stronger in women than men, likely explained by the higher rates of lipolysis of VAT in women compared to men.[46]

Greater lower-body peripheral fat mass was associated with a lower cardiometabolic risk, commensurate with findings from previous studies in African American and Caucasian men and women.[47] Similarly, the protective effect of lower-body peripheral fat was observed in a large sample of Asian men and women, showing that those with the MetS had less lower-body peripheral fat that those without the MetS.[13]

Notably, the study by Shorr *et al.*,[48] which examined the differences between gender, body composition and cardiometabolic risk, showed the protective effect of lower-body fat to be stronger in women than men, which supports our study results. The lower-body fat depot is seen as a 'metabolic sink', which traps excess free fatty acids due to the increased lipoprotein lipase activity and lower lipolytic activity in this depot compared to the abdominal fat depot, thus protecting other tissues from lipid overflow and insulin resistance associated with ectopic lipotoxicity.[11,12,44] The protective effect of lower-body peripheral fat on triglyceride concentrations was however not observed in the sample of men, who had significantly less lower-body peripheral fat than women.

We found positive associations between arm fat and cardiometabolic risk, in particular insulin resistance, similar to those found with central adiposity. A possible explanation for this may be that upper-body adiposity is more sensitive to lipolysis and secretes a greater number of inflammatory cytokines.[49] Accordingly, not all peripheral fat may be regarded as protective and these differences should be further investigated.

Contrary to the findings for triglyceride and HDL-C concentrations, TC and LDL-C concentrations were not associated with body fat in either men or women. This is at variance with findings from similar studies in other ethnic groups,[50] but similar to those shown in black SA women.[27] These findings suggest that factors other than body fat and its distribution, including genetics, dietary intake, physical activity and smoking influence HDL-C, TC and LDL-C concentrations.

Commensurate with the decline in oestrogen following menopause, the post-menopausal women had greater VAT and lower gynoid %FM compared to pre-menopausal women, corresponding to their greater cardiometabolic risk, as previously demonstrated.[18,19] However, the association between body fat distribution and cardiometabolic risk was weaker in the post- compared to pre-menopausal women. A possible explanation for this is that as oestrogen levels decline and levels of bioavailable testosterone increase at menopause, this results in a shift in body weight and body fat distribution and disruptions in glucose regulation.[43] Interestingly, studies have shown that aging and lack of physical activity rather than menopause are the main reasons for weight gain and obesity in midlife women.[19]

This study adds to the literature the associations between body composition and cardiometabolic risk factors in the mixed-ancestry population, which previously had not been researched. In particular, the women in our study had higher VAT than the men, which is in contrast to other studies and ethnicities.[48] This is possibly due to the vast difference in total body fat between men and women, which may be unique in this sample. Additionally, post-menopausal women had increased VAT compared to pre-menopausal women, which is commensurate with recent literature.[51] In clinical practice the importance of preventing weight gain and centralisation of body fat prior to menopause should be highlighted. Even though the women in our study had substantially more abdominal SAT, the relationship between abdominal SAT and insulin resistance was stronger in the men, a finding similar to that of the Netherlands Epidemiology of Obesity study.[52]

The strengths of the study include the proven accuracy of DXA to measure body composition, and the use of robust analytical approaches to carefully explore the targeted associations. Although there were multiple comparisons, the relationships were consistent, which suggests that false-positive results were unlikely.

Possible limitations were the cross-sectional nature of the study and the inclusion of a convenient sample of women and only a small sample of men. However, this is typical of a South African population survey in which more women are usually included than men.[31] Furthermore, the gender disparities in obesity prevalence shown in this study are similar to those reported in the national prevalence data.[53]

We did not have an objective measure of menopausal age. These findings could therefore reflect an age effect and warrant further investigation. We lacked information on important potential confounders such as socio-economic status, diet, physical activity and smoking, which are known to affect body fat and cardiometabolic risk. In addition, we did not adjust for medication use, but the participants were instructed not to take any medications prior to testing.

Conclusion

Central fat mass was associated with increased cardiometabolic risk, and lower body peripheral fat mass was associated with reduced risk. However, these associations were influenced by gender and menopausal status. Notably, VAT was the most consistent and significant correlate of insulin resistance. Future studies should focus on the mechanisms underlying the gender-specific associations between SAT (in particular dSAT and sSAT) and cardiometabolic risk. Additionally, the relationship between DXA-derived VAT and SAT and simpler anthropometry measurements to predict cardiometabolic risk should be investigated. Specific VAT cut-off points for cardiometabolic risk in the mixed-ancestry populations should be derived in an effort to identify high-risk individuals.

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Significant financial stress associated with 13-fold higher odds of having a heart attack

Significant financial stress is associated with a 13-fold higher odds of having a heart attack, according to research presented at the 18th Annual Congress of the South African Heart Association.

'The role of psychosocial factors in causing disease is a neglected area of study in South Africa, perhaps because there are so many other pressing health challenges such as tuberculosis and HIV,' said lead author Dr Denishan Govender, associate lecturer, University of the Witwatersrand, Johannesburg.

'The INTERHEART study showed that psychosocial factors are independently associated with acute myocardial infarction (heart attack) in Africa but as far as we are aware there are no other published local data,' said last author Professor Pravin Manga, professor of cardiology, University of the Witwatersrand.

This study included 106 patients with acute myocardial infarction who presented to a large public hospital in Johannesburg. A control group of 106 patients without cardiac disease was matched for age, gender and race. All participants completed a questionnaire about depression, anxiety, stress, work stress and financial stress in the previous month. The Likert scale was used to grade the experience of each condition.

Regarding financial stress, patients were graded with no financial stress if they were coping financially; mild financial stress if they were coping financially but needed added support; moderate financial stress if they had an income but were in financial distress; and significant financial stress if they had no income and at times struggled to meet basic needs. Levels of psychosocial conditions were compared between groups and used to calculate associations with having a heart attack.

Self-reported stress levels were common, with 96% of heart attack patients reporting any level of stress, and 40% reporting severe stress levels. There was a three-fold increased risk of myocardial infarction if a patient had experienced any level of depression (from mild to extremely severe) in the previous month compared to those with no depression.

Both work stress and financial stress were associated with a higher risk of acute myocardial infarction. The odds of myocardial infarction was 5.6 times higher in patients with moderate or severe work stress compared to those with minimal or no stress. Patients with significant financial stress had a 13-fold higher odds of having a myocardial infarction.

Dr Govender said: 'Our study suggests that psychosocial aspects are important risk factors for acute myocardial infarction. Often patients are counselled about stress after a heart attack but there needs to be more emphasis prior to an event. Few doctors ask about stress, depression or anxiety during a general physical and this should become routine practice, like asking about smoking. Just as we provide advice on how to quit smoking, patients need information on how to fight stress.'

continued on page 335…